

From Cell to Mind

How Excitable Cells, Nerve Nets, Brains and Minds Evolved. A Reference Work in Two Layers

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How to use this book

This book is the fourth of a series. *Plants on the Ladder* treated photosynthetic life. *The Company of Plants* treated the co-evolution of plants with the rest of life.

The Weaving of Life treated how all the kingdoms became interwoven. This book follows one line through animals: from the charged membrane of every cell to nerve nets, brains and minds.

Its question: how did excitable cells, nerve nets, brains and minds evolve? In what order, at what sizes and times, with what counts? And how can that evolution be described within the Vacuum.Net model?

The book is built in two layers, kept apart.

Layer A is biology only. Ten chapters, A1 to A10, each with the same sections. What it is; first appearance; partners or groups; sizes; times; counts; order of events; present quantities.

A closing **Pattern** of at most 150 words. Then what could not be verified, and the references of the chapter. Layer A mentions no theory.

Part C gathers the numbers of Layer A in seven tables across the chapters.

Layer B asks one question of Layer A. Do the measured patterns correlate with what the Vacuum.Net texts state, with nothing added? For this subject the texts say more than for the earlier ones: they name the membrane, the nerve cell, synchrony, sleep, seizure, memory and consciousness. Three tests were therefore fixed from the texts before any dossier was written, then run.

Their outcomes stand as they fell. Section B14 gives the answer to the question of the book.

The marks. *Measured*: read in the cited source, with a reference number [n].

Computed: arithmetic on measured numbers, shown. *Modelled*: the output of a published model, named as such.

Text: a statement of a Vacuum.Net text, quoted (Layer B only). *Read*: a pairing made in Layer B between a text statement and a measured pattern; a read is a hypothesis.

The ladder and the position. Every size and every time given as a number carries its position: $\log_3$ of the value over a unit. The unit of length is 4.558816×10^{-8} m, the unit of time 1.520655×10^{-16} s: Larson's natural units, as used in *From Atom to Body*. One year is 3.15576×10^7 s.

An age of A million years is placed as a duration of $A \times 10^6$ years. Positions are given to two decimals. A position is a coordinate.

Sources. Each chapter of Layer A has its own numbered reference list. Part C cites as "A3 [12]": chapter A3, reference 12. Citations were checked against OpenAlex or Crossref, or read on the publisher's or the institution's page.

Each chapter ends with a list "Not verified": items found only in secondary sources, or whose primary could not be opened. They are not facts of this book.

Statements about consciousness. Layer A reports positions on consciousness, such as the declarations of 2012 and 2024, as positions held by named authors on a date. They are not measurements.

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Part 0 — The Rules

0.1 Two layers

Layer A is written as if the theory did not exist. Its ten Pattern paragraphs and the tables of Part C are the data of Layer B. Nothing in Layer B adds a fact that Layer A does not hold, and nothing in Layer A leans on Layer B.

0.2 The marks

Four marks for fact, one for pairing; see “How to use this book”. A statement without a mark is a heading or a connective.

0.3 The ladder

Positions as defined above. The day sits at 43.50, the year at 48.87. A spike of 2 ms sits at 27.50; a human lifetime of 80 years at 52.86.

0.4 Depth, in two senses

Ring depth is the length of a closed ring of trits, 3, 6, 9; it is used only where the texts use it. *Position* is the depth of the Climate paper, “each depth n is one layer” (as quoted in *The Weaving of Life*); every measured size and time has one. No text equates the two, and this book does not.

0.5 What is not added

No rule is added to the theory. No sentence says that the net causes a biological pattern. Where the texts are silent, Layer B says none.

0.6 Tests

A test is fixed before its data are looked at: the quantity, the required outcome, the chance outcome where there is one, the data. Where a test could not be run on the fixed data, it is reported as not run. Where a classification or a reading was made after the data had been seen, it is marked so and is not a test.

The tests are run by Claude Code. The attestation is the author’s.

Layer A — From Cell to Mind

A1 The Excitable Cell

What it is

Every cell measured carries a voltage across its membrane. The inside is negative. Among the cells read, plant cells hold the largest values and bacteria the next.

An excitable cell changes that voltage in a pulse and returns. The pulse runs through channels in the membrane that open and close with voltage, ligand or touch. Channels for potassium, sodium and calcium occur in bacteria, archaea, protists, algae, plants and animals.

This chapter follows the membrane potential and the voltage-gated channel from prokaryotes to protists, algae and plants. It records sizes, durations, speeds and gene counts. Neurons enter only as a reference value.

First appearance

The membrane potential. No fossil dates the membrane potential. Clocks date the last universal common ancestor (LUCA), the ancestor of all cells now living.

One clock places LUCA at about 4.2 Ga, position 69.04 (modelled [1]). Its interval is 4.09–4.33 Ga, position 69.02–69.07 (modelled [1]). A composite range in the same study runs 3.94–4.52 Ga, position 68.98–69.11 (modelled [1]).

The first interval is $4,330 - 4,090 = 240$ Myr wide, position 66.43 (computed). The composite range is $4,520 - 3,940 = 580$ Myr wide, position 67.24 (computed).

A second study places LUCA before 3.9 Ga, position 68.97 (modelled [2]). It places crown Bacteria and crown Archaea after 3.4 Ga, position 68.85 (modelled [2]).

All bacteria and archaea in the sources read carry a membrane potential, negative inside. No prokaryotic group without one was found. No measured archaeal value was found either.

The voltage-gated sodium channel family. Genes of the Na^+ -channel type (Nav-like) occur in the apusozoan *Thecamonas* and the choanoflagellate *Monosiga* [3]. “NaV-like channels emerged before nervous systems or even multicellularity evolved” [3]. The emergence is placed “more than a billion years ago”, position 67.73 (modelled [3]).

Ca^{2+} -conducting Nav2 channels appeared before the split of fungi and animals [3]. Cav channels occur in green algae, which places Cav in the common ancestor of plants and animals [3]. NALCN diverged before Cav and Nav diversified [3].

“All voltage-gated channel families are present in choanoflagellates” [3]. The choanoflagellate Na^+ -channel homologue has a selectivity filter intermediate between Ca^{2+} and Na^+ channels [4]. In the same source, sodium channels “are believed to have evolved from calcium channels at the origin of the nervous system” [4].

Sodium selectivity in animals. Sodium selectivity arose twice: once in cnidarians, once in Bilateria [5]. Both came from ancestral non-selective channels that also passed Ca^{2+} [5].

The cnidarian Na⁺-selective group diverged from Ca²⁺-conducting homologues “more than 540 million years ago”, position 67.17 (modelled [5]). The cnidarian Nav2.5 channel, with a DKEA filter, arose by duplication at the same >540 Ma, position 67.17 (modelled [3]).

Nav1, Na⁺-selective with a DEKA filter, occurs only in Bilateria [3]. It appeared in the urbilaterian [3]. Cnidarian-specific Cav genes have been conserved “at least 500 million years”, position 67.10 (modelled [3]).

The four-domain Nav arose by two rounds of duplication from a single-domain gene [3].

The fast eukaryotic action potential. The fast Na⁺/Ca²⁺ action potential arose “in ancestral unicellular eukaryotes” [6]. It was retained in opisthokonts and stramenopiles [6]. No date is given.

Four-domain Na⁺/Ca²⁺ channels are “widespread” in eukaryotes [7]. Land plants and fungi have lost them [7]. Single-domain channels of a new kind, EukCats in three classes, are “broadly distributed across major phytoplankton lineages” [7].

Plants. Characean algae, the closest algal relatives of land plants, fire action potentials, as do flowering plants. No date for plant excitability was read.

Partners

Potassium in bacterial communities. In biofilms of *Bacillus subtilis* NCIB 3610, long-range electrical signals travel as waves of extracellular potassium [8]. The K⁺ leaves through the channel YugO, gated by an intracellular TrkA domain [8]. YugO is named “the only experimentally characterized K⁺ channel” of the species [8].

Intracellular K⁺ is about 300 mM, “nearly 40 times” the medium (measured [8]). The medium then holds about 300 / 40 = 7.5 mM (computed). Deletion of *yugO* removed the K⁺ release (measured [8]).

No extracellular Na⁺ oscillation was detected (measured [8]). More than 75 biofilms were analysed (measured [8]). Each holds “billions of densely packed cells” [8].

Metabolic coupling. The oscillations in these biofilms are metabolic [9]. Growth halts periodically, which raises the nutrient supply to interior cells [9]. The period “slightly increases over time” [9].

Other species drawn in. Motile *B. subtilis* cells peak 26 ± 9 min after the biofilm electrical peak, position 39.85, over 44 pulses (measured [10]). *Pseudomonas aeruginosa* cells peak 22 ± 13 min after, position 39.69, over 30 pulses (measured [10]).

A $\Delta trkA$ biofilm gives a signal 75 ± 4 % lower (measured [10]). $\Delta ktrA$ motile cells are 57 ± 6 % more polarised and 239 ± 25 % more attracted (measured [10]).

Ciliates. In *Paramecium caudatum* depolarization reverses the ciliary beat (measured [11]).

Green algae. *Chlamydomonas reinhardtii* has two light-regulated inward currents [12]. One arises at the eyespot, one in the flagellar region [12]. Both depend on Ca²⁺ and are blocked by verapamil and pimozide [12].

The photoreceptor current and a fast, action-potential-like flagellar current together precede the photophobic response [13]. During the flagellar current the flagella switch from forward to backward beating [13].

Diatoms. *Odontella sinensis* fires a fast $\text{Na}^+/\text{Ca}^{2+}$ -based action potential [6]. Its properties are close to those of invertebrate and vertebrate muscle [6]. The source calls it the “first demonstration” of voltage-activated Na^+ channels and Na^+ -based action potentials in a unicellular photosynthetic organism [6].

In *Phaeodactylum tricornutum* the single-domain EukCatA channels carry voltage-activated Ca^{2+} signalling [7]. They are voltage-gated, pass Na^+ and Ca^{2+} , and have fast kinetics like animal four-domain channels [7]. Mutants glide poorly [7].

Plants. In the Venus flytrap *Dionaea muscipula* action potentials close the trap and switch on digestion [14]. Three trigger hairs stand on each lobe [15]. About 37,000 glands line the inner trap surface (measured [14]).

In *Mimosa pudica* the Ca^{2+} rise precedes leaflet movement by up to 0.15 s, position 31.43 (measured [16]). *Mimosa* shows three signal classes [17]. They are the action potential (“steep spike-like waveform”), the slower variation potential and a faster “rapid unknown signal” [17].

In *Chara* cytoplasmic streaming stops after the spike and recovers (measured [18]; times in the table).

Animal cells without neurons. In the sea-urchin egg the fast block to polyspermy acts “within a few seconds” of sperm entry [19]. It results from depolarisation of the egg plasma membrane [19].

The glass sponge *Rhabdocalyptus dawsoni* has no neurons. Its all-or-none impulses are presumed to run in the syncytial trabecular reticulum “that penetrates all parts of the body” [20].

Sizes

Membrane potentials. *Escherichia coli* holds a membrane potential $\Delta\psi$ of about -140 mV during aerobic growth on glycerol (measured [21]). During fermentative growth on glucose it holds about -105 mV (measured [21]).

“A typical bacterial membrane potential is around 150 mV, corresponding to $\text{Cin}/\text{Cex} \approx 350$ ” (measured [22]). The value comes from a dye ratio [22].

The proton-motive force Δp of respiring *E. coli* is 230 ± 15 mV (measured [23]). For *Staphylococcus aureus* it is 211 ± 15 mV (measured [23]). Both rest on six determinations each at external pH ≈ 6.5 [23].

For eukaryotic cells, resting potentials “between -40 and -95 mV are typical” [24]. The bacterial range, -105 to -150 mV, lies beyond it in magnitude (computed).

A bacterial cell has a surface of about $6 \mu\text{m}^2$, a mammalian cell about $1,600 \mu\text{m}^2$ (measured [25]). The ratio is $1,600 / 6 = 267$ (computed).

Paramecium caudatum rests at about -62 , -55.5 , -44.7 and -30.3 mV at 0.1, 0.3, 1.1

and 5.1 mM external Ca^{2+} (measured [26]). Across 0.44–3.2 mM K^+ it rests at -38 to -43 mV (measured [26]). Individual cells range from -56 to -69 mV (measured [26]).

Membrane resistance is 45–90 M Ω (measured [26]).

In *Chara* a healthy cell rests “around -200 mV”, “up to -250 mV” (measured [18]). One cell rested at -170 mV (measured [18]). Peaks reach near 0 mV; amplitude was about 140 mV in a second cell (measured [18]).

The Nernst potentials in *Chara* are $E_{\text{K}} -177$, $E_{\text{Na}} -99$, $E_{\text{Ca}} +58$ and $E_{\text{Cl}} +100$ mV [18].

Flytrap gland cells rest at -116 ± 19 mV and at -122 ± 14 mV in activated glands (measured [14]). Oocytes were clamped at -140 mV as the approximate gland resting potential [14].

The neuron reference rests at -70 mV, with threshold -55 mV and peak $+30$ mV [27].

Spike amplitudes and currents. The *Paramecium* Ca^{2+} response overshoots by $+5$ to $+15$ mV (measured [28]). Its maximum rate of rise is about 7 V s^{-1} (measured [28]). The overshoot rises 22–25 mV per tenfold external Ca^{2+} , against a Nernst slope of 29 mV (measured [28]).

That is $22 / 29 = 76 \%$ to $25 / 29 = 86 \%$ of the Nernst slope (computed).

The overshoot stays at least 100 mV short of the Ca^{2+} equilibrium potential, $+64$ to $+133$ mV for 0.016–4 mM (measured [28]). Recordings were made at 18°C [28].

The *Odontella* action potential carries a peak inward current of -19.7 ± 2.6 nA (measured [29]). Activation $V_{1/2}$ is -58.5 ± 1.0 mV; inactivation $V_{1/2}$ is -69.4 ± 0.5 mV (measured [29]). The delayed outward current is 13.1 ± 1.1 nA (measured [29]).

The flytrap action potential is 1.6-fold higher at 40°C than at 10°C (measured [15]). It induces a biomagnetic signal of up to 0.5 pT (measured [15]).

The *Chara corallina* peak amplitude is almost independent of temperature (measured [30]).

Channel dimensions. KcsA is built of four identical subunits (measured [31]). Two K^+ ions occupy its filter (measured [31]). The NavAb pore of *Arcobacter butzleri* is closed with four activated voltage sensors [32].

Its filter is water-filled, with four acidic side chains at the narrowest point (measured [32]).

KvAP is the voltage-dependent K^+ channel of the archaeon *Aeropyrum pernix* [33]. Positively charged “voltage-sensor paddles” sit on its outer perimeter [33]. The table gives all dimensions and resolutions.

Communities. The *B. subtilis* biofilm signal was followed over a profile of about 1.5 mm, position 9.47 (measured [8]). Oscillations begin when the biofilm holds “over one million cells” (measured [10]).

Speeds. Mean swimming speed of *Chlamydomonas* is about $75 \mu\text{m s}^{-1}$, with peaks near $300 \mu\text{m s}^{-1}$ (measured [34]).

The glass-sponge impulse spreads at $0.27 \pm 0.1 \text{ cm s}^{-1}$ at 10°C (measured [20]). That is 2.7 mm s^{-1} (computed).

In *Mimosa* the touch-induced action potential on the rachilla runs at $5.52 \pm 0.43 \text{ mm s}^{-1}$ (measured [16]). The wound-induced one runs at $4.27 \pm 0.41 \text{ mm s}^{-1}$ (measured [16]).

Mimosa Ca^{2+} waves run at $1.31 \pm 0.17 \text{ mm s}^{-1}$ in the leaflet vein, $n = 6$, and $2.65\text{--}3.11 \text{ mm s}^{-1}$ on the rachilla at the first peak (measured [16]). They run at $5.87 \pm 0.75 \text{ mm s}^{-1}$ after touch and $4.13 \pm 0.45 \text{ mm s}^{-1}$ after wounding (measured [16]).

A general plant range is $0.01\text{--}0.04 \text{ m s}^{-1}$, against $0.4\text{--}200 \text{ m s}^{-1}$ in animals [18]. The flytrap action potential propagates “around 10 m/s ”, a value cited from Volkov 2019 [15]. The two plant values disagree: 10 m s^{-1} against $0.01\text{--}0.04 \text{ m s}^{-1}$.

Both are recorded.

The *Mimosa* action potential, 5.52 mm s^{-1} , is slower than the general plant range by a factor of $0.01 / 0.00552 = 1.8$ to $0.04 / 0.00552 = 7.2$ (computed).

In the human heart conduction runs at about 0.5 m s^{-1} in the atria and about 0.05 m s^{-1} in the atrioventricular (AV) node (measured [27][35]). It runs at about 2 m s^{-1} in the bundle branches and about 4 m s^{-1} in the Purkinje fibres (measured [27][35]).

Electrical conduction speeds read run from 2.7 mm s^{-1} (sponge) to 200 m s^{-1} (animal nerve). The ratio is $200 / 0.0027 = 74,000$ (computed). The slowest wave read is the *Mimosa* Ca^{2+} wave, 1.31 mm s^{-1} .

what	size	position	source
KvAP isolated voltage sensor, structure resolution	$1.9 \text{ \AA}$	-4.99	[33]
NavAb structure resolution	$2.7 \text{ \AA}$	-4.67	[32]
KcsA structure resolution	$3.2 \text{ \AA}$	-4.51	[31]
KvAP full channel, structure resolution	$3.2 \text{ \AA}$	-4.51	[33]
NavAb selectivity filter, width	about $4.6 \text{ \AA}$	-4.18	[32]
KcsA, distance between two K^+ ions in the filter	about $7.5 \text{ \AA}$	-3.74	[31]
KcsA water-filled cavity	about $10 \text{ \AA}$	-3.48	[31]
KcsA selectivity filter, length	$12 \text{ \AA}$	-3.31	[31]
KcsA pore, length	$45 \text{ \AA}$	-2.11	[31]
<i>Chlamydomonas</i> cell body, radius	$4.4 \pm 0.3 \text{ \mu m}$	4.16	[34]
<i>Chlamydomonas</i> cell body, diameter	$8.8 \text{ \mu m}$	4.79	(computed)
<i>Chlamydomonas</i> flagellum	$13.5 \pm 0.8 \text{ \mu m}$	5.18	[34]

<i>B. subtilis</i> biofilm signal profile	about 1.5 mm	9.47	[8]
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Times

Channels. KcsA passes up to 10^8 ions s^{-1} , which is $1 / 10^8 = 10$ ns per ion, position 16.39 (measured [31]; computed). K^+ is “at least 10,000 times more permeant than Na^+ ” (measured [31]). A comparison value gives about 0.1 μs per ion at 10^7 ions s^{-1} , position 18.48 [36].

NaChBac is voltage-gated and Na^+ -selective [37]. Its gating currents are detectable at -90 mV from a holding potential of -150 mV, and the charge saturates at -10 mV (measured [38]). The charge-voltage curve lies 22 mV negative of the conductance-voltage curve (measured [38]).

Each channel moves about 16 elementary charges (measured [38]). Holding at 0 mV shifts the charge-voltage curve by about -60 mV (measured [38]). The Cole-Moore shift of 533 μs , position 26.29, was found for a prepulse change from -160 to -80 mV (measured [38]).

In HEK cells NaChBac half-activates at -35.0 ± 1.3 mV, slope 7.3 ± 0.4 mV (measured [39]). It half-inactivates at -52.3 ± 1.3 mV, slope -4.6 ± 0.3 mV (measured [39]).

Bacteria. *E. coli* cells imaged with the voltage-sensitive protein PROPS spiked “at up to 1 hertz” (measured [40][41]). The spiking coincided with rapid efflux of a small-molecule fluorophore [40]. Biofilm periods were measured peak to peak, imaged at one frame per 10 min, position 38.98 [9].

A model gives a period “on the order of hours”, increasing with biofilm size, with onset only above a critical size [42]. The biofilm propagation data have a log-log slope of 1.1 ($R^2 = 0.96$), against 0.5 expected for diffusion (measured [8]).

The K^+ diffusion coefficient, $19.7 \times 10^{-6} \text{ cm}^2 \text{ s}^{-1}$ in water, was taken as 13.8×10^{-6} in biofilm [8]. That is $13.8 / 19.7 = 70\%$ (computed).

Ciliates. In *Paramecium* Ba^{2+} and Sr^{2+} make the graded response all-or-none (measured [28]). Ciliary reversal lengthens with stimulus strength, from shortest to longest by $2.4 / 0.05 = 48$ times (measured [11]; computed). Reversal is suppressed at $+70$ mV and above (measured [11]).

Before stimulation the cilia beat at 13–27 Hz (measured [26]). One beat lasts $1 / 27 = 37$ ms to $1 / 13 = 77$ ms, position 30.15–30.82 (computed).

Green algae. The *Chlamydomonas* flagellum beats at 43.2 ± 8.0 Hz, one beat per $1 / 43.2 = 23$ ms, position 29.73 (measured [34]; computed). The source gives a period of about 20–25 ms, position 29.59–29.80 [34]. The body rotates at 1.67 ± 0.35 Hz (measured [34]).

The product of rotation frequency and adaptation time is 1.27 ± 0.41 (measured [34]). The check $1.67 \times 0.764 = 1.28$ agrees (computed). The product is 1.20 ± 0.44 in *Volvox* and 0.95 ± 0.50 in *Gonium* (measured [34]).

Diatoms and charophytes. In *Chara corallina* the action potential lengthens 30 times

between 40 °C and 3.5 °C (measured [30]; computed). The activation enthalpy is about 7 kJ mol⁻¹ above 20 °C and about 350 kJ mol⁻¹ below 7 °C (measured [30]).

The Venus flytrap. For closing of the trap the Results give 15–20 s, position 35.62–35.88, and the Discussion “within about 30 s”, position 36.25 [14]. Half-depolarization is 0.29 / 0.13 = 2.2 times faster at 30 °C than at 10 °C (measured [15]; computed).

Heat-induced firing reaches 50 % at 33.8 °C (measured [15]). At 46 °C the trap fires a steady 3.8 action potentials per minute (measured [15]). Struggling prey elicit 63 ± 13 action potentials in the first hour, position 40.61, n = 5 (measured [14]).

More than 100 follow within 6 h, position 42.24 (measured [14]).

Heart. In the human heart the sinus node fires 80–100 min⁻¹ unaided, the AV node 40–60, the bundle 30–40 and the branches 20–30 [27][35].

The AV delay is 100 / 225 = 44 % of the conduction time from sinus node to last ventricular cell (computed). Heart muscle cells renew by 1 % per year (one year, position 48.87) at age 25 and 0.45 % at age 75 (measured [43]). Fewer than half are replaced in a lifetime [43].

what	duration	position	source
ion passage, KcsA at 10 ⁸ ions s ⁻¹	10 ns	16.39	(computed)
ion passage at 10 ⁷ ions s ⁻¹	about 0.1 μs	18.48	[36]
NaChBac Cole-Moore shift	533 μs	26.29	[38]
neuron action potential	about 2 ms	27.50	[27]
<i>Paramecium</i> “off” latency	2–4 ms	27.50–28.13	[11]
<i>Paramecium</i> reversal latency	30 to ≤4 ms	29.96–28.13	[11]
<i>Odontella</i> recovery from inactivation, τ	5.1 ± 0.4 ms	28.35	[29]
<i>Chlamydomonas</i> response time τ _r	0.018 ± 0.009 s	29.50	[34]
<i>Chlamydomonas</i> flagellar beat (43.2 Hz)	23 ms	29.73	(computed)
<i>Chlamydomonas</i> phototransduction delay	28 ± 11 ms; 38 ± 5 ms	29.90; 30.18	[34]
<i>Paramecium</i> regenerative component absent below	30 ms	29.96	[28]
<i>Paramecium</i> ciliary beat (13–27 Hz)	37–77 ms	30.15–30.82	(computed)
<i>Paramecium</i> electrotonic time constant	40–50 ms	30.22–30.43	[28]
<i>Paramecium</i> regenerative component	80 ms	30.85	[28]

reduced >75 % at			
<i>Odontella</i> action potential	50-100 ms	30.43-31.06	[29]
<i>Chlamydomonas</i> time to peak	97 ± 18 ms	31.03	[34]
heart AV delay	100 ms	31.06	[27]
flytrap half-depolarization, 30 °C and 10 °C	0.13 ± 0.02 s; 0.29 ± 0.08 s	31.30; 32.03	[15]
<i>Mimosa</i> Ca ²⁺ rise before leaflet movement	up to 0.15 s	31.43	[16]
<i>Paramecium</i> refractoriness, up to	200 ms	31.69	[28]
heart, sinus node to last ventricular cell	225 ms	31.80	[27]
ventricular muscle action potential	250-300 ms	31.89-32.06	[27]
<i>Paramecium</i> ciliary reversal	50 ms to 2.4 s	30.43-33.95	[11]
<i>Chlamydomonas</i> body rotation (1.67 Hz)	0.60 s	32.69	(computed)
sinus node interval (80-100 min ⁻¹)	0.60-0.75 s	32.69-32.89	(computed)
bundle-branch interval (20-30 min ⁻¹)	2-3 s	33.78-34.15	(computed)
<i>Chlamydomonas</i> adaptation time τ_a	0.764 ± 0.190 s	32.91	[34]
<i>Chlamydomonas</i> reorientation	0.96 ± 0.36 s	33.12	[34]
<i>E. coli</i> spike cycle at 1 Hz	1 s	33.15	(computed)
<i>Chara</i> streaming stops after spike, within	<1 s	33.15	[18]
<i>Chlamydomonas</i> recovery of flagellar asymmetry	about 1-2 s	33.15-33.78	[34]
<i>Chara corallina</i> action potential, 40 °C	about 1 s	33.15	[30]
flytrap action potential	2 s	33.78	[15]
<i>Chara</i> half-amplitude duration	about 2-3 s	33.78-34.15	[18]
<i>Chara</i> absolute refractory period	2-10 s	33.78-35.25	[18]
flytrap, two action potentials close the trap within	15-20 s; about 30 s	35.62-35.88; 36.25	[14]
glass sponge absolute refractory period	29 s	36.22	[20]
<i>Chara corallina</i> action	about 30 s	36.25	[30]

potential, 3.5 °C			
<i>Chara</i> relative refractory period, up to	90 s	37.25	[18]
glass sponge relative refractory period	95-100 s	37.30-37.34	[20]
<i>Chara</i> streaming recovery	about 250 s	38.18	[18]
<i>P. aeruginosa</i> lag after biofilm peak	22 ± 13 min	39.69	[10]
<i>B. subtilis</i> motile lag after biofilm peak	26 ± 9 min	39.85	[10]
flytrap, 63 ± 13 action potentials in	1 h	40.61	[14]
<i>P. aeruginosa</i> mean peak interval	2.1 h	41.28	[10]
flytrap DmHKT1 maximum after stimulation	4 h	41.87	[14]
flytrap, >100 action potentials within	6 h	42.24	[14]
heart muscle renewal, per	1 year	48.87	[43]
Cnidarian Cav genes conserved, at least	500 Myr	67.10	[3]

The durations read span from 10 ns to 500 Myr, positions 16.39 to 67.10. Electrical events alone run from 533 μ s to 100 s, positions 26.29 to 37.34.

Counts

Subunits and transmembrane segments. KcsA has 4 subunits of 2 transmembrane segments each [37][39][3]. NaChBac, from *Bacillus halodurans*, is encoded by one six-transmembrane (6TM) segment [37]. It forms “four identical subunits, each of which contains six transmembrane segments” [39].

The canonical eukaryotic Na⁺ and Ca²⁺ channels have four repeated 6TM domains in one chain [37][3]. Both arrangements give $4 \times 6 = 24$ transmembrane segments (computed).

NaChBac has a pore similar to that of voltage-gated Ca²⁺ channels and is blocked by Ca²⁺-channel blockers [37].

The archaeal Ca²⁺-gated K⁺ channel MthK from *Methanobacterium thermoautotrophicum* carries eight RCK domains on its intracellular side (measured [44]).

A genome survey found “two sodium channels and one calcium channel in prokaryota” [45]. The Na⁺ channels come from alkaliphilic bacteria, the Ca²⁺ channel from *Paracoccus* [45].

Genes per genome.

organism	count	source
<i>Bacillus subtilis</i>	1 characterised K ⁺ channel (YugO)	[8]
prokaryotes (survey)	2 Na ⁺ and 1 Ca ²⁺ channel sequences	[45]
<i>Monosiga brevicollis</i> (choanoflagellate)	1 T-type Cav + 1 high-voltage Cav; Nav-like; putative Kv	[3]
<i>Paramecium tetraurelia</i>	~40,000 genes; 34 Ca ²⁺ -release channel genes in 6 groups; K ⁺ channel multigene family (Pak1, Pak2 complete; three fragments)	[46][47][48]
<i>Thalassiosira pseudonana</i> (diatom)	1 putative four-domain Na ⁺ /Ca ²⁺ channel + single-domain channels	[29]
<i>Phaeodactylum tricornutum</i> (diatom)	0 four-domain channels; EukCatA single-domain	[29][7]
<i>Karenia brevis</i> (dinoflagellate)	7 four-domain channels (transcriptome)	[29]
<i>Arabidopsis thaliana</i>	9 Shaker-type + 6 KCO K ⁺ channels; 20 CNGC; ~880 transporters in 46 families	[49]
<i>Amphimedon queenslandica</i> (sponge)	two-TM Kir only; 0 Kv; 0 Nav	[3]
<i>Trichoplax</i> (placozoan), <i>Mnemiopsis</i> (ctenophore)	putative Kv; all Nav with DEEA filter	[3]
<i>Nematostella vectensis</i>	44 Kv (18 Shaker, 14 intron-less); 5 Nav2 (3 DEEA, 1 DEET, 1 DKEA)	[3]
sea anemones and corals	6 Cav	[3]
<i>Hydra magnipapillata</i>	35 Kv	[3]
<i>Caenorhabditis elegans</i>	38 K ⁺ + 2 CNG subunit genes in 8 families (1996); ≥80 K ⁺ channels, no voltage-gated Na ⁺ channel (1998)	[50][51]
<i>Drosophila melanogaster</i>	5 Kv; 1 Nav1 + 1 Nav2	[3]
most invertebrate bilaterians	3 Cav	[3]
<i>Homo sapiens</i>	27 Kv (or 35); 10 Nav (Nav1.1–1.9 and Nax); 8 Shaker (7 intron-less); 10 Cav	[3][45]

Protists. *Paramecium tetraurelia* is “one of the gene-richest organisms” [46]. Its 34 InsP₃/ryanodine Ca²⁺-release channel genes diversified by whole-genome duplication [47].

The *Paramecium* K⁺ channels Pak1 and Pak2 are distantly related to animal Kv channels, with a conserved pore [48]. By 1994 “over 50” K⁺ channel sequences were known (measured [52]). All but two, both from plants, came from triploblast animals [52].

Most diatom channel sequences are single-domain channels closest to NaChBac [29].

Only *T. pseudonana* has both single-domain and four-domain channels [29].

Plants. About 5 % of the *Arabidopsis* genome encodes membrane transport proteins (measured [49]). Its Shaker-type K⁺ channels are 1P/6TM, its KCO channels 2P/4TM; 1P/2TM and 2P/8TM K⁺ channels are absent [49].

The flytrap counts. More than three action potentials are needed to induce hydrolase genes, and five for significant expression (measured [14]). DmJAZ1 rises 5.5-fold after two (measured [14]).

DmHKT1 Na⁺-transporter expression is negligible up to three action potentials: 147 molecules per 10,000 actin (measured [14]). That is $147 / 10,000 = 1.5$ % of actin (computed). After 5–60 action potentials it rises up to 60-fold (measured [14]).

The DmHKT1 K_m is 10 mM (measured [14]).

Animals. The human counts differ between sources. Moran and colleagues give 27 Kv genes (measured [3]). Palaniappan and Jakobsson give 35, against 22 and 26 in two earlier counts cited there (measured [45]).

The same survey counts 123 non-redundant human K⁺ channel proteins, 23 with two pore signatures (measured [45]). It gives 7 CNG channels (6 in an earlier count) and 18 pore-forming K⁺ subfamilies (measured [45]). It gives the human K⁺ complement of Yu and Catterall as 88 [45].

The human voltage-gated-like ion channel superfamily has 143 members in eight families (measured [53]). The families are the voltage-gated Na⁺, Ca²⁺ and K⁺ channels, Ca²⁺-activated K⁺, cyclic-nucleotide-modulated, TRP, inward-rectifier K⁺ and two-pore K⁺ channels [53]. It is the third largest group of signal-transduction proteins after G-protein-coupled receptors and protein kinases [53].

More than 400 human genes encode ion channels [54]. At least 232 encode pore-forming parts of plasma-membrane channels [55].

The worm *C. elegans* has 38 K⁺ channel subunits and 2 cyclic-nucleotide-gated subunits in eight conserved families (measured [50]). At least 23 genes carry two tandem P domains (measured [50]).

A 1998 count gives at least 80 K⁺ channels, 90 neurotransmitter-gated ion channels and 50 peptide receptors (measured [51]). It gives up to 1,000 orphan receptors and no predicted voltage-gated Na⁺ channel [51]. The two worm K⁺ counts differ: 38 in 1996, at least 80 in 1998.

Both are recorded.

Order of events

1. 4.52–3.94 Ga, about 4.2 Ga (4.33–4.09 Ga) — LUCA (modelled [1]); position 69.11–68.98; 69.04 (69.07–69.02). >3.9 Ga in a second study (modelled [2]); position 68.97.
2. <3.4 Ga — crown Bacteria and crown Archaea (modelled [2]); position 68.85.
3. | 1 Ga — Nav-like channel genes, before multicellularity (modelled [3]); position

4. Before the fungal-animal split — Ca^{2+} -conducting Nav2 channels; Cav in the plant-animal ancestor [3]. No date given; no position.
5. Ancestral unicellular eukaryotes — fast $\text{Na}^+/\text{Ca}^{2+}$ action potential [6]. No date given; no position.
6. Later, undated — loss of four-domain $\text{Na}^+/\text{Ca}^{2+}$ channels in land plants and fungi [7], and in the pennate diatom *Phaeodactylum* [29].
7. 540 Ma — cnidarian Na^+ -selective channels diverge from Ca^{2+} -conducting homologues; cnidarian Nav2.5 duplication (modelled [5][3]); position 67.17.
8. ≥ 500 Myr of conservation — cnidarian-specific Cav genes (modelled [3]); position 67.10.
9. Urbilaterian — Nav1 with DEKA filter [3]. No date given; no position.

Present quantities

cell	resting potential	conduction speed	source
<i>E. coli</i>	−105 to −140 mV	—	[21]
bacteria, typical	about −150 mV	—	[22]
<i>Paramecium</i>	−30 to −69 mV	—	[26]
<i>Chara</i>	−170 to −250 mV	0.01–0.04 m s ^{−1} (plants, general)	[18]
<i>Dionaea</i> gland	−116 ± 19; −122 ± 14 mV (activated)	10 m s ^{−1} (cited)	[14][15]
<i>Mimosa</i>	—	4.27–5.52 mm s ^{−1}	[16]
glass sponge	—	2.7 mm s ^{−1}	[20]
human heart	—	0.05–4 m s ^{−1}	[27][35]
neuron	−70 mV	—	[27]
animals (general)	—	0.4–200 m s ^{−1}	[18]

Eukaryotic resting potentials of −40 to −95 mV are typical [24]. Human cells carry 143 VGL superfamily channels within more than 400 ion-channel genes [53][54].

Pattern

Every value read is negative inside. Magnitudes run plants (−116 to −250 mV), bacteria (−105 to −150 mV), protists and animals (−30 to −95 mV). The bacterial Na^+ channel already has a fourfold pore of 24 transmembrane segments.

The NavAb filter is about 4.6 Å wide; the KcsA filter is 12 Å long. KcsA passes up to 10^8 ions s^{−1}, a generic channel 10^7 ions s^{−1}.

Electrical events last 2 ms (neuron), 50–100 ms (diatom), 250–300 ms (heart), 2–3 s (plants), and hours (biofilm waves). Refractory periods run tens of ms to about 2 min. Conduction speeds span 2.7 mm s^{−1} to 200 m s^{−1}, a factor of 74,000.

The Na⁺ channel family is older than animals and passed Ca²⁺ first; Na⁺ selectivity arose twice. Four-domain channels were lost in land plants, fungi and one diatom. Kv counts run 0, 35–44, 5 and 27–35 across sponge, cnidarians, fly and human.

Not verified

- KcsA first described 1995 from *Streptomyces lividans* (Schrempf et al. 1995): content not read.
- KcsA opening at acidic pH; four K⁺ sites in the filter (TVGYG): encyclopedia only.
- Cnidarians separate from other animals “>600 million years ago”: press release only.
- *E. coli* proton-motive force $\approx$ 150 mV (Gabel & Berg 2003): assumed value, secondary.
- *Paramecium* steady-state model values (Al-Rudainy 2014): secondary.
- Fungal potentials –50 and –300 mV (BioNumbers 107759): page did not load.
- Action potentials widespread in higher plants (Pickard 1973): not opened.
- *Halobacterium* –100 mV (Koch 2005): worked example, not a measurement.
- Biofilm wave speed and period: not printed in the texts read.

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A2 Before the Neuron

What it is

Many parts of the neuron and the synapse occur in cells and animals without neurons. The scaffold of the post-synaptic density, the presynaptic secretion complex and all families of voltage-gated channels occur in choanoflagellates. Choanoflagellates are the unicellular sister group of animals [1].

Sponges and placozoans have no neurons. Sponges keep a nearly complete post-synaptic scaffold. Placozoans coordinate feeding with secreted peptides, without synapses.

In ctenophores “many bilaterian neuron-specific genes and genes of ‘classical’ neurotransmitter pathways either are absent or, if present, are not expressed in neurons” [2]. No known neuropeptide homologues are found, and L-glutamate is a candidate neuromuscular transmitter [2].

The sources read tie the question of one or two origins of neurons to the branching position of ctenophores [2][3]. This chapter records the parts, the counts, the dates of the early animal nodes and every statement found on division of neurons in early animals.

First appearance

Animals and their unicellular relatives. Animals and their unicellular relatives diverged “more than 800 million years ago”, position 67.53 (modelled [4]). No fossils record the split.

The metazoan stem, from the animal-choanoflagellate split to crown animals, lasted “about 150–200 million years”, position 66.01–66.27 (modelled [5]). It carried about 28 % of the substitutions between humans and choanoflagellates (modelled [5]).

The post-synaptic scaffold proteins Shank, Homer and DLG and some partners “were acquired in a unicellular ancestor” of choanoflagellates and animals [6]. The scaffold “emerged in a unicellular context and was probably not involved in cell-cell

communication" [6]. Most post-synaptic proteins did not originate together with synapses or neural-like cells [6].

The Munc18/syntaxin-1 complex was earlier found only in neuronal tissue [7]. It is present in the choanoflagellate *Monosiga brevicollis* and is "structurally and functionally very similar" to the vertebrate complex [7]. The source states that this secretion machinery of the common ancestor was later co-opted for synaptic roles [7].

"All voltage-gated channel families are present in choanoflagellates" [8]. The choanoflagellate Na⁺-channel homologue has a selectivity filter intermediate between Ca²⁺ and Na⁺ channels [1].

Sponges. Sponges "diverged from other animals more than 600 million years ago", position 67.27 (modelled [5]). Sponge sterane biomarkers are older than about 635 Ma, position 67.32 (measured [9][10]). An algal origin of the same molecule is also proposed [11].

Both readings are recorded.

Nerve cells "appear restricted to eumetazoans sensu stricto" [5].

Placozoans. In the 2008 genome analysis placozoans group with cnidarians and bilaterians in a eumetazoan clade, with sponges diverging earliest [12]. Moving Placozoa around the eumetazoan node "has a profound impact on the estimated age of the root" [13]. No placozoan fossils were read.

Ctenophores. Six sclerotised, armoured ctenophores come from the early Cambrian [14]. They have eight-fold symmetry and eight pairs of comb rows, and form the class Scleroctenophora [14]. No numerical age was printed on the pages read.

Living ctenophore diversity arose about 350 ± 88 Ma, position 66.78 (modelled [15]). The range 262–438 Ma has position 66.51–66.98 (computed). An earlier hypothesis gave about 65 Ma, position 65.25 [15].

About 200 ctenophore species are described [15].

Lobate and cydippid ctenophores diverged 160–260 Ma, position 66.07–66.51 (modelled [4]).

One origin of neurons or two. Two positions alternate in the record read.

The *Mnemiopsis leidyi* genome placed ctenophores, not sponges, as sister to all other animals [16]. Many genes of bilaterian mesodermal cell types are absent [16]. The neural gene set resembles that of sponges, which the abstract reads as a possible loss of a nervous system in ctenophores [16].

The *Pleurobrachia bachei* genome also placed ctenophores earliest [2]. The authors concluded that neural systems "evolved independently from those in other animals" [2]. They called a single origin "a less parsimonious scenario" [2].

In some analyses the support was weaker [2].

A 2015 review found a single origin "compatible" with shared molecular and cellular traits [3]. Under ctenophore-first "this ancestral nervous system was likely very simple"

[3]. The authors “favor the view of an independent complexification of nervous systems from a simple precursor state” [3].

The same review notes complete loss of a nervous system in only “two examples” of animals, both parasites [3]. It states that available data “do not strongly challenge” sponges as sister to the rest [3].

Twenty-seven new ctenophore transcriptomes placed Ctenophora as “sister group to all other animals” [15]. *Euplokamis dunlapae* is sister to the other ctenophores [15]. The ancestor reconstructs as pelagic, tentacled, bioluminescent and hermaphroditic, with at least 2 transitions to benthic life [15].

A dataset of 1,719 genes with a site-heterogeneous model “strongly” supports sponges as sister to all other animals, ctenophores second [17]. Ctenophore-sister appeared only under settings that worsen long-branch attraction [17].

Partitioned analyses with mixture models and recoding found that support for ctenophore-sister declines as model fit improves [18]. At the strongest recoding, datasets WEA15 and WEA17 recover Porifera-sister with 95 % and 99 % support (modelled [18]). Dataset REA weakly recovers Placozoa-sister, 52 % (modelled [18]).

Each test dataset held 133–146 genes [18].

Chromosome-scale genomes of 1 ctenophore, 2 sponges and 3 unicellular relatives were compared in 2023 [4]. Seven derived fusions are shared by sponges, bilaterians and cnidarians to the exclusion of ctenophores; 4 of them are fusion-with-mixing (measured [4]). The Bayesian posterior for ctenophore-sister is 1.0 (modelled [4]).

The clade of all other animals is named Myriazoa [4].

The count of positions read: ctenophore-sister in 2013, 2014, 2017 and 2023, four publications [16][2][15][4]. Sponge-sister in 2015 (review), 2017 and 2021, three publications [3][17][18].

Partners

The choanoflagellate toolkit. *Monosiga* carries Shank, Homer, DLG, CaMKII, Citron, Cortactin, the Ephrin receptor, IP₃R, PKCαβγ and Shaker K⁺ channels [6]. Three DLG partners, CRIPT, Shaker and PMCA, have clear orthologues [6].

The mammalian post-synaptic density holds “about one thousand proteins” [6]. Shank has five interacting domains, DLG three PDZ domains and GRIP seven [6].

Monosiga has one T-type (low-voltage) Cav and one high-voltage Cav, putative Kv channels and a Nav-like channel [8]. Its genome holds 78 protein domains otherwise found only in animals (measured [19]).

The sponge scaffold. The demosponge *Amphimedon queenslandica* has a “nearly complete set of post-synaptic protein homologs” among 36 post-synaptic gene families analysed [20]. Present are dlG, Shank, Homer, GRIP, CRIPT, GKAP, PICK1 and several mGluRs [20]. Absent are the whole ionotropic glutamate receptor (iGluR) family, Shaker-type Kv and neuroligin [20].

The 13 ligand-binding residues of the dlG PDZ domains are 100 % conserved between sponge and human (measured [20]). Within the domain about 88.5 % is conserved across four animals, against about 68 % for the rest of the domain (measured [20]). Rat and sponge PDZ3 are about 50 % identical; modelled binding differs less than twofold (measured [20]; modelled [20]).

Five genes, DLG, HOMER, GRIP, CRIPT and GKAP, are co-expressed in larval flask cells and in no other larval cell type (measured [20]).

Amphimedon also carries homologues of proneural proteins, taken as an ancestral “protoneuron” [5]. Metabotropic glutamate, dopamine and serotonin receptors are present [5]. An ephrin receptor is present without an ephrin ligand; slit, netrin, unc-5 and robo are absent [5].

Bilaterian peptide hormones were not detected in *Amphimedon* [5]. It has only two-TM Kir K⁺ channels, no Kv and no Nav homologue [8].

Sponge cells and impulses. The freshwater demosponge *Spongilla lacustris* has no nerves or muscles [21]. Whole-body single-cell RNA sequencing found 18 cell types (measured [21]). They include NO-sensitive contractile pinacocytes, amoeboid phagocytes and secretory “neuroid” cells beside the digestive choanocytes [21].

The neuroid cells contain secretory vesicles [21]. They send projections that wrap choanocyte microvilli and cilia [21].

The glass sponge *Rhabdocalyptus dawsoni* (Hexactinellida) conducts all-or-none impulses through a syncytial trabecular tissue (measured [22]). Glass sponges retain relicts of 10 of the 29 ancient bilaterian-cnidarian-sponge linkage groups (measured [4]).

Placozoan peptides. *Trichoplax adhaerens* has “just six identified cell types” [23]. Ciliated epithelial cells form about 70 % of the ventral epithelium (measured [23]). There are no gap junctions, and fibre cells “do not form chemical synapses” [23].

Secretory cells make up 4 % of the total (measured [23]). About 1,500 stand around a 500 µm animal (measured [23]).

Six peptidergic cell populations have distinct distributions (measured [24]). Each secretes one peptide: SIFGamide, TrIns3, SITFamide, YYamide, RWamide or FFNPamide [24]. Under some peptides animals flatten up to 5 times their default size (measured [24]).

Twelve peptides were tested in feeding: 3 commercial and 9 custom amidated (measured [23]). The threshold is 100 nmol l⁻¹; YPFFamide acted in 3 of 6 animals and YPWFamide in 3 of 3 (measured [23]). Full pausing occurs above 200 nmol l⁻¹ (measured [23]).

As few as 10 algae suffice for a pause (measured [23]). A pausing animal affects others up to about 200 µm away, position 7.63 (measured [23]).

Trichoplax lacks orthologues of Shank, GRIP, the ErbB receptor, mGluR and SynGAP [6]. The genome “contains most post-synaptic genes but lacks some of them” [6]. Shank is present in *Monosiga*, sponges and eumetazoans [6].

All placozoan Nav channels carry the DEEA filter, and putative Kv channels are present [8]. Placozoa keep Na⁺-channel homologues without a nervous system [1].

A neuropeptide precursor matching the large connected peptide-family network occurs in *Trichoplax*, “an animal without neurons” [25]. Placozoan genome analysis “revealed several genes encoding proteins with characteristics of neuropeptide precursors” [26].

Whole-organism single-cell RNA sequencing found several types of peptidergic cells in placozoans [27]. Ctenophores produce a greater diversity of cell types than placozoans and sponges [27].

The ctenophore nervous system. The *Pleurobrachia* authors “strongly suggest” that ctenophores do not use serotonin, acetylcholine, dopamine, noradrenaline, adrenaline, octopamine, histamine or glycine as intercellular messengers [2]. L-glutamate is a candidate neuromuscular transmitter, active at about 10⁻⁷ M (measured [2]). Other classical transmitters were ineffective up to 5 mM (measured [2]).

“Many bilaterian neuron-specific genes and genes of ‘classical’ neurotransmitter pathways either are absent or, if present, are not expressed in neurons” [2]. No known neuropeptide homologues were found [2].

In a 1-day-old *Mnemiopsis* cydippid, serial block-face electron microscopy reconstructed 5 subepithelial nerve-net neurons (measured [28]). It also reconstructed 6 mesogleal neurons and 22 putative sensory cells in five morphological groups (measured [28]).

The neurites of all five nerve-net cells form “an anastomosed continuous network” [28]. Their plasma membrane is continuous, a syncytium [28]. “Neither electrical nor chemical synapses were detected between the cells” of the net [28].

A reconstructed nerve-net neuron sends five neurites from its soma (measured [29]).

Of nine synthetic *Mnemiopsis* peptides tested, four raised swimming speed (measured [29]).

Neuropeptides across early animals. As of 2018, “neuropeptides that act as ligands for GPCRs have yet to be identified in any of the four non-bilaterian phyla” [26]. The four are Porifera, Placozoa, Ctenophora and Cnidaria [26].

“Homologues of the majority of bilaterian neuropeptides and their cognate receptors have not been found in non-bilaterians” [26]. In sponges no homologues of bilaterian neuropeptides or receptors were identified [26].

The cnidarian *Nematostella vectensis* has precursors with 12 C-terminal motifs, none orthologous to bilaterian neuropeptides (measured [26]). The motifs are RIamides, RPamides, RWamides, LWamides, ITamide, MTamide, VRamide, RRamide, PGamides, RGamides, PVamides and LVamide [26]. A family of 13 ENaC-type channels are receptors for *Hydra* RFamide peptides (measured [26]).

Two peptide families, GRFamide and X1PRX2amide, are present in all cnidarian classes investigated [30]. In *Pleurobrachia*, none of the 72 putative precursors is orthologous to those of other animals except glycoprotein-, bursicon- and insulin-type hormones [26].

About one quarter of animal peptide families form one large, loosely connected similarity network [25].

Division of neurons in early animals. Three statements were found.

In the *Mnemiopsis* cydippid the question is left open: “do neurons divide, but remain connected in the cydippid SNN or do neurites from different cell bodies reach out and fuse?” [28]. No answer is given [28].

In *Nematostella*, NvSoxB(2) is expressed in neural progenitors “before mitosis” and “transiently expressed in mitotically active cells” [31]. Some NvSoxB(2)⁺ cells carry a mitotic spindle (measured [31]). The paper does not test division of differentiated neurons [31].

In *Hydra attenuata* “nerves and nematocytes have 2n postmitotic nuclear DNA content” (measured [32]). Nerves differentiate directly from interstitial stem cells (measured [32]).

For placozoans and sponges, which have no neurons, no statement on neuronal division applies. No source read covers division of *Trichoplax* peptidergic or sponge neuroid cells.

Sizes

what	size	position	source
<i>Mnemiopsis</i> synaptic vesicle, median (n = 56)	51 nm	0.10	[29]
<i>Mnemiopsis</i> dense-core vesicle, median (n = 66)	202 nm	1.36	[29]
<i>Trichoplax</i> secretory granules	300–500 nm	1.72–2.18	[23]
<i>Trichoplax</i> secretory cells, spacing	about 5 µm	4.28	[23]
<i>Salpingoeca rosetta</i> cell, equivalent-sphere diameter (from 105.9 µm ³)	5.87 µm	4.42	(computed)
algae eaten by <i>Trichoplax</i>	9 × 6 µm	4.81 × 4.44	[23]
<i>Trichoplax</i> cilia	about 10 µm	4.91	[23]
<i>Trichoplax</i> , reach of a pausing animal	up to about 200 µm	7.63	[23]
<i>Trichoplax</i> animal, diameter	0.3–1.5 mm	8.00–9.47	[23]
<i>Trichoplax</i> animal holding about 1,500 secretory cells	500 µm	8.47	[23]
<i>Mnemiopsis</i> cydippids at 3–5 days	3–5 mm	10.10–10.56	[29]

The *Salpingoeca rosetta* cell volume is $105.9 \pm 8.8 \mu\text{m}^3$ (measured [33]). The diameter of a sphere of that volume is $(6 \times 105.9 / \pi)^{(1/3)} = 5.87 \mu\text{m}$ (computed). Rosettes hold 4–25 cells, mostly 8 (measured [33]).

Dense-core vesicles are $202 / 51 = 4.0$ times the synaptic vesicle diameter (computed).
A 500 μm *Trichoplax* is $500 / 5 = 100$ secretory-cell spacings across (computed).

The glass-sponge impulse runs at $0.27 \pm 0.1 \text{ cm s}^{-1}$ at 10 °C, which is 2.7 mm s^{-1} (measured [22]; computed).

Effective concentrations sit near 10^{-7} M : the *Trichoplax* threshold is 100–200 nM and ctenophore glutamate acts at about 10^{-7} M (measured [23][2]). Placozoan peptides were tested at 200 nM–50 μM , 20 μM for detail [24].

The sizes run from 51 nm to 5 mm, positions 0.10 to 10.56.

Times

what	duration	position	source
glass sponge, absolute refractory period	29 s	36.22	[22]
<i>Trichoplax</i> , onset of pause after a peptide pulse	about 30 s	36.25	[23]
glass sponge, relative refractory period (further)	95–100 s	37.30–37.34	[22]
<i>Trichoplax</i> , single feeding pause (n = 64)	$2.97 \pm 0.96 \text{ min}$	37.87 (37.52–38.13)	[23]
<i>Trichoplax</i> , group pause	4.13 min	38.17	[23]
<i>Trichoplax</i> , repeat of pause under peptide (n = 33)	$9.11 \pm 4.22 \text{ min}$	38.89 (38.32–39.24)	[23]
<i>Trichoplax</i> , PWN effect	about 10 min	38.98	[24]
<i>Trichoplax</i> , group pause cycle (n = 38)	$12.9 \pm 2.0 \text{ min}$	39.21 (39.05–39.34)	[23]
<i>Nematostella</i> , S phase to mitosis at gastrula	about 2–4 h	41.24–41.87	[31]
<i>Mnemiopsis</i> , eggs hatch after spawning	22–26 h	43.42–43.57	[29]
<i>Mnemiopsis</i> cydippid with syncytial net	1 day	43.50	[28]
<i>Hydra</i> , nerve differentiation from stem cells	about 1 day	43.50	[32]
<i>Hydra</i> , stem cell cycle	24 h	43.50	[32]
ctenophore neurons appear after muscle	about 2 days	44.13	[2]
<i>Mnemiopsis</i> cydippid age at 3–5 mm	3–5 days	44.50–44.96	[29]
Cambrian explosion, more than	22 Myr	64.26	[34]
about 1 % of genes move chromosome,	about 40 Myr	64.80	[4]

every			
metazoan stem	about 150–200 Myr	66.01–66.27	[5]

Ranges in parentheses are the positions of mean $\pm$ one standard deviation (computed). For example $2.97 - 0.96 = 2.01$ min and $2.97 + 0.96 = 3.93$ min (computed).

A single pause lasts $2.97 / 12.9 = 23$ % of a group cycle (computed). The behavioural units of *Trichoplax* run from 30 s to 13 min, positions 36.25 to 39.21.

Widths of the clock intervals. Crown Metazoa spans $833.5 - 649.8 = 184$ Myr, position 66.19 (computed). Crown Eumetazoa spans $746.2 - 625.9 = 120$ Myr, position 65.81 (computed). Crown Cnidaria spans $641.8 - 531.5 = 110$ Myr, position 65.73 (computed).

Crown Bilateria spans $688.3 - 595.7 = 93$ Myr, position 65.57 (computed).

Crown Deuterostomia and crown Protostomia each span 75 Myr, position 65.38 (computed). The lobate-cydropid window, $260 - 160 = 100$ Myr, has position 65.64 (computed).

Steps between first fossils. From the first complex Ediacaran fossils to *Dickinsonia* is $574.17 - 558 = 16$ Myr, position 63.98 (computed). From *Dickinsonia* to the Cambrian base is $558 - 538.8 = 19$ Myr, position 64.14 (computed). From the Cambrian base to Chengjiang is $538.8 - 518.03 = 21$ Myr, position 64.21 (computed).

The Ediacara biota spans $571 - 541 = 30$ Myr, position 64.54 (computed).

Counts

Genomes.

organism	genome	genes	source
<i>Monosiga brevicollis</i> (choanoflagellate)	~41.6 Mb	~9,200 (9,196 models)	[19]
<i>Salpingoeca rosetta</i> (choanoflagellate)	~55 Mb	11,629	[33]
<i>Trichoplax adhaerens</i> (placozoan)	~98 Mb	11,514	[12]
<i>Pleurobrachia bachei</i> (ctenophore)	156,146,497 bp draft (estimated 160–180 Mb)	19,523	[2]
<i>Amphimedon queenslandica</i> (sponge)	~167 Mb	~30,000 loci (called an overestimate)	[5]

Of the *Pleurobrachia* genes, 44 % have orthologues in other animals (measured [2]). That is $0.44 \times 19,523 = 8,590$ genes (computed). Of the *Amphimedon* loci, 18,693, or 63 %, have Swiss-Prot homologues (measured [5]).

The choanoflagellate. *Monosiga* has at least 23 cadherin genes, about 120 tyrosine kinase domains and about 80 SH2 domains (measured [19]). It has 58 PDZ-domain genes against 66 in *Nematostella* (measured [20]). Fifteen are orthologous between the two, seven with conserved full domain architecture (measured [20]).

At least 54 PDZ genes are inferred for the eumetazoan ancestor (modelled [20]).

Immunoglobulin-like proteins number 5 in *Monosiga* against 218 in *Amphimedon* (measured [5]). That is $218 / 5 = 44$ times more (computed).

The sponge. Of 4,670 pan-metazoan gene families, 1,286 are metazoan-specific, which is 27 % (measured [5]). On the metazoan stem 235 animal-specific domains and 769 animal-specific domain combinations arose (modelled [5]).

Amphimedon has 705 kinases, more than 150 of them receptor tyrosine kinases, and more than 200 GPCRs (measured [5]). It has 3 Wnt, 2 Frizzled, 8 TGF- β ligands, 5 TGF- β receptors, 1 Notch and 5 Delta genes (measured [5]).

For comparison, iGluR genes number at least 11 in *Nematostella* (8 NMDA-like), 18 in human and 20–30 in the fly (measured [20]). The sponge has none [20].

Cell types by grade. Non-bilaterian animals have about 5–15 cell types, invertebrate bilaterians about 50–100 and vertebrates about 225 (measured [5]). *Spongilla* has 18 (measured [21]). *Trichoplax* was known in 2008 to have four, possibly five, somatic cell types (measured [12]).

In 2017 the count was six (measured [23]).

Placozoan gene loss. The 2014 gain-and-loss reconstruction predicts a loss of 4,952 genes on the placozoan branch (modelled [2]).

The ctenophore genome. *Pleurobrachia* has 72 novel prohormones, with more than 50 homologues in other ctenophores (measured [2]). It has more than 100 orphan neuropeptide-like GPCRs and 12 pannexins/innexins (measured [2]). It has 29 ASIC-type Na⁺ channel genes and 8 glutaminases (measured [2]).

Pleurobrachia has 92 homeodomain genes, against 76 in *Mnemiopsis* and 32 in *Amphimedon* (measured [2]). HOX genes, Drosha, Pasha and most innate-immunity receptors are absent [2]. Ten further ctenophore transcriptomes were analysed with the genome (measured [2]).

Mnemiopsis has 129 putative neuropeptide precursors: 67 linear, 27 meeting all four models (measured [29]). Thirty are enriched in metacells (measured [29]). At least 42 mature peptides were found (measured [29]).

An earlier genome search had found one neuropeptide homologue [29]. *Mnemiopsis* has 35 Kv homologues, 2 Nav and 2 innexins (measured [29]).

Chromosome linkage. The 2023 study counts 31 ancestral metazoan syntenic groups of 5–29 genes each (measured [4]). Together they hold 291 genes of 2,474 orthology groups, which is 12 % (measured [4]; computed).

Of the 31 groups, 29 are shared with *Capsaspora*, 20 with *Salpingoeca* and 8 with *Creolimax* (measured [4]). There are 29 bilaterian–cnidarian–sponge (BCnS) linkage groups (measured [4]).

Haploid chromosome numbers are 36 in *Salpingoeca*, 16 in *Capsaspora*, 26 in *Creolimax* and 13 in ctenophores (measured [4]).

Neuropeptide systems. At least 30 neuropeptide signalling systems trace to the common ancestor of protostomes and deuterostomes [26]. Mirabeau and Joly counted

29 in 2013 and Jékely 27 in 2013 [26].

group	peptide count	source
<i>Trichoplax</i> (placozoan)	11 predicted peptides tested; 4 insulin-like peptides; 6 peptidergic populations	[24]
<i>Nematostella</i> (cnidarian)	precursors with 12 C-terminal motifs	[26]
Medusozoa and Octocorallia	66 preprohormones in all groups studied	[30]
Scyphozoa (3 species)	6 preprohormone genes	[30]
Staurozoa (5 species)	3 preprohormone genes	[30]
Cubozoa (5 species, earlier study)	6 families	[30]
Octocorallia (7 species)	5 families	[30]
<i>Pleurobrachia</i> (ctenophore)	72 putative precursors	[2][26]
<i>Mnemiopsis</i> (ctenophore)	129 predicted precursors; ≥ 42 mature peptides	[29]
bilaterian ancestor	≥ 30 systems (29; 27)	[26]

A cnidarian precursor carries up to 32 copies of its peptide (measured [30]). GPRRamide copies number 22 in *Briareum*, 15 in *Xenia*, 8 in *Eleutherobia*, 5 in *Clavularia* and 4 in *Heliopora* (measured [30]). RPRSamide copies number 3–16 in staurozoans (measured [30]).

Dividing cells. In *Nematostella* 10 % (mid-planula) to 25 % (early blastula) of NvSoxB(2)⁺ cells incorporate EdU, by the figure legend (measured [31]). The text gives 30 % [31]. Both values are recorded.

In 97 % of two-cell clusters only one cell is EdU-positive (measured [31]). The source reads this as “either one of the two cells is already post-mitotic (G0), or ... in an extended G1 phase” [31].

In *Hydra* 900 nerve cells differentiate per day per animal (measured [32]). Each animal holds 3,000–6,000 stem cells (measured [32]). About 60 % of daughters remain stem cells and about 40 % differentiate (measured [32]).

Order of events

1. 800 Ma — animals split from unicellular relatives; post-synaptic scaffold backbone, Munc18/syntaxin, Cav and Nav-like channels already present (modelled [4]; [6][7][8]); position 67.53.
2. 833.5–649.8 Ma — crown Metazoa (modelled [13]); position 67.57–67.34. First split: ctenophores [16][2][15][4] or sponges [17][18].
3. 746.2–625.9 Ma — crown Eumetazoa (modelled [13]); position 67.47–67.31.
4. 688.3–595.7 Ma — crown Bilateria (modelled [13]); position 67.39–67.26. At least 30 peptide systems in its ancestor [26].
5. 662.3–587.2 Ma — crown Deuterostomia (modelled [13]); position 67.36–67.25.

6. 653.1–578.1 Ma — crown Protostomia (modelled [13]); position 67.35–67.23.
7. 641.8–531.5 Ma — crown Cnidaria (modelled [13]); position 67.33–67.16.
8. 635 Ma — sponge steranes (measured [9][10]); algal origin also proposed [11]; position 67.32.
9. 600 Ma — sponges diverge from other animals (modelled [5]); position 67.27.
10. 574.17 ± 0.66 Ma — first complex Ediacaran macrofossils, Mistaken Point (measured [35]); position 67.23.
11. 571–541 Ma — Ediacara biota [36]; position 67.22–67.17.
12. 558 Ma — *Dickinsonia*, an animal by its sterols (measured [36]); position 67.20.
13. 540 Ma — cnidarian Na⁺-selective channel group diverges; cnidarian Nav2.5 duplication (modelled [37][8]); position 67.17.
14. 538.8 ± 0.2 Ma — base of the Cambrian [38]; position 67.17.
15. Early Cambrian — six armoured ctenophores, Scleroctenophora [14]; no numerical age read.
16. ≤ 518.03 Ma — Chengjiang biota (measured [34]); position 67.13.
17. ~ 450 Ma — cladorhizid and spongillid demosponges diverge (modelled [4]); position 67.01.
18. 350 ± 88 Ma — crown living ctenophores (modelled [15]); position 66.78 (66.51–66.98).
19. 260–160 Ma — lobate and cydippid ctenophores diverge (modelled [4]); position 66.51–66.07.

Present quantities

group	neurons	synapses	cell types	genes	source
choanoflagellates	none	none	—	$\sim 9,200$ – $11,629$	[19][33]
<i>Amphimedon</i> / <i>Spongilla</i> (sponges)	none	none	18 (<i>Spongilla</i>)	$\sim 30,000$ loci	[5][21]
<i>Trichoplax</i> (placozoan)	none	none; no gap junctions	6	11,514	[23][12]
<i>Mnemiopsis</i> cydippid (ctenophore)	5 net + 6 mesogleal; 22 sensory cells	none between net cells	—	—	[28]
<i>Pleurobrachia</i> (ctenophore)	present	—	—	19,523	[2]

About 200 ctenophore species are described [15]. The mammalian post-synaptic density holds about one thousand proteins [6].

Pattern

The unicellular sister of animals holds the post-synaptic scaffold backbone, the

presynaptic secretion complex and all voltage-gated channel families. Its genome holds about 9,200–11,600 genes.

The sponge lacks neurons, synapses, iGluRs, Kv and Nav. It keeps 5 scaffold genes co-expressed in one larval cell type and a secretory neuroid cell among 18 types. The placozoan, with 6 cell types and no synapses, coordinates feeding by peptides in units of 30 s to 13 min.

Cell-type counts step 5–15, 50–100, 225 by grade. Peptide counts per group run 11, 66, 72–129 and ≥ 27 –30; the ctenophore and cnidarian peptides are not orthologous to bilaterian ones.

Publications alternate: four ctenophore-sister, three sponge-sister. The ctenophore net at day 1 is 5 fused neurons without synapses. Clock intervals are 75–184 Myr wide.

No differentiated neuron was found dividing.

Not verified

- Cnidarians separated from other animals “more than 600 million years ago” (Gur Barzilai et al. 2012): press release only.
- About 80 mature neuropeptides in *Drosophila* (cited in Sachkova et al. 2021): secondary.
- Crown ages of Porifera, Ctenophora and Placozoa: not read from clocks.
- Numerical ages of the Cambrian armoured ctenophores and of *Haootia*-type early cnidarians: not found.
- Cell-type and metacell counts of Seb  -Pedr  s et al. 2018: not read.
- Full paper of Leys, Mackie and Meech 1999: not opened.
- Redmond and McLysaght 2021 author correction (2022) and Matters Arising (2023): not read.
- Published version of Sachkova et al. 2021: not opened; values may differ from the preprint.
- Division of placozoan or sponge secretory cells: no source found.

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 38. ICS chart v2023/09

A3 Nerve Nets

What it is

A nerve net is a nervous system without a central organ. Nerve cells lie spread through a body wall and join one another along neurites. In *Hydra* there are two separate nerve nets, one in the ectoderm and one in the endoderm [1].

The two nerve nets of *Hydra* do not mix. The endoderm of the tentacles holds no nerve cells [1]. Endodermal sensory cells make up more than 50 % of all endodermal nerve cells (measured [1]).

The cells of a *Hydra* nerve net are small and widely spaced. Ectodermal cell bodies are roughly 10 μm long, pos. 4.91 (measured [1]). The spacing between them is usually 50–100 μm , pos. 6.37–7.00 (measured [1]).

Neurites run singly or in bundles. In the ectoderm only about 20 % of cross-sectioned nerve tracks are single neurites; the rest are bundles (measured [1]). In the endoderm about half are single and half are bundles of two, and no endodermal bundle holds more than two neurites (measured [1]).

The bundle counts rest on 130 ectodermal and 47 endodermal tracks. These came from four electron-microscope sections spanning 40 μm , pos. 6.17 (measured [1]). A serial block-face block of 2,000 planes at 30 nm steps, pos. –0.38, gave the contact geometry (measured [1]).

In that block two reconstructed cell bodies lay about 50 μm apart, pos. 6.37 (measured [1]). At one contact the terminal neurite fingers overlapped over about 8 μm , pos. 4.70 (measured [1]). A second contact spanned about 4 μm , pos. 4.07 (measured [1]).

The block had a lateral resolution of $20 \times 20 \text{ nm}^2$, pos. –0.75 per side (measured [1]). Its volume was $40 \times 13 \times 56 \mu\text{m}^3$, sides at pos. 6.17, 5.15 and 6.47 (measured [1]). The nerve-cell antibody PNab stained 684 of 684 NeonGreen-expressing nerve cells, 149 of 149 Hym176B cells and 51 of 51 nGreen cells (measured [1]).

The *Hydra* nerve net has one local condensation. In *Hydra oligactis* a nerve ring around the hypostome holds 20–30 nerve cells (measured [1]). This hypostome nerve ring has at least four neuron subsets [2].

The cells fall into molecular classes. One account gives three sensory and five ganglion nerve-cell populations [1]. One ganglion population lies in the endoderm and two in the ectoderm; the ectodermal population ec3 expresses innexins 6 and 14 [1].

A single-cell atlas sequenced 24,985 *Hydra* cells by Drop-seq (measured [3]). It found 12 molecularly distinct neuronal subtypes, from 15 clusters of which 3 were neuronal progenitors (measured [3]). In the same atlas 46 % of all *Hydra* cells are nematoblasts or nematocytes (measured [3]).

The *Hydra* nerve net is not the only form. In the ctenophore *Mnemiopsis leidyi* the subepithelial nerve-net neurons share one continuous plasma membrane [4]. They form a syncytium, shown by volume electron microscopy with three-dimensional reconstruction [4].

Within this syncytial nerve net there are no electrical or chemical synapses between net cells [4]. Chemical synapses do run from the nerve net to polster cells [4]. Mesogleal neurons in the same animal showed no synapses [4].

Sea anemones carry nerve nets together with other conducting tissues. *Calliactis parasitica* has two slow conduction systems, SS1 and SS2, beside its nerve net [5]. Octocorals such as *Pennatula phosphorea* have a through-conducting nerve net and a slow system [6].

Medusae add conducting structures of larger size. The hydromedusa *Aglantha digitale* has a ring giant axon, motor giant axons and thin tentacle axons [7]. Box jellyfish and scyphozoans carry rhopalia, sense organs at the bell margin, with swim pacemakers [8].

Planarians are bilaterian flatworms with a brain. In flatworms “differentiated somatic cells do not divide”, and “the only somatic cells capable of mitosis are neoblasts” [9].

First appearance

No fossil nerve net is recorded in any source used here. The nerve net is dated only through the animals that carry it. The dates below are for those animals and for the rock record around them.

The cnidarian node is placed at 741 Ma by a mitochondrial clock, with a 95 % credible region of 686–819 Ma (modelled [10]). Positions are 67.46, with the region at 67.39–67.55. The same study places the diversification of major cnidarian taxa before the Cambrian, given as 543 Ma in its abstract, pos. 67.18 (modelled [10]).

Crown animals originated in the Cryogenian by molecular clock (modelled [11]).

Most crown-bilaterian phyla diversified in the Ediacaran (modelled [11]). Bilaterian phyla diverged more than 100 million years before the Cambrian (modelled [11]). With the Cambrian base at 538.8 Ma [12], that places them before 638.8 Ma, pos. 67.33 (computed).

The oldest architecturally complex Ediacaran macrofossils date to 574.17 ± 0.66 Ma at Mistaken Point, Newfoundland, pos. 67.23 (measured [13]). This is 166.83 Myr after the clock age of the cnidarian node (computed: $741 - 574.17$). That interval has pos. 66.10 (computed).

Haootia quadriformis, from Newfoundland at about 560 Ma, pos. 67.21, is an impression of twisted fibrous bundles in a square pattern [14]. It has four bifurcating corner branches. The authors compare it with the muscles of living Staurozoa and propose it as the earliest body-fossil evidence of animal musculature [14].

The base of the Cambrian is 538.8 ± 0.2 Ma, pos. 67.17 (measured [12]). The interval from *Haootia* to the Cambrian base is 21.2 Myr, pos. 64.23 (computed: $560 - 538.8$).

The oldest free-swimming medusa is *Burgessomedusa phasmiformis*, from the middle Cambrian Burgess Shale [15]. The paper describes 182 specimens (measured [15]). Its cuboidal umbrella reached 20 cm in height, pos. 13.92, with more than 90 short finger-like tentacles (measured [15]).

Muscle appears in the record before any nerve does. The first proposed cnidarian muscle, *Haootia*, is 14.17 Myr younger than the first complex macrofossils, pos. 63.86 (computed: $574.17 - 560$). Nerve tissue itself is not seen in any of these fossils.

Partners

A *Hydra* nerve net depends on a stem-cell pool. Interstitial stem cells cycle every 24 h, pos. 43.50 (measured [16]). A later account gives “about 24–30 hours” in asexually growing tissue, pos. 43.50–43.70 (measured [17]).

The stem pool holds 3,000–6,000 cells per *Hydra* (measured [16]). By an in vivo estimate about 4 % of all cells in a whole *Hydra* are stem cells (measured [18]). Per generation about 60 % of stem-cell daughters stay stem cells and about 40 % differentiate (measured [16]).

The stem cells give rise to nerve cells and to nematocytes. About 900 nerve cells differentiate per day per *Hydra*, and about 1,760 nematocyte nests (measured [16]). The nematocyte to nerve ratio is 3 : 1 over the whole animal and about 7 : 1 in the gastric region (measured [16]).

Nerve differentiation consumes about 10 % of stem cells (measured [17]). The stem-cell population doubles at the rate of the epithelial tissue, in about 3–4 days, pos. 44.50–44.76 (measured [17]). Hydroxyurea lowers interstitial cells to 1–2 % of normal (measured [17]).

Commitment to nerve fate occurs in S phase of a precursor [17]. In the source’s words, “Committed cells completed the cell cycle, divided, and daughter cells differentiated to nerve cells” [17]. Nerve-cell density is higher in head, tentacles and basal disk [17].

Cloning confirms a shared origin of nerve cells and nematocytes. About 1.2 % of input cells formed clones, scored after 1–2 weeks, pos. 45.27–45.90 (measured [18]). Nine clones contained both nerve cells and nematocytes (measured [18]).

In the peduncle of *Hydra oligactis* about 50 % of interstitial cells grow rapidly (measured [19]). Moved to a gastric environment, these give rise to nematocyte precursors [19]. The rest sit in G1 and behave as committed, non-cycling nerve precursors [19].

Epithelial cells are the second partner. Every epithelial cell is continuously displaced, carrying neurons toward the head or the foot [2]. The ectoderm in and around the hypostome nerve ring is a stationary zone, and nerve differentiation there is much slower than around it [2].

Muscle is the third partner. In *Aglantha* the motor giant axons drive a myoepithelium, with a synaptic delay of about 1.6 ms, pos. 27.29 (measured [7]). The myoepithelial impulse travels at 0.22–0.29 m s⁻¹ (measured [7]).

Sense organs are the fourth partner in medusae. A cubozoan rhopalium carries two lensed eyes, two pit ocelli and two slit ocelli [8]. A nerve ring connects the four rhopalia and four tentacle bases [8].

In *Tripedalia cystophora* that nerve ring has two or three immunoreactive tracts of small fibres (measured [8]). Each rhopalium holds six eyes of four types, 24 eyes per medusa (measured [20]). The rhopalial central nervous system holds “several thousand nerve cells” [20].

In the ctenophore the partners are sensory and effector cells. A 1-day-old cydippid held

22 putative sensory cells of five morphological types beside its nerve net (measured [4]). The nerve net synapses onto polster cells [4].

The *Mnemiopsis* statocyst carries four clusters of ciliated balancer cells bearing the statolith [21]. Some neurons synapse onto balancer cells, with reciprocal connections to bridge cells [21].

A sponge has no nerves and no muscles. *Spongilla lacustris* has 18 cell types by whole-body single-cell RNA sequencing (measured [22]). It is an animal without a nerve net.

In planarians all division sits in the neoblasts. “BrdU was incorporated only into neoblasts and appeared in differentiated cells later” [9]. Planarian neoblasts incorporate BrdU in S phase, and continuous labelling shows no large slow-cycling neoblast population in intact animals [23].

Sizes

what	size	position	source
SBF-SEM lateral resolution, <i>Hydra</i>	20 nm	−0.75	measured [1]
SBF-SEM step, <i>Hydra</i>	30 nm	−0.38	measured [1]
Second neurite contact, <i>Hydra</i>	~4 µm	4.07	measured [1]
Tentacle axon, <i>Aglantha</i>	3.6–7.8 µm	3.98–4.68	measured [7]
Motor giant axon, one <i>Aglantha</i>	7.5–32 µm	4.64–5.97	measured [7]
Ring giant axon, one 10 mm <i>Aglantha</i>	5–24 µm	4.28–5.70	measured [7]
Neurite finger overlap at a contact, <i>Hydra</i>	~8 µm	4.70	measured [1]
Ectodermal nerve cell body, <i>Hydra</i>	~10 µm	4.91	measured [1]
SBF-SEM block, short side	13 µm	5.15	measured [1]
Ring giant axon, <i>Aglantha</i>	22–35 µm	5.62–6.05	measured [7]
Motor giant axon, <i>Aglantha</i>	up to 40 µm	6.17	measured [7]
TEM sections span, <i>Hydra</i>	40 µm	6.17	measured [1]
Distance between two reconstructed cell bodies	~50 µm	6.37	measured [1]
Spacing of ectodermal cell bodies, <i>Hydra</i>	50–100 µm	6.37–7.00	measured [1]
SBF-SEM block, long side	56 µm	6.47	measured [1]
Small <i>Hydra</i> in imaging work	~0.3 mm	8.00	measured [24]

Small <i>Nematostella</i> (20–40 longitudinal neurons)	2.5–5 mm	9.93–10.56	measured [25]
<i>Tripedalia</i> bell	7–9 mm	10.87–11.10	measured [20]
<i>Aglantha</i> specimen	10 mm	11.19	measured [7]
Large <i>Hydra</i> in imaging work	~1 cm	11.19	measured [24]
<i>Aurelia</i> in nerve-net model	~4 cm diameter	12.46	modelled [26]
Smallest <i>Aurelia</i> , fastest beats	~5.08 cm (~2 inch)	12.67	computed from [27]
Larger <i>Aurelia</i>	~7.62 cm (~3 inch)	13.04	computed from [27]
<i>Burgessomedusa</i> umbrella height	up to 20 cm	13.92	measured [15]

The sizes span from 20 nm in imaging to 20 cm in a fossil umbrella. Axons in one *Aglantha* run from 3.6 μm to 40 μm . Within that animal conduction speed rises with axon diameter (see Present quantities).

The *Aurelia* sizes are given in the source as about 2 and 3 inches [27]. They are converted at 2.54 cm per inch to 5.08 and 7.62 cm (computed). The model size of about 4 cm belongs to a model estimate of neuron number [26].

Times

what	duration	position	source
Chronaxie, <i>Virgularia</i> nerve net	0.6–1 ms	26.40–26.87	measured [6]
Chronaxie, <i>Pennatula</i> nerve net	~0.8 ms	26.66	measured [6]
Motor giant spike at half amplitude, <i>Aglantha</i>	1.2–1.4 ms	27.03–27.17	measured [7]
Ring giant spike, <i>Aglantha</i>	~1.6 ms	27.29	measured [7]
Synaptic delay motor giant $\rightarrow$ myoepithelium	~1.6 ms	27.29	measured [7]
Synaptic delay ring giant $\rightarrow$ motor giant	1.6–1.8 ms	27.29–27.40	measured [7]
Escape-burst impulse, <i>Aglantha</i>	2–3 ms	27.50–27.87	measured [7]
Minimum repeat interval, ring giant	3.5 ms	28.01	measured [7]
Myoepithelial impulse, <i>Aglantha</i>	15–70 ms	29.33–30.73	measured [7]
Time to peak of escape contraction	40.5 ms (shortest)	30.23	measured [7]
Absolute refractory period, <i>Pennatula</i> nerve net	40–50 ms	30.22–30.43	measured [6]
Half relaxation of	94 ms	31.00	measured [7]

escape contraction			
Escape contraction complete	~100 ms	31.06	measured [7]
Facilitation peak, paired interval, <i>Pennatula</i>	~250 ms	31.89	measured [6]
Shortest beat interval, small <i>Aurelia</i>	~0.25 s	31.89	measured [27]
SS1 absolute refractory period, <i>Calliactis</i>	~300 ms	32.06	measured [5]
Shortest common beat interval, <i>Dactylometra</i>	0.4 s	32.32	measured [27]
Pacemaker period at 2.4 Hz, <i>Tripedalia</i>	0.42 s	32.36	computed from [20]
Second facilitation peak, <i>Pennatula</i>	~600 ms	32.69	measured [6]
Pacemaker period at 1.6 Hz	0.625 s	32.73	computed from [20]
Absolute refractory period, <i>Aurelia</i>	0.7 s	32.83	Bullock 1943 (cited in [27])
Beat interval, larger <i>Aurelia</i>	0.75 s	32.89	measured [27]
Pacemaker period at ~1 Hz, dark	~1 s	33.15	computed from [20]
SS1 relative refractory period	~1,400 ms	33.46	measured [5]
Pacemaker period at 0.5 Hz	2 s	33.78	computed from [20]
SS1 fails above one shock per	3 s	34.15	measured [5]
Pacemaker period, regenerating rhopalium, day 8 (0.2 Hz)	5 s	34.62	computed from [28]
Pacemaker counting window, <i>Tripedalia</i>	10 s	35.25	measured [20]
Pacemaker period, regenerating rhopalium, day 6 (0.03 Hz)	~33 s	36.34	computed from [28]
Window for 4–5 peristaltic waves, <i>Nematostella</i>	5 min	38.34	measured [25]
Early or late block of pacemaker record	7 min	38.65	measured [20]
Peak of cell death after amputation, <i>Nematostella</i>	1.5–12 h	40.98–42.87	measured [25]
Median G2, planarian neoblasts	~6 h	42.24	measured [23]
First proliferation after amputation, <i>Nematostella</i>	12 h	42.87	measured [25]

Labelling to nematoblast, <i>Hydra</i>	12 h	42.87	measured [16]
Labelling to visible nerve cell, <i>Hydra</i>	~18 h	43.24	measured [16]
Interstitial stem-cell cycle, <i>Hydra</i>	24 h; 24–30 h	43.50; 43.50–43.70	measured [16]; [17]
Age of reconstructed ctenophore cydippid	1 day	43.50	measured [4]
Neurite extension in grafts, <i>Hydra</i>	by days 2 and 3	44.13–44.50	measured [1]
Labelling to nematocyte, <i>Hydra</i>	72–96 h	44.50–44.76	measured [16]
Doubling of stem-cell population	3–4 days	44.50–44.76	measured [17]
Tentacle tissue renewal, <i>Hydra</i>	4–5 days	44.76–44.96	measured [1]
Variation of resting length, <i>Nematostella</i>	over 5 days	44.96	measured [25]
Nematocyte differentiation, <i>Hydra</i>	5–7 days	44.96–45.27	measured [16]
Oral regeneration, <i>Nematostella</i> (82 of 83)	7 days	45.27	measured [25]
Doubling of FMRFamide giant neurons, 7 → 14	~1 week	45.27	measured [28]
Clone scoring, <i>Hydra</i>	1–2 weeks	45.27–45.90	measured [18]
Regrowth of most rhopalial neural elements	within 2 weeks	45.90	measured [28]
Whole-tissue renewal including nerve net, <i>Hydra</i>	2–3 weeks	45.90–46.27	measured [1]
Growth of fed-then-starved <i>Nematostella</i> by 75.9 %	3 weeks	46.27	measured [25]
Shrinkage of starved-then-fed <i>Nematostella</i> by 26.1 %	7 weeks	47.04	measured [25]
Shrinkage of fed-then-starved <i>Nematostella</i> by 38.6 %	11 weeks	47.45	measured [25]

Durations of electrical events in cnidarians run from 0.6 ms (chronaxie, *Virgularia* sea pen) to about 1.4 s (relative refractory period, *Calliactis* anemone). Pacemaker periods of medusae reach about 33 s (regenerating *Tripedalia* rhopalium).

Durations of cell supply and tissue renewal run from about 6 h to 11 weeks. The two groups do not overlap in the table.

Frequencies were converted to periods as $1/f$. For example $1/1.6 \text{ Hz} = 0.625 \text{ s}$ and $1/0.03 \text{ Hz} = 33.3 \text{ s}$ (computed).

Counts

Cells in a *Hydra* nerve net. The ratio of nerve cells to epithelial cells is 0.12 by two methods (measured [1]). By region it is 0.10–0.19 in body-column endoderm and 0.15–0.22 in the ectoderm of gastric region and peduncle (measured [1]).

Samples held 80–400 nerve cells per body-column or peduncle sample and 20–30 per hypostome sample (measured [1]). Tissue bands representing about 4 % of the body column held 133 nerve cells, 57 ectodermal and 76 endodermal (measured [1]). Scaled up, $133 / 0.04 = 3,325$ nerve cells per body column at that sampling (computed; not a value the paper gives).

Classes. One study gives 3 sensory and 5 ganglion populations, 8 in all [1]. A single-cell atlas gives 12 neuronal subtypes [3]. The hypostome nerve ring has at least four neuron subsets [2].

Supply. About 900 nerve cells are made per day per *Hydra* (measured [16]). The stem pool holds 3,000–6,000 cells (measured [16]). About 1,760 nematocyte nests are made per day, 1.96 times the nerve-cell output (computed: $1,760 / 900$).

Nematostella. In 146 adults the counts of longitudinal neurons ($r = 0.854$, $p < 0.001$) and tripolar neurons ($r = 0.791$, $p < 0.001$) rise with body length (measured [25]). Neuron numbers in both nerve nets fall as animals shrink [25]. Small animals have 20–40 longitudinal neurons (measured [25]).

The *Nematostella* paper reports subtype counts, not a total neuron count [25]. Tentacular neuron number is “not stereotyped” between tentacles or animals [25]. Regenerates are smaller than before cutting and show 4–5 peristaltic waves per 5 min (measured [25]).

Rhopalia and eyes. Swim pacemakers of cubomedusae are restricted to four rhopalia [8]. “Most scyphozoans have eight or more rhopalia, typically with species-specific numbers that are multiples of four” [8]. A box jellyfish has $6 \times 4 = 24$ eyes (computed; also stated in [20]).

Whole *Aurelia aurita* and *Dactylometra quinquecirrha* had eight marginal ganglia (measured [27]). Some *Aurelia* had only five or three marginal bodies (measured [27]).

Regenerating rhopalium. In *Tripedalia* the FMRFamide-positive giant neurons rose from 7 to 14 in about one week (measured [28]). RFamide-positive neurons rose from 8 on day 8 to 16 on day 14 (measured [28]). Both counts double (computed: $14 / 7 = 2$; $16 / 8 = 2$).

Aurelia model. A model estimate gives “of the order of 10000 neurons” in the motor nerve net of a jellyfish about 4 cm in diameter (modelled [26]).

Ctenophore. The main block of a 1-day-old *Mnemiopsis* cydippid held 5 nerve-net neurons, 6 mesogleal neurons and 22 putative sensory cells (measured [4]). Two further cydippids served for confirmation [4]. The statocyst connectome reconstructed 1,011 cells by volume electron microscopy (measured [21]).

Fossils. *Burgessomedusa* is described from 182 specimens with more than 90 tentacles each (measured [15]). *Haootia* shows four bifurcating corner branches [14].

Sponge. *Spongilla* has 18 cell types and no nerve cells (measured [22]).

Order of events

1. 741 Ma (686–819 Ma), pos. 67.46 (67.39–67.55): origin of Cnidaria by mitochondrial clock (modelled [10]).
2. Cryogenian (no bounds given in the sources here): crown animals by clock (modelled [11]).
3. Before 638.8 Ma, pos. 67.33: bilaterian phyla diverge, more than 100 Myr before the Cambrian (modelled [11]; computed).
4. 574.17 ± 0.66 Ma, pos. 67.23: oldest architecturally complex Ediacaran macrofossils (measured [13]).
5. About 560 Ma, pos. 67.21: *Haootia*, the earliest proposed muscle impression, cnidarian [14].
6. Before 543 Ma, pos. 67.18: major cnidarian taxa diversified (modelled [10]).
7. 538.8 ± 0.2 Ma, pos. 67.17: base of the Cambrian (measured [12]).
8. Middle Cambrian: *Burgessomedusa*, the oldest free-swimming medusa [15]. The source age is not used here (see Not verified).

543 Ma is given in the abstract [10]. The chart gives 538.8 Ma [12]. Both are recorded.

Steps between dated events are 166.83 Myr (741 to 574.17 Ma), 14.17 Myr (574.17 to 560 Ma) and 21.2 Myr (560 to 538.8 Ma) (computed). Their positions are 66.10, 63.86 and 64.23 (computed).

Present quantities

Conduction speeds. In *Calliactis* at 11–14 °C, SS1 runs at 4.4–14.6 cm s⁻¹ (measured [5]). Its oral-disc mean is 12.3 cm s⁻¹ and its column mean 5.2 cm s⁻¹ (measured [5]). SS2 runs at 3.0–5.3 cm s⁻¹ (measured [5]).

The *Pennatula* nerve net conducts at a mean 7.5 cm s⁻¹ at 10 °C and its slow system at about 6 cm s⁻¹ (measured [6]). The *Virgularia* nerve net conducts at 40–60 cm s⁻¹ at about 16 °C (measured [6]). In *Virgularia* velocity rises with repetitive stimulation [6].

In *Aglantha* at 15 ± 1 °C the ring giant axon conducts at 1–2.6 m s⁻¹ (measured [7]). Motor giant axons conduct at 1–4 m s⁻¹ and tentacle axons at 0.4–0.8 m s⁻¹ (measured [7]). The myoepithelial impulse travels at 0.22–0.29 m s⁻¹ (measured [7]).

Across these tissues the speeds span from 3.0 cm s⁻¹ to 4 m s⁻¹. That is a factor of 133 (computed: 400 / 3.0). The two octocoral nerve nets differ by a factor of up to 8, at different temperatures (computed: 60 / 7.5).

Spikes. The ring giant spike of *Aglantha* reaches up to 68 mV (measured [7]). An escape burst holds 2–6 impulses (measured [7]). The *Hydra* imaging paper gives no conduction velocity and states that action potentials “likely propagate through gap junctions” [24].

Refractory periods. The *Pennatula* nerve net has an absolute refractory period of 40–50 ms, pos. 30.22–30.43 (measured [6]). SS1 in *Calliactis* has about 300 ms absolute and about 1,400 ms relative, pos. 32.06 and 33.46 (measured [5]). The ratio of relative

to absolute in SS1 is 4.67 (computed: $1,400 / 300$).

Swim pacemakers. In *Tripedalia* at 28 ± 0.5 °C the pacemaker frequency in darkness is “close to 1Hz” (measured [20]). Over 10 s windows it ranges 0.5–1.6 Hz (measured [20]). The first 7 min average about 1.25 Hz and the last 7 min about 0.9 Hz, a difference that is not significant (measured [20]).

Light steps shift the rate. Light-off after lower-lens-eye stimulation overshoots to 2.4 Hz in the first 10 s (measured [20]). Light-on via the upper lens eye gives more than 1.8 Hz, then about 1.5 Hz (measured [20]).

Pit-eye stimulation gives 1.7–1.9 Hz at light-on and 0.3–0.6 Hz at light-off (measured [20]). Slit-eye stimulation gives at most 1.7 Hz, about 1.3 Hz in light (measured [20]). The full range under light steps is 0.3–2.4 Hz, a factor of 8 (computed: $2.4 / 0.3$).

In a regenerating *Tripedalia* rhopalium the pacemaker runs at about 0.03 Hz on day 6 and about 0.2 Hz on day 8 (measured [28]). The rate rises by a factor of 6.7 in two days (computed: $0.2 / 0.03$). Days 6 and 8 have pos. 45.13 and 45.39.

Beat intervals. In *Aurelia* at 16–18 °C beat intervals are as short as about 0.25 s in the smallest animals and 0.75 s in larger ones (measured [27]). The ratio is 3 (computed: $0.75 / 0.25$). *Dactylometra* at 12–13 °C has intervals commonly as short as 0.4 s (measured [27]).

Nematostella growth. Fed-then-starved animals grew 75.9 ± 20.8 % in 3 weeks, then shrank 38.6 ± 9.1 % in 11 weeks (measured [25]). Starved-then-fed animals shrank 26.1 ± 7.4 % in 7 weeks, then grew 164 ± 34.9 % (measured [25]). Resting length varies 14 ± 3 % over 5 days (measured [25]).

Hydra renewal. “All *Hydra* tissues, including the nerve net, are newly formed every 2–3 weeks in well-fed animals” [1]. Tentacle tissue is renewed in 4–5 days by displacement of epithelial tissue [1]. In grafts most differentiating nerve cells had extended neurites along the existing nerve net by days 2 and 3 [1].

The authors propose growth by addition of new nerve cells alongside existing ones [1]. None of the sources used here states that a differentiated *Hydra* nerve cell divides. The divisions recorded are of stem cells and committed precursors [17].

Planarian cycle. Planarian neoblasts have a median G2 of about 6 h, pos. 42.24 (measured [23]). Freshwater planarians show at least two cell-cycle periods; the source gives no durations [9].

Pattern

A *Hydra* holds 0.12 nerve cells per epithelial cell in two nerve nets that do not mix. Cell bodies are about 10 μm long and 50–100 μm apart.

A stem pool of 3,000–6,000 cells, cycling every 24–30 h, supplies about 900 nerve cells per day. The whole nerve net is renewed in 2–3 weeks; division is recorded only upstream of the nerve cell.

Conduction speeds in cnidarian tissues span a factor of 133, from 3.0 cm s^{-1} to 4 m s^{-1} . Within one medusa speed rises with axon diameter.

Rhopalia occur as 4, or 8 and more in multiples of 4. Swim pacemakers run near 1 Hz, between 0.3 and 2.4 Hz under light steps.

The ctenophore nerve net is a syncytium without internal synapses. Dated animals carrying nerve nets begin with a clock age of 741 Ma; muscle enters the fossil record at about 560 Ma.

Not verified

- *Hydra* total of 500–2,000 nerve cells (Keramidioti et al. 2023, citing Bode et al. 1973; secondary).
- Three non-overlapping activity networks CB, RP1, RP2 in *Hydra* (Dupré & Yuste 2017; secondary via citing papers).
- A fourth coactive group (STN) and “hundreds of neurons” imaged (Ji & Flavell 2017 dispatch; secondary).
- Whole-animal cell replacement “approximately every 20 days” (Siebert et al. 2018 bioRxiv, citing an earlier study; secondary).
- An explicit statement that differentiated *Hydra* nerve cells are post-mitotic (not found; UNVERIFIED).
- Fourteen distinct conducting systems in *Aglantha digitale* (Satterlie 2011, citing Mackie 2004; secondary).
- *Aurelia* motor nerve net conduction 45 cm s⁻¹ to 1 m s⁻¹, diffuse nerve net about 15 cm s⁻¹ (Pallasdies et al. 2019, citing Horridge 1956 and Passano 1965; secondary).
- *Aurelia* synapse spacing about 70 µm, refractory periods about 30 ms and 70 ms, cross-body delay about 30 ms (Pallasdies et al. 2019, citing others; secondary).
- *Burgessomedusa* age of 505 Ma and “about 200 specimens” (Royal Ontario Museum release 2023; secondary; the paper gives 182).
- *Cassiopea* sleep-like state with quiescence, reduced responsiveness and homeostatic regulation (Nath et al. 2017; V-bib, no numbers read).
- *Cassiopea* about 39 pulses per minute at night against about 58 by day; arousal delay up to 5 s; deprivation every 10 s for 20 min (ScienceDaily 2017; secondary).
- *Cassiopea* 23 animals over six days, pulsing 32 % lower at night, lower activity after up to 12 h of disturbance (Science News 2017; secondary).
- Planarian brain of 1,000–10,000 cells, “several thousand neurons” (Brown & Pearson 2017, citing Cebrià 2007; secondary).
- Planarian brain turnover about 25 % per week against about 1–2 % per year in humans (Brown & Pearson 2017, citing others; secondary).
- Neoblasts about 20 % of planarian cells; brain regenerated in about 7 days; brain rescaling about 10-fold in length and 100-fold in area (Brown & Pearson 2017, citing others; secondary).
- Mean planarian neuron residence of about 4 weeks (computed from secondary values; not used).
- Primary *Hydra* CB and RP frequencies and conduction speed (Dupré & Yuste 2017 abstract absent).
- Total neuron count of *Nematostella* (not given in the source).

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A4 Centralisation

What it is

Centralisation is the gathering of nerve cells into cords, commissures and brains. In Bilateria nerve cords run along the body and a brain sits at the front. The sources here differ on how often this arrangement arose.

One account starts from a nerve net with two centres at opposite ends [1]. An “apical nervous system” served body physiology, and a “blastoporal nervous system” served feeding and locomotion [1]. Their expansion, integration and fusion gave the bilaterian nerve cord and brain, by this account [1].

A second account rests on gene expression in nerve cords across five clades [2]. The clades sampled are Xenacoelomorpha, Rotifera, Nemertea, Brachiopoda and Annelida [2]. No species studied shows a conserved dorsoventral molecular regionalisation of its nerve cords [2].

This holds also for the annelid *Owenia fusiformis* [2]. Its medially condensed trunk cord

resembles those of vertebrates and flies [2]. The authors conclude that ventral nerve cords likely evolved convergently, “many times” [2].

Nerve cords also differ in position. Nemertodermatids have dorsal cords and nemerteans ventral cords [2]. The xenacoelomorph *Nemertoderma westbladi* has an anterior ring-like commissure and a pair of ventral condensations [2].

The position of Xenacoelomorpha in the animal tree bears on the first centralised animal. One study places them as sister to Nephrozoa, the remaining Bilateria [3]. By that placement the last common bilaterian ancestor “was probably a benthic, ciliated acoelomate worm” with one gut opening [3].

In that same study nerve cords, excretory organs and coeloms arose after the xenacoelomorphs split off [3]. The data were 11 new xenacoelomorph transcriptomes and 25 experimental data sets (measured [3]). Matrices ran from 212 genes to 336 genes $\times$ 56 taxa and 881 genes $\times$ 77 taxa (measured [3]).

The 336-gene matrix held 81,451 amino acids and was 89 % complete (measured [3]). The 881-gene matrix held 337,954 amino acids and was 62 % complete (measured [3]). A larger matrix was thus less complete in this study.

A second study applies corrections for systematic error and places Xenacoelomorpha as sister to Ambulacraria [4]. “We conclude that the Xenacoelomorpha are simplified relatives of the Ambulacraria” [4]. The two placements disagree; both are recorded.

An acoel shows a brain at small size. A juvenile *Symsagittifera roscoffensis* averages 200 μm long and 100 μm wide, pos. 7.63 and 7.00 (measured [5]). Its brain cortex of “approximately 700 cells” fills the anterior third of the body [5].

The acoel neuropil is linked by three commissures; the whole-body model has seven, c1–c7 (measured [5]). Three pairs of nerve cords run along the body (measured [5]). Anterior cords carry about 50–100 neurites and posterior cords about 15–30 (measured [5]).

The acoel statocyst has three cells, two parietal cells and a lithocyte (measured [5]). There are eight ocellar cells, three sensory and one pigment cell per ocellus (measured [5]). The counts are approximate because of gaps between sections [5].

A second paper on the same species calls the brain “a centralized anterior brain made up of about 700 neurons” [6]. The first paper says about 700 “cells” [5]. Both wordings are recorded.

In arthropods and vertebrates the brain has divisions. Fossil arthropods show brains of one, two or three parts (see First appearance). Two studies propose that specific centres are shared between arthropods and vertebrates.

The arthropod central complex and the vertebrate basal ganglia both derive from embryonic forebrain lineages specified by a conserved genetic programme [7]. Both lie at the midline of the forebrain-midbrain boundary [7]. Both use GABAergic inhibitory and dopaminergic modulatory circuits for action selection, and the authors propose “deep homology” [7].

Against a single origin, tripartite brains of euarthropods and chordates “are the result

of convergent adaptations” by one reading [8]. Ventral nerve cords are convergent “many times” by another [2]. These positions stand against the homology claim; both are recorded.

The vertebrate brain is divided into regions early. The inshore hagfish *Eptatretus burgeri* develops domains equivalent to the medial ganglionic eminence (MGE) and the rhombic lip [9]. Lamprey larvae also have them [9].

Lamprey *Nkx2.1/2.4B* and *Nkx2.1/2.4C* are expressed in the rostral telencephalon, with no *Hedgehog* there [9]. Hagfish *Hedgehog* genes are expressed in hypothalamus, zona limitans intrathalamica and MGE [9]. The authors state that “brain regionalization as seen in crown gnathostomes is not an evolutionary innovation of this group” [9].

The lamprey pallium has a separate visual area with retinotopic representation [10]. An adjacent lateral-pallial area serves head and trunk somatosensation [10]. Both flank a non-primary motor area, and vision and somatosensation are relayed via the thalamus [10].

First appearance

Crown animals originated in the Cryogenian by molecular clock (modelled [11]). Most crown-bilaterian phyla diversified in the Ediacaran (modelled [11]).

Bilaterian phyla diverged more than 100 million years before the Cambrian (modelled [11]). With the Cambrian base at 538.8 ± 0.2 Ma [12], this is before 638.8 Ma, pos. 67.33 (computed). The Cambrian base itself has pos. 67.17.

The Ediacara biota spans about 571–539 Ma, pos. 67.22–67.17 [13]. That is about 32 Myr, pos. 64.60 (computed: 571 – 539). Chapter A2 gives 571–541 Ma from a different source; both spans are recorded.

Ikaria wariootia, from the Ediacaran of South Australia, is presented as one of the oldest bilaterians [13].

Ikaria is presented as matching predictions for a small, simple last common bilaterian ancestor [13]. Its size and an exact age come only from a press release (see Not verified). No brain is reported for it.

Fossil brains appear in Cambrian Stage 3. The base of Stage 3 is about 521 Ma, pos. 67.14 [12].

The Chengjiang biota has a maximum depositional age of $518.03 \pm 0.69/0.71$ Ma by U–Pb on the youngest detrital zircon, pos. 67.13 (measured [14]). The Chengjiang fossils are thus no older than 518.03 Ma [14].

Kerygmachela kierkegaardi comes from Sirius Passet, Buen Formation, Cambrian Stage 3, North Greenland [8]. Its brain is “unipartite”, a small protocerebral brain innervating eyes and frontal appendages [8]. There are no ganglia in the frontal appendages [8].

Fuxianhuia protensa from Chengjiang has “a tripartite pre-stomodaeal brain” of protocerebrum, deutocerebrum and tritocerebrum [15]. It shows “traces of three nested optic centres serving forward-viewing eyes” [15]. The source gives its age as 520 million years, pos. 67.14 [15].

Alalcomenaeus sp., a great-appendage arthropod from Chengjiang, has one optic neuropil separate from a protocerebrum [16]. This is contiguous with four head ganglia, followed by eight more contiguous ganglia in an eleven-segment trunk [16]. The source states that this nervous system evolved “by 520 million years ago” [16].

The 520 Ma of [15] and [16] and the maximum age of ≤ 518.03 Ma for Chengjiang [14] disagree. Both are recorded.

Lyrarapax unguispinus, a radiodont from Chengjiang, has paired pre-protocerebral ganglia at the origin of its paired frontal appendages [17]. These join a dorsal, segmented, bilateral pre-oral brain that receives the eyestalk neuropils [17]. The source page gives no age [17].

The fossil brain readings are disputed. In “numerous articulated individuals” of *Fuxianhuia protensa* from Chengjiang, structures read as brain may instead be microbial biofilms [18]. These would have formed as gut, muscle and connective tissue decayed [18].

The same critique covers structures read as nerve cords or vessels along the body [18]. The descriptions of brains [15, 16, 17] and the biofilm reading [18] disagree. Both are recorded.

The first vertebrates also come from Chengjiang. *Mylokunmingia fengjiao* is lamprey-like and *Haikouichthys ercaicunensis* closer to hagfish [19]. Both are from the Lower Cambrian Chengjiang Lagerstätte at Haikou, Yunnan [19].

The abstract gives the Cambrian as 545–490 Ma, pos. 67.18–67.08 [19]. It suggests chordates may have arisen in the Ediacaran, at about 555 Ma, pos. 67.20 [19]. Its base of 545 Ma lies 6.2 Myr before the current base of 538.8 Ma (computed); both are recorded.

Cyclostomes and gnathostomes diverged more than 500 million years ago, by one source, pos. 67.10 [9]. A second source places the last common ancestor of cyclostomes and gnathostomes at around 560 million years ago, pos. 67.21 [10]. By that source the sensorimotor plan and thalamocortical relay “had already evolved” in that ancestor [10].

The ~560 Ma date is 41.97 Myr older than the Chengjiang maximum age, pos. 64.85 (computed: 560 – 518.03). The >500 Ma date is a lower bound that lies 18.03 Myr below the Chengjiang age (computed: 518.03 – 500). That bound does not by itself place the split before the fossils.

At the printed 520 Ma, fossil brains follow the Cambrian base by 18.8 Myr, pos. 64.12 (computed: 538.8 – 520). At the Chengjiang maximum age of 518.03 Ma, they follow it by at least 20.77 Myr, pos. 64.21 (computed: 538.8 – 518.03).

Partners

A brain depends on the cells around it. In the 72-hour *Platynereis dumerilii* larva, 2,905 non-neuronal cells fall into 90 types beside 892 classified neurons (measured [20]). The larva also holds 5,230 unclassified cells, including 1,692 undifferentiated and 62 dividing cells (measured [20]).

The *Platynereis* larva has three chaetigerous trunk segments, a cryptic anterior segment and a pygidium [20]. Its grouped graph has 45 sensory, 61 interneuron and 35 motoneuron types (measured [20]). Sensory, inter- and motor types total 141 (computed: $45 + 61 + 35$).

In *Ciona intestinalis* the tadpole larva holds a peripheral nervous system of 28 neurons (measured [21]). These sit 8 on the left, 6 in the centre and 14 on the right (measured [21]). Of the larval synapses 1,772 are neuromuscular junctions (measured [21]).

In *C. elegans* about 2,000 neuromuscular junctions join neurons to muscle (measured [22]). The worm also has about 600 gap junctions (measured [22]).

In the adult fly brain, 5,512 sensory neurons project into the central brain (measured [23]). There are 1,303 descending and 2,362 ascending neurons, which link brain and nerve cord (measured [23]). The ascending neurons outnumber the descending by a factor of 1.81 (computed: $2,362 / 1,303$).

In the male fly nerve cord, intrinsic neurons other than motor neurons number 21,683 (measured [24]). Descending plus motor neurons number 2,065 (measured [24]). Intrinsic neurons are 91 % of the 23,748 in these two groups (computed: $21,683 / 23,748$).

The acoel brain partners with sense cells. Collared receptors with granular bodies make up 50 % of sensory cells and those with rootlets 16 % (measured [5]). About nine granular-body receptors lie along each cord (measured [5]).

The lamprey forebrain partners with the thalamus, which relays vision and somatosensation to the pallium [10]. The arthropod central complex and the vertebrate basal ganglia both use dopaminergic modulatory circuits [7].

Sizes

what	size	position	source
TEM pixel size, <i>Platynereis</i> (finest)	2.2 nm	−2.76	measured [20]
TEM pixel size, <i>Platynereis</i>	3.7 nm	−2.29	measured [20]
TEM pixel size, <i>Platynereis</i> (coarsest)	5.7 nm	−1.89	measured [20]
Voxel side, fly hemibrain	8 nm	−1.58	measured [25]
TEM section thickness, <i>Platynereis</i>	40 nm	−0.12	measured [20]
Slab thickness, male fly nerve cord	~25 µm	5.74	measured [24]
Width, juvenile acoel	100 µm	7.00	measured [5]
Length, juvenile acoel	200 µm	7.63	measured [5]
Height of recorded volume, larval zebrafish	200 µm	7.63	measured [26]
Side of hemibrain sample	~250 µm	7.84	measured [25]

Diameter of nerve-cord sample	up to 250 μm	7.84	measured [24]
Edge of cube with fly neuropil volume 0.0175 mm^3	0.26 mm	7.87	computed from [27]
Length of nerve-cord sample	>500 μm	8.47	measured [24]
Width of recorded volume, larval zebrafish	600 μm	8.63	measured [26]
Median intrinsic neuron path length, fly brain	685 μm	8.75	measured [27]
Length of recorded volume, larval zebrafish	800 μm	8.90	measured [26]
<i>Ciona</i> tadpole larva	~1 mm	9.10	measured [21]
Mean path length per neuron, fly brain	1.07 mm	9.16	computed from [27]
Acoel phototaxis distance before decapitation	2.59 cm	12.06	measured [6]
Neuronal cable, male fly nerve cord	44 m	18.83	measured [24]
Neuronal path length, fly brain	~149 m	19.94	measured [27]

The edge of a cube with 0.0175 mm^3 volume is $(0.0175 \times 10^{-9} \text{ m}^3)^{(1/3)} = 2.60 \times 10^{-4} \text{ m}$ (computed). The mean path per neuron is $149 \text{ m} / 139,255 = 1.07 \times 10^{-3} \text{ m}$ (computed).

The larval zebrafish volume is $800 \times 600 \times 200 \mu\text{m}^3 = 0.096 \text{ mm}^3$ (computed). That is 5.5 times the adult fly neuropil volume (computed: $0.096 / 0.0175$).

Times

what	duration	position	source
Volume period at 0.8 Hz, larval zebrafish imaging	1.25 s	33.36	computed from [26]
Acoel geotaxis before decapitation	8.6 s (mean, N = 69)	35.11	measured [6]
Acoel locomotion test after decapitation	1 day	43.50	measured [6]
<i>Platynereis</i> larva at reconstruction	72 h	44.50	measured [20]
Acoel phototaxis not restored by	5 days	44.96	measured [6]
Acoel brain neuropil regenerated in ~70 %	50 days	47.06	measured [6]
Interval >500 Ma bound to Chengjiang age	18.03 Myr	64.08	computed from [9, 14]
Interval Cambrian base	18.8 Myr	64.12	computed from [12, 15]

to fossil brains at 520 Ma (as printed)			
Interval Cambrian base to Chengjiang maximum age 518.03 Ma	≥ 20.77 Myr	64.21	computed from [12, 14]
Ediacara biota, 571–539 Ma	~ 32 Myr	64.60	computed from [13]
Interval ~ 560 Ma split to Chengjiang age	41.97 Myr	64.85	computed from [10, 14]

Counts

Platynereis larva. The 72-hour larva holds 8,852 cells with a soma (measured [20]). The final connectome holds 2,728 cells (measured [20]). There are 892 neurons classified into 180 neuronal cell types, and 270 cell types in all (measured [20]).

Classified neurons are 10.1 % of cells with a soma (computed: $892 / 8,852$). There are 4.96 neurons per neuronal type (computed: $892 / 180$). Skeletons with a soma carry 27,943 presynaptic and 26,433 postsynaptic sites (measured [20]).

The connectome has 25,509 synapses in 11,437 edges, at a graph density of 0.0015 (measured [20]). That is 28.6 synapses per classified neuron (computed: $25,509 / 892$). It was traced through 4,845 serial sections (measured [20]).

The later version gives “over 9000” reconstructed cells, 202 neuronal and 92 non-neuronal cell types (measured [28]). The preprint gives 180 and 90 [20]. Both are recorded.

Ciona larva. The larva has “a mere ~ 2600 cells” (measured [21]). Its central nervous system has about 330 cells, 301 imaged, and 177 neurons with axons and presynaptic sites (measured [21]). These form at least 25 types and 52 subtypes (measured [21]).

CNS neurons are 6.8 % of all cells (computed: $177 / 2,600$). The synapse total is 6,618 in the abstract, 8,768 in the Results and 8,617 in Table 1 (measured [21]). Gap junctions are 1,206 in the abstract, 2,105 in the Results and 3,205 in Table 1 (measured [21]).

Per neuron the *Ciona* larva has 37 presynaptic sites and 7 gap junctions (measured [21]). The same paper gives 28 synapses and 3.2 gap junctions per non-pharyngeal *C. elegans* neuron (measured [21]). It gives about 8,200 synapses for a mouse somatosensory cortex neuron (measured [21]).

C. elegans. The hermaphrodite has 302 neurons in 118 classes (measured [22]). It has about 5,000 chemical synapses, 2,000 neuromuscular junctions and 600 gap junctions (measured [22]). That is 16.6 chemical synapses per neuron (computed: $5,000 / 302$).

Full brains of eight isogenic *C. elegans* individuals were reconstructed from birth to adulthood (measured [29]). “The overall geometry of the brain is preserved from birth to adulthood” [29]. With age the brain becomes “progressively more feedforward and discernibly modular” [29].

Fly larva. The whole-brain connectome of the *Drosophila* larva has 3,016 neurons and about 548,000 synapses (measured [30]). That is 182 synapses per neuron (computed:

548,000 / 3,016). Most recurrent circuits involve the mushroom body [30].

Fly hemibrain. The adult hemibrain has “around 25,000 neurons”, 15,912 traced to cell bodies and 22,594 typed and named (measured [25]). It has about 20 million chemical synapses, with 9.5 million T-bars and 64 million PSDs (measured [25]). There are 6.7 PSDs per T-bar (measured [25]; computed $64 / 9.5 = 6.74$).

The hemibrain graph has about 25,000 nodes and 3 million edges (measured [25]). It has 5,229 morphology types and 5,609 connectivity types (measured [25]). It covers about 36 % of all synaptic neuropil by volume and 54 % of central-brain neuropil (measured [25]).

The imaging produced 26 teravoxels (measured [25]). The sample was cut into 37 slabs, 13 of them imaged (measured [25]). Synapses per neuron are 800 (computed: $2 \times 10^7 / 25,000$).

Fly whole brain. FlyWire holds 139,255 proofread neurons (measured [27]). Chemical synapses are about 5×10^7 in the abstract, 54.5 million between reconstructed neurons in the text and about 130 million in the whole volume (measured [27]). There are 2,700,513 connections of at least five synapses among 134,181 identified neurons (measured [27]).

Synapses per neuron are 391 (computed: $5.45 \times 10^7 / 139,255$). Of 118,501 intrinsic neurons, 32,388 lie wholly in the central brain and 77,536 in the optic lobes and ocellar ganglia (measured [27]). The optic share of intrinsic neurons is 65.4 % and the central share 27.3 % (computed).

The annotation paper gives 77,536 (54 %) and 32,388 (23 %) for the same groups (measured [23]). Its percentages use a different base from the 118,501 intrinsic neurons. The brain has 78 neuropils (measured [27]).

The annotation lists 8,453 cell types, 3,643 proposed in the hemibrain and 4,581 new (measured [23]). Singleton types are 59 % of all types (measured [23]). Hemilineages hold 60–282 neurons, 10th to 90th percentile (measured [23]).

Kenyon cells number 2,597 on the right and 2,580 on the left in FlyWire, and 1,917 in the hemibrain (measured [23]). The source gives about 30 % more per hemisphere in FlyWire (measured [23]). The computed ratios are 1.35 and 1.35 (computed: $2,597 / 1,917$; $2,580 / 1,917$).

Of 5,235 hemibrain types, 2,920 (56 %) were found unambiguously in FlyWire (measured [23]). About 13 % were found after merging or splitting, and 1,651 (32 %) were not reidentified (measured [23]). The left-right difference in central-brain intrinsic neurons is 27 neurons, 0.1 % (measured [23]).

About one type in six differs in count between hemispheres and one in three across brains (measured [23]). The mean difference per type is 0.3 ± 1.8 within brains and 0.8 ± 10 across brains (measured [23]). The annotations number more than 870,000 at four levels (measured [23]).

Two fly-brain totals. The hemibrain paper gives the whole fly brain as “approximately 100,000 neurons” [25]. FlyWire gives 139,255 proofread neurons [27]. Both are recorded.

Fly nerve cord. The male ventral nerve cord holds “roughly 23 thousand traced neurons” (measured [24]). It has 10 million T-bars and 74 million PSDs (measured [24]). That is 7.4 PSDs per T-bar and 435 T-bars per neuron (computed: $74 / 10$; $10^7 / 23,000$).

Brain plus nerve cord gives $139,255 + 23,000 = 162,255$ neurons in the adult fly central nervous system (computed). The two counts come from different animals and sexes. The nerve cord is 14.2 % of that total (computed: $23,000 / 162,255$).

Zebrafish. Light-sheet imaging records “more than 80% of all neurons at single-cell resolution” in the larval brain at 0.8 Hz volume rate (measured [26]). The source page gives no total neuron count [26].

Scale of counts. From 302 neurons in the worm to 139,255 in the fly brain is a factor of 461 (computed: $139,255 / 302$). The counted systems in order of size are 177 (*Ciona* CNS), 302 (*C. elegans*), 892 (*Platynereis*, classified), 3,016 (fly larva), about 25,000 (hemibrain) and 139,255 (fly brain).

Acoel. Of 50 decapitated acoels 42 began head regeneration (measured [6]). That is 84 % (computed: $42 / 50$). About 70 % had regenerated a brain neuropil “virtually indistinguishable” from intact animals by 50 days (measured [6]).

Fossils. *Kerygmachela* is described from 15 new specimens with 11 pairs of trunk flaps (measured [8]). *Alalcomenaeus* shows 4 head ganglia and 8 trunk ganglia in an 11-segment trunk (measured [16]). The specimens are YKLP 15006 (*Fuxianhuia*), 11075 (*Alalcomenaeus*) and 13304a/b and 13306a/b (*Lyrarapax*) [15, 16, 17].

Phylogeny. Five clades were sampled for nerve-cord patterning [2]. No source here gives a count of independent origins of the central nervous system [2, 1].

Order of events

1. Cryogenian (no bounds given in the sources here): crown animals by clock (modelled [11]).
2. Before 638.8 Ma, pos. 67.33: bilaterian phyla diverge, more than 100 Myr before the Cambrian (modelled [11]; computed).
3. About 571–539 Ma, pos. 67.22–67.17: Ediacara biota, including *Ikaria wariootia* [13]; chapter A2 gives 571–541 Ma from another source.
4. About 560 Ma, pos. 67.21: last common ancestor of cyclostomes and gnathostomes by one estimate (modelled [10]).
5. About 555 Ma, pos. 67.20: chordates proposed to arise in the Ediacaran [19].
6. 538.8 ± 0.2 Ma, pos. 67.17: base of the Cambrian (measured [12]).
7. About 521 Ma, pos. 67.14: base of Cambrian Stage 3; Sirius Passet *Kerygmachela* with a unipartite brain falls in Stage 3 [12, 8].
8. About 520 Ma as printed, pos. 67.14: Chengjiang *Fuxianhuia* tripartite brain and *Alalcomenaeus* ganglia [15, 16]; this disagrees with item 9.
9. $\leq 518.03 \pm 0.69/0.71$ Ma, pos. 67.13: Chengjiang fossils, below the maximum depositional age, with *Fuxianhuia*, *Alalcomenaeus*, *Lyrarapax*, *Myllokunmingia* and *Haikouichthys* (measured [14]; [15, 16, 17, 19]).
10. More than 500 Ma, pos. 67.10: cyclostome–gnathostome split by a second estimate [9].

The “>500 Ma” date is a lower bound. It is listed after the Chengjiang age because its value is younger. The true split may be older.

Present quantities

Acoel behaviour. Before decapitation, acoels took 8.6 s on average for geotaxis (measured [6]; N = 69). Phototaxis distance was 2.59 cm before decapitation and was not restored at 5 days (measured [6]).

Locomotion was 1.63 mm s⁻¹ in controls and 1.37 mm s⁻¹ one day after decapitation (measured [6]). The headless speed is 84 % of the control speed (computed: 1.37 / 1.63).

Imaging rates. Larval zebrafish brains were imaged at a 0.8 Hz volume rate (measured [26]). This is one volume every 1.25 s (computed: 1 / 0.8).

Connectome effort. The hemibrain needed “over 50 person-years” of proofreading over about 2 calendar years (measured [25]). FlyWire needed about 33 person-years for a brain with 5.6 times as many neurons (measured [27]; computed: 139,255 / 25,000).

Synapse density per neuron. In the maps counted here, chemical synapses per neuron are 16.6 in the worm and 28.6 in *Platynereis* (computed). They are 182 in the fly larva, 391 in the FlyWire brain and 800 in the hemibrain (computed).

Ciona has 37 presynaptic sites per neuron (measured [21]). A mouse cortical neuron has about 8,200 synapses (measured [21]).

Variation between brains. In the fly, one cell type in three differs in count across brains (measured [23]). Left and right central brains differ by 0.1 % in intrinsic neurons (measured [23]). Kenyon cells differ by 17 between left and right in FlyWire (computed: 2,597 – 2,580).

Pattern

Counted systems run 177 (*Ciona* CNS), 302 (*C. elegans*), 892 (*Platynereis*, classified, of 8,852 cells), 3,016 (fly larva brain), about 25,000 (hemibrain, part of a brain) and 139,255 (fly brain) neurons. Synapses per neuron run 16.6 to 800. In the fly, optic lobes hold 65.4 % of intrinsic neurons.

Fossil brains occur in Cambrian Stage 3. Sources print 520 Ma, 18.8 Myr after the Cambrian base; the Chengjiang maximum age, 518.03 Ma, gives at least 20.77 Myr. They come in one, two and three parts; one study reads such structures as biofilms.

Molecular dates sit before the fossils: crown animals in the Cryogenian, bilaterian phyla before 638.8 Ma, and the vertebrate split at about 560 Ma. Cyclostome brains already carry MGE, rhombic lip, pallial sensory areas and thalamic relay. Origins of nerve cords are recorded as one fused system and as convergent “many times”; no count is given.

Not verified

- *Ikaria wariootia* size of 2–7 mm by about 1–2.5 mm and age of “more than 555 million years” (UC Riverside release 2020; secondary).
- Bilaterian burrows accepted for 15 years before the *Ikaria* body was found (UC

Riverside release 2020; secondary).

- “Several hundred specimens” of fuxianhuiids and an age of “about 500 million years” (Museum für Naturkunde Berlin release; secondary).
- Common origin of annelid mushroom bodies and vertebrate pallium (Tomer et al. 2010; V-bib, abstract not read).
- Earlier claim that the lamprey lacks an MGE-like domain (cited by Sugahara et al. 2016; primary not opened; secondary).
- *C. elegans* hermaphrodite graph of 460 nodes and male graph of 579 nodes with 385 neurons (Cook et al. 2019 via OpenWorm; secondary).
- *C. elegans* sex-specific neurons 8 and 91, median 19 neighbours, 10–30 % sex effect, 54,000 images (The Transmitter 2019; secondary).
- *C. elegans* 282 somatic plus 20 pharyngeal neurons, 222 at hatching, 113 motor neurons, about 6,400 chemical synapses, 900 gap junctions and 1,500 neuromuscular junctions (WormAtlas; secondary).
- *C. elegans* 80 neurons added after hatching (computed from WormAtlas values; not used).
- Male *C. elegans* 302 + 79 = 381 neurons against 385 (computed from secondary values; not used).
- Larval zebrafish about 100,000 neurons; adult about 10 million (Zanichelli et al. 2025 report, citing others; secondary).
- Mouse visual cortex volume of 1 mm³ with about 120,000 neurons and 523 million synapses (Zanichelli et al. 2025, citing MICrONS; secondary).
- Lamprey basal ganglia as a conserved action-selection mechanism (Stephenson-Jones et al. 2011; V-bib, abstract not read).
- Origin of cortex pushed back “some 300 million years” and lamprey brain parts with “much fewer nerve cells” (Neuroscience News 2020; secondary).
- About 700 motor and about 1,300 descending neurons in the male fly nerve cord (companion-paper summaries cited by Takemura et al. 2023).
- A count of independent CNS origins (none given); hemichordate cord data (not read).

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A5 Speed and Size

What it is

This chapter records how fast nerve impulses travel, what they cost, and how many neurons brains hold. It covers four lines of data.

The first is conduction speed: myelin, giant axons and nodes. The second is energy: the ATP cost of a spike and the brain's share of the body's budget.

The third line is size: neuron numbers across mammals, birds and reptiles, brain-body scaling and neuron density. The fourth is the division status of vertebrate neurons. It records whether a differentiated neuron re-enters the cell cycle and whether division is completed.

Speed in an axon rises with diameter or with insulation. In unmyelinated axons, axial resistance “drops as the square of diameter” and speed rises “in proportion to the

square root of the interior diameter” [1]. In myelinated fibres speed shows “a first power (rather than square root) dependence on diameter over a substantial range” [1].

A ten-fold speed gain by diameter alone needs axons “100 times larger” [1]. The arithmetic is $\sqrt{100} = 10$ (computed). Rapidly conducting axons “in all animals tend to be larger than slowly conducting ones” [2].

Myelin is a sheath of membrane layers around an axon, interrupted at nodes. Penaeid shrimp have a “fenestration node” with saltatory conduction [3].

First appearance

The oldest dated element in this chapter is molecular. The paranodal proteins Caspr and neurexin IV are conserved “over 750 million years of evolution” [1].

Several myelin proteins are older than the sheath itself. CNP, PMP22, MAL and PLP are “evolutionarily older than vertebrates” [4].

MPZ (P0) belongs to an Ig-CAM superfamily present in vertebrates and invertebrates [4].

The first myelinated vertebrate “was likely to have been a placoderm” [1]. No date in Ma is given in that review [1].

A second source states that myelin is thought to have arisen around the time of hinged jaws [4]. It names placoderms “the most ancient group of jawed vertebrates” [4].

It also states that “lamprey axons are not ensheathed by myelin” [4]. No date in Ma is given there either [4].

Two readings exist of one lamprey sequence. A lamprey protein segment is “86% identical over 22 amino acids” to a fragment of myelin basic protein (MBP), as reported by Smith et al. 2013 and cited in [4].

Werner argues that the segment is homologous to GOLLI, not to MBP [4]. Both readings are recorded.

In a survey of 20 calanoid copepod species, two of the more ancient superfamilies lacked myelin [5]. It was “present in the species from three more recently evolved superfamilies” [5]. No date was read.

Giant axons “evolved in invertebrates such as squid” [2], without a date.

Neuron numbers have a dated frame in amniotes. Kverková et al. record “four major shifts in neuron–brain scaling” over 300 Myr of amniote evolution [6].

For the human cortex the first appearance of each neuron is dated by carbon-14. Neurons of the human cerebral cortex date from around birth [7].

They are not made in adulthood at detectable levels [7]. Non-neuronal cortical cells are replaced [7].

Partners

Myelin appears in “each of the major bilaterian lineages” [1]. The deuterostomes are represented by gnathostomes.

The lophotrochozoa are represented by polychaetes and oligochaetes. The ecdysozoa are represented by copepods and malacostracans [1].

The count is three superclades and five groups (computed from the groups named in [1]). Myelin “seems to have arisen independently in evolution several times in vertebrates, annelids and crustacea” [1].

Molluscs and insects are named as groups without myelin [1]. Jawless lampreys lack it [4].

Each sheath has its own structure. Copepod sheaths reach “up to 60 layers” around sensory and motor axons [5].

Earthworm myelin has “60 to 200 such layers” [1]. Copepod fibres carry “well-developed myelin-like sheaths” [8].

Penaeid shrimp myelinated fibres occur in “at least six species of *Penaeus* shrimp” [3]. They combine a fenestration node, a compact multilayered sheath, a microtubular sheath around the axon and a wide submyelinic space [3].

At the vertebrate node, nodal microdomains lie within “just a few microns of length in either direction from the centre of the node” [1]. Caspr and neurexin IV mark the paranode [1].

Random glial sealing of over half of an axon’s surface is predicted to raise speed by about 20 % (modelled [1]).

Mitochondria are the energy partners at the synapse. Neocortical presynaptic terminals hold 0.3–1.4 mitochondria each (measured [9]).

Dendrites hold about one mitochondrion per 7 μm (measured [9]). About 80 % of mitochondria are stationary [9].

Mitochondria supply about 93 % of ATP and glycolysis about 7 % [9]. Oxygen and glucose are consumed in a ratio near 6:1 [9].

Non-neuronal cells are the partners in brain mass. In six rodent species, larger structures hold more and larger neurons plus many more non-neuronal cells of roughly constant size [10]. Non-neuronal cell density lies at 50,000–120,000 cells/mg in mammals, birds and reptiles (measured [11]).

Sizes

what	size	position	source
Squid (<i>Loligo pealei</i>) giant axon, May	506 μm (SEM 26.8)	8.48	measured [12]
Squid giant axon, August	383 μm (SEM 14.68)	8.23	measured [12]
Penaeid shrimp myelinated fibre	120 μm	7.17	measured [1]

Rushton's critical diameter (disputed)	1 μm	2.81	[13]
Dendrite length per mitochondrion	7 μm	4.58	measured [9]
Human myelinated fibre length, men aged 20	176,000 km	32.67	measured [14]
Human myelinated fibre length, women aged 20	149,000 km	32.52	measured [14]
Human myelinated fibre length, men aged 80	97,200 km	32.13	measured [14]
Human myelinated fibre length, women aged 80	82,000 km	31.97	measured [14]

Squid axon diameter was 506 μm in May and 383 μm in August, in collections of 1997–1998 (measured [12]). May waters were about 10–12 °C and August waters about 20 °C [12]. Records numbered 5–11 per season [12].

Giant axons are “several times larger” than other large axons in the same animals [1]. No single diameter is given there [1]. The squid May axon is $506 / 120 = 4.2$ times the diameter of the shrimp fibre (computed).

Speeds follow diameter and sheath. Squid conduction velocity was 9.56 m/s at 5 °C and 18.94 m/s at 20 °C (measured [12]).

The May axon conducted 12.45 m/s at 10 °C (measured [12]). The ratio over 15 °C is $18.94 / 9.56 = 1.98$ (computed).

The implied Q10 is $1.98^{(10/15)} = 1.58$ (computed). Penaeid shrimp fibres of 120 μm conduct “over 200 m s^{-1} ”, “the fastest speeds known” (measured [1]; also [3]). The fastest recorded myelinated vertebrate axons reach about 100 m/s [1].

A textbook gives other ranges. Unmyelinated axons conduct at 0.5–10 m/s and myelinated axons up to 150 m/s [2]. Two values for the vertebrate maximum are therefore recorded: about 100 m/s [1] and 150 m/s [2].

The shrimp exceeds the vertebrate maximum by $200 / 100 = 2.0$ or $200 / 150 = 1.33$ (computed). It exceeds the warm squid axon by $200 / 18.94 = 10.6$ (computed) with a diameter 4.2 times smaller. The full span runs from 0.5 m/s to >200 m/s, a factor of 400 (computed).

Myelin raises speed by a stated factor. For fibres of a few μm or more, myelin speeds conduction “by a factor of ten or more” over unmyelinated fibres of the same diameter [1]. Copepod sheaths are compared to “those that give a tenfold boost” in vertebrates [8].

Another source states that myelin “has sped up nerve conduction velocity more than 20-fold” [4]. Two factors are recorded: ≥ 10 [1, 8] and > 20 [4]. Earthworm myelinated fibres are “a few fold” faster than unmyelinated fibres of the same diameter [1].

The lower size limit of the gain is disputed. Rushton's “critical diameter” of 1 μm is the size below which myelin gives no gain [13]. Waxman and Bennett report that “myelinated fibres considerably smaller than 1 μm ” may conduct faster than unmyelinated fibres of similar size [13].

Node length varies between axons. It spans a 4.4-fold range in rat optic nerve and an 8.7-fold range in cortex (measured [15]).

Variation along one axon is much smaller than between axons [15]. Absolute node lengths in μm were not read.

Node length is modelled to shift conduction speed by about 20 % (modelled [15]). The membrane area change needed at the node is more than 270-fold less than in the sheath for the same effect (modelled [15]).

The same ~ 20 % appears for random glial sealing (modelled [1]).

Human white matter holds 176,000 km of myelinated fibre at age 20 in men and 149,000 km in women (measured [14]). At 80 the values are 97,200 and 82,000 km [14].

The loss is $(176,000 - 97,200) / 176,000 = 44.8$ % in men and $(149,000 - 82,000) / 149,000 = 45.0$ % in women (computed). The source states 45 % [14].

Times

what	duration	position	source
Minimum reaction time, <i>Undinula vulgaris</i> (myelinated copepod)	1.5 ms	27.23	measured [5]
Minimum reaction time, <i>Neocalanus gracilis</i> (myelinated)	1.6 ms	27.29	measured [5]
Minimum reaction time, <i>Labidocera madurae</i> (non-myelinated)	3.1 ms	27.90	measured [5]
Minimum reaction time, <i>Pleuromamma xiphias</i> (non-myelinated)	6.6 ms	28.58	measured [5]
Copepod reaction time, upper value	2.5 ms	27.70	measured [5]
<i>Acartia</i> typical response to a hydrodynamic disturbance	4 ms	28.13	measured [5]
Interval between copepod kicks	5 ms	28.33	measured [5]
<i>Acartia</i> stroke and recovery	7 ms	28.64	measured [5]
Interval for one spike plus downstream events	2.5 ms	27.70	modelled [9]
Isotropic fractionator estimate	24 h	43.50	[16]
BrdU incorporation window after forced re-entry	2-4 days	44.13-44.76	measured [17]
Viability unchanged after forced re-entry	3 days	44.50	measured [17]

Progressive death after forced re-entry, through	7 days	45.27	measured [17]
Rb-TKO cortical neurons in culture	4 days	44.76	measured [18]
Human sample ages, hippocampal study	18–77 years	51.50–52.82	[19]
Ages with few young hippocampal neurons	7 and 13 years	50.64 and 51.21	[19]
Human white-matter fibre length measured	20 and 80 years	51.60 and 52.86	measured [14]
Conservation of Caspr / neurexin IV	>750 Myr	67.47	[1]
Span of amniote neuron-brain scaling shifts	300 Myr	66.64	[6]

The copepod times compare sheath against no sheath. Myelinated species reacted in 1.5 and 1.6 ms (measured [5]).

Non-myelinated species reacted in 6.6 and 3.1 ms (measured [5]). The ratios are $6.6 / 1.5 = 4.4$ and $3.1 / 1.6 = 1.9$ (computed).

Spike heights in the two non-myelinated species were 1–4 mV (measured [5]). These are about an order of magnitude larger than in the two myelinated species [5].

Acartia spp. often reached a maximum speed of >500 mm/s (measured [5]). Acceleration was usually >100 m/s² (measured [5]). Turning reached about 30° per ms (measured [5]).

Copepod reaction times were “under 2.5 ms following stimulus onset”, with intervals of 5 ms between kicks (measured [5]). Escape accelerates copepods “to 200 body lengths per second” “within milliseconds” [8].

Cycle re-entry in disease has a long duration. Polyploid neurons in Alzheimer’s disease survive “hundreds of days” or “many months” before dying [20].

For many months such neurons “appear incapable of either completing the cycle or dying” [21]. No exact duration in days is given, so no position is computed.

Counts

Myelin. Myelin occurs in five named groups [1]. It arose “several times in vertebrates, annelids and crustacea”, three taxa [1].

Calanoid copepods: 3 of 5 surveyed superfamilies have it, across 20 species (measured [5]). Sheaths hold up to 60 layers in copepods (measured [5]) and 60–200 in earthworms (measured [1]).

Ions and ATP per spike. The Na⁺ entry needed for a spike is quadrupled to allow for simultaneous Na⁺ and K⁺ channel activation, after Hodgkin 1975 [22]. This gives 11.5×10^8 Na⁺ per action potential, requiring 3.84×10^8 ATP (modelled [22]).

Rodent signalling at 4 Hz costs $4 \times (3.84 \times 10^8 + 3.28 \times 10^8) = 2.85 \times 10^9$ ATP per

neuron per second (modelled [22]). The product checks as 2.848×10^9 (computed). With the resting potential added, the total is 3.29×10^9 ATP per neuron per second [22].

The resting share is then $(3.29 - 2.85) / 3.29 = 13 \%$ (computed). This matches the 13 % share stated for the resting potential [22].

The budget split is: action potentials 47 %, postsynaptic glutamate effects 34 %, resting potential 13 %, glutamate recycling 3 % (modelled [22]). The sum is $47 + 34 + 13 + 3 = 97 \%$ (computed). One extra action potential per cortical neuron per second raises O_2 consumption by 145 mL per 100 g grey matter per hour (modelled [22]).

Measurement in rat hippocampal mossy fibres gives a lower overlap. Na^+ influx and energy per action potential are “only 1.3 times the theoretical minimum”, “in contrast to the factor of 4” used in earlier budgets (measured [23]). Two overlap factors are recorded: 4 [22] and 1.3 [23].

Na^+ load per spike, per cm^2 of membrane, varies across neuron models (all modelled [24]). Squid giant axon: 1,098 nC/ cm^2 at 6.3 °C (about 2.3×10^{12} ATP/ cm^2 , efficiency about 9 %) and 331 nC/ cm^2 at 18 °C (about 24 %). Mouse thalamocortical relay neuron: 65 nC/ cm^2 (about 1.35×10^{11} ATP/ cm^2 , about 100 %).

Rat granule cell 72 nC/ cm^2 (about 100 %); rat hippocampal interneuron 76 (74 %); honeybee Kenyon cell 186 (33 %). Mouse fast-spiking interneuron 315 (41 %); crab motor neuron 364 (29 %). Spike heights run from 55.5 to 129 mV, and resting use is below 1.5 % of spike use, at 3 Na^+ per ATP [24].

The squid load divided by the thalamocortical load is $1,098 / 65 = 16.9$ (computed); the source states “about 17×” [24].

Myelin gives “a several hundred-fold improvement in metabolic efficiency” [1].

Synaptic budget. At 4 Hz, synaptic transmission takes 55 % of ATP spent on signalling, which is 41 % of total cortical ATP (modelled [9]). Housekeeping is assumed at 25 % [9].

A second split is given in the same source: postsynaptic receptors 50 %, action potentials 22 %, resting potential 20 %, glutamate recycling 4 %, presynaptic Ca^{2+} 4 % (modelled [9]). Two budgets are therefore recorded. Action potentials take 47 % [22] or 22 % [9]; postsynaptic effects take 34 % [22] or 50 % [9].

One vesicle released costs 1.64×10^5 ATP (modelled [9]). One bit costs about 24,000 ATP, or 20,500 at release probability 1 (modelled [9]). A vesicle is $1.64 \times 10^5 / 2.4 \times 10^4 = 6.8$ bits’ worth of ATP (computed).

One spike plus downstream events costs 4.5×10^8 ATP per 2.5 ms interval, against 3×10^6 for resting and housekeeping (modelled [9]). The ratio is $4.5 \times 10^8 / 3 \times 10^6 = 150$ (computed), as stated [9].

White matter uses 3-fold less energy than grey matter (modelled [9]). Synapse density in white matter is 80-fold lower [9]. The fly retina uses 10 % of the fly’s resting ATP consumption [9].

Brain share of body energy. The human brain is “only 2% of the body’s mass” and uses “~20% of the O_2 consumed by the resting body” [9]. A second source states that

the nervous system accounts for 20 % of the body's resting metabolic budget [1]. The ratio of energy share to mass share is $20 / 2 = 10$ (computed).

During development the share is larger. At birth brain glucose use is 52.5 % and 59.8 % of resting metabolic rate (RMR) in males and females (measured [25]). As a share of daily energy expenditure (DER) the values are 35.4 % and 38.7 % [25].

The childhood peak is 66.3 % and 65.0 % of RMR, and 43.3 % and 43.8 % of DER (measured [25]). The age of the peak is not given in the abstract read [25].

Body-weight growth is inversely related to brain demand [25]. The peak of 66.3 % is a share of RMR [25]; the adult 20 % is a share of resting O_2 or energy [9, 1]. The bases differ, so no ratio is formed here.

Glucose per neuron. Across six species (mouse, rat, squirrel, macaque, baboon, human), glucose use per neuron varies by only 40 % (measured [26]). The whole-brain average is 5.79×10^{-9} μmol glucose per minute per neuron [26]. A brain of one billion neurons then uses 5.79 $\mu\text{mol}/\text{min}$ [26].

Cerebral cortex neurons use $1.50 \times 10^{-8} \pm 0.49 \times 10^{-8}$ $\mu\text{mol}/\text{min}$ each (measured [26]). Cerebellar neurons use $0.87 \times 10^{-9} \pm 0.36 \times 10^{-9}$ $\mu\text{mol}/\text{min}$ each (measured [26]). The ratio is $1.50 \times 10^{-8} / 0.87 \times 10^{-9} = 17.2$ (computed).

The source states the cortex at “nearly 20×” the cerebellum in its Results and “at least 10×” in its abstract [26]. Both are recorded. A human brain of 86×10^9 neurons at 5.79 $\times 10^{-9}$ $\mu\text{mol}/\text{min}$ each uses 498 μmol glucose/min (computed).

Glucose use scales with brain mass at exponent 0.873 (95 % CI 0.830–0.915) for the whole brain, 0.850 for cortex and 0.844 for cerebellum [26]. Against neuron number the exponents are 0.988 (whole brain), 0.944 (cortex) and 0.880 (cerebellum) [26].

Neuron numbers, rat. The adult rat brain holds about 330 million cells and 200 million neurons (200.13 ± 21.17 million; measured [16]). The neuron share is $200.13 / 330 = 61$ % (computed); the source states about 60 % [16].

The rat cortex holds about 80 million cells and about 30 million neurons, 40 % of its cells (measured [16]). The cerebellum holds about 170 million cells, over 80 % neurons [16]. Almost 70 % of the rat's neurons are in the cerebellum [16].

Neuron numbers, human. The human brain holds 86 billion neurons and 85 billion other cells [27]. The cerebral cortex holds 16 billion neurons in 1,233 g, 82 % of brain mass [27].

The cerebellum holds 69 billion in 154 g, 80 % of neurons [27]. The share checks as $69 / 86 = 80$ % (computed).

A second source gives the human cortex 16.3 billion neurons [28]. Human cortical grey matter holds 21,450 neurons/mg and 80,064 neurons per mm^2 of cortex (measured [28]). Hippocampus plus amygdala hold about 250 million neurons [28].

Neuron numbers, elephant. The African elephant brain holds 257.0 billion neurons in 4,618.6 g without olfactory bulb (measured [28]). The cerebral cortex holds 5.6 billion [28].

The cerebellum holds 250.7 billion, 97.5 % of the total [28]. The share checks as $250.7 / 257.0 = 97.5 \%$ (computed).

There are 44.8 cerebellar neurons per cortical neuron [28]; $250.7 / 5.6 = 44.8$ (computed). Elephant cortical neurons are $5.6 / 16.3 = 0.34$ times the human count (computed).

Neuron numbers, 41 mammals. Data cover 41 species in 6 mammalian clades [29]. About 2 cortical and about 8 cerebellar neurons are added per neuron added in the rest of the brain [29]. Cortex runs from 9.8 million neurons (smoky shrew) to 16 billion (human) [29].

The cortical range is $16 \times 10^9 / 9.8 \times 10^6 = 1,630$ -fold (computed). The cerebellum runs from 21 million (smoky shrew) to 69 billion (human), a range of 3,290-fold (computed from [29]). The rest of the brain runs from 6 million to 690 million neurons [29].

The human olfactory bulb holds 15–16 million neurons and the mouse lemur olfactory bulb 7.6 million [29]. In rodents, the cerebellar share of total neurons grows with brain size [10].

Neuron numbers, birds. Parrots and songbirds have on average twice as many neurons as primates of the same brain mass [30]. Corvids and parrots have much higher proportions of neurons in the pallial telencephalon [30]. Large-brained parrots and corvids have forebrain neuron counts equal to or greater than primates with much larger brains [30].

In 111 bird species, pallial neuron number is positively associated with innovation propensity [31]. Pallial counts are higher in brains large in absolute and relative terms and with longer post-hatching development [31].

Neuron numbers, amniotes. Reptile average neuron numbers are “over 20 times lower” than in birds and mammals of similar body size [6]. A preprint dataset of amniotes runs from the Algerian sand gecko to the African elephant [11]. The gecko has just under 2 million neurons and the elephant 257 billion [11].

The range is $257 \times 10^9 / 2 \times 10^6 = 1.3 \times 10^5$ -fold (computed). The Sumatran flying dragon has barely more than 5 million neurons [11].

Species counts differ between sections of that preprint: reptiles 107 or 108, mammals 75, 69 or 68, birds 65 [11]. All are recorded.

Ratios between structures are given in [11]: mammals about 4 cerebellar per cortical neuron; birds 4.5 cerebellar per hindbrain neuron; reptiles 1.4 ± 0.6 telencephalic per rest-of-brain neuron. Most bird clades have about 3 pallial per rest-of-brain neuron, owls 12, and primates can exceed 20 [11].

Brain-body allometry. In 1,552 mammal species from 28 orders, an ordinary least squares fit gives $\log \text{ brain mass} = -1.26 + 0.75 \log \text{ body mass}$ [32]. The slope's 95 % CI is 0.742–0.758, excluding 2/3 and 1 [32]. A phylogenetic fit (PGLS, $\lambda = 0.935$) gives $\log \text{ brain mass} = -0.83 + 0.57 \log \text{ body mass}$ [32].

Per-order slopes, for orders with more than 10 species, run from 0.24 (Peramelemorphia) to 0.81 (Chiroptera), median 0.64 [32]. The family level is the only

level distinguishable from 0.75 [32]. More than 70 % of extant mammals lack brain data [32].

The exponents recorded in [32] are 0.75 (OLS), 0.57 (PGLS), “about 0.5” and “about 2/3” (other studies cited).

A larger dataset covers 20,213 specimens of 4,587 jawed-vertebrate species [33]. Brain-body allometries among species stay constant across classes and taxonomic levels [33].

Within-species allometries of birds and mammals are shallower and more variable [33]. Birds and mammals extend fetal brain growth relative to fishes [33].

A critique holds that static allometries of indeterminate growers (fish, reptiles, amphibians) cannot be compared with those of determinate growers (birds, mammals) [34]. Two positions are recorded [33, 34]. Brain size may be linked to maternal metabolic turnover rather than body surface area in mammals, birds and reptiles [35].

Structure mass against neuron number. For the cerebral cortex the exponent is 1.087 ± 0.074 in primates and 1.688 ± 0.051 in all other clades jointly [29]. For the cerebellum it is 0.976 ± 0.036 (primates), 1.028 ± 0.084 (eulipotyphlans) and 1.296 ± 0.043 (other clades) [29].

The rest of the brain scales at 1.400 ± 0.077 in non-artiodactyls [29]. The olfactory bulb scales at 0.823 (eulipotyphlans), 1.309 (artiodactyls) and 1.185 (scandentians, afrotherians and glires) [29].

Doubling cortical neurons multiplies cortical mass by $2^{1.087} = 2.12$ in primates (computed). In other mammals it multiplies cortical mass by $2^{1.688} = 3.22$ (computed).

Neuron density. Human cortical grey matter holds 21,450 neurons/mg; elephant cortical grey matter 3,661 neurons/mg (measured [28]). The ratio is 5.9 (computed).

The elephant table prints “3.661”, which disagrees with the text value 3,661 [28]. Both are recorded.

Per mm² of cortex, the human value is 80,064 and the elephant value 10,752 (measured [28]). The ratio is 7.4 (computed).

Across six species, neuronal density falls with brain mass at exponent -0.116 [26]. Glucose use per gram rises with neuronal density at exponent 0.986 [26].

In mammals, adding neurons is “accompanied by a decrease in neuronal density”, with little change in glial density [29]. Average neuron size therefore grows in larger brains [29].

Avian brains have “higher neuron packing densities than mammalian brains” [30]. Late-derived birds have telencephalic densities that barely decline with neuron number [11].

Early-derived birds are comparable to reptiles and mammals [11]. Non-neuronal density spans $120,000 / 50,000 = 2.4$ -fold across all three amniote classes (computed from [11]).

Division status of vertebrate neurons. Three outcomes are recorded for vertebrate

neurons that re-enter the cell cycle: DNA replication without mitosis, endoreplication, and completed division.

In Alzheimer's disease, hippocampal pyramidal and basal forebrain neurons replicate four loci on three chromosomes [20]. "Nearly 4% of the at-risk neurons are in a polyploid state" in the hippocampus (measured [20]). The range is 0.005–0.100 and the mean 0.037 ± 0.028 SD, from 6 AD and 4 control cases [20].

No control hippocampal cell had more than two signals [20]. "Because mitosis is not initiated, the cells remain tetraploid" [20]. "No neuron has ever been observed in M phase" [20].

In the normal human brain about 10 % of neurons have more than diploid DNA content and fewer than 1 % are tetraploid (measured [36]). In AD a cyclin B1-positive tetraploid population makes up about 2 % of all neurons [36].

Tetrasomic neurons increase six-fold in early AD (Braak I-II), to 2.4 ± 0.7 % [36]. The implied baseline is $2.4 / 6 = 0.4$ % (computed).

A review states: "Adult CNS neurons are typically described as permanently postmitotic, but there is probably nothing permanent about the neuronal cell cycle arrest" [21]. Neurons that fail to hold the cycle in check "will re-enter a cell cycle that they will not be able to complete" [21].

Forced re-entry has been induced with SV40 large T antigen in differentiated mouse cortical neurons in culture [17]. About 70 % became hyperploid (measured [17]). At 2–4 days, 30–40 % still incorporated BrdU and about 30 % were refractory [17].

Some cells exceeded 4C, which is endoreplication: DNA replication without division [17]. Viability was unchanged for 3 days, followed by progressive death through day 7 [17]. Mitosis or cytokinesis is not reported [17].

Completed division with neuronal identity kept is documented in mouse. Rb-triple-knockout (CAG-Rb-TKO) Satb2-positive cortical neurons in culture were 13.9 ± 1.2 % EdU-positive and 2.02 ± 0.06 % phospho-histone-H3-positive at 4 days (measured [18]). The neurons "continued to cycle after cell division", with 6.4 % EdU-positive [18].

Camptothecin-treated (1 nM) neurons after oxygen-glucose deprivation "underwent cell division, while maintaining their neurites" [18]. "The daughter cells were both Satb2 positive" [18]. The source states that "neuronal division occurred without de-differentiation" [18].

In contrast, 14.21 ± 5.36 % of G2/M cells in MAP2-Rb-TKO cultures were positive for activated caspase-3, a marker of dying cells (measured [18]). The same source states that mouse horizontal interneurons "differentiate into mature horizontal interneurons that proliferate and form tumors" [18]. It also states that "Mouse horizontal/amacrine cells and human cone photoreceptors can proliferate and form tumors" [18].

Every completed division recorded here follows loss of Rb-family genes or added DNA damage [18].

New neurons in the adult human hippocampus. One study reports about 700 new neurons per day in each hippocampus [37]. Another found no young neurons in 17 post-

mortem brains and 12 surgical samples, ages 18–77 [19]. Only a few were found at 7 and 13 years [19].

Two positions are recorded. Both concern new neurons from progenitors, not division of neurons.

Order of events

Positions of ages are computed as durations of $A \times 10^6 \times 3.15576 \times 10^7$ s.

1. More than 750 Myr ago: paranodal Caspr and neurexin IV proteins conserved from this time onward [1]. Position 67.47.
2. Before vertebrates: CNP, PMP22, MAL and PLP present; the P0 family present in vertebrates and invertebrates [4]. No date read; no position.
3. Early jawed vertebrates: placoderms named as the first myelinated vertebrates; lampreys lack myelin [1, 4]. No date in Ma read; no position.
4. Within calanoid copepods: myelin absent in two ancient superfamilies and present in three younger ones [5]. No date read; no position.
5. Over the last 300 Myr: four major shifts in neuron–brain scaling in amniotes [6]. Position of the span 66.64.
6. Around birth, in humans: cortical neurons generated; not added in adulthood at detectable levels [7]. No duration; no position.
7. Age 20 to 80, in humans: myelinated fibre length falls by about 45 % [14]. Positions 51.60 and 52.86.

Present quantities

Human brain: 2 % of body mass, 20 % of resting O_2 or energy [1, 9]; glucose about 498 $\mu\text{mol}/\text{min}$ (computed from [26]); 86 billion neurons [27]. Human white matter at age 20: 176,000 km (men) and 149,000 km (women) of myelinated fibre [14]. Rodent grey matter: 3.29×10^9 ATP per neuron per second at 4 Hz (modelled [22]).

Fly retina: 10 % of resting ATP [9]. African elephant: 257.0 billion neurons in 4,618.6 g without olfactory bulb [28].

Pattern

Conduction speeds span 0.5 to >200 m/s, a factor of 400. Myelin occurs in five groups of three bilaterian superclades.

Its speed gain is given as ≥ 10 -fold and >20 -fold. Myelinated copepods react in 1.5–1.6 ms, non-myelinated ones in 3.1–6.6 ms.

One action potential costs 3.84×10^8 ATP [22]; a spike with downstream events, 4.5×10^8 [9]. Two budgets disagree on the spike share, 47 % and 22 %. The adult human brain takes 20 % of resting energy at 2 % of body mass; the childhood share reaches 65–66 % of RMR.

Glucose per neuron varies 40 % across six species. Neuron numbers run about 2 million (gecko) to 257 billion (elephant). Mammal brain–body exponents are 0.75 and 0.57.

Neuronal density falls with brain size in mammals and stays high in late-derived birds. Completed neuronal division is recorded only after loss of Rb-family genes or added DNA damage.

Not verified

- Placoderm myelination programme and 10-fold longer oculomotor nerves than in osteostracans (Zalc, Goujet & Colman 2008; secondary summary only).
- Copepod myelinate and amyelinate lineages diverged possibly 270 Ma (Hartline web page; secondary).
- Myelin in vertebrates plus at least three invertebrate taxa, ≥ 4 origins (Hartline "Myelin Evolution" page; secondary).
- Squid giant axon first described 1909 by Williams; Young 1938; Hodgkin-Huxley 1952 (Wikipedia; secondary).
- Typical 0.5 mm squid axon at about 25 m/s; diameter up to 1.5 mm (Wikipedia; secondary).
- Squid 12.3 m/s at 6.3 °C; axoplasm 35 $\Omega\cdot\text{cm}$; shrimp extracellular fluid 23 $\Omega\cdot\text{cm}$; 25 % speed gain (Hartline web page; secondary).
- Doubling all dimensions lengthens unmyelinated travel time by about 40 %; speed need scales with body length^{2/3} (Hartline web page; secondary).
- Human fibre classes A α to C with diameters and speeds; clinical velocities 41–74 m/s (Wikipedia; secondary).
- Node of Ranvier 1–2 μm ; internodes up to 1.5 mm; Ranvier 1871 or 1878 (Wikipedia; secondary).
- Whole-brain neuron counts for mouse, cat, dog, macaque, chimpanzee and pilot whales (Wikipedia list; secondary).
- Bird neuron counts per species, zebra finch to macaw (Wikipedia list; secondary).
- 28 bird species; 2–4 times the neurons of rodent brains of equal mass (Sci.News; secondary).
- Rb-family-deficient horizontal interneurons multiplying up to 50-fold (Ajioka et al. 2007; numbers via ScienceDaily; secondary).

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A6 Senses

What it is

This chapter records the receptor molecules and organs of light, smell, taste, touch, hearing and electric fields. For each it gives first appearance, families, sizes, response times and gene counts. Light is covered in most detail.

Animal light reception rests on opsins. An opsin is a membrane protein of 30–50 kDa that binds retinal (measured [1]).

Retinal is bound at lysine K296 on helix VII [1]. The counterion is E113 in vertebrate visual and non-visual opsins and E181 in other opsins [1].

The first step of vision is the 11-cis to all-trans isomerization of retinal, on a femtosecond time scale [2]. No number of femtoseconds is restated in the source [2]. Microbes use a second class, the type 1 or microbial rhodopsins [3].

Smell and taste rest on receptor gene families. In vertebrates these are the olfactory receptor (OR) genes [4, 5]. In insects they are the odorant receptors (Or) and gustatory receptors (Gr) [6].

Touch and hearing rest on mechanosensitive channels. These range from the bacterial MscL to Piezo proteins and the vertebrate hair cell [7, 8, 9]. Electoreception uses

receptor cells of the lateral line in fishes and amphibians, and trigeminal endings in monotremes [10].

First appearance

Opsins. Opsins share a common ancestor with melatonin receptors [11]. Placozoa have opsins [11]. The first opsin arose by gene duplication in a eumetazoan ancestor and “may not have been light-sensitive” [11].

Two further duplications in the ancestral neuralian lineage gave the progenitors of three subfamilies [11]. These are the ciliary (C), rhabdomeric (R) and Go/RGR subfamilies [11].

All known neuralian opsins fall within these three [11]. No date in Ma is given in the abstract read [11].

A second phylogeny, built from sequences of 14 animal phyla, counts ancestral paralogs [12]. The last common ancestor of Cnidaria and Bilateria had at least four opsins [12].

The bilaterian ancestor had at least nine [12]. Opsins were duplicated and lost many times [12].

Cone and rod pigments. Gene duplication “produced all of the different kinds of cone pigments before the evolution of rod pigments” [13]. Cone-like cells “first appear among cnidarians” [13].

Microbial rhodopsins. Channelrhodopsin-2 (ChR2) is “a directly light-switched cation-selective ion channel” [14]. It is expressed in the green alga *Chlamydomonas reinhardtii*, mainly under low light [14]. In continuous light it desensitizes to a smaller steady-state conductance [14].

Eyes. The earliest dated eyes in this chapter are Early Cambrian fossils from the Emu Bay Shale, South Australia, at about 515 Ma [15, 16]. Arthropod compound eyes there carry “over 3,000 large ommatidial lenses” per eye [16]. *Anomalocaris* eyes from the same shale carry “at least 16,000 hexagonally packed ommatidial lenses” [15].

Compound eyes evolved before a hardened exoskeleton [15]. Non-biomineralized eyes of similar complexity do not reappear in the record until about 85 Myr later [16]. That gives about $515 - 85 = 430$ Ma (computed).

The Cambrian radiation “may have lasted for as little as 25 million years” [17]. Ordovician agnathans are dated at 450 Ma [17]. *Nautilus* is described as having had “half a billion years” to improve its eye [17].

Eye development genes. *Drosophila eyeless* carries a paired domain and a homeodomain [18]. It is homologous to mouse *Small eye (Pax-6)* and human *Aniridia* [18].

The *eyeless* mutation was identified by Hoge in 1915 [19]. The fly Pax6 homolog was isolated about 80 years later [19].

Mouse Pax6 was cloned in 1991 [19]. Homologs are named in vertebrates, ascidians, insects, cephalopods and nemerteans [18]. The cnidarian relative is PaxB [19].

Electroreception. Lateral-line electroreception is present in lampreys and in jawed fishes [10]. It was later lost in frogs, amniotes and neopterygian fishes [10].

It was regained at least twice within teleosts [10]. No dates in Ma are given [10].

Mechanoreception. Mechanosensitive channels are recorded in bacteria, fungi, plants and animals [20]. Piezo homologs occur in invertebrates, plants and protozoa [8].

Partners

Opsin partners. One activated rhodopsin activates the G protein transducin at about 1,000 molecules per second [2]. Each activated enzyme breaks about 4,000 cGMP per second [2]. One photon changes more than 10^5 molecules [2].

All seven *Drosophila* opsin genes are Gq-coupled and belong to the melanopsin subfamily [1]. Opsins share ancestry with melatonin receptors [11].

Bovine rhodopsin was sequenced by protein sequencing in 1982 and by cDNA in 1983 [1]. The β -adrenergic receptor sequence followed in 1986 [1].

Eye partners. Targeted expression of *eyeless* produced ectopic eyes on wings, legs and antennae (measured [18]).

These eyes had differentiated ommatidia and a full set of photoreceptor cells [18]. Mouse Pax6 also induced ectopic compound eyes in *Drosophila* [19].

Cnidarian PaxB is identical to mouse genes at 82 % (Pax2) and 75 % (Pax6) in the paired domain (measured [19]). In the homeodomain the identity is 60 % (Pax3/7) and 55 % (Pax6) [19]. Gehring argues from Pax6 for a single origin of eyes [19].

Lipid partners. Mechanosensitive channels purified from bacteria “sense forces from the lipid bilayer in the absence of other proteins” [20]. Lipids are involved in gating in fungal, plant and animal channels [20].

Ion partners. The vertebrate hair-cell receptor current is carried in vivo by K^+ [9]. The channel is permeable to Li^+ , Na^+ , K^+ , Rb^+ , Cs^+ , Ca^{2+} and at least one small organic cation [9]. ChR2 unitary conductance depends on the permeant ion [21].

Olfactory partners. Each human olfactory receptor neuron carries one receptor type [2]. In the honey bee the number of Ors roughly equals the number of antennal-lobe glomeruli, about 160–170 [6].

Electric partners. The electric organ has evolved six times in fishes [22]. Three lineages compared share transcription factors and developmental pathways [22]. Passive prey detection uses fields in the microvolt range [23].

Sizes

what	size	position	source
Bacteriorhodopsin diameter	4.3 ± 0.5 nm	−2.15	measured [24]
Fly microvillus width	~55 nm	0.17	measured [25]
Human cone value	420 nm	2.02	[2]

Macaque blue cone reference	430 nm	2.04	[26]
Human melanopsin value	~480 nm	2.14	[2]
Human rod value	498 nm	2.18	[2]
Wavelength of light (Land)	~0.5 μ m	2.18	[17]
Macaque green cone reference	530 nm	2.23	[26]
Human cone value	534 nm	2.24	[2]
Macaque red cone reference	560 nm	2.28	[26]
Human cone value	564 nm	2.29	[2]
Fly microvillus length	~1 μ m	2.81	measured [25]
Hair-bundle deflection read	0.3 nm	-4.57	[2]
Bee ommatidial lens diameter	25 μ m	5.74	measured [17]
Decapod facet	~50 μ m	6.37	measured [17]
Small pigmented pit eyes	<100 μ m	7.00	[17]
Merkel disc spatial resolution	0.5 mm	8.47	[2]
Scallop eye	~1 mm	9.10	measured [17]
Human pupil	~2.5 mm	9.93	measured [17]
Object detectable at a 5° acceptance angle	1 cm	11.19	[17]
<i>Anomalocaris</i> eye	2-3 cm	11.83-12.19	measured [15]
Human cochlea	35 mm	12.33	reused [2]
Distance for the 1 cm object	11 cm	13.38	[17]
Compound eye with reduced peripheral resolution matching human acuity	~1 m	15.39	modelled [17]
Compound eye matching human resolution	~12 m	17.65	modelled [17]

Resolution. Acceptance angles reach 90° in pigment-pit eyes [17]. About 5° is a likely threshold for post-Cambrian tasks [17]. At 5° a 1 cm object is detectable at 11 cm [17].

Many insects resolve about 1° [17]. The human fovea resolves about 1 arc minute, “60 times better than a typical insect” [17]. No insect is better than about 0.25° [17].

The span from pit eye to fovea is $90 \times 60 = 5,400$ -fold (computed). The best insect value is $0.25 \times 60 = 15$ arc minutes, 15 times coarser than the fovea (computed).

Lenses. The bee ommatidial lens is 25 μ m across, with blur of about 0.02 rad, or 1.15°

[17]. The human pupil, about 2.5 mm, is “a hundred times the diameter of a bee lens” [17]. The ratio checks as $2.5 \text{ mm} / 25 \text{ }\mu\text{m} = 100$ (computed).

A compound eye matching human resolution would be about 12 m across, after Mallock 1894 [17]. With reduced peripheral resolution it would be about 1 m, after Kirschfeld 1976 [17].

Fish lenses follow Matthiessen’s ratio. Focal length is about 2.5 lens radii, against about 4 for a homogeneous lens of index 1.52 [17]. Refractive index rises from about 1.34 (sea water) and 1.38 (lens cortex) to about 1.52 at the lens centre [17].

Cambrian eyes. The *Anomalocaris* eyes are paired, 2-3 cm and up to 3 cm long (measured [15]). They hold at least 16,000 lenses each [15].

The Emu Bay arthropod eyes hold over 3,000 lenses [16]. The lens counts differ by a factor of at least $16,000 / 3,000 = 5.3$ (computed).

Hearing and touch. The human ear spans 20-20,000 Hz [2]. The range is $20,000 / 20 = 1,000$ -fold (computed). The hair bundle reads deflections of 0.3 nm [2].

Skin receptors divide vibration into bands [2]. The Merkel disc resolves 0.5 mm and reads 5-15 Hz [2]. Meissner corpuscles read below 50 Hz and Pacinian corpuscles about 250 Hz [2].

Microvilli. A fly compound-eye microvillus is about 1 μm long and about 55 nm wide (measured [25]). It holds about 1,000 rhodopsin molecules [25]. The cockroach recordings in that study were made at 22-24 °C [25].

Times

what	duration	position	source
Hair cell forms its receptor potential	~10 μs	22.67	[2]
Human cone inactivation time constant, fast	~3 ms	27.87	[27]
Human cone inactivation time constant, slow	~10 ms	28.96	[27]
Proteorhodopsin photocycle	15 ms	29.33	measured [3]
Macaque green cone integration time	$19 \pm 9.8 \text{ ms}$	29.55	measured [26]
Transport rhodopsin photocycle, upper value	<20 ms	29.59	measured [3]
Human cone dim-flash time to peak	~20 ms	29.59	measured [27]
Macaque red cone integration time	$28 \pm 14 \text{ ms}$	29.90	measured [26]
Mouse activated-rhodopsin lifetime	40-45 ms	30.22-30.33	[13]
Macaque cone time to	$47 \pm 14 \text{ ms}$	30.37	measured [26]

peak, within 1 mm of fovea			
Macaque green cone time to peak	51 ± 13 ms	30.44	measured [26]
Macaque red cone time to peak	55 ± 18 ms	30.51	measured [26]
Mouse GNAT2C rod decay time constant	122 ms	31.24	measured [13]
Mouse wild-type rod decay time constant	258 ms	31.92	measured [13]
Sensory rhodopsin photocycle, lower value	≥300 ms	32.06	measured [3]
Vertebrate phototransduction cascade	~1 s	33.15	[2]
Upper bound, light-sensitive patch to lens eye	<5 × 10 ⁵ generations (≈ years at 1 generation per year [17]); “a few hundred thousand years” [28]	60.81	modelled [17, 28]
Cambrian radiation, as little as	25 Myr	64.38	[17]
Gap before complex soft-bodied eyes reappear	~85 Myr	65.49	fossil [16]
Next complex non-biomineralized eyes	~430 Ma	66.97	computed from [16]
Ordovician agnathans	450 Ma	67.01	[17]
Emu Bay Shale compound eyes	~515 Ma	67.13	fossil [15, 16]

Microbial rhodopsins. Transport rhodopsins (bacteriorhodopsins and halorhodopsins) have photocycles “typically <20 ms” [3]. Sensory rhodopsins have photocycles of at least 300 ms [3].

The proteorhodopsin photocycle is 15 ms [3]. The sensory band is at least 300 / 20 = 15 times the pump band (computed).

ChR2 drives spikes “with millisecond precision” [29]. Many cells cannot follow ChR2-driven trains above about 40 Hz (measured [29]). Plateau potentials of 10 mV or more occur [29].

The engineered variant ChETA allows sustained trains up to at least 200 Hz (measured [29]). The C128 mutation extends the open-state lifetime “vastly” [30]. Such channels respond at orders of magnitude lower light [30].

Cones. Macaque cones (*Macaca fascicularis*) were recorded at 37 °C [26]. Linear flash responses peaked at 55 ± 18 ms (red-sensitive) and 51 ± 13 ms (green-sensitive) (measured [26]). Cones within 1 mm of the fovea peaked at 47 ± 14 ms [26].

Integration time was 28 ± 14 ms (red) and 19 ± 9.8 ms (green) (measured [26]). Human cone dim-flash responses “peak in about 20 ms” (measured [27]). They are monophasic,

with inactivation time constants of about 3 and 10 ms [27].

Two cone time-to-peak values are recorded: about 20 ms (human [27]) and 47–55 ms (macaque [26]). The macaque value is $47 / 20 = 2.4$ to $55 / 20 = 2.75$ times the human value (computed).

Rods. Mouse rods were recorded at 37 °C [13]. Small-response decay time constants were 258 ms in wild type and 122 ms in GNAT2C rods (measured [13]). The ratio is $258 / 122 = 2.1$ (computed).

The activated-rhodopsin lifetime is “probably as short as 40–45 ms” [13]. The amplification constant is 20.5 s^{-2} in wild type and 10.2 s^{-2} in GNAT2C rods (measured [13]). Amplification is “at least 2–3 times larger in rods than in cones” [13].

The vertebrate cascade as a whole lasts about 1 s [2].

Fly photoreceptors. Fly photoreceptors respond to a flash with a slow graded depolarisation [31]. Responses are “typically hundreds of milliseconds long” [31]. Small-signal transduction shows underdamped resonance and a pure time delay [31].

In *Drosophila* at 25 °C, information capacity “starts to saturate at ~200 bits/s” with light adaptation (measured [32]). Rising temperature accelerates the cascade and membrane dynamics [33]. The effective Q10 for information capacity is 6.5 (measured [33]).

The fly retina uses 10 % of the fly’s resting ATP [34].

Eye evolution time. Optical theory gives a light-sensitive patch becoming a focused lens eye in “only a few hundred thousand years” [28]. The assumptions are deliberately pessimistic [28]. Land restates the figure as “less than half a million generations”, at about one generation per year for a small animal [17].

Hair cells. The hair cell forms its receptor potential in about 10 μs [2].

Counts

Opsin families. More than a thousand opsins have been identified [1]. They fall into seven subfamilies [1]. Amino-acid similarity is below about 25 % between subfamilies and above about 40 % within them [1].

Three counts of opsin classes are recorded. Terakita gives 7 subfamilies [1].

Feuda et al. give 3 major neurelian subfamilies (C, R, Go/RGR) [11]. Ramirez et al. give at least 9 ancestral bilaterian paralogs and at least 4 in the Cnidaria + Bilateria ancestor [12].

Opsin genes per genome. The human genome holds 9 opsin genes in 6 of the 7 subfamilies [1]. *Drosophila* holds 7, all Gq-coupled [1].

Amphioxus holds at least 6 opsin genes from 4 subfamilies [1]. No opsin gene has been found in *C. elegans* [1].

Microbial rhodopsin numbers. A SAR86 bacterial cell holds 24,000 proteorhodopsin molecules (measured [3]). Purple membrane holds more than 100,000 proton-pumping

rhodopsins per cell [24]. The oceans hold an estimated 10^{28} proteorhodopsin-expressing bacteria [24].

Bacteriorhodopsin has a quantum efficiency of about 60 % [24]. It translocates 188 H^+ per molecule per minute (measured [24]).

ChR2 unitary conductance. At -60 mV , single-channel conductance is $42 \pm 7 \text{ fS}$ with Na^+ and $61 \pm 18 \text{ fS}$ with Li^+ (measured [21]). It is $91 \pm 25 \text{ fS}$ with guanidinium and $37 \pm 14 \text{ fS}$ with methylammonium [21].

The maximum is $129 \pm 9 \text{ fS}$, with K_m $82 \pm 14 \text{ mM}$ [21]. The density is 226 active channels per μm^2 [21].

Eye origins. Salvini-Plawen and Mayr concluded that “at least 40 different lines of photoreceptor differentiation must be postulated”, as reported by Land [17]. Gehring reports their claim as independent origin in “at least 40 but possibly up to 65 or more phyletic lines” [19]. Gehring calls a 40- to 65-fold independent origin extremely unlikely [19].

Two counts are recorded: at least 40 [17] and 40 up to 65 or more [19]. Two positions are recorded: many independent origins, and a single Pax6-controlled origin [19].

Of the Precambrian lines “only about [a] quarter” gave rise to resolving eyes [17]. The rest are small pigmented pits under $100 \mu\text{m}$ [17]. A quarter of 40 is 10 lines (computed).

Three phyla have “good” eyes: molluscs, arthropods and chordates [17]. Eight optical types are illustrated [17].

Receptors per eye. Insect ommatidia typically hold 8 or 9 receptors [17]. Tiger beetle larval ocelli hold about 6,300 receptors each, with an inter-receptor angle of about 1.8° [17].

A scallop has about 100 eyes of about 1 mm each [17]. The *Nautilus* eye has perhaps a million receptors [17].

Olfactory receptor genes, mammals. Thirteen placental mammals hold more than 10,000 intact OR genes in total (measured [4]). These fall into 781 orthologous gene groups (OGGs) [4]. “Only three OGGs” show complete one-to-one orthology across the 13 species without gains or losses [4].

The mean is more than $10,000 / 13 = 769$ intact genes per species (computed). African elephants have “~2000” functional OR genes in enlarged clusters [4].

The human genome holds about 800 OR genes, about 50 % pseudogenes [5]. The mouse holds about 1,400, with a pseudogene fraction of 20–25 % [5].

The platypus has fewer than 400 functional genes [5]. Its pseudogene fraction is about 50 % if truncated genes are counted as functional [5].

The opossum pseudogene fraction is below 20 % [5]. The cow has nearly 1,000 functional genes with nearly as many pseudogenes [5].

The macaque has fewer than 400 functional genes [5]. Species other than platypus and primates have “800–1,200 functional OR genes” [5].

Dog and rat hold 1,094 and 1,493 OR genes, with pseudogene fractions of 20.3 % and 19.5 %, after Quignon et al. 2005 [5]. The human-mouse common ancestor had about 690 genes, or about 750 by another method [5].

Gains and losses are large. The opossum lineage gained more than 750 genes [5].

The cetartiodactyl and rodent lineages gained more than 400 each [5]. Each branch to the placental orders lost more than 170 [5].

Total gains and losses are 4,968 or 5,134, depending on the tree [5]. Both are recorded. The elephant repertoire is about $2,000 / 400 = 5$ times the primate and platypus repertoires (computed).

Olfactory receptor genes, human. The human genome holds 339 intact OR genes and 297 broken ones, at 51 places on 21 chromosomes, after Malnic, Godfrey and Buck 2004 [2]. A second count gives 400 working genes, after Gilad and Lancet 2003 [2]. The intact share is $339 / 636 = 53$ % (computed).

Human counts recorded here are 339 and about 400 intact or working genes [2], about 800 total [5], and 636 total [2]. The human nose holds 6–20 million receptor neurons in about 5 cm^2 [2]. Each carries 5–20 cilia and projects to a little under 2,000 collecting points [2].

Insect chemoreceptor genes. *Drosophila melanogaster* has 62 odorant receptors and *Anopheles gambiae* 79 [6]. The honey bee has 170 annotated, of which 7 are pseudogenes [6]. One bee subfamily is expanded to 157 genes with 15–99 % identity, and one tandem array holds 60 genes [6].

Gustatory receptors number 10 in the bee, 68 in *D. melanogaster* and 76 in *A. gambiae* [6]. The bee Or/Gr ratio is $163 \text{ intact} / 10 = 16$ (computed). The fly ratio is $62 / 68 = 0.9$ (computed).

Mechanoreceptor counts. *E. coli* MscL is a large-conductance mechanosensitive channel encoded by *mscL* alone [7]. The protein has 136 amino acids [7].

Piezo1 (Fam38A) and Piezo2 (Fam38B) are multipass membrane proteins required for mechanically activated cation currents [8]. Piezo2 in dorsal root ganglion neurons carries rapidly adapting currents [8].

Each human ear holds about 3,500 inner hair cells in one row and about 12,000 outer hair cells [2]. About 90 % of auditory nerve fibres come from inner hair cells [2]. A hair bundle holds 30 to a few hundred stereocilia [2].

The utricle holds about 30,000 hair cells and the saccule about 16,000 [2]. Cochlear hair cells total $3,500 + 12,000 = 15,500$ per ear (computed). Vestibular counts for utricle and saccule total $30,000 + 16,000 = 46,000$ (computed).

Electroreception counts. Electroreceptive groups include lampreys (end buds) and chondrichthyans: sharks, batoids and holocephalans [10]. They also include lungfishes, coelacanths, salamanders and caecilians, and bichirs, paddlefishes and sturgeons [10].

Among teleosts they include mormyriforms (with *Gymnarchus*), gymnotiforms and siluriforms [10]. Monotremes sense fields by trigeminal endings, separate from the lateral-line system [10].

Electroreception “evolved independently at least twice within teleosts” [10]. Ampullary receptors arose independently in Osteoglossomorpha and Ostariophysi [10]. Independent losses are named in frogs, amniotes and neopterygian fishes, with later losses in Asian notopterids and characiforms [10].

The count is at least 2 teleost origins, 1 ancestral vertebrate system and 1 monotreme system, at least 4 in all (computed from the groups named in [10]). Losses named number 3 plus 2 later ones (computed from [10]).

Lamprey electroreceptive end buds hold up to 30 receptor cells, each with 80–90 apical microvilli [10].

About 16 % of fish species have passive electroreception (measured [23]). About 1.5 % have electric organs [23]. The ratio is $16 / 1.5 = 10.7$ (computed).

Weak discharges are below 1 V in electrolocating taxa and below 10 V in other weak groups [23]. Strong discharges exceed 50 V [23]. From 1 μV to 50 V is $50 / 10^{-6} = 5 \times 10^7$, more than seven orders of magnitude (computed).

The electric organ “has evolved six times in fishes” [22].

Human taste. Humans have 2,000–4,000 taste buds with 10–50 cells each [2].

Order of events

Positions of ages are computed as durations of $A \times 10^6 \times 3.15576 \times 10^7$ s.

1. Eumetazoan ancestor: first opsin by gene duplication, possibly not light-sensitive [11]. No date read; no position.
2. Cnidaria + Bilateria ancestor: at least 4 opsin paralogs [12]; cone-like cells first among cnidarians [13]. No date read; no position.
3. Neuralian ancestor: two duplications give the C, R and Go/RGR progenitors [11]. Bilaterian ancestor: at least 9 opsin paralogs [12]. No date read; no position.
4. Before rod pigments: all kinds of cone pigments produced by duplication [13]. No date read; no position.
5. About 515 Ma: Emu Bay Shale compound eyes with over 3,000 lenses and *Anomalocaris* eyes with at least 16,000 lenses [15, 16]. Position 67.13.
6. 450 Ma: Ordovician agnathans [17]. Position 67.01.
7. About 430 Ma (515 – 85, computed): next record of non-biomineralized eyes of similar complexity [16]. Position 66.97.

Undated events (no date read; no position):

- Early vertebrates: lateral-line electroreception in lampreys and jawed fishes [10].
- After early vertebrates: losses of electroreception in frogs, amniotes and neopterygians; at least two regains in teleosts [10].
- Electric organs: six independent origins in fishes [22].

Present quantities

Opsin genes per genome: human 9, *Drosophila* 7, amphioxus at least 6, *C. elegans* 0 [1].

Olfactory receptor genes: African elephant about 2,000; most placentals 800–1,200 functional; primates and platypus below 400 [4, 5]. Insect odorant receptors: bee 170, mosquito 79, fly 62 [6].

Fishes: about 16 % of species electroreceptive and about 1.5 % electrogenic [23].

Oceans: about 10^{28} proteorhodopsin-expressing bacteria [24].

Human: 6–20 million olfactory receptor neurons; 3,500 inner and 12,000 outer hair cells per ear; 2,000–4,000 taste buds [2].

Pattern

Opsin classes are counted as 3, 7 and at least 9; genomes hold 0 to 9 opsin genes. Microbial rhodopsin cycles fall in two bands: pumps at or under 20 ms and sensory rhodopsins at or over 300 ms. Eye or photoreceptor origins are counted at least 40, up to 65 or more; a quarter reached resolving eyes.

The first dated compound eyes, at about 515 Ma, hold 3,000 and 16,000 lenses. Resolution spans 5,400-fold from pit eye to fovea. Cone time to peak is about 20 ms in human and 47–55 ms in macaque; mouse rod decay is 122–258 ms.

Mammal OR repertoires span about 400 to about 2,000 genes, five-fold, with about 5,000 gains and losses. Insects hold 62–170 Ors. Electroreception has at least 4 origins and at least 5 losses; electric organs have 6 origins.

Not verified

- Salvini-Plawen & Mayr 1977 primary not opened; the 40–65 count is taken through Land and Gehring.
- ChR2 kinetics: τ_{rise} 0.2 ms, τ_{off} 9.8–11.1 ms, time to peak 2.4–2.65 ms, ChETA τ_{off} 5.2 ms, opening <1 ms, desensitization 10–400 ms (Stefanescu et al., arXiv 1304.5635; secondary).
- Primate rod time to peak ~200 ms, amplitude 0.1–1 pA, integration ~300 ms; cone time to peak 30 ms (Adler's Physiology of the Eye; secondary).
- Primate rod temporal resolution ~50 ms against a response duration of ~750 ms (bioRxiv 10.1101/421263, introduction; secondary).
- Human OR counts of 387 protein-coding and ~600 pseudogenes; mammals up to 2,000 OR genes or 5 % of coding genes; Buck & Axel 1991 discovery (Wikipedia; secondary).
- Insect olfactory receptors as ligand-gated ion channels (Hallem et al. 2006, via Wikipedia; secondary).
- Fly quantum-bump latency and time to peak (not read).
- *C. elegans* chemoreceptor gene counts and ant Or counts (not read).
- Opsin origin dates in Ma (not read).

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A7 Rhythms and Sleep

What it is

Networks of neurons in the mammalian forebrain show several bands of oscillation. The bands cover frequencies “from approximately 0.05 Hz to 500 Hz” [1], [2]. Their mean frequencies “form a linear progression on a natural logarithmic scale” [1].

The classes were defined by Penttonen and Buzsáki in 2003 [3]. The 2004 paper reproduces them [1].

The full list of classes is printed in Figure 1 of a 2012 review, reproduced from the 2004 paper [2]. The figure is titled “Oscillatory classes in the cortex”. It gives ten classes, slowest to fastest, copied here exactly as printed (measured [2]).

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#	Label as printed	Unit printed
1	"15-40 s, slow 4"	period
2	"5-15 s, slow 3"	period
3	"2-5 s, slow 2"	period
4	"0.7-2 s, slow 1"	period
5	"1.5-4 Hz, delta"	frequency
6	"4-10 Hz, theta"	frequency
7	"10-30 Hz, beta"	frequency
8	"30-80 Hz, gamma"	frequency
9	"80-200 Hz, fast"	frequency
10	"200-600 Hz, ultra fast"	frequency

The legend reads: "Note the linear progression of the frequency classes" "on the natural log scale" [2]. It adds that "these frequency families" "were defined based on phenomenological correlates" [2].

The axis is ticked at 0.05, 0.37, 2.72, 20.09 and 148.41 Hz [2]. These equal e^{-3} , e^{-1} , e^1 , e^3 and e^5 (computed: 0.0498, 0.3679, 2.7183, 20.0855, 148.4132).

The text states that neighbouring bands "tend to have constant ratios" (p. 346) [2]. No numeric value of the ratio is printed in either paper [1], [2]. The abstract of the defining primary states that centre frequencies and ranges "form an arithmetic progression on the natural logarithmic scale" [3].

The four slow classes convert to frequency as 0.025–0.0667, 0.0667–0.200, 0.200–0.500 and 0.500–1.429 Hz (computed). The centre of each class is taken as the geometric mean of its limits. All values below are computed from the printed labels [2].

Class	Limits (Hz)	Upper/lower	Geometric centre (Hz)	ln(centre)
slow 4	0.025–0.0667	2.67	0.0408	–3.20
slow 3	0.0667–0.200	3.00	0.1155	–2.16
slow 2	0.200–0.500	2.50	0.3162	–1.15
slow 1	0.500–1.429	2.86	0.8452	–0.17
delta	1.5–4	2.67	2.4495	0.90
theta	4–10	2.50	6.3246	1.84
beta	10–30	3.00	17.3205	2.85
gamma	30–80	2.67	48.9898	3.89
fast	80–200	2.50	126.4911	4.84
ultra fast	200–600	3.00	346.4102	5.85

Adjacent centres differ by factors of 2.83, 2.74, 2.67, 2.90, 2.58, 2.74, 2.83, 2.58 and 2.74 (computed). The geometric mean over the nine steps is $(346.41 / 0.0408)^{(1/9)} = 2.73$ (computed). Each class spans a factor 2.50–3.00; the factors 2.50, 2.67 and 3.00 occur three times each, 2.86 once (computed).

Eight of the nine adjacent pairs share a limit (computed). The one gap lies between slow 1, ending at 1.43 Hz, and delta, starting at 1.5 Hz (computed).

Other lists differ. One gives “<0.5 Hz (ultra-slow oscillations), 0.5–1 Hz (slow oscillations), 1–3.5 Hz (delta), 3.5–8 Hz (theta)”, then alpha, beta, gamma and “>80 Hz (fast oscillations)” [4]. The text of the 2012 review gives theta as “4 to 9 Hz” and gamma as “30 to 90 Hz” (p. 348), against 4–10 and 30–80 Hz in its figure [2].

Sleep is the second subject. In *Drosophila*, rest is “characterized by an increased arousal threshold” and “is homeostatically regulated independently of the circadian clock” [5].

First appearance

The oldest clock read here is a three-protein loop of cyanobacteria. Of its genes, “kaiC is evolutionarily the oldest, and kaiA is the youngest and likely evolved only in cyanobacteria” [6]. The order was drawn from “≈70 complete prokaryotic genomes”; homologues “occur in Archaea and Proteobacteria as well” [6].

No absolute date is given in the abstract [6].

Sleep-like states occur in Cnidaria, “an earlier-branching metazoan lineage” [7]. A sleep-like state is also reported in *Hydra vulgaris* [8]. Neither source gives a date.

In a lizard, slow-wave and REM sleep push the dynamics back “at least to the emergence of amniotes” [9]. An infraslow sleep rhythm is “conserved across amniotes” [10]. No date of the amniote node is given [9], [10].

In zebrafish, “common neural signatures of sleep may have emerged in the vertebrate brain over 450 million years ago” [11]. An age of 450 Myr is $450 \times 10^6 \times 3.15576 \times 10^7 \text{ s} = 1.42 \times 10^{16} \text{ s}$, position 67.01 (computed).

Within mammals, the classes are “largely preserved throughout the mammalian evolution” [1]. “All known oscillations in humans are present in all other mammals investigated to date” (p. 348) [2].

Partners

In all seven lizard species tested, heart rate was modulated by the beta phase [10]. Breathing and muscle tone were modulated in five of the seven [10]. In the bearded dragon, the cerebral-blood-volume rhythm was strongly rhythmic only in sleep and absent in wake [10].

In the octopus, sleep shows “wake-like skin patterning” [12]. Active sleep shows prominent 30-Hz oscillations; quiet sleep shows 12–18-Hz events in the superior frontal lobe [12].

In *Hydra*, the sleep-like state is regulated by homeostasis and needed for cell proliferation [8]. Sleep deprivation changed expression of “212 genes, including cGMP-dependent protein kinase 1 (PRKG1) and ornithine aminotransferase” [8]. Melatonin, GABA and PRKG1 promoted sleep; dopamine induced it [8].

In *Drosophila*, homeostatic regulation of rest depends on *timeless*, not on *period* [13]. Flies lacking arylalkylamine N-acetyltransferase “show increased rest after rest deprivation” [5]. In the fly clock, PER accumulation attenuates *period* mRNA, TIM binds

PER and DBT phosphorylates PER [14].

In mammals, isolated neurons of the suprachiasmatic nucleus each keep a rhythm; coupling holds them in step [15]. Daytime feeding shifts the phase of mouse peripheral tissues by up to 12 h, the nucleus unchanged [16].

The cyanobacterial oscillation was reconstituted “by incubating KaiC with KaiA, KaiB, and adenosine triphosphate” [17]. The cycle “persists even without transcription or translation” [17]. *Synechocystis* sp. PCC 6803 carries two further Kai systems; KaiC1 and KaiC3 “exhibit phase-locked free-running phosphorylation rhythms”, and both systems are needed for the ~24-h rhythm [18].

Sizes

The sizes are spatial reaches of synchrony in cat neocortex, from field potentials in natural states, three animals [19]. Positions use central values.

What	Size	Position	Source
LFP correlation length λ , waking (n = 8)	3.7 ± 0.4 mm	10.29	measured [19]
λ , SWS (n = 15)	13.0 ± 1.2 mm	11.43	measured [19]
λ , REM sleep (n = 11)	3.1 ± 0.5 mm	10.13	measured [19]
Biexponential λ_1 , waking	10.6 ± 0.6 mm	11.25	measured [19]
Biexponential λ_2 , waking and REM	0.03 ± 0.01 mm	5.91	measured [19]
Biexponential λ_1 , REM	7.5 ± 0.5 mm	10.93	measured [19]
Biexponential λ_1 , SWS	16.1 ± 1.5 mm	11.63	measured [19]
Biexponential λ_2 , SWS	13.3 ± 0.9 mm	11.45	measured [19]
Reach of joint silence and firing in SWS	7 mm	10.87	measured [19]

The SWS/waking ratio of λ is $13.0 / 3.7 = 3.5$ (computed).

Times

Ten classes as periods. Limits measured [2]; periods computed as $1/f$, positions of both limits computed.

What	Period	Position
slow 4	15–40 s	35.62–36.51
slow 3	5–15 s	34.62–35.62
slow 2	2–5 s	33.78–34.62
slow 1	0.7–2 s	32.83–33.78
delta	0.25–0.667 s	31.89–32.78
theta	0.1–0.25 s	31.06–31.89
beta	33.3–100 ms	30.06–31.06
gamma	12.5–33.3 ms	29.16–30.06

fast	5-12.5 ms	28.33-29.16
ultra fast	1.67-5 ms	27.33-28.33
Span of the figure	1.67 ms-40 s	27.33-36.51
Span in the text (500-0.05 Hz)	2 ms-20 s	27.50-35.88

The figure spans $40 / 0.00167 = 24,000$ in period, 4.38 decades (computed). Each class spans 0.83-1.00 in position, as $\log_3 2.50 = 0.83$ and $\log_3 3.00 = 1.00$ (computed).

Named rhythms and events. Frequencies measured; periods computed as 1/f.

What	Duration	Position	Source
Alpha, "8 to 12 Hz"	83.3-125 ms	30.89-31.26	[1], [2]
Ultra-slow rhythm, 0.1 Hz	10 s	35.25	[2]
Spindles, "12 to 18 Hz" (p. 349)	55.6-83.3 ms	30.52-30.89	[2]
Spindles, "12 to 16 Hz" (p. 353)	62.5-83.3 ms	30.63-30.89	[2]
Slow oscillation, 0.5-2 Hz	0.5-2 s	32.52-33.78	[2]
Neocortical slow oscillation, 0.5-1.5 Hz	0.667-2 s	32.78-33.78	[2]
Hippocampal ripples, 140-200 Hz	5-7.14 ms	28.33-28.65	[2]
Sharp-wave ripple event	80-150 ms	30.85-31.43	[2]
Cycle of a 40-Hz oscillation	25 ms	29.80	[2]
Membrane time constant	10-30 ms	28.96-29.96	[2]
Mouse hippocampal theta, 6-9 Hz (exploration, REM)	111-167 ms	31.15-31.52	[20]
Mouse hippocampal gamma, 40-100 Hz	10-25 ms	28.96-29.80	[20]
Rodent theta, 6-12 Hz	83.3-167 ms	30.89-31.52	[2]
Carnivore theta, 4-6 Hz	167-250 ms	31.52-31.89	[2]
Human theta, 1-4 Hz	0.25-1 s	31.89-33.15	[2]
Gamma across species, 30-90 Hz	11.1-33.3 ms	29.06-30.06	[2]

Infraslow rhythm of sleep across amniotes, medians as given (measured [10]).

What	Duration	Position
Lizards, beta power, range across individuals	84-134.5 s	37.19-37.61
Lizards, mean across species	113.2 ± 6.8 s	37.46
Human, N2	51 s	36.73
Rat, NREM	47 s	36.66
Pigeon, NREM	49 s	36.70

Mouse, cerebral blood volume	50 s	36.71
Bearded dragon, cerebral blood volume	100 s	37.34
Panther chameleon, skin brightness	175.7 ± 18.3 s	37.86

Human, rat and pigeon periods are “roughly half” those of lizards [10]. The lizard mean over the pigeon value is $113.2 / 49 = 2.31$ (computed). Period correlated with body temperature across species, $R^2 = 0.88$ [10].

Sleep bouts, cycles and daily amounts.

What	Duration	Position	Source
Lizard <i>Pogona vitticeps</i> , SW-REM cycle	~80 s	37.14	measured [9]
Lizard, continuous oscillation per night	6–10 h	42.24–42.70	measured [9]
Octopus, quiet-sleep events	up to 1 s	33.15	measured [12]
Octopus, active-sleep bout	75 ± 28 s	37.08	measured [12]
Octopus, interval between active bouts	~60 min	40.61	measured [12]
Octopus, quiet-sleep bout	50.5 ± 16.43 min	40.45	measured [12]
Octopus, quiet sleep per 24 h (12 × 50.5 min)	~10.1 h	42.71	computed [12]
<i>Hydra</i> , ultradian rhythm	4 h	41.87	measured [8]
<i>Drosophila</i> , longest immobility	up to 157 min	41.48	measured [13]
Zebrafish larvae at recording	7 days post-fertilisation	45.27	measured [11]
Bird in flight, daily sleep	0.69 h	40.27	measured [21]
Bird, SWS episode in flight	10.89 ± 0.81 s	35.33	measured [21]
Bird, SWS episode on land	28.25 ± 1.75 s	36.19	measured [21]
Bird, longest flight	10.02 days	45.60	measured [21]
Bats and opossums, daily sleep	18–20 h	43.24–43.33	measured [22]
Elephant and giraffe, daily sleep	3–4 h	41.61–41.87	measured [22]
Bushtail possum, REM	6.6 h	42.32	measured [22]
African elephant (captive), sleep / REM	3.9 h / 1.8 h	41.85 / 41.14	measured [22]
Platypus, adult REM	8 h	42.50	measured [22]
Guinea pig, REM	1 h	40.61	measured [22]
Sleep cycle, short-tailed shrew	~8 min	38.77	measured [22]

Sleep cycle, Asiatic elephant	1.8 h	41.14	measured [22]
Wild elephant matriarchs, daily sleep	2.3 and 1.8 h	41.36, 41.14	measured [23]
Wild elephants, longest without sleep	up to 46 h	44.09	measured [23]
Captive elephants, reported	3.10–6.90 h	41.64–42.36	measured [23]
Regression prediction for elephants	5.46–5.87 h	42.15–42.22	modelled [23]
Human sleep cycle	90–110 min	40.98–41.16	measured [24]
Human, first / last REM period	~10 min / up to 1 h	38.98 / 40.61	measured [24]

Windows of firing and periods of clocks.

What	Duration	Position	Source
Spike-count windows, V1	1,000 and 200 ms	33.15, 31.69	measured [25]
Window of fast-oscillation synchrony, cat	100–500 ms	31.06–32.52	measured [19]
Population ON / OFF period in NREM, rat	815.5 ± 119.9 / 85.8 ± 5.9 ms	32.97 / 30.92	measured [26]
KaiC phosphorylation cycle	24 h	43.50	measured [27]
<i>S. elongatus</i> luminescence in vivo, 30 °C	25.6 ± 0.1 h	43.56	measured [27]
Human intrinsic circadian period	24.18 h	43.51	measured [28]
Peripheral phase shift by feeding, mouse	up to 12 h	42.87	measured [16]
Age at which common vertebrate sleep signatures “may have emerged”	over 450 Myr	67.01	inferred [11]

Counts

The list has ten classes, four printed as periods and six as frequencies [2]. Across mammals “brain rhythms vary little across species (30% to 100%), brain size increases hundreds- to thousands-fold” (p. 350) [2]. Gamma has “the same frequency range (30 to 90 Hz)” across the species discussed, and spindles “the same frequency (12 to 18 Hz)” [2].

The infraslow study recorded 7 lizard species at 20–27 °C, 5 rats, 11 pigeons and 8 humans; ultrasound covered 4 bearded dragons and 4 mice [10]. The octopus has two sleep stages, with 10 ± 3.5 active and 12 ± 3 quiet bouts per 24 h [12]. *C. elegans* lethargus “occurs before each of the four moults” [29].

Zebrafish show “at least two major sleep signatures”, “slow bursting sleep” and “propagating wave sleep” [11]. A lizard night holds 6 h / 80 s = 270 to 10 h / 80 s = 450 SW-REM cycles (computed).

Birds in flight slept 7.4 % of their sleep on land [21]. Time asleep was 2.89 ± 0.58 % in flight against 53.28 ± 4.82 % on land; N = 14 and 9 [21]. Unihemispheric share of asymmetric SWS was 47.27 ± 5.30 % against 24.96 ± 2.26 % [21].

In mammals, log body weight against sleep amount gives $R = -0.5$, $P < 0.0001$, $n = 71$, about 25 % of the variance [22]. Brain weight and encephalisation “correlate poorly and negatively” with NREM and REM amounts [22]. The sleep cycle ratio, elephant over shrew, is $108 / 8 = 13.5$ (computed).

The wild elephants were recorded 35 days each; recumbent sleep came on 10 of 35 days [23]. Days without sleep for up to 46 h number 4 in the results and 5 in the discussion [23]. The all-mammal regression is $TST = 17.946 \times Mb^{-0.076}$, $r^2 = 0.25$ (modelled [23]).

A human night holds 4 to 6 cycles: N1 5 %, N2 45 %, N3 25 %, REM 25 % [24]. The intrinsic period of 24.18 h holds in young and older adults [28].

KaiC consumes “15 ATPs” “per day per KaiC subunit”; the null mutant KaiC-AA is “reported to consume 27 ATP molecules per day” [27]. That is $15 / 24 = 0.63$ ATP per hour, and $27 / 15 = 1.8$ times the wild-type rate (computed). The period in vitro “was stable despite temperature change (temperature compensation)” [17].

Order of events

One source gives an age, inferred. Other entries follow the sources’ order of sequence without dates, so they carry no position.

- Not dated: *kaiC* oldest of the clock genes; *kaiA* youngest, likely cyanobacterial only [6].
- Not dated: sleep-like states in Cnidaria and *Hydra* [7], [8].
- More than 450 Ma: common neural signatures of sleep “may have emerged” in the vertebrate brain (inferred [11]). Position 67.01 (computed).
- Not dated: SW and REM dynamics at least from the emergence of amniotes [9]; infraslow rhythm across amniotes [10].
- Not dated: oscillation classes preserved through mammalian evolution [1].

Present quantities

Spike-count correlations in awake cortex. Trial-to-trial correlations of spike counts between pairs recorded together (r_{sc}). All values measured.

#	Value	Species, area	State	Source
1	0.12	monkey, area not named	awake	[30]
2	0.20 (SD 0.15), $n = 57$	macaque MT	awake task; $\Delta PD < 90^\circ$	[31]
3	-0.02 (SD 0.09), n	macaque MT	awake task; $\Delta PD \geq$	[31]

	= 12		90°; ≈ 0	
4	0.06 (SD 0.15), n = 34	macaque MT	awake task; non-directional cell; ≈ 0	[31]
5	0.058 ± 0.001 , 3,240 pairs	macaque V4	awake fixation, evoked	[32]
6	0.110 ± 0.003 , 1,122 pairs	macaque V4	awake fixation, spontaneous	[32]
7	around 0.08	macaque V4	awake, desynchronized	[33]
8	0.10 ± 0.02	macaque V1, supragranular	awake, 1 s window	[25]
9	0.09 ± 0.02	macaque V1, granular	awake, 1 s window	[25]
10	0.08 ± 0.02	macaque V1, infragranular	awake, 1 s window	[25]
11	0.05 ± 0.01	macaque V1, supragranular	awake, 200 ms window	[25]
12	0.01 ± 0.01	macaque V1, granular	awake, 200 ms window	[25]
13	0.05 ± 0.01	macaque V1, infragranular	awake, 200 ms window	[25]

Nine values lie below 0.1, one equals 0.1 and three lie above; range -0.02 to 0.20 (computed). The pair-weighted MT mean is $(57 \times 0.20 + 12 \times -0.02 + 34 \times 0.06) / 103 = 0.128$ (computed).

Measure	Value	Species, area	State	Source
r_signal against r_noise, 103 pairs	$r = 0.61$	macaque MT	awake	[31]
Spontaneous / evoked r_sc	$1.9 (0.110 / 0.058, \text{computed})$	macaque V4	awake	[32]
V4 against V1 variability	about one-third of V1	macaque	awake	[32]
r_sc, 703 pairs	"relatively close to zero"	macaque V4	awake, desynchronized	[33]
Synchronized against desynchronized	higher; delay $P < 0.0001$, evoked $P < 0.001$	macaque V4	awake	[33]
Decrease, synchronized to desynchronized	approximately 20 %	macaque V4	awake	[33]
Nearby similarly tuned neurons	"virtually no correlated variability"	macaque V1	awake	[34]
Mean correlation	"Near-zero"	rodent neocortex	in vivo	[35]
Attentional gain from lower correlation	over 80 %	macaque V4	awake, attention	[36]

The desynchronized V4 state carries two phrases in one paper, “close to zero” and “around 0.08” [33]. The V1 values were a bit higher than in the authors’ earlier studies with awake fixating animals [25]. Attention “can either increase or decrease spike count correlations” [37].

Under anaesthesia or of unstated state. All values measured.

Measure	Value	Area	State	Source
Corrected mean (Smith & Kohn 2008), rate 3.4 Hz	0.18	V1	not stated	[38]
Median noise correlation, 1,291 / 759 / 1,014 pairs	0.020 / 0.015 / 0.007	macaque IT / V4 / V1	anaesthetised	[39]
Median signal correlation	0.070 / 0.039 / 0.083	macaque IT / V4 / V1	anaesthetised	[39]
Spontaneous, total and noise correlations	“uniformly higher in synchronized states”	visual cortex	anaesthetised	[40]
Pairwise correlations	lower when awake	rat visual cortex	awake against anaesthetised	[41]

Slow-wave sleep against waking. Same animals in each row. All values measured.

Measure	Wake	SWS / NREM	REM	Direction	Source
LFP correlation length λ , cat	3.7 mm	13.0 mm	3.1 mm	higher in SWS	[19]
Joint silence and firing of units, cat	fast (15–75 Hz) synchrony only between neighbouring electrodes	within 7 mm	as wake	higher in SWS	[19]
Pairs with significant CCG peak, rat (14,343 pairs)	not read	10.8 $\pm$ 6.3 %	not read	wake value not read	[42]
Pairs with significant trough, rat	not read	3.6 $\pm$ 3.4 %	not read	wake value not read	[42]
Pairs negative only in that state, wake/NREM	0.66 %	2.31 %	—	more in NREM	[42]
Pairs negative only in that state, NREM/REM	—	2.56 %	0.06 %	more in NREM	[42]
NREM coupling against other state	R = 0.33	—	R = 0.16	—	[42]
Zero-lag E-I	0.726	0.47	0.503	lower in SWS	[43]

ensemble correlation, human					
E-I correlation, monkey	—	differs from awake, $P = 10^{-3}$	—	lower in SWS	[43]
LFP-blood-volume coupling, dragon, mouse	absent or weak	stronger ($P < 0.001$, mouse)	weaker than NREM	higher in sleep	[10]
Principal-cell synchrony, hippocampus	lowest in theta	highest	—	higher in SWS	[2]

The rows form five sleep comparisons:

1. Cat LFP correlation length: 13.0 mm in SWS against 3.7 mm awake; higher [19].
2. Cat units: joint silence and firing within 7 mm in SWS; higher [19].
3. Dragon and mouse infraslow coupling, present only or stronger in sleep; higher [10].
4. Human E-I ensemble correlation: 0.47 in SWS against 0.726 awake; lower [43].
5. Rat pairs: more synchronised and more anticorrelated pairs in NREM; wake peak values not read; mixed [42].

The count is 3 higher, 1 lower and 1 mixed or not fully read (computed). The human E-I value in SWS is $0.47 / 0.726 = 0.65$ of the awake one (computed). The rat abstract states that “most pairs of neurons were synchronized”, with a minority desynchronized in NREM [42].

NREM shows “a several fold increase in long ISIs (>100 ms)” against waking and REM [26]. Synchrony at ON-OFF transitions “decreased by 18% from early to late sleep”, and by 24 % at OFF-ON transitions [26].

In human sleep (13 patients, 600 units), firing at EEG positivity was 39 ± 1 % of the mean NREM rate, at negativity 198 ± 11 % [44]. “85% $\pm$ 0.7% of slow waves were detected in less than half of the recording sites”; mean involvement was 27.1 ± 0.4 % of regions [44]. Spindles of 10-16 Hz were in less than half the regions in 75.8 ± 0.9 % of cases [44].

Seizures against the period before. All values measured.

Measure	Outside seizure	Seizure	Direction	Source
Cross-correlation, rat slices, 4AP (22 slices, 8 rats)	interictal	lower in 27 of 30 pairs	lower	[45]
Mutual information, same	interictal	lower in 28 of 30	lower	[45]
Broadband phase correlation, same	interictal	lower in 28 of 30	lower	[45]
Interictal bursts	synchronized in 14 of 16	—	—	[45]
Onset cross-	mean during	66 % of that mean	lower	[45]

correlation, Schaffer collaterals intact	bursts			
Single-neuron spiking, human	—	“not hypersynchronous” at onset; “nearly homogenous” at end	not higher; higher at end	[46]
Multiscale synchrony, human iEEG	pre-seizure	up at smallest and largest scales	higher	[47]
Network flexibility, human ECoG (88 seizures, 21 patients)	0.665 ± 0.205	0.274 ± 0.165	lower	[48]
Connection density, same	not printed	S0 0.304, S1 0.333, S2 0.338	rising within	[48]
Connection-type index, same	about -0.401	S0 0.023, S1 0.437, S2 0.512	strong links dominate	[48]
E-I population correlation, human (6 seizures, 2 patients)	balanced	“disrupted”	lower	[43]

The rows form five seizure comparisons:

1. Rat slices, 4AP: pairwise measures lower in 27–28 of 30 pairs; lower [45].
2. Human single neurons: “not hypersynchronous” at onset and spread; not higher [46].
3. Human iEEG: synchrony up at the smallest and largest scales; higher [47].
4. Human ECoG: connection-type index -0.401 before against 0.023 – 0.512 within; strong links dominate; higher [48].
5. Human E–I population correlation: “disrupted”; disrupted [43].

The count is 2 higher and 3 lower, not higher or disrupted (computed).

The slice authors write: “Unexpectedly, seizure-like events in 4AP were desynchronous events” [45]. In human focal epilepsy, neurons outside the onset zone changed “minutes before the seizure” [46]. Network flexibility fell by a factor $0.665 / 0.274 = 2.43$ (computed).

Pattern

One group publishes ten classes, from 15–40 s to 200–600 Hz. Positions run from 36.51 to 27.33. Computed centres step by 2.58–2.90, mean 2.73; each class spans a factor 2.50–3.00.

Frequencies vary 30–100 % across mammals while brain size varies hundreds- to thousands-fold. The 12–18 Hz range is printed for mammalian spindles and octopus quiet-sleep events.

Infraslow sleep periods are 47–51 s in endotherms and 84–134.5 s in lizards. Sleep-like states occur from *Hydra* to mammals; daily sleep spans 0.69 h to 20 h.

Nine of thirteen awake spike-count means lie below 0.1. Of five sleep comparisons, 3 show more co-activity in SWS, 1 lower E-I correlation, 1 mixed. Of five seizure comparisons, 2 show higher synchrony and 3 lower, not higher or disrupted.

Not verified

- The class table of the 2003 primary; only its abstract was read [3].
- A secondary count of “10 frequency bands extending from 0.02 to 600 Hz” [49].
- A binary hierarchy with centres 2.5, 5, 10, 20 and 40 Hz; preprint author unconfirmed [50].
- The 2013 Neuron review on rhythms preserved across brain sizes; text not read [51].
- *Cassiopea* pulsing ~39 against ~58 per minute (night/day), floating up to 5 s after disturbance [52].
- Near-zero correlations in anaesthetised rat auditory cortex, as described by a later paper [33].
- The numeric means behind “virtually no” and “near-zero” correlation [34], [35].
- Duration of lethargus in *C. elegans* [29].
- Absolute dates of the kai genes [6].
- Species of the octopus and of the birds in flight [12], [21].

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A8 Learning and Memory

What it is

The sources record three forms of learning: habituation, sensitisation and association. They also record the synaptic and cellular changes that accompany memory, and its durations.

In the slime mould *Physarum polycephalum*, habituation was tested “with chemotaxis as the behavioural output and quinine or caffeine as the stimulus” [1]. The organism “learnt to ignore the stimuli when they were repeated, but responded again when the stimulus was withheld” [1]. The criteria met were “responsiveness decline and spontaneous recovery”, plus “stimulus specificity” [1].

In the sea hare *Aplysia*, the gill-withdrawal reflex is mediated by identified motor neurons of the abdominal ganglion [2]. It habituates to repeated touch of siphon or mantle shelf [2]. It recovers after rest and is dishabituated by a strong stimulus elsewhere [2].

After long-term sensitisation in *Aplysia*, monosynaptic sensory-to-motor connections

were “significantly larger (2.2x)” than in controls [3]. Inhibitors of protein synthesis (anisomycin, emetine) and of RNA synthesis (actinomycin D, alpha-amanitin) “blocked long-term facilitation without interfering with short-term facilitation” [3].

In cultured rat hippocampal neurons, postsynaptic spiking “within a time window of 20 msec after presynaptic activation resulted in long-term potentiation” [4]. Spiking “within a window of 20 msec before” presynaptic activation led to long-term depression [4]. The mean changes were $+48.4 \pm 9.9 \%$ and $-18.0 \pm 3.2 \%$ [4].

Long-term potentiation has an early and a late phase. The early phase lasts “less than three hours”, and “The synaptic tag decays in less than three hours” [5]. Late LTP needs transcription and translation [5].

The term “engram” was introduced by Richard Semon in 1904 for the neural substrate of a memory, as given by a 2020 review [6]. An experience activates a subset of cells that undergo lasting chemical and/or physical change; reactivation induces retrieval [6].

In mice, light stimulation of dentate-gyrus cells labelled during fear conditioning recalled the fear. “The mice showed increased freezing only upon light stimulation” [7]. Recall came from “activating a sparse but specific ensemble of hippocampal neurons” [7].

First appearance

No source read gives a fossil or molecular-clock date for learning. The record consists of living species only.

Groups without neurons in which learning is recorded: a ciliate, *Stentor coeruleus* [8]; an amoebozoan plasmodium, *Physarum* [1]; and a flowering plant, *Mimosa pudica* [9]. Learning in pea seedlings is reported [10] and not replicated [11].

Groups with centralised nervous systems in which learning is recorded: planarian [12], nematode [13], molluscs (*Aplysia* [2], octopus [14]), insects (fly [15], bee [16]) and mammals [17].

Partners

The long phase of memory needs protein synthesis in four groups. In *Aplysia*, long-term facilitation needs protein and RNA synthesis; short-term facilitation does not [3]. In *C. elegans*, a heat-shock block of protein synthesis during training “blocked consolidation” [13].

In the honeybee, the early long-term memory (eLTM) is protein-synthesis independent; the late one (lLTM) is protein-synthesis dependent [16]. In the rat, late LTP needs transcription and translation [5].

In the bee, the reinforcing neuron VUMmx1 is one of 15 ventral unpaired median neurons of the suboesophageal ganglion [16].

The hippocampus is a partner of early memory in mammals. In rats conditioned to tone and context, hippocampal lesions were made at 1, 7, 14 or 28 days after training [18]. Contextual fear was abolished only by lesions 1 day after training; tone fear was

unaffected at any interval [18].

In humans, memories of everyday life “depend initially on the medial temporal lobe system, including the hippocampus” [19]. Damage there disrupts recent memories more than older ones, in humans and rodents [19].

Replay occurs in sleep. Place cells co-active at nearby positions during a task were more likely to fire together in the following slow-wave sleep, in three rats [20]. The tendency declined over each post-task sleep session [20].

Sharp-wave ripple events “last 80-150 ms” and carry ripples of 140–200 Hz [21]. The number of cell assemblies that can nest in one theta period is “7 to 9” [21].

In the slime mould, a learned response passes by fusion. Transfer of the habituated response occurred “when fusion was lengthened to 3 h”; 1 h was not enough [22]. “Veins between the two slime moulds are apparent after 2 h” [22].

“A minimum of habituated individuals is required” for transfer [22]. The habituation index rose with the proportion of habituated plasmodia up to about 0.4 and then levelled [22].

In plants, the context of growth modifies habituation. In *Mimosa*, habituation of leaf folding was “more pronounced and persistent for plants growing in energetically costly environments” [9]. In pea seedlings, “learning was successful only when it occurred during the subjective day” [10].

Sizes

What	Size	Position	Source
Scale bar on the <i>Stentor</i> cell image	200 μm	7.63	measured [8]
Reversal distance after a tap, <i>C. elegans</i>	around 1 mm	9.10	measured [13]
Honeybee brain volume, 1 μL = 1 mm^3 ; edge of an equal cube	1 mm	9.10	computed from [16]

The bee brain holds 950,000 neurons in 1 mm^3 , a density of 9.5×10^5 neurons per mm^3 (computed from [16]).

Times

Training schedules and stimulus intervals.

What	Duration	Position	Source
<i>Stentor</i> , stimulus interval	1 min	36.88	measured [8]
<i>Stentor</i> , other intervals	2.5 min; 1.2 s	37.71; 33.32	measured [8]
<i>Stentor</i> , pause before recovery test	15 min	39.34	measured [8]
<i>Physarum</i> , habituation	5 days	44.96	measured [1]

phase			
<i>Physarum</i> , whole experiment	9 days	45.50	measured [1]
<i>Physarum</i> , fusion needed for transfer	3 h	41.61	measured [22]
<i>Aplysia</i> , intersession interval, rapid protocol	1.5 h	40.98	measured [23]
<i>Aplysia</i> , whole rapid protocol	5 h	42.07	measured [23]
<i>C. elegans</i> , tap interval, short-term	10 s	35.25	measured [13]
<i>C. elegans</i> , tap interval, long-term	60 s	36.88	measured [13]
<i>C. elegans</i> , interval between blocks	1 h	40.61	measured [13]
<i>C. elegans</i> , salt exposure without food	4 h	41.87	measured [13]
<i>C. elegans</i> , oxygen learning at 1 % O ₂	4–6 h	41.87–42.24	measured [13]
Honeybee, spaced trials	10 min apart	38.98	measured [16]
Honeybee, massed trials	30 s apart	36.25	measured [16]
Pea, training	3 days	44.50	measured [10]
Optogenetic recall, light-on period	3 min	37.88	measured [7]
LTP-inducing train, 400 Hz	25 ms	29.80	measured [17]

Memory and plasticity durations.

What	Duration	Position	Source
Spike-timing window, before or after	20 ms	29.59	measured [4]
Sharp-wave ripple event	80–150 ms	30.85–31.43	measured [21]
Honeybee colour memory, early minimum	roughly 2–3 min	37.51–37.88	measured [24]
Honeybee colour memory, rise after the minimum	10–20 min	38.98–39.61	measured [24]
<i>Stentor</i> , recovery of 90 % of cells	within 15 min	39.34	measured [8]
<i>Drosophila</i> mutants (<i>amnesiac</i> , <i>rutabaga</i> , <i>dunce</i>), rapid decay	first 30 min	39.98	measured [15]
<i>Drosophila</i> mutants, memory still measurable	at least 3 h	41.61	measured [15]
Early LTP; synaptic tag	< 3 h	41.61	measured [5]
<i>Physarum</i> , crossing time of trained plasmodia on day 1	4 h	41.87	measured [1]

<i>Physarum</i> , crossing time of controls	about 1 h	40.61	measured [1]
<i>Drosophila</i> wild type, gradual decay	first 7 h	42.38	measured [15]
<i>Drosophila</i> wild type, memory present	24 h	43.50	measured [15]
<i>C. elegans</i> , long-term habituation tested	24 h	43.50	measured [13]
<i>Aplysia</i> , synaptic decrement in isolated ganglion	24 h later	43.50	measured [23]
Honeybee eLTM	1–2 d	43.50–44.13	measured [16]
<i>Physarum</i> , stimulus withheld before recovery	2 days	44.13	measured [1]
Honeybee ILTM	≥ 3 d	44.50	measured [16]
Octopus, correct choice without further conditioning	5 days	44.96	measured [14]
<i>Aplysia</i> , rapid long-term habituation	> 1 week	45.27	measured [23]
Planarian, familiarisation memory	≥ 14 days	45.90	measured [12]
<i>Aplysia</i> , long-term habituation	≥ 3 weeks	46.27	measured [25]
<i>Mimosa</i> , learned response kept, undisturbed	a month (30 d taken)	46.60	measured [9]
LTP decay τ , 5 trains	0.7 d	43.17	measured [17]
LTP decay τ , 20 trains	1.0 d	43.50	measured [17]
LTP decay τ , 4×5 trains (decremental)	3.3 d	44.59	measured [17]
LTP decay τ , 50 trains, short baseline	32 d	46.65	measured [17]
LTP decay τ , lateral perforant path	42 d	46.90	measured [17]
LTP decay τ , the one-year animal	127 d	47.91	measured [17]
Stable-LTP animals, recording span	42–119 days (mean 68)	46.90–47.85 (47.34)	measured [17]
LTP, longest record	369 days	48.88	measured [17]

Ebbinghaus intervals in the replication [26].

Interval	Position
20 minutes	39.61
1 hour	40.61
9 hours	42.61

1 day	43.50
2 days	44.13
6 days	45.13
31 days	46.63

All intervals measured [26].

Dendritic spines, school Spanish and hippocampal dependence.

What	Duration	Position	Source
Hippocampal dependence of contextual fear, rat	lesion at 1 day abolishes; at 7 days spares	43.50; 45.27	measured [18]
Mean spine lifetime, mouse CA1	approximately 1-2 weeks	45.27-45.90	measured [27]
Full CA1 turnover, 2-3 × 1-2 weeks	2-6 weeks	45.90-46.90	computed from [27]
Stable spines (about 50 %), barrel cortex	at least a month (30 d taken)	46.60	measured [28]
Adult spine half-life, cortex	> 13 months (390 d taken)	48.93	measured [29]
Spanish, exponential loss	first 3-6 years	49.87-50.50	measured [30]
Spanish, roughly unchanged	up to 30 years	51.97	measured [30]
Spanish, permastore response life span	6-25 years	50.50-51.80	measured [30]
Spanish, whole study span	50 years	52.43	measured [30]

One year is taken as 3.15576×10^7 s and one month as 30 d (computed). The durations read run from 0.02 s to 1.58×10^9 s, 10.90 decades (computed). In position, they run from 29.59 to 52.43 (computed).

Counts

C. elegans has “302 neurons”; “959 cells make up the entire adult hermaphrodite”; it has “about 5000 chemical synapses” [13]. The honeybee has “a brain as small as 1 μ L containing 950,000 neurons” [16]. The ratio of bee to worm neurons is $950,000 / 302 = 3,146$ (computed).

Chapter A9 gives the honeybee brain as about 960,000 neurons, from Menzel & Giurfa 2001.

Stentor habituation used 30 stimuli at 1-min intervals, in 31 cells (Fig. 1G) and 44 cells (Fig. 1H) [8]. The 2.5-min interval used 43 cells [8]. “Within 15 minutes, 90% of habituated cells became fully responsive again” [8].

Physarum studies introduced 416 plasmodia, excluded 6 and used 410: quinine 140, caffeine 70, control 200 [1]. Quinine was 4 mM and caffeine 1 mM; caffeine was crossed only below 2 mM in tests at 1-4 mM [1]. Trained plasmodia later “crossed the bridge

twice as fast” [1].

Aplysia long-term habituation took “Five” daily ten-trial sessions [25]. Spaced sessions gave longer-lasting habituation than massed training [25]. The rapid protocol used “Four ten-trial training sessions”, “only 40 patterned stimuli” [23].

C. elegans tap habituation plateaus “after about seven taps at a 10-sec ISI” [13]. Long-term memory followed “four blocks (each separated by 1 h) of 20 taps at a 60-sec ISI” [13]. Worms “massed trained with 80 taps” did not retain at 24 h [13].

Larval regimes were “seven blocks (separated by 1 h) of 15 taps” and “five blocks (separated by 1 h) of 20 taps” [13]. Salt aversion reversed “within 10 min” if NaCl came with food [13]. AFD thresholds were 15, 17 and 21 °C for cultivation at 15, 20 and 25 °C [13].

In the honeybee, “Three learning trials produce a stable long-term memory” [16]. “A life-long memory of a colour signal is already established after 3 operant learning trials” [24]. The spontaneous response of hungry bees to an odour is “a few percent up to 30%” [24].

In *Drosophila*, about 150 flies per chamber received twelve shock pulses with the first odour [15]. “Typically, 95% of trained flies avoided the shock-associated odor” [15].

Order of events

The sources read give no evolutionary dates for learning. The capacities are listed in the order of the groups as the chapter describes them, without dates or positions.

- Ciliate, *Stentor coeruleus*: habituation with recovery [8].
- Slime mould, *Physarum*: habituation with recovery; transfer of the habituated response by fusion [1], [22].
- Flowering plant, *Mimosa pudica*: habituation of leaf folding [9].
- Pea seedlings: conditioning reported [10] and not replicated [11].
- Planarian: familiarisation memory [12].
- Nematode, *C. elegans*: tap habituation and long-term memory [13].
- Mollusc, *Aplysia*: habituation, dishabituation and long-term sensitisation [2], [3], [25].
- Mollusc, octopus: observational learning [14].
- Insect, *Drosophila*: classical conditioning [15].
- Insect, honeybee: stable long-term memory after three trials [16].
- Mammals, rat: long-term potentiation lasting months [17].

Present quantities

Long-term potentiation in vivo, rat. Trains of “400 Hz, 25 msec”; all values measured [17].

Protocol	Animals with stable LTP	τ of decay
5 trains	0/6	0.7 d
20 trains	1/6	1.0 d
4 × 5 trains	3/6	3.3 d (decremental animals)

50 trains, long baseline	8/12	—
50 trains, short baseline	1/9	32 d
Lateral perforant path	3/4	42 d
One animal, 369 days	—	127 d

The asymptote was 21 ± 3 % in the stable group against 0.4 ± 1 % in the decremental group [17]. The one-year animal kept 13 % on the 119-day fit and 10 % on the 369-day fit [17]. The τ values span $127 / 0.7 = 181$ -fold (computed).

Dendritic spines. All values measured.

Measure	Value	Species, region	Source
Stable spines, persisting at least a month	about 50 %	mouse barrel cortex	[28]
Other spines	“a few days or less”	mouse barrel cortex	[28]
Spines stable over one month, young	~73 %	mouse cortex	[29]
Spines stable over one month, adult	~96 %	mouse cortex	[29]
Adult half-life	“greater than 13 months”	mouse cortex	[29]
Mean lifetime	approximately 1-2 weeks	mouse CA1	[27]
Full turnover	“~2-3 times this interval”	mouse CA1	[27]
New spines from novel experience kept	“a small fraction”, “throughout the entire life”	mouse	[32]

The two 2002 papers disagree for adult cortex over one month: about 50 % against about 96 % stable [28], [29]. Both are recorded. CA1 turnover “differed sharply” from neocortex [27].

Plants. Habituation in *Mimosa* “exhibits clear habituation”, with the learned response shown “even when left undisturbed in a more favourable environment for a month” [9]. A 2016 review states that “it is critical that the Gagliano et al. (2014) results be repeated by an independent laboratory” [33]. It also states that without data across intertrial intervals “it is difficult to separate sensory adaptation from habituation” [33].

Pea conditioning, original and replication. All values measured.

Measure	Original 2016	Replication 2020	Source
Fan and light on the same arm: share towards the fan	62 %	—	[10]
Fan and light on opposite arms: share away from the fan	69 %	—	[10]
Training in the subjective day / light-dark / dark	61 % / 47 % / 20 % (83 seedlings)	—	[10]

Counted plants, F + L / control	31 / 20	61 / 60	[11]
Counted plants, F vs L / control	13 / 9	42 / 40	[11]
F + L against control	p = 0.0027 (n = 13 + 10)	p = 0.335 (n = 61 + 60)	[11]
F vs L against control	p = 0.0017 (n = 13 + 9)	p = 0.387 (n = 42 + 40)	[11]
Fan opposite against fan adjacent	—	p = 0.1713	[11]

Experiment 1 of the original used 45 seedlings: 26 test, 13 per condition, 19 controls, over 3 training days and 1 test day [10]. Controls all grew to the last light [10]. The replication describes the original as “approximately two thirds of experimental plants showed behavior influenced by the fan” [11].

Forgetting curves. The Ebbinghaus replication used 104 nonsense syllables per list, 8 rows of 13 [26]. Savings at 31 days were 0.0410, 0.137 corrected [26]. The curve shows “a jump upwards starting at the 24 hour data point”, with fitted boosts of 0.030 (Ebbinghaus) and 0.131 (Mack & Seitz) [26].

School Spanish was tested in 733 people over 50 years [30]. Retention fell exponentially for the first 3–6 years, then held roughly unchanged up to 30 years before a final decline [30]. Responses fell into two groups with life spans of 0–6 years and 6–25 years (“permastore”) [30].

Other. The sleep spectrum in the 8–16 Hz band allows “>90% correct discrimination among individuals” [21]. The twin correlation of gamma is “r = 0.9” [21].

Pattern

Habituation with recovery is recorded in a ciliate, a slime mould and animals from worms to mammals; habituation in a plant is also recorded. Spaced training gives memory of days to weeks in *Aplysia*, worm and bee; massed training gives shorter-lasting habituation in *Aplysia* and no retention at 24 h in the worm. The phase lasting beyond hours needs protein synthesis in rat, *Aplysia*, worm and bee.

Plasticity has a 20-ms timing window, position 29.59. Durations read reach 50 years, position 52.43, a span of 10.90 decades. LTP decay constants run 0.7–127 days; one record lasts 369 days.

Adult cortical spines are 50 % or 96 % stable over a month in two studies; CA1 spines live 1–2 weeks.

Two forgetting curves show breaks, at 24 h and at 3–6 years. Pea conditioning did not replicate.

Not verified

- *Stentor* forgetting timescales of “2–6 hours” and “less than 1 hour”, cited from 1970 [34].
- Journal of publication of the *Stentor* study [8].

- Associative learning in the box jellyfish *Tripedalia cystophora*; citation verified, numbers not read [35].
- First LTP report: potentiation of 1 h to 3 days on 26 % of occasions; the abstract read may belong to a companion paper [36].
- Transient and persistent spines in neocortex; citation verified, numbers not read [37].
- Loss of recent memory after bilateral hippocampal lesions; contents not read [38].
- Iconic memory in brief visual presentations; values not read [39].
- Recall decrements after 10 s (1940) and 5 s (1958), as summarised in a 1959 abstract [31].
- Plant habituation from Pfeffer 1873, Holmes & Gruenberg 1965 (recovery about 15 min) and Applewhite 1972, via a review [33].
- Drop protocol and exact retention in days of the 2014 *Mimosa* study [9].
- Numbers for lifelong spines formed by learning [32].

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A9 Minds in Many Bodies

What it is

This chapter collects measured nervous systems and measured capacities outside the human line. It covers cephalopods, insects, birds, teleost fish, elephants and whales. It closes with dated statements by named authors on which animals are conscious.

Complex brains are recorded in several lineages that do not share a complex-brained ancestor [1]. One review names insects, octopodid molluscs, teleosts, corvid and psittacid birds, cetaceans, elephants and primates as groups where complex brains and high intelligence “evolved several times independently” [1]. The same review pairs each group with a multimodal brain centre: mushroom bodies in insects, the vertical lobe in octopodids, the pallium in birds and the cerebral cortex in primates [1].

The capacities recorded include counting, self-control, planning, tool construction, social learning, play and mirror self-recognition. The statements on consciousness at the end are positions held by the authors named, with their dates. They are reported as positions, not as findings about consciousness.

First appearance

Cephalopods. A molecular clock built from 180 genes, about 36,000 amino acids and 26 species dates the coleoid cephalopods (squid, cuttlefish, octopus) [2]. The study places the crown coleoid divergence in the Silurian-Devonian [2]. It dates the vampire squid and dumbo octopus lineages to 242 ± 38 Ma, in the Early Mesozoic [2].

The decabrachians (squid and cuttlefish) diversified in the Jurassic in the same study [2]. The authors note that this timing coincides with the Mesozoic Marine Revolution [2]. The interval 242 ± 38 Ma runs from 204 Ma to 280 Ma (computed).

Amniotes. Neuron numbers were compared across reptiles, birds and mammals in one analysis [3]. The high neuron counts of endothermic land vertebrates are reached through “as few as four major changes in neuron-brain scaling over 300 million years” [3]. Mammals and birds have “dramatically increased neuron numbers in the telencephalon and cerebellum” compared with reptiles [3].

Vertebrate sensory consciousness, as dated by Feinberg and Mallatt (2013).

Feinberg and Mallatt state that vertebrates arose in the Cambrian, before 520 Ma [4]. They propose multiple levels of isomorphic somatotopic maps as a marker of sensory consciousness. Because all living vertebrates have such maps, they date sensory consciousness to the origin of the group [4].

In the same paper the lamprey is proposed to have the basic requirements for the simplest qualia [4]. This is the authors’ stated position.

Insect subjective experience, as dated by Barron and Klein (2016). Barron and Klein propose that “at least one invertebrate clade”, the insects, has the capacity for subjective experience [5]. They base this on insect brain structures that perform functions analogous to integrated vertebrate midbrain structures [5]. They state that the origins of consciousness “can be traced to the Cambrian” [5].

Birds, as stated by Nieder, Wagener and Rinnert (2020). Single pallial neurons in crows tracked reported perception in a visual detection task [6]. The response came in two stages: the first stage followed mainly stimulus intensity, the later stage the crows’ report [6]. The authors conclude that the neural basis may have arisen before the bird-mammal split, or independently in birds, without a layered cortex [6].

Fish nociceptors. Trigeminal receptors in rainbow trout respond to mechanical pressure, to temperatures in the noxious range “more than 40 degrees C” and to 1 % acetic acid [7]. Noxious stimulation raised the opercular beat rate [7]. It also lengthened the time taken to resume feeding “over a prolonged period of time” [7].

Partners

The octopus genome. The genome of *Octopus bimaculoides*, the California two-spot octopus, has a core gene repertoire like that of other invertebrate bilaterians [8]. Two gene families “formerly thought” vertebrate-specific are expanded: the protocadherins and the C2H2 zinc-finger transcription factors [8]. The genome shows extensive RNA editing and hundreds of cephalopod-specific genes [8].

RNA editing in coleoids. Coleoid cephalopods carry “tens of thousands of evolutionarily conserved sites” of RNA editing [9]. The sites are enriched in the nervous system, in molecules for excitability and neuronal morphology [9]. The genomic

sequence flanking the sites is highly conserved [9].

Neurogenesis in the octopus embryo. In *Octopus vulgaris* embryos the neural progenitors lie outside the central brain cords [10]. They sit near the lateral lips beside the eyes [10]. Newly formed postmitotic neurons migrate from there into the cords over long distances [10].

Lineage tracing shows that lip location sets the lobe supplied [10]. No division of differentiated neurons is reported [10].

Honeybee mushroom-body development. In stage 1 honeybee larvae there are about 40 neuroblasts per brain hemisphere in the protocerebrum, each about 20 μm across [11]. Kenyon cell precursors form clusters of about 20 cells at larval stage 2 [11].

Hymenopteran brain cell numbers. Brain cell numbers were estimated by isotropic fractionator for 32 species of Hymenoptera in seven subfamilies [12]. The estimates match whole-brain counts available for two species [12]. Ants have smaller brains than bees and wasps, by mass and by cell number [12].

Smaller Hymenoptera have higher brain cell densities [12]. The same holds in most vertebrates and not in primates [12]. The cell-number ranges are not given in the abstract.

Tool-using wrasses. At least three different brain organisations support higher-order cognition, in mammals, birds and teleosts [13]. In the tool-using wrasses *Choerodon anchorago* and *Thalassoma hardwicke* the ventral forebrain and midbrain regions are enlarged [13]. The enlargement is built from fibre bundles that link the pallium to the inferior lobe, not from larger cells [13].

The inferior lobe is a midbrain structure absent in amniotes [13].

Sizes

Octopus arms. The axial nerve cord of the octopus arm is segmented [14]. In *O. bimaculoides* the number of segments per sucker stays constant along the arm, at an average of about 7.5 [14]. Arm 1 gave 7.64 and arm 2 gave 7.88, with $n = 2$ per condition [14].

The squid *Doryteuthis pealeii* has about 4.5 segments per sucker ($n = 3$) [14]. Each octopus arm also has four smaller intramuscular nerve cords and “hundreds of chemotactile suckers” [14]. The oral roots cover about 65 % of the sucker [14].

The smallest insects. The smallest insects measured have body lengths of 170 μm (*Megaphragma caribea*) and 200 μm (*M. mymaripenne*) [15]. The central nervous system of *M. mymaripenne* has a volume of 93,600 μm^3 in the pupa and 52,200 μm^3 in the adult [15]. The adult volume is 0.56 of the pupal volume (computed: 52,200 / 93,600).

The honeybee brain. The honeybee brain holds about 960,000 neurons in a volume of about 1 mm^3 [16, 17]. Chapter A8 gives 950,000 neurons, from Menzel 2001.

Fish. The cleaner wrasses in the mark test measured 51–68 mm; the mirror was 45 × 30 cm [18].

Volumes are placed as the edge of a cube of equal volume (computed, cube root).

what	size	position	source
neuroblast, honeybee larva stage 1 (diameter)	20 μm	5.54	(measured [11])
<i>M. mymaripenne</i> adult CNS, 52,200 μm^3 , cube edge	37.4 μm	6.11	(computed) from [15]
<i>M. mymaripenne</i> pupal CNS, 93,600 μm^3 , cube edge	45.4 μm	6.28	(computed) from [15]
<i>Megaphragma caribea</i> body length	170 μm	7.49	(measured [15])
<i>M. mymaripenne</i> body length	200 μm	7.63	(measured [15])
honeybee brain, about 1 mm^3 , cube edge	1 mm	9.10	(measured [16]; edge computed)
cleaner wrasse body length, lower	51 mm	12.68	(measured [18])
cleaner wrasse body length, upper	68 mm	12.94	(measured [18])
mirror, short side	0.30 m	14.29	[18]
mirror, long side	0.45 m	14.66	[18]

Times

Self-control in cuttlefish. Cuttlefish sustained delays “up to 50-130 s” for a preferred food [19]. Individuals that waited longer learned a reversal task better [19]. The authors give “several seconds” for other species and “up to several minutes” for large-brained vertebrates [19].

Planning in ravens. Ravens tolerated delays “up to 17 hours” in planning for tool use and bartering [20]. The authors report that this matches great apes [20]. The raven delay is 471 times the upper cuttlefish delay (computed: 61,200 s / 130 s).

Crow numerosity. In the crow numerosity task a 500 ms sample followed a 500 ms baseline, and a 1,000 ms delay followed the sample [21]. The average visual response latency of neurons in the nidopallium caudolaterale (NCL) was 144 ms [21].

Compound tools. New Caledonian crows built their first compound tools “within only 4-6 min of engaging with the tool elements” [22].

Bumblebee string pulling. Stepwise training to pull a string took on average 309 ± 18 min per bee [23]. Naïve attempts lasted 5 min, controls ran 5 days and practice 48 h [23].

Bumblebee ball rolling. The ball-rolling experiment ran 3 h a day for 18 days [24]. Younger bees, 3-7 days from eclosion, rolled more [24]. The age test compared three-day-old bees with bees older than 10 days [24].

Lifespan of the smallest insect. The adult lifespan of *M. mymaripenne* is 5 days at 25

°C and 8.8 days at 15 °C [15].

Octopus arm study. The adults studied were at least 6 months old; the juveniles were 6 weeks old [14].

Mirror test in the cleaner wrasse. Mouth fighting at the mirror fell to zero by day 7 [18]. Atypical mirror-directed behaviour peaked on days 3–5, at about 36 per hour on days 3–4 in seven fish [18]. It had nearly ended by day 10 [18].

Years are converted at 365.25 days. Ages are placed as durations.

what	duration	position	source
crow NCL visual response latency	144 ms	31.39	(measured [21])
crow task baseline; sample	500 ms	32.52	[21]
crow task delay	1,000 ms	33.15	[21]
cuttlefish delay, lower	50 s	36.71	(measured [19])
cuttlefish delay, upper	130 s	37.58	(measured [19])
first compound tool, lower	4 min	38.14	(measured [22])
bumblebee naïve attempt	5 min	38.34	[23]
first compound tool, upper	6 min	38.51	(measured [22])
ball rolling per day	3 h	41.61	[24]
string-pulling training per bee (mean)	309 min	42.10	(measured [23])
raven planning delay	17 h	43.19	(measured [20])
bumblebee practice, colourless flower	48 h	44.13	[23]
youngest ball-rolling bees	3 d	44.50	(measured [24])
<i>M. mymaripenne</i> adult lifespan, 25 °C	5 d	44.96	(measured [15])
string-pulling control period	5 d	44.96	[23]
wrasse mouth fighting at zero	7 d	45.27	(measured [18])
upper age of younger ball-rolling bees	7 d	45.27	(measured [24])
<i>M. mymaripenne</i> adult lifespan, 15 °C	8.8 d	45.48	(measured [15])
wrasse mirror behaviour nearly ended	10 d	45.60	(measured [18])
older ball-rolling bees, more than	10 d	45.60	[24]
ball-rolling experiment	18 d	46.13	[24]
juvenile octopus age	6 weeks	46.90	[14]

adult octopus age, at least	6 months	48.24	[14]
crow ages	5 y; 6 y	50.34; 50.50	[21]
vampire squid / dumbo octopus lineages, lower	204 Ma	66.29	(modelled [2])
vampire squid / dumbo octopus lineages	242 Ma	66.44	(modelled [2])
vampire squid / dumbo octopus lineages, upper	280 Ma	66.57	(modelled [2])
amniote neuron-scaling history	300 Myr	66.64	[3]
vertebrate origin, stated as before	520 Ma	67.14	[4]

Counts

Octopus brain connectivity. A preprint maps 32 cortical and subcortical regions in the octopus brain [25]. Its connection totals differ within the document [25]. The abstract gives “more than 350 main neural connections”, the results 249 directed edges between the 32 regions, the discussion 439 connections, and the methods 2,178 literature hits [25].

The 249 edges are described as an underestimate; all four totals are recorded as printed [25].

Cephalopod species. About 750 living cephalopod species are counted in the LSE sentence review [26].

The smallest insect. The adult CNS of *M. mymaripenne* has 339–372 nuclei (mean 361, $n = 3$) [15]. Of these, 179–253 (mean 215) lie in the brain [15]. The pupal CNS has about 7,199–7,593 cells (mean 7,396, $n = 2$) [15].

The adult carries “about 7000 anucleate cells” [15]. Nuclei and cell bodies lyse “in over 95% of the neurons” [15]. The adult mean of nuclei is 4.9 % of the pupal mean of cells (computed: $361 / 7,396 = 0.049$), so 95.1 % lack a nucleus (computed).

Insect counting and concepts. Honeybees “can count up to four objects, when they are encountered sequentially during flight” [27]. They also count novel objects [27].

Individual honeybees were trained on “greater than” and “less than” with stimuli of one to six elements [28]. They placed the empty set at the low end of the numerical continuum [28].

Honeybees form “sameness” and “difference” concepts in delayed matching-to-sample and non-matching-to-sample tasks [29]. They transfer the concepts to new stimuli, including across senses [29]. The abstract gives no numbers [29].

Bumblebee string pulling (*Bombus terrestris*) [23]: - Trained stepwise: 23 of 40 bees (57.5 %, computed). - Naïve bees tested singly from eight colonies: 0 of 291 solved on the first 5-min attempt. - In a second 5-min session 2 of 25 solved, given as “about 1 %” of the 291 (computed 0.69 %). - Control bees: 0 further spontaneous solvers among 165

over 5 days. - Observers of a trained demonstrator: 15 of 25 (60 %) solved on first test. - Observers of a “ghost” flower moved by the experimenter: 0 of 15. - Colourless-flower control: 2 of 15 at first, 11 of 15 after 48 h practice. - Coiled string: 0 of 27 observers; 3 of 8 experienced bees. - Seeded colonies after 150 paired foraging bouts: 25 of 47, 17 of 29 and 12 of 28 foragers (53 %, 59 % and 43 %, computed). - Later in the same colonies: 34 of 47 and 18 of 28 (72 % and 64 %, computed). - Control colonies: 0 of 51, 0 of 58 and 0 of 57.

Bumblebee ball rolling (*Bombus terrestris*) [24]: - 45 tagged bees from one colony recorded 910 ball-rolling actions; 20 per bee on average (computed: 910 / 45). - Rolls per bee over the experiment: 1–117; up to 44 on one day. - Three-day-old bees: 11 of 13 rolled (85 %, computed), with 11 ± 3.7 actions (mean $\pm$ SE). - Bees older than 10 days: 14 of 33 rolled (42 %, computed), with 4 ± 1.4 actions. - Age difference: Wilcoxon $Z = 2.30$, $P = 0.02$. - Conditioned place preference: 42 female bees from four colonies, two groups of 21, preferred the colour of the chamber where they had rolled balls. - Place preference statistics: GLM estimate 1.696, SE 0.761, $Z = 2.228$, $P = 0.026$. - Five behavioural criteria for play are stated as fulfilled.

Bird brains against primate brains. Parrots and songbirds have on average twice as many neurons as primate brains of the same mass [30].

Corvid telencephalon, per hemisphere [31] ($n = 4$ per corvid species):

species	telencephalon mass	telencephalic neurons	pallial neurons	mesopallium	nidopallium
hooded crow	2,666 mg	352.7 million	301.8 million	81.1 million	156.9 million
carrion crow	2,512 mg	409.9 million	336.1 million	89.4 million	182.7 million
rook	2,401 mg	483.0 million	408.7 million	116.0 million	214.2 million
ostrich	8,168 mg	228.3 million	208.1 million	41 million	—

The text of the same paper gives 282 million telencephalic neurons for the ostrich [31]. Both figures are recorded. Rooks hold 1.37 times the telencephalic neurons of hooded crows (computed: 483.0 / 352.7).

Telencephalic neurons per milligram are 132,000 in the hooded crow, 163,000 in the carrion crow, 201,000 in the rook and 28,000 in the ostrich (computed from the table). The pallium holds 86 %, 82 % and 85 % of telencephalic neurons in the three corvids and 91 % in the ostrich (computed). With the text figure of 282 million the ostrich share is 74 % (computed).

The paper names primate comparators: 68 million neurons in one hemisphere of rhesus prefrontal cortex and 115 million in one hemisphere of baboon prefrontal cortex [31]. It predicts “fewer than 300 million” per hemisphere for the chimpanzee. That figure is a prediction, not a measurement [31].

Crow numerosity neurons [21]: - Two male carrion crows (*Corvus corone corone*), aged 6 and 5 years. - Numerosities 0–4. - 501 NCL neurons recorded (233 and 268). - Numerosity-selective in the sample period: 27 % (134 of 501); in the delay: 31 % (153 of 501). - Of the numerosity-selective neurons, 35.8 % ($n = 34$) preferred zero in the sample period and 41.8 % ($n = 38$) in the delay. - The n and the percentages imply a base of about 95, not 134 (computed: 34 / 0.358). Both are recorded as printed.

Compound tools. Four of 8 naïve New Caledonian crows combined elements into functional compound tools [22]. One bird built tools of 3 and 4 pieces [22].

Teleost brains (11 species: 3 wrasses, 4 cichlids, 4 outgroup species) [13]: - Brain mass: wrasses 34.62–338.8 mg; cichlids 42.43–96.94 mg; outgroup 8.38–354.73 mg. - Total brain cells (not neurons): wrasses 45.7–185.08 million; one large *C. anchorago* 301.9 million. - Cichlids 37.54–61.78 million; outgroup 6.66–100.84 million. - Teleosts have more brain cells than rodent brains of similar body mass and fewer than birds and primates.

Cleaner wrasse mark test (*Labroides dimidiatus*) [18]: - 10 fish; 7 aggressive to the mirror at first. - 4 fish marked on the throat; 3 of 4 scraped the mark while viewing the mirror. - No scraping in control, sham-mark or no-mirror periods. - 37 scrapes in total (15, 16 and 6); Friedman $\chi^2 = 9.0$, $df = 3$, $P = 0.029$.

After passing the mark test, cleaner wrasses stopped attacking still photographs of themselves [32]. They kept attacking photographs of unfamiliar fish [32]. The abstract gives no sample sizes [32].

Elephant. The African elephant brain weighs 4,618.6 g without the olfactory bulb, about three times the human brain [33]. It holds 257 billion neurons [33]. Of these, 251 billion (97.5 %) lie in the cerebellum and 5.6 billion in the cerebral cortex [33].

The cortical figure is about one third of the human cortex figure of 16.3 billion cited in the same paper (computed: $5.6 / 16.3 = 0.34$) [33].

Pilot whale. Ten long-finned pilot whales from the Faroe Islands had total brain weights of 3,062–4,618 g [34]. The neocortex held about 37.2×10^9 neurons, range 29.1–46.3 $\times 10^9$, “almost twice as many as humans” [34]. It held 127×10^9 glial cells, range 99.9–183 $\times 10^9$, or 3.4 glial cells per neuron (computed: $127 / 37.2$) [34].

Independent origins. Counted from the abstract of the convergence review: 7 named groups (insects, octopodids, teleosts, birds, cetaceans, elephants, primates) [1]. These fall in 3 major bilaterian lineages: ecdysozoans, lophotrochozoans and vertebrates [1]. A separate study counts at least 3 brain organisations for higher-order cognition (mammal, bird, teleost) [13].

Frameworks and declarations, as counts. Dimensions: 5 (Birch, Schnell and Clayton 2020) [35]. Criteria: 8, drawn from “over 300” studies (LSE review, 2021) [26]. Statements: 3 (New York Declaration, 2024) [36]; steps in the vertebrate model: 2 (Feinberg and Mallatt 2013) [4].

Order of events

Geological ages first. Numbered ages are placed as durations; named periods without a number in the source carry no position.

1. Before 520 Ma, Cambrian. Vertebrates arise; Feinberg and Mallatt (2013) date vertebrate sensory consciousness here [4]. Position 67.14.
2. Cambrian. Barron and Klein (2016) trace the origins of insect subjective experience here [5]. No number in the source; no position.
3. 300 Myr of amniote history with as few as four major changes in neuron-brain

- scaling [3]. Position 66.64 (duration).
4. Silurian-Devonian. Crown coleoid divergence [2]. No number in the source; no position.
 5. 242 ± 38 Ma (280–204 Ma). Vampire squid and dumbo octopus lineages [2]. Positions 66.57, 66.44, 66.29.
 6. Jurassic. Decabrachian diversification [2]. No number in the source; no position.

Dated positions on consciousness. These are statements by named authors, with their dates; they carry no positions.

- 7 July 2012: the Cambridge Declaration on Consciousness, written by Philip Low, names “all mammals and birds, and many other creatures, including octopuses” [37].
- November 2021: the LSE review for DEFRA, by Birch, Burn, Schnell, Browning and Crump, recommends that all cephalopods and decapods be regarded as sentient [26].
- 28 April 2022: the UK Animal Welfare (Sentience) Act 2022 includes any cephalopod mollusc and any decapod crustacean in “animal” [38].
- 19 April 2024: the New York Declaration on Animal Consciousness is announced [36].

Present quantities

Living cephalopods. About 750 species [26].

Living decapods. About 15,000 species, as counted in the LSE review [26].

The Cambridge Declaration (Low and co-authors, 7 July 2012). The declaration was proclaimed at the Francis Crick Memorial Conference on Consciousness in Human and non-Human Animals, Churchill College, University of Cambridge [37]. It was written by Philip Low and signed by conference participants that evening “in the presence of Stephen Hawking” [37]. Its position: “all mammals and birds, and many other creatures, including octopuses” possess the neurological substrates of consciousness [37].

Dimensions of animal consciousness (Birch, Schnell and Clayton 2020). The authors propose five dimensions [35]. These are perceptual richness, evaluative richness, integration at a time, integration across time, and self-consciousness [35]. On their position each species has its own “consciousness profile”, and “no single scale” ranks species [35].

The LSE sentience review (Birch, Burn, Schnell, Browning and Crump, November 2021). The review draws on “over 300 scientific studies” and uses eight criteria of sentience [26]. The criteria, as summarised from the report, are: 1. nociceptors; 2. integrative brain regions; 3. connections from nociceptors to those regions; 4. responses altered by anaesthetics or analgesics; 5. motivational trade-offs; 6. flexible self-protection; 7. associative learning; 8. valuing analgesics when injured.

The review states, by group, how many criteria are met with high or very high confidence [26]:

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group	criteria at high or very high confidence (of 8)
octopods	7 (medium for the 8th)
true crabs	5
squid and cuttlefish	4
anomuran crabs	3
astacid lobsters and crayfish	3
spiny lobsters	2
caridean shrimps	2
penaeid shrimps	1

The review recommends that all cephalopods and decapods be regarded as sentient for UK animal welfare law [26].

UK law (28 April 2022). Section 5(1) of the Animal Welfare (Sentience) Act 2022 defines “animal” as any vertebrate other than *Homo sapiens*, any cephalopod mollusc and any decapod crustacean [38]. With the LSE species counts, the Act covers all non-human vertebrates, about 750 cephalopod species and about 15,000 decapod species [38, 26].

The New York Declaration on Animal Consciousness (19 April 2024). The declaration makes three statements [36]: 1. There is “strong scientific support” for conscious experience in other mammals and in birds. 2. There is “at least a realistic possibility” of conscious experience in all vertebrates (reptiles, amphibians, fishes) and many invertebrates, “at minimum, cephalopod mollusks, decapod crustaceans, and insects”. 3. Ignoring a realistic possibility in decisions affecting an animal is “irresponsible”.

The declaration page showed 611 signatures on 14 Oct 2026 [36].

The vertebrate framework (Feinberg and Mallatt 2013). The authors’ minimal brain for qualia comprises forebrain, midbrain and hindbrain, with widespread activity of the reticular formation [4]. They propose two steps. The optic tectum is the first centre of multisensory perception (fish, amphibians); the dorsal pallium follows (mammals, reptiles, birds) [4].

They propose vision as the first conscious sense [4].

Pattern

Complex brains are recorded in seven named groups across three bilaterian lineages [1]. Four groups are paired with a multimodal centre [1]; in tool-using wrasses enlarged regions are built from pallium-inferior-lobe fibre bundles [13]. Counts span 361 nuclei (*Megaphragma*) [15], about 960,000 neurons (honeybee) [16], 352.7–483.0 million telencephalic neurons per corvid hemisphere [31] and 257 billion neurons (elephant) [33].

Measured delays run from 50–130 s (cuttlefish) to 17 h (raven) [19, 20]. Spontaneous string pulling is rare (2 of 291) [23]. The stated positions widen by date: 2012 mammals, birds, octopuses; 2016 insects; 2021–2022 cephalopods and decapods [37, 5, 26, 38].

In 2024 all vertebrates and, at minimum, cephalopods, decapods and insects are named as a realistic possibility [36].

Not verified

- Octopus-vertebrate last common ancestor “about 600 million years ago” (eLife digest of [10]) — secondary.
- Cephalopod and vertebrate brains compared over “more than 500 million years of independent evolution” [39] — secondary.
- Squid-octopus divergence 270 Ma ([14] citing Albertin et al. 2022) — secondary.
- Centralisation of nervous systems “on more than five occasions” ([39] citing Moroz 2009) — secondary.
- Octopus protocadherins with “over 70 extracellular cadherin domains” [39] — secondary.
- More than 60 % of RNA transcripts in the squid brain recoded, against under 1 % in humans and fruit flies (University of Chicago release on [9]) — secondary.
- Squid giant fibres “reaching over 250 µm in diameter” ([39] citing Young 1939) — secondary.
- Vertical lobe about 14 % of the supra-oesophageal mass, with over 25 million nerve cells [39] — secondary.
- *Octopus vulgaris* with “over half a billion” neurons, two thirds in the arms (eLife digest 2021), against about 200 million ([25] citing Young 1963) — secondary; the two may refer to different totals.
- Very small neurons over 50 % of the octopus neural cell population [25] — secondary.
- Lobe counts “more than 30” (Young 1971; Packard 1972, via [39]) and 25 by diffusion MRI (Jacobs 2022, via [25]) — secondary.
- Squid *Sepioteuthis lessoniana*: 426 connections between 23 areas ([25] citing Chung et al. 2020) — secondary.
- Octopus brain 11-15 main tracts and four pairs of brachial nerves [39] — secondary.
- Honeybee mushroom body 10 % of brain volume ([11] citing Mobbs 1982) — secondary.
- Honeybee 170,000 Kenyon cells per mushroom body ([11] citing Witthöft 1967) — secondary.
- Bird counts in “more than two dozen species”, and two to four times the neurons of rodent brains (Vanderbilt release on [30]) — secondary.
- Pallial share of neurons 55 % in parrots, 61 % in songbirds, against 19 % cortical in primates [40] — secondary.
- Pallial neurons kea 1.28 billion, raven 1.2 billion, chimpanzee 7.4 billion, and corvid-pigeon ratios [40] — secondary.
- Whole-brain neuron counts and endocranial volumes for ten bird and twelve mammal species, raven 2.17 billion in 14.5 cm³ [41] — secondary.
- Rhesus macaque 6.38 and chimpanzee 28 billion brain neurons [41] — secondary.
- Brain cell number ranges for the 32 hymenopteran species [12] — not read.

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A10 The Human Brain and Beyond

What it is

This chapter records the human brain in numbers. It covers hominin brain size, brain energy, growth from the second trimester to old age, human-specific cortex genes and neuron count. It ends with two records beyond the single brain: social insect colonies, and the dated record of tools, images and internet use.

The human brain holds 86.1 ± 8.1 billion neurons and 84.6 ± 9.8 billion non-neuronal cells [1]. Its proportions of neurons to other cells match those of other primates [1]. The authors describe it as “an isometrically scaled-up primate brain” [1].

The brain is about 2 % of body mass [2]. It “consumes about 20% of the whole body energy budget” [2].

First appearance

Brain size before *Homo*. *Australopithecus* had an endocranial volume (ECV) of “~450 cc”, roughly unchanged from 3.5 to 2.0 Ma [3]. This is about 20 % larger than *Sahelanthropus*, *Ardipithecus* or chimpanzees [3].

The rise of brain size. Across the hominin clade ECV rose gradually [4]. Change within hypothesised lineages accounts for 64 % (finer taxonomy) or 88 % (less speciose taxonomy) of the change [4]. The rest comes from the appearance of larger-brained *Homo* and the loss of smaller-brained *Australopithecus* and *Paranthropus* [4].

Within-lineage change fits episodes of directional selection with stasis and/or drift [4].

Change points in brain size. A change-point analysis used 981 cranial capacity estimates over the last 10 Myr, excluding small-brained Pleistocene *Homo* [3]. Before the first change point the rate of increase was $0.03 \pm 0.01 \log_{10} \text{ cc per Myr}$ [3]. The first change point lies at $2.10 \pm 0.07 \text{ Ma}$, after which the rate was 0.35 ± 0.05 [3].

The second change point lies at $1.49 \pm 0.14 \text{ Ma}$, with a rate after of 0.19 ± 0.01 [3]. A third lies at $0.003 \pm 0.001 \text{ Ma}$, with a rate of -17.16 ± 6.69 [3]. The rate after the first change point is 11.7 times the rate before it (computed: $0.35 / 0.03$).

With small-brained *Homo* included (985 estimates), the first change point lies at $2.10 \pm 0.05 \text{ Ma}$, rate 0.72 ± 0.51 [3]. The second lies at $1.97 \pm 0.12 \text{ Ma}$, rate 0.20 ± 0.01 ; the third at $0.003 \pm 0.001 \text{ Ma}$, rate -16.74 ± 7.55 [3].

Human-specific gene duplications. SRGAP2 was duplicated three times only in humans [5]. The promoter and first nine exons of SRGAP2A (1q32.1) were copied to 1q21.1 as SRGAP2B about 3.4 million years ago [5]. Larger copies of SRGAP2B went to 1p12 as SRGAP2C about 2.4 mya, and to proximal 1q21.1 as SRGAP2D about 1 mya [5].

The authors propose that the new function arose “at birth” 2–3 mya [5]. They place this at the transition from *Australopithecus* to *Homo* and the start of neocortex expansion [5]. The window of 2–3 mya contains the first change point in brain size at 2.10 Ma (computed comparison of [5] and [3]).

ARHGAP11B arose by partial duplication of *ARHGAP11A*, a Rho GTPase-activating protein gene [6]. The duplication occurred “on the human lineage after separation from the chimpanzee lineage” [6]. A later study states that “a single nucleotide substitution” underlies its properties [7].

Stone tools. Stone tools at Lomekwi 3, West Turkana, Kenya, are 3.3 million years old [8]. They predate the Oldowan by 700,000 years [8]. Before them, the earliest sharp-edged tools were about 2.6 million years old, in Ethiopia [8].

Oldowan tools at Gona, Ethiopia, are “securely dated between 2.6–2.5 Myr” [9]. The ages come from radio-isotopic dating and magnetic polarity stratigraphy [9].

The Acheulean first appears at Kokiselei 4, Nachukui Formation, West Turkana, at 1.76 Myr ago [10]. This is “350,000 years older” than the previous earliest record [10]. The previous record was therefore about 1.41 Myr (computed: $1.76 - 0.35$).

Images. An abstract drawing at Blombos Cave, South Africa, comes from Middle Stone

Age levels about 73,000 years old [11]. It is at least 30,000 years older than earlier abstract and figurative drawings, which date after 40,000 years ago [11].

Narrative cave art at Leang Karampuang, South Sulawesi, was painted at least 51,200 years ago [12]. The minimum age for the scene is 53.5 ± 2.3 ka [12]. The hunting scene at Leang Bulu' Sipong 4, previously dated to 43.9 ka, was re-dated to at least 50.2 ± 2.2 ka [12].

The dates come from laser-ablation U-series imaging [12].

Ants. A molecular phylogeny of the ants used 4.5 kb of six gene regions, 139 of 288 extant genera and 19 of 20 subfamilies [13]. It was calibrated with 43 fossils [13]. Most subfamilies arose earlier than previously proposed, and diversification took off in the Late Cretaceous to Early Eocene, with the rise of angiosperms [13].

The abstract gives no Ma values [13]. In Hymenoptera, mushroom-body elaboration “preceded the evolution of eusociality”, stated without a date [3].

The first synapses of a human brain. Synapse formation in human cerebral cortex begins before the 27th week of pregnancy [14].

Partners

Genes of cortical progenitors. A screen found 56 genes preferentially expressed in human apical radial glia that lack mouse orthologs [6]. *ARHGAP11B* showed the highest radial-glia specificity among them [6]. Expressed in embryonic mouse neocortex, it increased basal progenitors and their self-renewal, enlarged the cortical plate and induced gyrification [6].

A second screen found 35 hominid-specific duplicated genes with dynamic expression during human cortical neurogenesis [15]. *NOTCH2NL* promotes progenitor maintenance and clonal expansion by inhibiting cis Delta/Notch interactions [15].

Three *NOTCH2NL* paralogs are highly expressed in radial glia [16]. The *NOTCH2NL* genes form the breakpoints of the 1q21.1 distal deletion/duplication syndrome [16]. Duplications go with macrocephaly and autism; deletions go with microcephaly and schizophrenia [16].

FOXP2. The Nature abstract of Enard and co-authors (2002) states that “two functional copies of *FOXP2* seem to be required for acquisition of normal spoken language” [17]. A reanalysis of “hundreds” of globally distributed genomes finds no evidence of recent positive or balancing selection at *FOXP2* [18]. It attributes the earlier signal to sample composition [18].

The same reanalysis reports that the two nonsynonymous substitutions are present in archaic hominins [18]. It identifies an intronic *FOXP2* region enriched for highly conserved sites that are polymorphic in humans [18]. The region is compatible with loss of function and lowly expressed in human prefrontal cortex [18].

Energy per neuron. Average glucose use per neuron is near constant across six species of rodents and primates, including humans [2]. It varies about 0.4-fold while neuron numbers vary about 1,000-fold, given as 1,213-fold in the paper [2].

Myelination, human and chimpanzee. Myelinated axon fibre length density and myelin-protein expression were measured across postnatal life in somatosensory, motor, prefrontal and visual cortex [19]. Chimpanzees (N = 20) reach adult-like levels around sexual maturity [19]. In humans (N = 33) maturation extends “past late adolescence” [19].

Eusociality. A comparison of 267 species of eusocial bees, wasps and ants found single mating ancestral in all eight independent lineages of eusociality examined [20]. Multiple mating is always derived [20]. High polyandry, more than two effective mates, occurs only where workers had lost reproductive ability [20].

Ant brains and colonies. Workers of species with larger colonies have larger brains [3]. In monomorphic fungus-growing ants, larger colonies go with smaller brains [3]. Both are recorded.

Sizes

Hominin endocasts. ECV ranges given in a primary text: *H. habilis* “500 to >700 mL” and *H. erectus* “550 to >1,200 mL”, including Dmanisi and Ngandong [21]. *H. naledi* and *H. floresiensis* fall “within or just above the range of *Australopithecus*” [21].

H. naledi from the Dinaledi Chamber gave water-displacement ECVs of 555 mL (DH1) and 460 mL (DH3) [21]. Earlier virtual composites gave 560 mL (DH1/DH2) and 465 mL (DH3/DH4) [21].

H. floresiensis LB1 measured 426 cc by micro-CT [22]. Published estimates run 380–430 cc, and the earlier commonly cited value is 400 cc [22]. The study took human brain-body scaling from 20 modern populations [22].

Modern cranial capacity. The modern mean in the DeSilva dataset is 1,297 cc [23]. Other published estimates run about 1,340–1,460 cc, as stated by the same reanalysis [23]. The modern mean in the DeSilva dataset is 2.9 times the *Australopithecus* value of about 450 cc (computed: 1,297 / 450).

Holocene body size. A 5 kg fall in body size would account for only 22 mL of brain reduction [3]. The reported reduction is “more than 5x greater” [3].

Cortex surface. The surface of the human cerebral cortex is 973 cm² per hemisphere [24].

Myelinated fibre. The total length of myelinated fibre is 176,000 km in men and 149,000 km in women at age 20 [25]. At age 80 it is 97,200 km and 82,000 km [25]. The loss is 45 %, about 10 % per decade, in a sample of 36 people [25].

The Argentine ant supercolony. In southern Europe the Argentine ant (*Linepithema humile*) forms two supercolonies [26]. The main one extends over 6,000 km from Italy to the Spanish Atlantic coast [26]. The authors describe it as the largest cooperative unit ever recorded [26].

Volumes and areas are placed as the edge of a cube or square of equal measure (computed).

what	size	position	source
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reduction from a 5 kg fall in body size, 22 mL, cube edge	2.80 cm	12.13	(computed) from [3]
<i>H. floresiensis</i> LB1, 426 cc, cube edge	7.52 cm	13.03	(measured [22]; edge computed)
<i>Australopithecus</i> , about 450 cc, cube edge	7.66 cm	13.05	[3]; edge computed
<i>H. naledi</i> DH3, 460 mL, cube edge	7.72 cm	13.05	(measured [21]; edge computed)
<i>H. naledi</i> DH3/DH4 composite, 465 mL, cube edge	7.75 cm	13.06	[21]; edge computed
<i>H. habilis</i> , lower, 500 mL, cube edge	7.94 cm	13.08	[21]; edge computed
<i>H. erectus</i> , lower, 550 mL, cube edge	8.19 cm	13.11	[21]; edge computed
<i>H. naledi</i> DH1, 555 mL, cube edge	8.22 cm	13.11	(measured [21]; edge computed)
<i>H. naledi</i> DH1/DH2 composite, 560 mL, cube edge	8.24 cm	13.11	[21]; edge computed
<i>H. habilis</i> , upper, 700 mL, cube edge	8.88 cm	13.18	[21]; edge computed
<i>H. erectus</i> , upper, 1,200 mL, cube edge	10.63 cm	13.35	[21]; edge computed
modern mean, DeSilva dataset, 1,297 cc, cube edge	10.91 cm	13.37	[23]; edge computed
modern, other estimates, lower, 1,340 cc, cube edge	11.02 cm	13.38	[23]; edge computed
modern, other estimates, upper, 1,460 cc, cube edge	11.34 cm	13.41	[23]; edge computed
cortex surface, 973 cm ² per hemisphere, square edge	31.2 cm	14.33	[24]; edge computed
Argentine ant main supercolony, more than	6,000 km	29.59	(measured [26])
myelinated fibre, women, age 80	82,000 km	31.97	(measured [25])
myelinated fibre, men, age 80	97,200 km	32.13	(measured [25])
myelinated fibre, women, age 20	149,000 km	32.52	(measured [25])
myelinated fibre, men, age 20	176,000 km	32.67	(measured [25])

Times

The first 90 days. A study scanned 87 infants 211 times between ages 2 and 90 days [27]. At birth whole-brain volume is about one third of elderly brain volume [27]. Growth runs about 1 % per day and slows to 0.4 % per day by 3 months, when volume is just over half of adult [27].

Total growth in 90 days is 64 % [27]. The cerebellum more than doubles and the hippocampus grows by 47 % [27]. A birth one week earlier gives a brain 5 % smaller, still 2 % smaller at 90 days [27].

Lifespan peaks. Brain charts were built from 123,984 MRI scans of 101,457 participants in more than 100 primary studies [28]. The ages run from 115 days post-conception to 100 years [28]. Peak ages, with 95 % bootstrap intervals, are given in the table below [28].

measure	peak age (years)	95 % bootstrap CI	position of peak
cortical thickness	1.7	1.3-2.1	49.35
grey matter volume	5.9	5.8-6.1	50.49
total cerebrum volume	12.5	12.14-12.89	51.17
subcortical grey matter	14.4	14.0-14.7	51.30
white matter volume	28.7	28.1-29.2	51.93

Cerebrospinal fluid volume rises to age 2 and then plateaus to age 30 [28].

Synapses and spines. Synapse density peaks near 3 months after birth in auditory cortex and after 15 months in frontal cortex [14]. Net elimination of synapses has ended by 12 years in auditory cortex [14].

Dendritic spines were counted on layer IIIC and V pyramidal neurons of prefrontal cortex, from newborn to 91 years [29]. Childhood spine density is two- to threefold the adult value, and decline begins at puberty [29]. Overproduction and remodelling continue “into the third decade of life” [29].

Adult neurogenesis: two records. Carbon-14 dating of DNA gives about 700 new neurons per day in each adult hippocampus, a turnover of 1.75 % per year [30]. At that rate the renewing population turns over in 57 years (computed: $1 / 0.0175$). In 17 post-mortem brains and 12 surgical samples aged 18-77 years, no young neurons were found in adults, only a few at 7 and 13 years [31].

Both records are kept: about 700 a day against none detected. In both, new neurons come from progenitor cells; no division of a differentiated neuron is reported [30, 31].

The Holocene: two records. DeSilva and co-authors report a decrease in brain size from about 3,000 years ago [3]. They give its rate as “50 times greater” than the Pleistocene increase [3]. A reanalysis of the same dataset (987 specimens; 988 in one place) finds human brain size stable over the last 300 ka [23].

In the reanalysis the slopes do not differ from zero ($p = 0.754$ for 300 ka and for 30 ka) [23]. No change point appears near 3 ka (Davies test $p = 0.739$ for 300 ka, $p = 0.259$ for 30 ka) [23]. The reanalysis notes that 578 of 987 specimens come from two sources, more than half fall in the final 100-year bin, and only 23 crania cover 5-1 ka [23].

Dates of *H. naledi*. The Dinaledi fossils are dated “between 236,000 and 335,000 y

ago” in the main text; the significance statement gives 226,000 [21].

Years are converted at 365.25 days. Ages are placed as durations.

what	duration	position	source
youngest infant scan	2 d	44.13	[27]
infant growth at 1 % → 0.4 % per day; last scan	90 d	47.60	(measured [27])
auditory synapse density peak	3 months	47.61	(measured [14])
earliest age in lifespan charts, post-conception	115 d	47.82	[28]
synaptogenesis begins, before	27 weeks	48.27	(measured [14])
frontal synapse density peak, after	15 months	49.07	(measured [14])
cortical thickness peak	1.7 y	49.35	(modelled [28])
CSF rise ends	2 y	49.50	(modelled [28])
grey matter peak	5.9 y	50.49	(modelled [28])
few young hippocampal neurons, last seen	7 y; 13 y	50.64; 51.21	(measured [31])
auditory synapse elimination ended	12 y	51.13	(measured [14])
total cerebrum peak	12.5 y	51.17	(modelled [28])
subcortical grey matter peak	14.4 y	51.30	(modelled [28])
youngest adult sample, no young neurons	18 y	51.50	(measured [31])
myelinated fibre, first age	20 y	51.60	(measured [25])
white matter peak	28.7 y	51.93	(modelled [28])
CSF plateau ends	30 y	51.97	(modelled [28])
hippocampal turnover at 1.75 % per year	57 y	52.55	(computed) from [30]
oldest adult sample	77 y	52.82	(measured [31])
myelinated fibre, second age	80 y	52.86	(measured [25])
oldest prefrontal spine sample	91 y	52.98	[29]
latest age in lifespan charts	100 y	53.06	[28]
final bin in the Holocene dataset	100 y	53.06	[23]
reanalysis interval, lower	1 ka	55.16	[23]
proposed Holocene decrease, from about	3 ka	56.16	(modelled [3])

reanalysis interval, upper	5 ka	56.62	[23]
reanalysis window	30 ka	58.25	[23]
Blombos margin, at least	30 kyr	58.25	(measured [11])
earlier drawings, after	40 ka	58.52	[11]
Leang Bulu' Sipong 4, previous date	43.9 ka	58.60	[12]
Leang Bulu' Sipong 4, re-dated, at least	50.2 ka	58.72	(measured [12])
Leang Karampuang, at least	51.2 ka	58.74	(measured [12])
Leang Karampuang scene, minimum	53.5 ka	58.78	(measured [12])
Blombos drawing	73 ka	59.06	(measured [11])
<i>H. naledi</i> , significance statement	226 ka	60.09	[21]
<i>H. naledi</i> , lower	236 ka	60.13	(measured [21])
reanalysis window; stable brain size	300 ka	60.35	[23]
<i>H. naledi</i> , upper	335 ka	60.45	(measured [21])
Acheulean margin	350 kyr	60.49	[10]
Lomekwian margin over the Oldowan	700 kyr	61.12	[8]
SRGAP2D	1 Ma	61.45	(modelled [5])
previous earliest Acheulean	1.41 Ma	61.76	(computed) from [10]
second change point	1.49 Ma	61.81	(modelled [3])
first Acheulean, Kokiselei 4	1.76 Ma	61.96	(measured [10])
second change point, small-brained <i>Homo</i> included	1.97 Ma	62.06	(modelled [3])
<i>Australopithecus</i> flat period, end	2.0 Ma	62.08	[3]
first change point	2.10 Ma	62.12	(modelled [3])
SRGAP2C	2.4 Ma	62.24	(modelled [5])
Oldowan at Gona, lower	2.5 Ma	62.28	(measured [9])
Oldowan at Gona, upper; previous earliest tools	2.6 Ma	62.32	(measured [9]; [8])
proposed SRGAP2C function, upper	3 Ma	62.45	[5]
Lomekwi 3 tools	3.3 Ma	62.53	(measured [8])
SRGAP2B	3.4 Ma	62.56	(modelled [5])
<i>Australopithecus</i> flat period, start	3.5 Ma	62.59	[3]

Counts

Neurons and other cells. Whole brain: 86.1 ± 8.1 billion NeuN-positive neurons and 84.6 ± 9.8 billion non-neuronal cells, in adult male brains [1]. The ratio is 1.02 to one (computed: $86.1 / 84.6$). The cerebral cortex holds 19 % of all neurons in 82 % of brain mass [1].

The cortex holds 16 billion neurons and the cerebellum 69 billion, leaving about 1 billion for the rest (computed) [32]. The cerebellum holds 80 % of the neurons (computed: $69 / 86$) in 154 g [32]. The ratio of ten glia to one neuron holds only in a few deep nuclei [32].

The brain of the men studied weighed about 1.5 kg, with the cerebral cortex at 1,233 g [32].

Synapses. Cortex holds about 10^9 synapses per mm^3 ; the whole brain holds 10^{13} – 10^{15} [33]. With 5.2×10^{14} synapses and 16 billion cortical neurons this gives about 33,000 synapses per cortical neuron (computed: $5.2 \times 10^{14} / 1.6 \times 10^{10} = 32,500$) [33, 32].

Comparators. The African elephant brain holds 257 billion neurons, 97.5 % in the cerebellum, and 5.6 billion in the cerebral cortex [34]. The long-finned pilot whale neocortex holds 37.2×10^9 neurons [35].

Computed ratios: - elephant to human brain neurons: $257 / 86 = 3.0$; - human to elephant cortical neurons: $16.3 / 5.6 = 2.9$, with the human cortex at 16.3 billion as cited in [34]; - pilot whale to human neocortical neurons: $37.2 / 16.3 = 2.3$.

Energy per neuron [2]: - Cerebral cortex: $1.50 \times 10^{-8} \pm 0.49 \times 10^{-8}$ μmol glucose per neuron per min. - Cerebellum: $0.87 \times 10^{-9} \pm 0.36 \times 10^{-9}$ μmol per neuron per min. - Whole-brain average: $5.79 \times 10^{-9} \pm 0.76 \times 10^{-9}$ μmol per neuron per min. - Cortical neurons use “nearly 20 $\times$ ” (results) or “at least 10 $\times$ ” (abstract) more than cerebellar neurons; the ratio of the two means is 17 (computed: $1.50 \times 10^{-8} / 0.87 \times 10^{-9} = 17.2$). - Model: 1 billion neurons use 5.79 μmol glucose per min; 100 billion use 579 μmol per min.

For 86 billion neurons: $86 \times 10^9 \times 5.79 \times 10^{-9} = 498$ μmol glucose per min (computed). Over a day this is $498 \times 1,440 = 717,000$ μmol , or $0.717 \text{ mol} \times 180.16 \text{ g/mol} = 129 \text{ g}$ glucose per day (computed).

Oxygen. The brain uses 3.5 mL O_2 per 100 g per min [36]. A brain of about 1,400 g uses about 49 mL O_2 per min, close to one fifth of basal body oxygen use in a healthy young adult [36]. Over a day this is $49 \times 1,440 = 70.6 \text{ L } \text{O}_2$ (computed).

Share of resting metabolism. The adult brain uses 20 % of resting metabolism [36]. In childhood the share is far higher [37]:

stage	share of resting metabolic rate, males	females	share of daily energy, males	females
birth	52.5 %	59.8 %	35.4 %	38.7 %
childhood peak	66.3 %	65.0 %	43.3 %	43.8 %

The peak lies in childhood, not at birth [37]. Body growth rate is inversely related to

brain glucose use until puberty [37]. The abstract does not state the ages of the peak [37].

Gene copies and screens. SRGAP2: 3 human-specific copies (B, C, D) [5]. NOTCH2NL: 3 paralogs highly expressed in radial glia [16]. Screens: 56 human radial-glia genes without mouse orthologs [6]; 35 hominid-specific duplicated genes [15].

Ants on Earth [38]: - Individuals: almost 20×10^{15} ($19.8 \pm 5 \times 10^{15}$); ground-dwelling ants over 3×10^{15} . - Dry biomass: about 12 Mt C (12.3 ± 3.1 Mt C). - Biomass comparisons: more than wild birds and mammals combined; about 20 % of human dry biomass. - Basis: 489 studies (abstract) or 465 studies at 1,306 sampling locations (results); both counts are printed in the paper. - Named ant species and subspecies: “more than 15,700”.

Known ant species rose from “roughly 5,000–6,000 circa 1,940” to “> 14,000 today”, and subfamilies from 6 to about 20 [3].

Internet users (ITU, 17 November 2025) [39]: - About 6 billion people online in 2025, about three quarters of the world population. - Growth in 2025: more than 240 million. - 2024 revised from 5.5 to 5.8 billion (71 %). - Offline: 2.2 billion in 2025; 2.3 billion in 2024, revised from 2.6 billion (29 %). - 96 % of the offline live in low- and middle-income countries. - Use: 94 % in high-income against 23 % in low-income countries. - Use: men 77 % against women 71 %; urban 85 % against rural 58 %. - 5G: about 3 billion subscriptions, about one third of mobile broadband.

Order of events

1. 3.5–2.0 Ma. *Australopithecus* at about 450 cc, roughly unchanged [3]. Positions 62.59–62.08.
2. About 3.4 Ma. SRGAP2B formed [5]. Position 62.56.
3. 3.3 Ma. Lomekwian stone tools, West Turkana [8]. Position 62.53.
4. 2.6–2.5 Ma. Oldowan tools at Gona [9]. Positions 62.32–62.28.
5. About 2.4 Ma. SRGAP2C formed [5]. Position 62.24.
6. 2.10 Ma. First change point in brain size; the rate rises from 0.03 to 0.35 $\log_{10}$ cc per Myr [3]. Position 62.12.
7. 1.97 Ma. Second change point with small-brained *Homo* included; rate 0.20 [3]. Position 62.06.
8. 1.76 Ma. First Acheulean, Kokiselei 4 [10]. Position 61.96.
9. 1.49 Ma. Second change point without small-brained *Homo*; rate 0.19 [3]. Position 61.81.
10. About 1 Ma. SRGAP2D formed [5]. Position 61.45.
11. 335–236 ka. *H. naledi* at 460–560 mL [21]. Positions 60.45–60.13.
12. About 73 ka. Abstract drawing at Blombos Cave [11]. Position 59.06.
13. At least 51.2 ka. Narrative cave art at Leang Karampuang [12]. Position 58.74.
14. About 3 ka. Proposed decrease in brain size [3]; no change detected in the reanalysis [23]. Position 56.16.

Two dated events carry no number in the source and no position. These are the *ARHGAP11B* duplication after the chimpanzee split [6] and the Late Cretaceous to Early Eocene diversification of ants [13].

The life course, placed by age:

1. Before 27 weeks of gestation. Synaptogenesis begins [14]. Position 48.27.
2. Birth. Whole brain about one third of elderly volume [27]; brain uses 52.5–59.8 % of resting metabolism [37].
3. 0–90 days. Growth from 1 % to 0.4 % per day; 64 % in total [27]. Position 47.60.
4. About 3 months. Auditory synapse density peak [14]. Position 47.61.
5. After 15 months. Frontal synapse density peak [14]. Position 49.07.
6. 1.7 y. Cortical thickness peak [28]. Position 49.35.
7. 5.9 y. Grey matter peak [28]. Position 50.49.
8. Childhood. Brain share of resting metabolism peaks at 65.0–66.3 % [37].
9. 12 y. Auditory synapse elimination ended [14]. Position 51.13.
10. 12.5 y and 14.4 y. Total cerebrum and subcortical grey matter peak [28]. Positions 51.17 and 51.30.
11. Puberty. Prefrontal spine decline begins [29].
12. Past late adolescence. Human myelination still rising, unlike chimpanzee [19].
13. Third decade. Prefrontal spine remodelling continues [29].
14. 28.7 y. White matter volume peak [28]. Position 51.93.
15. Range 20–80 y, spanning items 13 and 14. Myelinated fibre length falls by 45 % over this range [25]. Positions 51.60–52.86.

Present quantities

Brain mass at autopsy. Men: 1,407 g, range 1,070–1,767 [40]. Women: 1,233 g, range 1,000–1,618 [40].

Adult energy. About 20 % of resting energy at about 2 % of body mass [36, 2]. 49 mL O₂ per min for a brain of about 1,400 g [36]. 129 g glucose per day, computed from neuron number and per-neuron use.

Myelinated fibre at age 20. 176,000 km in men and 149,000 km in women [25].

Ants. 19.8×10^{15} individuals, 12.3 Mt C, more than 15,700 named ant taxa [38].

Internet. Users rose from 5.8 billion in 2024 to about 6 billion in 2025; 2.2 billion were offline in 2025 [39].

Pattern

ECV runs from about 450 cc (*Australopithecus*) through 426–560 mL (*H. floresiensis*, *H. naledi*) to 1,297–1,460 cc in modern humans [3, 22, 21, 23]. The rate of increase steps up at 2.10 Ma and changes again at 1.49 or 1.97 Ma [3]. SRGAP2 copies date to 3.4, 2.4 and 1 mya [5].

Tool and image dates run 3.3, 2.6–2.5 and 1.76 Ma, then 73 and 51.2 ka [8, 9, 10, 11, 12]. Synaptogenesis begins before 27 weeks; peaks of growth follow one another from 3 months to 28.7 years [14, 28]. The brain's share of resting energy runs from 52.5–59.8 % at birth to 65.0–66.3 % in childhood and 20 % in adults [37, 36].

Not verified

- Du dataset of 94 fossil specimens of 13 species, 3.2 Ma to 500,000 years ago (University of Chicago Medicine release on [4]) — secondary.
- A 3.8-million-year-old hominin cranium from Woranso-Mille [41] — V-bib; *A. anamensis* 365–370 cm³ [42] — secondary.
- Earliest *H. erectus* revised to about 860 cc against a previous mean of about 991 cc; modern humans about 1,300 cc (Royal Society release on [22]) — secondary.
- ECV table values for *H. habilis* to *H. sapiens*; *A. afarensis* 438 and *A. africanus* 452; modern average 1,473 cm³ [42] — secondary.
- Jebel Irhoud *H. sapiens* about 300,000 years ago at present-day brain size, about 1,400 mL; globular shape between 100,000 and 35,000 years ago (Max Planck release on [43]) — secondary.
- *ARHGAP11B* duplication about 5 million years ago; splice substitution between 1.5 million and 500,000 years ago; 47 human-specific amino acids; 55 nucleotides absent (Max Planck release on [7]) — secondary.
- NOTCH2NL functional and duplicated twice more about 3 to 4 million years ago (University of Amsterdam release on [16]) — secondary.
- Human-specific SRGAP2 paralogs induce neoteny of spine maturation [44] — V-bib (title statement).
- FOXP2: two human-specific amino-acid changes against chimpanzee, three against mouse; fixation within the past 200,000 years; 44 human chromosomes without polymorphism (Genome Biology news on [17]) — secondary.
- Derived FOXP2 variant shared with Neandertals [45] — V-bib (title statement).
- Honeybee colony 40,000–80,000 bees; workers replaced about every four months; queen 3–5 years, up to 8; age-graded tasks [42] — secondary.
- Army ant colonies over 15 million workers; 3,000 prey items per hour [42] — secondary.
- Army ant queens laying several million eggs per month; nomadic phase about 15 days; trails over 20 m wide [42] — secondary.
- Proto-cuneiform: numerical tablets c. 3500–3350 BC; non-numerical signs from about 3350–3300 BC; about 5,000 tablets; about 2,000 signs; 85 % administrative [42] — secondary.
- Gorilla 33.4 and chimpanzee 28 billion brain neurons (Karger table, see A9) — secondary.

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Part C — Tables Across the Chapters

All values are copied from the ten Layer A chapters of *From Cell to Mind* (A1–A10) and their data files. References are chapter-local: “A3 [12]” is reference 12 of chapter A3. A dash (—) means no value or no position is printed or computable.

An age of A Myr is placed as a duration of $A \times 10^6 \times 3.15576 \times 10^7$ s; positions are

computed with the ladder tool (pos.py time) and given to two decimals.

C1 First appearances

All FIRST rows of the ten data files with an age in Ma, merged and ordered from oldest to youngest by the older printed age. Rows with the same wording and the same age are merged and list every chapter. For a range the position of each end is given; for $\pm$ the central position is followed by the ends in brackets.

structure, capacity or lineage	age (Ma)	position	evidence	chapter [ref]
last universal common ancestor (LUCA), all cells with a membrane potential	about 4,200 (4,090–4,330); composite 3,940–4,520	69.04 (69.02–69.07); composite 68.98–69.11	molecular	A1 [1]
last universal common ancestor (LUCA)	>3,900	68.97	molecular	A1 [2]
crown Bacteria and crown Archaea	<3,400	68.85	molecular	A1 [2]
Nav-like voltage-gated channel genes (before multicellularity)	>1,000	67.73	molecular	A1 [3]
crown Metazoa	649.8–833.5	67.34–67.57	molecular	A2 [13]
Cnidaria (origin)	741 (686–819)	67.46 (67.39–67.55)	molecular	A3 [10]
split of animals from unicellular relatives; post-synaptic scaffold backbone (Shank, Homer, DLG), Munc18/syntaxin-1, Cav and Nav-like channels already present	>800	67.53	molecular	A2 [4, 6, 7, 8]
Paranodal Caspr / neurexin IV proteins	>750 (conserved “over 750 million years”)	67.47	molecular	A5 [1]
crown Eumetazoa	625.9–746.2	67.31–67.47	molecular	A2 [13]
crown Bilateria (ancestor with ≥ 30 neuropeptide systems)	595.7–688.3	67.26–67.39	molecular	A2 [13, 26]
crown Deuterostomia	587.2–662.3	67.25–67.36	molecular	A2 [13]
crown Protostomia	578.1–653.1	67.23–67.35	molecular	A2 [13]

crown Cnidaria	531.5–641.8	67.16–67.33	molecular	A2 [13]
Bilaterian phyla (divergence)	>100 Myr before the Cambrian (before 638.8, computed)	67.33	molecular	A3 [11]; A4 [11]
sponge sterane biomarkers (algal origin also proposed)	>635	67.32	geochemical	A2 [9, 10, 11]
sponges, divergence from other animals	>600	67.27	molecular	A2 [5]
first complex Ediacaran macrofossils (Mistaken Point)	574.17 ± 0.66	67.23 (67.23–67.23)	fossil	A2 [35]
Architecturally complex Ediacaran macrofossils	574.17 ± 0.66	67.23 (67.23–67.23)	fossil	A3 [13]
Ediacara biota	541–571	67.17–67.22	fossil	A2 [36]
Ediacara biota, including <i>Ikaria</i> (oldest bilaterian)	~571–539 (chapter A2 source: 571–541)	67.22–67.17 (chapter A2 source: 67.22–67.17)	fossil	A4 [13]
Animal musculature (proposed, cnidarian, <i>Haootia</i>)	~560	67.21	fossil	A3 [14]
Cyclostome–gnathostome last common ancestor, with sensorimotor pallium and thalamocortical relay	~560	67.21	phylogenetic	A4 [10]
<i>Dickinsonia</i> , animal by its sterols	558	67.20	fossil	A2 [36]
Chordates (proposed)	Ediacaran, ~555	67.20	fossil (proposal from fossils)	A4 [19]
Vertebrates (<i>Myllokunmingia</i> , <i>Haikouichthys</i>)	Lower Cambrian, Chengjiang (≤518.03; Cambrian given as 545–490)	67.13; Cambrian 67.18–67.08	fossil	A4 [19, 14]
Major cnidarian taxa (diversification)	before the Cambrian (543 in abstract)	67.18	molecular	A3 [10]
cnidarian Na ⁺ -selective channel group (divergence from Ca ²⁺ -conducting	>540	67.17	molecular	A1 [5]

homologues)				
cnidarian Nav2.5 (DKEA filter), by duplication	>540	67.17	molecular	A1 [3]
cnidarian Na ⁺ -selective channel group; cnidarian Nav2.5 duplication	>540	67.17	molecular	A2 [37, 8]
base of the Cambrian	538.8 ± 0.2	67.17 (67.17–67.17)	fossil (chart)	A2 [38]
Unipartite brain (<i>Kerygmachela</i>)	Cambrian Stage 3 (base ~521)	67.14	fossil	A4 [8, 12]
Tripartite brain with three optic centres (<i>Fuxianhuia</i>)	520 as printed (disagrees with Chengjiang ≤518.03 [14])	67.14; Chengjiang 67.13	fossil	A4 [15, 14]
Optic neuropil, head and trunk ganglia (<i>Alalcomenaeus</i>)	by 520 as printed (disagrees with Chengjiang ≤518.03 [14])	67.14; Chengjiang 67.13	fossil	A4 [16, 14]
vertebrates; vertebrate sensory consciousness (stated position, Feinberg & Mallatt 2013)	before 520 (Cambrian)	67.14	as stated in framework	A9 [4]
Chengjiang biota	≤518.03	67.13	fossil	A2 [34]
Pre-protocerebral ganglia (<i>Lyrarapax</i>)	Chengjiang (≤518.03)	67.13	fossil	A4 [17, 14]
Arthropod compound eyes, >3,000 lenses per eye	~515	67.13	fossil	A6 [16]
<i>Anomalocaris</i> compound eyes, ≥16,000 lenses per eye	~515	67.13	fossil	A6 [15]
cnidarian-specific Cav genes, conserved at least	500	67.10	molecular	A1 [3]
Cyclostome–gnathostome split, with MGE and rhombic lip before it	>500	67.10	phylogenetic	A4 [9]
cladorhizid and spongillid demosponges, divergence	~450	67.01	molecular	A2 [4]
Ordovician agnathans	450	67.01	fossil	A6 [17]

Common neural signatures of sleep in the vertebrate brain	“may have emerged” over 450 (inferred)	67.01	phylogenetic (comparison of zebrafish with amniote sleep)	A7 [11]
crown living ctenophores	350 ± 88 (earlier hypothesis ~65)	66.78 (66.51–66.98); earlier hypothesis 65.25	molecular	A2 [15]
Next non-biomineralized eyes of similar complexity	~85 Myr after 515, i.e. ~430 (computed)	66.97	fossil	A6 [16]
Four major shifts in amniote neuron–brain scaling	over 300 Myr	66.64	phylogenetic	A5 [6]
amniote neuron–brain scaling history (≥4 major changes)	over 300 Myr	66.64	phylogenetic	A9 [3]
vampire squid and dumbo octopus lineages	242 ± 38	66.44 (66.29–66.57)	molecular	A9 [2]
lobate and cydippid ctenophores, divergence	160–260	66.07–66.51	molecular	A2 [4]
<i>Australopithecus</i> ECV about 450 cc, roughly unchanged	3.5–2.0	62.59–62.08	fossil	A10 [3]
SRGAP2B (first human-specific SRGAP2 duplication)	about 3.4	62.56	molecular	A10 [5]
stone tools, Lomekwi 3	3.3	62.53	fossil (archaeological)	A10 [8]
proposed onset of new SRGAP2 function (stated position)	2–3	62.08–62.45	molecular	A10 [5]
Oldowan tools, Gona	2.6–2.5	62.32–62.28	fossil (archaeological)	A10 [9]
SRGAP2C	about 2.4	62.24	molecular	A10 [5]
first change point in hominin brain size	2.10 ± 0.07 (2.10 ± 0.05 with small-brained <i>Homo</i>)	62.12 (62.09–62.15); with small-brained <i>Homo</i> 62.12 (62.10–62.14)	fossil (modelled)	A10 [3]
second change point in hominin brain size	1.49 ± 0.14 (1.97 ± 0.12 with small-brained <i>Homo</i>)	61.81 (61.72–61.89); with small-brained <i>Homo</i> 62.06 (62.01–62.12)	fossil (modelled)	A10 [3]
Acheulean, Kokiselei 4	1.76	61.96	fossil (archaeological)	A10 [10]

SRGAP2D	about 1	61.45	molecular	A10 [5]
<i>H. naledi</i> , Dinaledi Chamber	0.335–0.236 (0.226 in the significance statement)	60.45–60.13 (significance statement 60.09)	fossil	A10 [21]
abstract drawing, Blombos Cave	about 0.073	59.06	fossil (archaeological)	A10 [11]
narrative cave art, Leang Karampuang	at least 0.0512	58.74	fossil (archaeological)	A10 [12]

C1, continued: first appearances without an age in Ma. These rows give only a period name, an ancestor or a relative time, so no position is computed. They are listed in chapter order.

structure, capacity or lineage	age as given	evidence	chapter [ref]
Ca ²⁺ -conducting Nav2 channels	before the fungal–animal split (no Ma given)	phylogenetic	A1 [3]
Cav channels in the plant–animal common ancestor	not given	phylogenetic	A1 [3]
fast Na ⁺ /Ca ²⁺ action potential, ancestral unicellular eukaryotes	not given	phylogenetic	A1 [6]
Nav1 (DEKA filter), urbilaterian	not given	phylogenetic	A1 [3]
armoured ctenophores, Scleroctenophora	early Cambrian (no Ma given)	fossil	A2 [14]
Crown animals	Cryogenian (no bounds given)	molecular	A3 [11]; A4 [11]
Free-swimming medusa (<i>Burgessomedusa</i>)	middle Cambrian	fossil	A3 [15]
Nerve cords, excretory organs, coeloms	after the xenacoelomorph split	phylogenetic	A4 [3]
Myelin proteins CNP, PMP22, MAL, PLP	“evolutionarily older than vertebrates”; no Ma given	molecular	A5 [4]
Myelin in vertebrates (placoderms, first jawed vertebrates)	“around the time of hinged jaws” [4]; no date in Ma given	phylogenetic	A5 [1, 4]
Myelin in calanoid copepods (three younger superfamilies)	no date read	phylogenetic	A5 [5]
Giant axons (“invertebrates such as squid”)	no date given	not stated	A5 [2]
First opsin (gene duplication; possibly not light-sensitive)	eumetazoan ancestor; no Ma given	phylogenetic	A6 [11]
At least 4 opsin paralogs	Cnidaria + Bilateria	phylogenetic	A6 [12]

	ancestor; no Ma given		
C, R and Go/RGR opsin progenitors	neuralian ancestor; no Ma given	phylogenetic	A6 [11]
At least 9 opsin paralogs	bilaterian ancestor; no Ma given	phylogenetic	A6 [12]
Cone-like cells	“first appear among cnidarians”; no Ma given	phylogenetic	A6 [13]
All kinds of cone pigments	before rod pigments; no Ma given	molecular	A6 [13]
Lateral-line electroreception (lampreys, jawed fishes)	early vertebrates; no Ma given	phylogenetic	A6 [10]
Mechanosensitive channels (bacteria, fungi, plants, animals)	no Ma given	phylogenetic	A6 [20]
Piezo homologs (invertebrates, plants, protozoa)	no Ma given	molecular	A6 [8]
Slow-wave and REM sleep dynamics	not given (“at least to the emergence of amniotes”)	phylogenetic	A7 [9]
Infraslow sleep rhythm	not given (“conserved across amniotes”)	phylogenetic	A7 [10]
Sleep-like state in Cnidaria	not given (“an earlier-branching metazoan lineage”)	phylogenetic	A7 [7]
<i>kaiC</i> (oldest of the kai clock genes)	not given	molecular (≈ 70 prokaryotic genomes)	A7 [6]
<i>kaiA</i> (youngest kai gene, likely cyanobacteria only)	not given	molecular (≈ 70 prokaryotic genomes)	A7 [6]
insect subjective experience (stated position, Barron & Klein 2016)	Cambrian (no number given)	as stated in framework	A9 [5]
crown coleoid cephalopods	Silurian–Devonian (no number given)	molecular	A9 [2]
decabrachian diversification	Jurassic (no number given)	molecular	A9 [2]
neural basis of sensory consciousness in birds (stated position, Nieder et al. 2020)	before the bird–mammal split, or independently in birds (no number given)	as stated	A9 [6]
<i>ARHGAP11B</i> partial duplication	after human–chimpanzee split (no number given)	molecular	A10 [6]
ant diversification	Late Cretaceous–Early Eocene (no number given)	molecular/phylogenetic	A10 [13]
mushroom-body	before eusociality (no	phylogenetic	A10 [3]

elaboration in Hymenoptera	number given)		
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C2 Repeated origins

Every ORIGINS row of the ten data files, in chapter order. Chapters A3 and A8 give no number of origins or losses.

trait	origins	losses	chapter [ref]
Na ⁺ selectivity of animal voltage-gated Na ⁺ channels	2 (cnidarians; Bilateria)	—	A1 [5, 3]
four-domain Na ⁺ /Ca ²⁺ channels	not given	not given as a number; losses named in land plants and fungi	A1 [7]
four-domain Na ⁺ /Ca ²⁺ channels	not given	absent in the pennate diatom <i>Phaeodactylum tricornutum</i>	A1 [29]
four-domain Nav from a single-domain gene	not given (two rounds of duplication)	—	A1 [3]
neural systems (ctenophore-first reading)	independent in ctenophores; single origin called “a less parsimonious scenario”	—	A2 [2]
nervous systems (review)	single origin “compatible”; independent complexification favoured	complete loss in “two examples” of animals, both parasites	A2 [3]
nervous system in ctenophores (<i>Mnemiopsis</i> genome)	not given	possible loss read in the abstract	A2 [16]
placozoan genes	—	4,952 genes lost (modelled)	A2 [2]
Ventral nerve cords	“many times” (convergent; no number)	not given	A4 [2]
Dorsoventral patterning and trunk neuroanatomy similarities	evolved independently (no number)	not given	A4 [2]
Bilaterian nerve cord and brain	one fused system from two centres	not given	A4 [1]
Tripartite brain (euarthropods, chordates)	convergent (no number)	not given	A4 [8]
Central complex and basal ganglia	one (“deep homology”, proposed)	not given	A4 [7]
Brain regionalisation as in crown gnathostomes	not an innovation of gnathostomes (present in cyclostomes)	not given	A4 [9]

Xenacoelomorph body plan	"simplified relatives of the Ambulacraria" (no number)	not given	A4 [4]
Myelin	"several times" in vertebrates, annelids and crustacea (3 taxa); occurs in 5 groups in 3 bilaterian superclades	not given	A5 [1]
Myelin within calanoid copepods	present in 3 younger of 5 surveyed superfamilies (20 species); absent in 2 older	not given	A5 [5]
Eyes / photoreceptor lines	at least 40	not given	A6 [17]
Eyes / photoreceptor lines	at least 40, possibly up to 65 or more	not given	A6 [19]
Resolving eyes	about a quarter of the Precambrian lines	not given	A6 [17]
Electroreception within teleosts	at least 2	not given	A6 [10]
Ampullary electroreceptors	2 (Osteoglossomorpha, Ostariophysi)	not given	A6 [10]
Electroreception, all vertebrates	at least 4 (computed: ≥ 2 teleost + 1 ancestral + 1 monotreme)	3 (frogs, amniotes, neopterygians) + 2 later (Asian notopterids, characiforms)	A6 [10]
Electric organ	6	not given	A6 [22]
Opsin genes	"duplicated ... many times"	"lost many times"	A6 [12]
Olfactory receptor genes, mammals	gains: >750 (opossum lineage); >400 each (cetartiodactyl, rodent)	>170 on each branch to placental orders; gains plus losses 4,968 or 5,134	A6 [5]
Prokaryotic kai clock genes	not numbered ("multiple lateral transfers, and gene duplications")	not numbered ("losses" stated)	A7 [6]
complex brains and high intelligence	7 named groups (insects, octopodids, teleosts, birds, cetaceans, elephants, primates) in 3 bilaterian lineages	not given	A9 [1]
brain organisations for higher-order cognition	at least 3 (mammals, birds, teleosts)	not given	A9 [13]
eusociality (Hymenoptera examined; single mating ancestral in each)	8	not given	A10 [20]
human-specific SRGAP2 copies (duplication events)	3 (B, C, D)	not given	A10 [5]

<i>ARHGAP11B</i> (partial duplication of <i>ARHGAP11A</i>)	1	not given	A10 [6]
NOTCH2NL paralogs highly expressed in radial glia	3	not given	A10 [16]

C3 Sizes

All rows of the Sizes tables of the ten chapters, sorted by position, smallest first. A row with several positions is placed by its smallest. The mark after the reference is the chapter's own (computed, modelled); rows the chapter marks as measured carry no mark.

what	size	position	chapter [ref]
KvAP isolated voltage sensor, structure resolution	1.9 Å	−4.99	A1 [33]
NavAb structure resolution	2.7 Å	−4.67	A1 [32]
Hair-bundle deflection read	0.3 nm	−4.57	A6 [2]
KcsA structure resolution	3.2 Å	−4.51	A1 [31]
KvAP full channel, structure resolution	3.2 Å	−4.51	A1 [33]
NavAb selectivity filter, width	about 4.6 Å	−4.18	A1 [32]
KcsA, distance between two K ⁺ ions in the filter	about 7.5 Å	−3.74	A1 [31]
KcsA water-filled cavity	about 10 Å	−3.48	A1 [31]
KcsA selectivity filter, length	12 Å	−3.31	A1 [31]
TEM pixel size, <i>Platynereis</i> (finest)	2.2 nm	−2.76	A4 [20]
TEM pixel size, <i>Platynereis</i>	3.7 nm	−2.29	A4 [20]
Bacteriorhodopsin diameter	4.3 ± 0.5 nm	−2.15	A6 [24]
KcsA pore, length	45 Å	−2.11	A1 [31]
TEM pixel size, <i>Platynereis</i> (coarsest)	5.7 nm	−1.89	A4 [20]
Voxel side, fly hemibrain	8 nm	−1.58	A4 [25]
SBF-SEM lateral resolution, <i>Hydra</i>	20 nm	−0.75	A3 [1]
SBF-SEM step, <i>Hydra</i>	30 nm	−0.38	A3 [1]
TEM section thickness,	40 nm	−0.12	A4 [20]

<i>Platynereis</i>			
<i>Mnemiopsis</i> synaptic vesicle, median (n = 56)	51 nm	0.10	A2 [29]
Fly microvillus width	~55 nm	0.17	A6 [25]
<i>Mnemiopsis</i> dense-core vesicle, median (n = 66)	202 nm	1.36	A2 [29]
<i>Trichoplax</i> secretory granules	300–500 nm	1.72–2.18	A2 [23]
Human cone value	420 nm	2.02	A6 [2]
Macaque blue cone reference	430 nm	2.04	A6 [26]
Human melanopsin value	~480 nm	2.14	A6 [2]
Human rod value	498 nm	2.18	A6 [2]
Wavelength of light (Land)	~0.5 μm	2.18	A6 [17]
Macaque green cone reference	530 nm	2.23	A6 [26]
Human cone value	534 nm	2.24	A6 [2]
Macaque red cone reference	560 nm	2.28	A6 [26]
Human cone value	564 nm	2.29	A6 [2]
Rushton's critical diameter (disputed)	1 μm	2.81	A5 [13]
Fly microvillus length	~1 μm	2.81	A6 [25]
Tentacle axon, <i>Aglantha</i>	3.6–7.8 μm	3.98–4.68	A3 [7]
Second neurite contact, <i>Hydra</i>	~4 μm	4.07	A3 [1]
<i>Chlamydomonas</i> cell body, radius	4.4 $\pm$ 0.3 μm	4.16	A1 [34]
<i>Trichoplax</i> secretory cells, spacing	about 5 μm	4.28	A2 [23]
Ring giant axon, one 10 mm <i>Aglantha</i>	5–24 μm	4.28–5.70	A3 [7]
<i>Salpingoeca rosetta</i> cell, equivalent-sphere diameter (from 105.9 μm^3)	5.87 μm	4.42	A2 (computed)
algae eaten by <i>Trichoplax</i>	9 $\times$ 6 μm	4.81 $\times$ 4.44	A2 [23]
Dendrite length per mitochondrion	7 μm	4.58	A5 [9]
Motor giant axon, one <i>Aglantha</i>	7.5–32 μm	4.64–5.97	A3 [7]
Neurite finger overlap at a contact, <i>Hydra</i>	~8 μm	4.70	A3 [1]
<i>Chlamydomonas</i> cell body, diameter	8.8 μm	4.79	A1 (computed)

<i>Trichoplax</i> cilia	about 10 μm	4.91	A2 [23]
Ectodermal nerve cell body, <i>Hydra</i>	$\sim 10 \mu\text{m}$	4.91	A3 [1]
SBF-SEM block, short side	13 μm	5.15	A3 [1]
<i>Chlamydomonas</i> flagellum	$13.5 \pm 0.8 \mu\text{m}$	5.18	A1 [34]
neuroblast, honeybee larva stage 1 (diameter)	20 μm	5.54	A9 [11]
Ring giant axon, <i>Aglantha</i>	22–35 μm	5.62–6.05	A3 [7]
Slab thickness, male fly nerve cord	$\sim 25 \mu\text{m}$	5.74	A4 [24]
Bee ommatidial lens diameter	25 μm	5.74	A6 [17]
Biexponential λ_2 , waking and REM	$0.03 \pm 0.01 \text{ mm}$	5.91	A7 [19]
<i>M. mymaripenne</i> adult CNS, 52,200 μm^3 , cube edge	37.4 μm	6.11	A9 [15] (computed)
Motor giant axon, <i>Aglantha</i>	up to 40 μm	6.17	A3 [7]
TEM sections span, <i>Hydra</i>	40 μm	6.17	A3 [1]
<i>M. mymaripenne</i> pupal CNS, 93,600 μm^3 , cube edge	45.4 μm	6.28	A9 [15] (computed)
Distance between two reconstructed cell bodies	$\sim 50 \mu\text{m}$	6.37	A3 [1]
Spacing of ectodermal cell bodies, <i>Hydra</i>	50–100 μm	6.37–7.00	A3 [1]
Decapod facet	$\sim 50 \mu\text{m}$	6.37	A6 [17]
SBF-SEM block, long side	56 μm	6.47	A3 [1]
Width, juvenile acoel	100 μm	7.00	A4 [5]
Small pigmented pit eyes	$< 100 \mu\text{m}$	7.00	A6 [17]
Penaeid shrimp myelinated fibre	120 μm	7.17	A5 [1]
<i>Megaphragma caribea</i> body length	170 μm	7.49	A9 [15]
<i>Trichoplax</i> , reach of a pausing animal	up to about 200 μm	7.63	A2 [23]
Length, juvenile acoel	200 μm	7.63	A4 [5]
Height of recorded volume, larval zebrafish	200 μm	7.63	A4 [26]
Scale bar on the <i>Stentor</i>	200 μm	7.63	A8 [8]

cell image			
<i>M. mymaripenne</i> body length	200 μm	7.63	A9 [15]
Side of hemibrain sample	$\sim 250 \mu\text{m}$	7.84	A4 [25]
Diameter of nerve-cord sample	up to 250 μm	7.84	A4 [24]
Edge of cube with fly neuropil volume 0.0175 mm^3	0.26 mm	7.87	A4 [27] (computed)
<i>Trichoplax</i> animal, diameter	0.3–1.5 mm	8.00–9.47	A2 [23]
Small <i>Hydra</i> in imaging work	$\sim 0.3 \text{ mm}$	8.00	A3 [24]
Squid giant axon, August	383 μm (SEM 14.68)	8.23	A5 [12]
<i>Trichoplax</i> animal holding about 1,500 secretory cells	500 μm	8.47	A2 [23]
Length of nerve-cord sample	$> 500 \mu\text{m}$	8.47	A4 [24]
Merkel disc spatial resolution	0.5 mm	8.47	A6 [2]
Squid (<i>Loligo pealei</i>) giant axon, May	506 μm (SEM 26.8)	8.48	A5 [12]
Width of recorded volume, larval zebrafish	600 μm	8.63	A4 [26]
Median intrinsic neuron path length, fly brain	685 μm	8.75	A4 [27]
Length of recorded volume, larval zebrafish	800 μm	8.90	A4 [26]
<i>Ciona</i> tadpole larva	$\sim 1 \text{ mm}$	9.10	A4 [21]
Scallop eye	$\sim 1 \text{ mm}$	9.10	A6 [17]
Reversal distance after a tap, <i>C. elegans</i>	around 1 mm	9.10	A8 [13]
Honeybee brain volume, 1 $\mu\text{L} = 1 \text{ mm}^3$; edge of an equal cube	1 mm	9.10	A8 [16] (computed)
honeybee brain, about 1 mm^3 , cube edge	1 mm	9.10	A9 [16] (measured; edge computed)
Mean path length per neuron, fly brain	1.07 mm	9.16	A4 [27] (computed)
<i>B. subtilis</i> biofilm signal profile	about 1.5 mm	9.47	A1 [8]
Small <i>Nematostella</i> (20–40 longitudinal neurons)	2.5–5 mm	9.93–10.56	A3 [25]
Human pupil	$\sim 2.5 \text{ mm}$	9.93	A6 [17]
<i>Mnemiopsis</i> cydippids at 3–5 days	3–5 mm	10.10–10.56	A2 [29]

λ , REM sleep (n = 11)	3.1 ± 0.5 mm	10.13	A7 [19]
LFP correlation length λ , waking (n = 8)	3.7 ± 0.4 mm	10.29	A7 [19]
<i>Tripedalia</i> bell	7–9 mm	10.87–11.10	A3 [20]
Reach of joint silence and firing in SWS	7 mm	10.87	A7 [19]
Biexponential λ_1 , REM	7.5 ± 0.5 mm	10.93	A7 [19]
<i>Aglantha</i> specimen	10 mm	11.19	A3 [7]
Large <i>Hydra</i> in imaging work	~1 cm	11.19	A3 [24]
Object detectable at a 5° acceptance angle	1 cm	11.19	A6 [17]
Biexponential λ_1 , waking	10.6 ± 0.6 mm	11.25	A7 [19]
λ , SWS (n = 15)	13.0 ± 1.2 mm	11.43	A7 [19]
Biexponential λ_2 , SWS	13.3 ± 0.9 mm	11.45	A7 [19]
Biexponential λ_1 , SWS	16.1 ± 1.5 mm	11.63	A7 [19]
<i>Anomalocaris</i> eye	2–3 cm	11.83–12.19	A6 [15]
Acoel phototaxis distance before decapitation	2.59 cm	12.06	A4 [6]
reduction from a 5 kg fall in body size, 22 mL, cube edge	2.80 cm	12.13	A10 [3] (computed)
Human cochlea	35 mm	12.33	A6 [2] (reused)
<i>Aurelia</i> in nerve-net model	~4 cm diameter	12.46	A3 [26] (modelled)
Smallest <i>Aurelia</i> , fastest beats	~5.08 cm (~2 inch)	12.67	A3 [27] (computed)
cleaner wrasse body length, lower	51 mm	12.68	A9 [18]
cleaner wrasse body length, upper	68 mm	12.94	A9 [18]
<i>H. floresiensis</i> LB1, 426 cc, cube edge	7.52 cm	13.03	A10 [22] (measured; edge computed)
Larger <i>Aurelia</i>	~7.62 cm (~3 inch)	13.04	A3 [27] (computed)
<i>Australopithecus</i> , about 450 cc, cube edge	7.66 cm	13.05	A10 [3] (edge computed)
<i>H. naledi</i> DH3, 460 mL, cube edge	7.72 cm	13.05	A10 [21] (measured; edge computed)
<i>H. naledi</i> DH3/DH4 composite, 465 mL, cube edge	7.75 cm	13.06	A10 [21] (edge computed)
<i>H. habilis</i> , lower, 500 mL, cube edge	7.94 cm	13.08	A10 [21] (edge computed)
<i>H. erectus</i> , lower, 550 mL, cube edge	8.19 cm	13.11	A10 [21] (edge computed)
<i>H. naledi</i> DH1, 555 mL,	8.22 cm	13.11	A10 [21] (measured;

cube edge			edge computed)
<i>H. naledi</i> DH1/DH2 composite, 560 mL, cube edge	8.24 cm	13.11	A10 [21] (edge computed)
<i>H. habilis</i> , upper, 700 mL, cube edge	8.88 cm	13.18	A10 [21] (edge computed)
<i>H. erectus</i> , upper, 1,200 mL, cube edge	10.63 cm	13.35	A10 [21] (edge computed)
modern mean, DeSilva dataset, 1,297 cc, cube edge	10.91 cm	13.37	A10 [23] (edge computed)
Distance for the 1 cm object	11 cm	13.38	A6 [17]
modern, other estimates, lower, 1,340 cc, cube edge	11.02 cm	13.38	A10 [23] (edge computed)
modern, other estimates, upper, 1,460 cc, cube edge	11.34 cm	13.41	A10 [23] (edge computed)
<i>Burgessomedusa</i> umbrella height	up to 20 cm	13.92	A3 [15]
mirror, short side	0.30 m	14.29	A9 [18]
cortex surface, 973 cm ² per hemisphere, square edge	31.2 cm	14.33	A10 [24] (edge computed)
mirror, long side	0.45 m	14.66	A9 [18]
Compound eye with reduced peripheral resolution matching human acuity	~1 m	15.39	A6 [17] (modelled)
Compound eye matching human resolution	~12 m	17.65	A6 [17] (modelled)
Neuronal cable, male fly nerve cord	44 m	18.83	A4 [24]
Neuronal path length, fly brain	~149 m	19.94	A4 [27]
Argentine ant main supercolony, more than	6,000 km	29.59	A10 [26]
Human myelinated fibre length, women aged 80	82,000 km	31.97	A5 [14]
myelinated fibre, women, age 80	82,000 km	31.97	A10 [25]
Human myelinated fibre length, men aged 80	97,200 km	32.13	A5 [14]
myelinated fibre, men, age 80	97,200 km	32.13	A10 [25]
Human myelinated fibre length, women aged 20	149,000 km	32.52	A5 [14]

myelinated fibre, women, age 20	149,000 km	32.52	A10 [25]
Human myelinated fibre length, men aged 20	176,000 km	32.67	A5 [14]
myelinated fibre, men, age 20	176,000 km	32.67	A10 [25]

C4 Times

All rows of the Times tables of the ten chapters, sorted by position, smallest first. A row with several positions is placed by its smallest. Ages that the chapters enter in their Times tables as durations are kept.

Tables printed without a source column take the source named in the chapter sentence above them (A7 [2], A7 [10], A8 [26], A10 [28]).

what	duration	position	chapter [ref]
ion passage, KcsA at 10^8 ions s^{-1}	10 ns	16.39	A1 (computed)
ion passage at 10^7 ions s^{-1}	about 0.1 μs	18.48	A1 [36]
Hair cell forms its receptor potential	$\sim 10 \mu s$	22.67	A6 [2]
NaChBac Cole-Moore shift	533 μs	26.29	A1 [38]
Chronaxie, <i>Virgularia</i> nerve net	0.6–1 ms	26.40–26.87	A3 [6]
Chronaxie, <i>Pennatula</i> nerve net	~ 0.8 ms	26.66	A3 [6]
Motor giant spike at half amplitude, <i>Aglantha</i>	1.2–1.4 ms	27.03–27.17	A3 [7]
Minimum reaction time, <i>Undinula vulgaris</i> (myelinated copepod)	1.5 ms	27.23	A5 [5]
Ring giant spike, <i>Aglantha</i>	~ 1.6 ms	27.29	A3 [7]
Synaptic delay motor giant $\rightarrow$ myoepithelium	~ 1.6 ms	27.29	A3 [7]
Synaptic delay ring giant $\rightarrow$ motor giant	1.6–1.8 ms	27.29–27.40	A3 [7]
Minimum reaction time, <i>Neocalanus gracilis</i> (myelinated)	1.6 ms	27.29	A5 [5]
ultra fast	1.67–5 ms	27.33–28.33	A7 [2] (periods computed)
Span of the figure	1.67 ms–40 s	27.33–36.51	A7 [2] (periods computed)
neuron action potential	about 2 ms	27.50	A1 [27]

<i>Paramecium</i> "off" latency	2-4 ms	27.50-28.13	A1 [11]
Escape-burst impulse, <i>Aglantha</i>	2-3 ms	27.50-27.87	A3 [7]
Span in the text (500-0.05 Hz)	2 ms-20 s	27.50-35.88	A7 [2] (periods computed)
Copepod reaction time, upper value	2.5 ms	27.70	A5 [5]
Interval for one spike plus downstream events	2.5 ms	27.70	A5 [9] (modelled)
Human cone inactivation time constant, fast	~3 ms	27.87	A6 [27]
Minimum reaction time, <i>Labidocera madurae</i> (non-myelinated)	3.1 ms	27.90	A5 [5]
Minimum repeat interval, ring giant	3.5 ms	28.01	A3 [7]
<i>Paramecium</i> reversal latency	30 to ≤ 4 ms	29.96-28.13	A1 [11]
<i>Acartia</i> typical response to a hydrodynamic disturbance	4 ms	28.13	A5 [5]
Interval between copepod kicks	5 ms	28.33	A5 [5]
fast	5-12.5 ms	28.33-29.16	A7 [2] (periods computed)
Hippocampal ripples, 140-200 Hz	5-7.14 ms	28.33-28.65	A7 [2]
<i>Odontella</i> recovery from inactivation, τ	5.1 ± 0.4 ms	28.35	A1 [29]
Minimum reaction time, <i>Pleuromamma xiphias</i> (non-myelinated)	6.6 ms	28.58	A5 [5]
<i>Acartia</i> stroke and recovery	7 ms	28.64	A5 [5]
Human cone inactivation time constant, slow	~10 ms	28.96	A6 [27]
Membrane time constant	10-30 ms	28.96-29.96	A7 [2]
Mouse hippocampal gamma, 40-100 Hz	10-25 ms	28.96-29.80	A7 [20]
Gamma across species, 30-90 Hz	11.1-33.3 ms	29.06-30.06	A7 [2]
gamma	12.5-33.3 ms	29.16-30.06	A7 [2] (periods computed)
Myoepithelial impulse, <i>Aglantha</i>	15-70 ms	29.33-30.73	A3 [7]

Proteorhodopsin photocycle	15 ms	29.33	A6 [3]
<i>Chlamydomonas</i> response time τ_r	0.018 ± 0.009 s	29.50	A1 [34]
Macaque green cone integration time	19 ± 9.8 ms	29.55	A6 [26]
Transport rhodopsin photocycle, upper value	<20 ms	29.59	A6 [3]
Human cone dim-flash time to peak	~20 ms	29.59	A6 [27]
Spike-timing window, before or after	20 ms	29.59	A8 [4]
<i>Chlamydomonas</i> flagellar beat (43.2 Hz)	23 ms	29.73	A1 (computed)
Cycle of a 40-Hz oscillation	25 ms	29.80	A7 [2]
LTP-inducing train, 400 Hz	25 ms	29.80	A8 [17]
<i>Chlamydomonas</i> phototransduction delay	28 ± 11 ms; 38 ± 5 ms	29.90; 30.18	A1 [34]
Macaque red cone integration time	28 ± 14 ms	29.90	A6 [26]
<i>Paramecium</i> regenerative component absent below	30 ms	29.96	A1 [28]
beta	33.3–100 ms	30.06–31.06	A7 [2] (periods computed)
<i>Paramecium</i> ciliary beat (13–27 Hz)	37–77 ms	30.15–30.82	A1 (computed)
<i>Paramecium</i> electrotonic time constant	40–50 ms	30.22–30.43	A1 [28]
Absolute refractory period, <i>Pennatula</i> nerve net	40–50 ms	30.22–30.43	A3 [6]
Mouse activated-rhodopsin lifetime	40–45 ms	30.22–30.33	A6 [13]
Time to peak of escape contraction	40.5 ms (shortest)	30.23	A3 [7]
Macaque cone time to peak, within 1 mm of fovea	47 ± 14 ms	30.37	A6 [26]
<i>Odontella</i> action potential	50–100 ms	30.43–31.06	A1 [29]
<i>Paramecium</i> ciliary reversal	50 ms to 2.4 s	30.43–33.95	A1 [11]
Macaque green cone time to peak	51 ± 13 ms	30.44	A6 [26]
Macaque red cone time	55 ± 18 ms	30.51	A6 [26]

to peak			
Spindles, “12 to 18 Hz” (p. 349)	55.6–83.3 ms	30.52–30.89	A7 [2]
Spindles, “12 to 16 Hz” (p. 353)	62.5–83.3 ms	30.63–30.89	A7 [2]
<i>Paramecium</i> regenerative component reduced >75 % at	80 ms	30.85	A1 [28]
Sharp-wave ripple event	80–150 ms	30.85–31.43	A7 [2]
Sharp-wave ripple event	80–150 ms	30.85–31.43	A8 [21]
Alpha, “8 to 12 Hz”	83.3–125 ms	30.89–31.26	A7 [1, 2]
Rodent theta, 6–12 Hz	83.3–167 ms	30.89–31.52	A7 [2]
Population ON / OFF period in NREM, rat	815.5 ± 119.9 / 85.8 ± 5.9 ms	32.97 / 30.92	A7 [26]
Half relaxation of escape contraction	94 ms	31.00	A3 [7]
<i>Chlamydomonas</i> time to peak	97 ± 18 ms	31.03	A1 [34]
heart AV delay	100 ms	31.06	A1 [27]
Escape contraction complete	~100 ms	31.06	A3 [7]
theta	0.1–0.25 s	31.06–31.89	A7 [2] (periods computed)
Window of fast- oscillation synchrony, cat	100–500 ms	31.06–32.52	A7 [19]
Mouse hippocampal theta, 6–9 Hz (exploration, REM)	111–167 ms	31.15–31.52	A7 [20]
Mouse GNAT2C rod decay time constant	122 ms	31.24	A6 [13]
flytrap half- depolarization, 30 °C and 10 °C	0.13 ± 0.02 s; 0.29 ± 0.08 s	31.30; 32.03	A1 [15]
crow NCL visual response latency	144 ms	31.39	A9 [21]
<i>Mimosa</i> Ca ²⁺ rise before leaflet movement	up to 0.15 s	31.43	A1 [16]
Carnivore theta, 4–6 Hz	167–250 ms	31.52–31.89	A7 [2]
<i>Paramecium</i> refractoriness, up to	200 ms	31.69	A1 [28]
Spike-count windows, V1	1,000 and 200 ms	33.15, 31.69	A7 [25]
heart, sinus node to last ventricular cell	225 ms	31.80	A1 [27]
ventricular muscle action potential	250–300 ms	31.89–32.06	A1 [27]
Facilitation peak, paired interval, <i>Pennatula</i>	~250 ms	31.89	A3 [6]

Shortest beat interval, small <i>Aurelia</i>	~0.25 s	31.89	A3 [27]
delta	0.25-0.667 s	31.89-32.78	A7 [2] (periods computed)
Human theta, 1-4 Hz	0.25-1 s	31.89-33.15	A7 [2]
Mouse wild-type rod decay time constant	258 ms	31.92	A6 [13]
SS1 absolute refractory period, <i>Calliactis</i>	~300 ms	32.06	A3 [5]
Sensory rhodopsin photocycle, lower value	≥300 ms	32.06	A6 [3]
Shortest common beat interval, <i>Dactylometra</i>	0.4 s	32.32	A3 [27]
Pacemaker period at 2.4 Hz, <i>Tripedalia</i>	0.42 s	32.36	A3 [20] (computed)
Slow oscillation, 0.5-2 Hz	0.5-2 s	32.52-33.78	A7 [2]
crow task baseline; sample	500 ms	32.52	A9 [21]
<i>Chlamydomonas</i> body rotation (1.67 Hz)	0.60 s	32.69	A1 (computed)
sinus node interval (80-100 min ⁻¹)	0.60-0.75 s	32.69-32.89	A1 (computed)
Second facilitation peak, <i>Pennatula</i>	~600 ms	32.69	A3 [6]
Pacemaker period at 1.6 Hz	0.625 s	32.73	A3 [20] (computed)
Neocortical slow oscillation, 0.5-1.5 Hz	0.667-2 s	32.78-33.78	A7 [2]
Absolute refractory period, <i>Aurelia</i>	0.7 s	32.83	A3 [27] (Bullock 1943, cited)
slow 1	0.7-2 s	32.83-33.78	A7 [2] (periods computed)
Beat interval, larger <i>Aurelia</i>	0.75 s	32.89	A3 [27]
<i>Chlamydomonas</i> adaptation time τ_a	0.764 ± 0.190 s	32.91	A1 [34]
<i>Chlamydomonas</i> reorientation	0.96 ± 0.36 s	33.12	A1 [34]
<i>E. coli</i> spike cycle at 1 Hz	1 s	33.15	A1 (computed)
<i>Chara</i> streaming stops after spike, within	<1 s	33.15	A1 [18]
<i>Chlamydomonas</i> recovery of flagellar asymmetry	about 1-2 s	33.15-33.78	A1 [34]
<i>Chara corallina</i> action potential, 40 °C	about 1 s	33.15	A1 [30]

Pacemaker period at ~1 Hz, dark	~1 s	33.15	A3 [20] (computed)
Vertebrate phototransduction cascade	~1 s	33.15	A6 [2]
Octopus, quiet-sleep events	up to 1 s	33.15	A7 [12]
crow task delay	1,000 ms	33.15	A9 [21]
<i>Stentor</i> , other intervals	2.5 min; 1.2 s	37.71; 33.32	A8 [8]
Volume period at 0.8 Hz, larval zebrafish imaging	1.25 s	33.36	A4 [26] (computed)
SS1 relative refractory period	~1,400 ms	33.46	A3 [5]
bundle-branch interval (20–30 min ⁻¹)	2–3 s	33.78–34.15	A1 (computed)
flytrap action potential	2 s	33.78	A1 [15]
<i>Chara</i> half-amplitude duration	about 2–3 s	33.78–34.15	A1 [18]
<i>Chara</i> absolute refractory period	2–10 s	33.78–35.25	A1 [18]
Pacemaker period at 0.5 Hz	2 s	33.78	A3 [20] (computed)
slow 2	2–5 s	33.78–34.62	A7 [2] (periods computed)
SS1 fails above one shock per	3 s	34.15	A3 [5]
Pacemaker period, regenerating rhopalium, day 8 (0.2 Hz)	5 s	34.62	A3 [28] (computed)
slow 3	5–15 s	34.62–35.62	A7 [2] (periods computed)
Acoel geotaxis before decapitation	8.6 s (mean, N = 69)	35.11	A4 [6]
Pacemaker counting window, <i>Tripedalia</i>	10 s	35.25	A3 [20]
Ultra-slow rhythm, 0.1 Hz	10 s	35.25	A7 [2]
<i>C. elegans</i> , tap interval, short-term	10 s	35.25	A8 [13]
Bird, SWS episode in flight	10.89 ± 0.81 s	35.33	A7 [21]
flytrap, two action potentials close the trap within	15–20 s; about 30 s	35.62–35.88; 36.25	A1 [14]
slow 4	15–40 s	35.62–36.51	A7 [2] (periods computed)
Bird, SWS episode on land	28.25 ± 1.75 s	36.19	A7 [21]

glass sponge absolute refractory period	29 s	36.22	A1 [20]
glass sponge, absolute refractory period	29 s	36.22	A2 [22]
<i>Chara corallina</i> action potential, 3.5 °C	about 30 s	36.25	A1 [30]
<i>Trichoplax</i> , onset of pause after a peptide pulse	about 30 s	36.25	A2 [23]
Honeybee, massed trials	30 s apart	36.25	A8 [16]
Pacemaker period, regenerating rhopalium, day 6 (0.03 Hz)	~33 s	36.34	A3 [28] (computed)
Rat, NREM	47 s	36.66	A7 [10]
Pigeon, NREM	49 s	36.70	A7 [10]
Mouse, cerebral blood volume	50 s	36.71	A7 [10]
cuttlefish delay, lower	50 s	36.71	A9 [19]
Human, N2	51 s	36.73	A7 [10]
<i>Stentor</i> , stimulus interval	1 min	36.88	A8 [8]
<i>C. elegans</i> , tap interval, long-term	60 s	36.88	A8 [13]
Octopus, active-sleep bout	75 ± 28 s	37.08	A7 [12]
Lizard <i>Pogona vitticeps</i> , SW-REM cycle	~80 s	37.14	A7 [9]
Lizards, beta power, range across individuals	84-134.5 s	37.19-37.61	A7 [10]
<i>Chara</i> relative refractory period, up to	90 s	37.25	A1 [18]
glass sponge relative refractory period	95-100 s	37.30-37.34	A1 [20]
glass sponge, relative refractory period (further)	95-100 s	37.30-37.34	A2 [22]
Bearded dragon, cerebral blood volume	100 s	37.34	A7 [10]
Lizards, mean across species	113.2 ± 6.8 s	37.46	A7 [10]
Honeybee colour memory, early minimum	roughly 2-3 min	37.51-37.88	A8 [24]
<i>Trichoplax</i> , single feeding pause (n = 64)	2.97 ± 0.96 min	37.87 (37.52-38.13)	A2 [23]
cuttlefish delay, upper	130 s	37.58	A9 [19]
Panther chameleon, skin brightness	175.7 ± 18.3 s	37.86	A7 [10]
Optogenetic recall,	3 min	37.88	A8 [7]

light-on period			
first compound tool, lower	4 min	38.14	A9 [22]
<i>Trichoplax</i> , group pause	4.13 min	38.17	A2 [23]
<i>Chara</i> streaming recovery	about 250 s	38.18	A1 [18]
<i>Trichoplax</i> , repeat of pause under peptide (n = 33)	9.11 ± 4.22 min	38.89 (38.32–39.24)	A2 [23]
Window for 4–5 peristaltic waves, <i>Nematostella</i>	5 min	38.34	A3 [25]
bumblebee naïve attempt	5 min	38.34	A9 [23]
first compound tool, upper	6 min	38.51	A9 [22]
Early or late block of pacemaker record	7 min	38.65	A3 [20]
Sleep cycle, short-tailed shrew	~8 min	38.77	A7 [22]
<i>Trichoplax</i> , PWN effect	about 10 min	38.98	A2 [24]
Human, first / last REM period	~10 min / up to 1 h	38.98 / 40.61	A7 [24]
Honeybee, spaced trials	10 min apart	38.98	A8 [16]
Honeybee colour memory, rise after the minimum	10–20 min	38.98–39.61	A8 [24]
<i>Trichoplax</i> , group pause cycle (n = 38)	12.9 ± 2.0 min	39.21 (39.05–39.34)	A2 [23]
<i>Stentor</i> , pause before recovery test	15 min	39.34	A8 [8]
<i>Stentor</i> , recovery of 90 % of cells	within 15 min	39.34	A8 [8]
20 minutes (Ebbinghaus interval)	20 minutes	39.61	A8 [26]
<i>P. aeruginosa</i> lag after biofilm peak	22 ± 13 min	39.69	A1 [10]
<i>B. subtilis</i> motile lag after biofilm peak	26 ± 9 min	39.85	A1 [10]
<i>Drosophila</i> mutants (<i>amnesiac</i> , <i>rutabaga</i> , <i>dunce</i>), rapid decay	first 30 min	39.98	A8 [15]
Bird in flight, daily sleep	0.69 h	40.27	A7 [21]
Octopus, quiet-sleep bout	50.5 ± 16.43 min	40.45	A7 [12]
flytrap, 63 ± 13 action potentials in	1 h	40.61	A1 [14]
Octopus, interval between active bouts	~60 min	40.61	A7 [12]

Guinea pig, REM	1 h	40.61	A7 [22]
<i>C. elegans</i> , interval between blocks	1 h	40.61	A8 [13]
<i>Physarum</i> , crossing time of controls	about 1 h	40.61	A8 [1]
1 hour (Ebbinghaus interval)	1 hour	40.61	A8 [26]
Peak of cell death after amputation, <i>Nematostella</i>	1.5–12 h	40.98–42.87	A3 [25]
Human sleep cycle	90–110 min	40.98–41.16	A7 [24]
<i>Aplysia</i> , intersession interval, rapid protocol	1.5 h	40.98	A8 [23]
African elephant (captive), sleep / REM	3.9 h / 1.8 h	41.85 / 41.14	A7 [22]
Sleep cycle, Asiatic elephant	1.8 h	41.14	A7 [22]
Wild elephant matriarchs, daily sleep	2.3 and 1.8 h	41.36, 41.14	A7 [23]
<i>Nematostella</i> , S phase to mitosis at gastrula	about 2–4 h	41.24–41.87	A2 [31]
<i>P. aeruginosa</i> mean peak interval	2.1 h	41.28	A1 [10]
<i>Drosophila</i> , longest immobility	up to 157 min	41.48	A7 [13]
Elephant and giraffe, daily sleep	3–4 h	41.61–41.87	A7 [22]
<i>Physarum</i> , fusion needed for transfer	3 h	41.61	A8 [22]
<i>Drosophila</i> mutants, memory still measurable	at least 3 h	41.61	A8 [15]
Early LTP; synaptic tag	< 3 h	41.61	A8 [5]
ball rolling per day	3 h	41.61	A9 [24]
Captive elephants, reported	3.10–6.90 h	41.64–42.36	A7 [23]
flytrap DmHKT1 maximum after stimulation	4 h	41.87	A1 [14]
<i>Hydra</i> , ultradian rhythm	4 h	41.87	A7 [8]
<i>C. elegans</i> , salt exposure without food	4 h	41.87	A8 [13]
<i>C. elegans</i> , oxygen learning at 1 % O ₂	4–6 h	41.87–42.24	A8 [13]
<i>Physarum</i> , crossing time of trained plasmodia on day 1	4 h	41.87	A8 [1]
<i>Aplysia</i> , whole rapid protocol	5 h	42.07	A8 [23]
string-pulling training	309 min	42.10	A9 [23]

per bee (mean)			
Regression prediction for elephants	5.46–5.87 h	42.15–42.22	A7 [23] (modelled)
flytrap, >100 action potentials within	6 h	42.24	A1 [14]
Median G2, planarian neoblasts	~6 h	42.24	A3 [23]
Lizard, continuous oscillation per night	6–10 h	42.24–42.70	A7 [9]
Bushtail possum, REM	6.6 h	42.32	A7 [22]
<i>Drosophila</i> wild type, gradual decay	first 7 h	42.38	A8 [15]
Platypus, adult REM	8 h	42.50	A7 [22]
9 hours (Ebbinghaus interval)	9 hours	42.61	A8 [26]
Octopus, quiet sleep per 24 h (12 × 50.5 min)	~10.1 h	42.71	A7 [12] (computed)
First proliferation after amputation, <i>Nematostella</i>	12 h	42.87	A3 [25]
Labelling to nematoblast, <i>Hydra</i>	12 h	42.87	A3 [16]
Peripheral phase shift by feeding, mouse	up to 12 h	42.87	A7 [16]
LTP decay τ , 5 trains	0.7 d	43.17	A8 [17]
raven planning delay	17 h	43.19	A9 [20]
Labelling to visible nerve cell, <i>Hydra</i>	~18 h	43.24	A3 [16]
Bats and opossums, daily sleep	18–20 h	43.24–43.33	A7 [22]
<i>Mnemiopsis</i> , eggs hatch after spawning	22–26 h	43.42–43.57	A2 [29]
<i>Mnemiopsis</i> cydippid with syncytial net	1 day	43.50	A2 [28]
<i>Hydra</i> , nerve differentiation from stem cells	about 1 day	43.50	A2 [32]
<i>Hydra</i> , stem cell cycle	24 h	43.50	A2 [32]
Interstitial stem-cell cycle, <i>Hydra</i>	24 h; 24–30 h	43.50; 43.50–43.70	A3 [16, 17]
Age of reconstructed ctenophore cydippid	1 day	43.50	A3 [4]
Acoel locomotion test after decapitation	1 day	43.50	A4 [6]
Isotropic fractionator estimate	24 h	43.50	A5 [16]
KaiC phosphorylation cycle	24 h	43.50	A7 [27]

<i>Drosophila</i> wild type, memory present	24 h	43.50	A8 [15]
<i>C. elegans</i> , long-term habituation tested	24 h	43.50	A8 [13]
<i>Aplysia</i> , synaptic decrement in isolated ganglion	24 h later	43.50	A8 [23]
Honeybee eLTM	1-2 d	43.50-44.13	A8 [16]
LTP decay τ , 20 trains	1.0 d	43.50	A8 [17]
1 day (Ebbinghaus interval)	1 day	43.50	A8 [26]
Hippocampal dependence of contextual fear, rat	lesion at 1 day abolishes; at 7 days spares	43.50; 45.27	A8 [18]
Human intrinsic circadian period	24.18 h	43.51	A7 [28]
<i>S. elongatus</i> luminescence in vivo, 30 °C	25.6 $\pm$ 0.1 h	43.56	A7 [27]
Wild elephants, longest without sleep	up to 46 h	44.09	A7 [23]
ctenophore neurons appear after muscle	about 2 days	44.13	A2 [2]
Neurite extension in grafts, <i>Hydra</i>	by days 2 and 3	44.13-44.50	A3 [1]
BrdU incorporation window after forced re-entry	2-4 days	44.13-44.76	A5 [17]
<i>Physarum</i> , stimulus withheld before recovery	2 days	44.13	A8 [1]
2 days (Ebbinghaus interval)	2 days	44.13	A8 [26]
bumblebee practice, colourless flower	48 h	44.13	A9 [23]
youngest infant scan	2 d	44.13	A10 [27]
<i>Mnemiopsis</i> cydippid age at 3-5 mm	3-5 days	44.50-44.96	A2 [29]
Labelling to nematocyte, <i>Hydra</i>	72-96 h	44.50-44.76	A3 [16]
Doubling of stem-cell population	3-4 days	44.50-44.76	A3 [17]
<i>Platynereis</i> larva at reconstruction	72 h	44.50	A4 [20]
Viability unchanged after forced re-entry	3 days	44.50	A5 [17]
Pea, training	3 days	44.50	A8 [10]
Honeybee lLTM	$\geq$ 3 d	44.50	A8 [16]
youngest ball-rolling	3 d	44.50	A9 [24]

bees			
LTP decay τ , 4×5 trains (decremental)	3.3 d	44.59	A8 [17]
Tentacle tissue renewal, <i>Hydra</i>	4–5 days	44.76–44.96	A3 [1]
Rb-TKO cortical neurons in culture	4 days	44.76	A5 [18]
Variation of resting length, <i>Nematostella</i>	over 5 days	44.96	A3 [25]
Nematocyte differentiation, <i>Hydra</i>	5–7 days	44.96–45.27	A3 [16]
Acoel phototaxis not restored by	5 days	44.96	A4 [6]
<i>Physarum</i> , habituation phase	5 days	44.96	A8 [1]
Octopus, correct choice without further conditioning	5 days	44.96	A8 [14]
<i>M. mymaripenne</i> adult lifespan, 25 °C	5 d	44.96	A9 [15]
string-pulling control period	5 d	44.96	A9 [23]
6 days (Ebbinghaus interval)	6 days	45.13	A8 [26]
Oral regeneration, <i>Nematostella</i> (82 of 83)	7 days	45.27	A3 [25]
Doubling of FMRFamide giant neurons, $7 \rightarrow 14$	~1 week	45.27	A3 [28]
Clone scoring, <i>Hydra</i>	1–2 weeks	45.27–45.90	A3 [18]
Progressive death after forced re-entry, through	7 days	45.27	A5 [17]
Zebrafish larvae at recording	7 days post-fertilisation	45.27	A7 [11]
<i>Aplysia</i> , rapid long-term habituation	> 1 week	45.27	A8 [23]
Mean spine lifetime, mouse CA1	approximately 1–2 weeks	45.27–45.90	A8 [27]
wrasse mouth fighting at zero	7 d	45.27	A9 [18]
upper age of younger ball-rolling bees	7 d	45.27	A9 [24]
<i>M. mymaripenne</i> adult lifespan, 15 °C	8.8 d	45.48	A9 [15]
<i>Physarum</i> , whole experiment	9 days	45.50	A8 [1]
Bird, longest flight	10.02 days	45.60	A7 [21]
wrasse mirror behaviour nearly ended	10 d	45.60	A9 [18]
older ball-rolling bees,	10 d	45.60	A9 [24]

more than			
Regrowth of most rhopalial neural elements	within 2 weeks	45.90	A3 [28]
Whole-tissue renewal including nerve net, <i>Hydra</i>	2-3 weeks	45.90-46.27	A3 [1]
Planarian, familiarisation memory	≥ 14 days	45.90	A8 [12]
Full CA1 turnover, 2-3 $\times$ 1-2 weeks	2-6 weeks	45.90-46.90	A8 [27] (computed)
ball-rolling experiment	18 d	46.13	A9 [24]
Growth of fed-then-starved <i>Nematostella</i> by 75.9 %	3 weeks	46.27	A3 [25]
<i>Aplysia</i> , long-term habituation	≥ 3 weeks	46.27	A8 [25]
<i>Mimosa</i> , learned response kept, undisturbed	a month (30 d taken)	46.60	A8 [9]
Stable spines (about 50 %), barrel cortex	at least a month (30 d taken)	46.60	A8 [28]
31 days (Ebbinghaus interval)	31 days	46.63	A8 [26]
LTP decay τ , 50 trains, short baseline	32 d	46.65	A8 [17]
LTP decay τ , lateral perforant path	42 d	46.90	A8 [17]
Stable-LTP animals, recording span	42-119 days (mean 68)	46.90-47.85 (47.34)	A8 [17]
juvenile octopus age	6 weeks	46.90	A9 [14]
Shrinkage of starved-then-fed <i>Nematostella</i> by 26.1 %	7 weeks	47.04	A3 [25]
Acoel brain neuropil regenerated in ~ 70 %	50 days	47.06	A4 [6]
Shrinkage of fed-then-starved <i>Nematostella</i> by 38.6 %	11 weeks	47.45	A3 [25]
infant growth at 1 % $\rightarrow$ 0.4 % per day; last scan	90 d	47.60	A10 [27]
auditory synapse density peak	3 months	47.61	A10 [14]
earliest age in lifespan charts, post-conception	115 d	47.82	A10 [28]
LTP decay τ , the one-year animal	127 d	47.91	A8 [17]
adult octopus age, at least	6 months	48.24	A9 [14]
synaptogenesis begins,	27 weeks	48.27	A10 [14]

before			
heart muscle renewal, per	1 year	48.87	A1 [43]
LTP, longest record	369 days	48.88	A8 [17]
Adult spine half-life, cortex	> 13 months (390 d taken)	48.93	A8 [29]
frontal synapse density peak, after	15 months	49.07	A10 [14]
cortical thickness peak	1.7 y (95 % CI 1.3-2.1)	49.35	A10 [28]
cortical thickness peak	1.7 y	49.35	A10 [28] (modelled)
CSF rise ends	2 y	49.50	A10 [28] (modelled)
Spanish, exponential loss	first 3-6 years	49.87-50.50	A8 [30]
crow ages	5 y; 6 y	50.34; 50.50	A9 [21]
grey matter volume peak	5.9 y (95 % CI 5.8-6.1)	50.49	A10 [28]
grey matter peak	5.9 y	50.49	A10 [28] (modelled)
Spanish, permastore response life span	6-25 years	50.50-51.80	A8 [30]
Ages with few young hippocampal neurons	7 and 13 years	50.64 and 51.21	A5 [19]
few young hippocampal neurons, last seen	7 y; 13 y	50.64; 51.21	A10 [31]
auditory synapse elimination ended	12 y	51.13	A10 [14]
total cerebrum volume peak	12.5 y (95 % CI 12.14-12.89)	51.17	A10 [28]
total cerebrum peak	12.5 y	51.17	A10 [28] (modelled)
subcortical grey matter peak	14.4 y (95 % CI 14.0-14.7)	51.30	A10 [28]
subcortical grey matter peak	14.4 y	51.30	A10 [28] (modelled)
Human sample ages, hippocampal study	18-77 years	51.50-52.82	A5 [19]
youngest adult sample, no young neurons	18 y	51.50	A10 [31]
Human white-matter fibre length measured	20 and 80 years	51.60 and 52.86	A5 [14]
myelinated fibre, first age	20 y	51.60	A10 [25]
white matter volume peak	28.7 y (95 % CI 28.1-29.2)	51.93	A10 [28]
white matter peak	28.7 y	51.93	A10 [28] (modelled)
Spanish, roughly unchanged	up to 30 years	51.97	A8 [30]
CSF plateau ends	30 y	51.97	A10 [28] (modelled)
Spanish, whole study	50 years	52.43	A8 [30]

span			
hippocampal turnover at 1.75 % per year	57 y	52.55	A10 [30] (computed)
oldest adult sample	77 y	52.82	A10 [31]
myelinated fibre, second age	80 y	52.86	A10 [25]
oldest prefrontal spine sample	91 y	52.98	A10 [29]
latest age in lifespan charts	100 y	53.06	A10 [28]
final bin in the Holocene dataset	100 y	53.06	A10 [23]
reanalysis interval, lower	1 ka	55.16	A10 [23]
proposed Holocene decrease, from about	3 ka	56.16	A10 [3] (modelled)
reanalysis interval, upper	5 ka	56.62	A10 [23]
reanalysis window	30 ka	58.25	A10 [23]
Blombos margin, at least	30 kyr	58.25	A10 [11]
earlier drawings, after	40 ka	58.52	A10 [11]
Leang Bulu' Sipong 4, previous date	43.9 ka	58.60	A10 [12]
Leang Bulu' Sipong 4, re-dated, at least	50.2 ka	58.72	A10 [12]
Leang Karampuang, at least	51.2 ka	58.74	A10 [12]
Leang Karampuang scene, minimum	53.5 ka	58.78	A10 [12]
Blombos drawing	73 ka	59.06	A10 [11]
<i>H. naledi</i> , significance statement	226 ka	60.09	A10 [21]
<i>H. naledi</i> , lower	236 ka	60.13	A10 [21]
reanalysis window; stable brain size	300 ka	60.35	A10 [23]
<i>H. naledi</i> , upper	335 ka	60.45	A10 [21]
Acheulean margin	350 kyr	60.49	A10 [10]
Upper bound, light-sensitive patch to lens eye	<5 × 10 ⁵ generations (≈ years at 1 generation per year [17]); “a few hundred thousand years” [28]	60.81	A6 [17, 28] (modelled)
Lomekwian margin over the Oldowan	700 kyr	61.12	A10 [8]
SRGAP2D	1 Ma	61.45	A10 [5] (modelled)
previous earliest Acheulean	1.41 Ma	61.76	A10 [10] (computed)

second change point	1.49 Ma	61.81	A10 [3] (modelled)
first Acheulean, Kokiselei 4	1.76 Ma	61.96	A10 [10]
second change point, small-brained <i>Homo</i> included	1.97 Ma	62.06	A10 [3] (modelled)
<i>Australopithecus</i> flat period, end	2.0 Ma	62.08	A10 [3]
first change point	2.10 Ma	62.12	A10 [3] (modelled)
SRGAP2C	2.4 Ma	62.24	A10 [5] (modelled)
Oldowan at Gona, lower	2.5 Ma	62.28	A10 [9]
Oldowan at Gona, upper; previous earliest tools	2.6 Ma	62.32	A10 [9, 8]
proposed SRGAP2C function, upper	3 Ma	62.45	A10 [5]
Lomekwi 3 tools	3.3 Ma	62.53	A10 [8]
SRGAP2B	3.4 Ma	62.56	A10 [5] (modelled)
<i>Australopithecus</i> flat period, start	3.5 Ma	62.59	A10 [3]
Interval >500 Ma bound to Chengjiang age	18.03 Myr	64.08	A4 [9, 14] (computed)
Interval Cambrian base to fossil brains at 520 Ma (as printed)	18.8 Myr	64.12	A4 [12, 15] (computed)
Interval Cambrian base to Chengjiang maximum age 518.03 Ma	≥ 20.77 Myr	64.21	A4 [12, 14] (computed)
Cambrian explosion, more than	22 Myr	64.26	A2 [34]
Cambrian radiation, as little as	25 Myr	64.38	A6 [17]
Ediacara biota, 571–539 Ma	~ 32 Myr	64.60	A4 [13] (computed)
about 1 % of genes move chromosome, every	about 40 Myr	64.80	A2 [4]
Interval ~ 560 Ma split to Chengjiang age	41.97 Myr	64.85	A4 [10, 14] (computed)
Gap before complex soft-bodied eyes reappear	~ 85 Myr	65.49	A6 [16] (fossil)
metazoan stem	about 150–200 Myr	66.01–66.27	A2 [5]
vampire squid / dumbo octopus lineages, lower	204 Ma	66.29	A9 [2] (modelled)
vampire squid / dumbo octopus lineages	242 Ma	66.44	A9 [2] (modelled)
vampire squid / dumbo	280 Ma	66.57	A9 [2] (modelled)

octopus lineages, upper			
Span of amniote neuron-brain scaling shifts	300 Myr	66.64	A5 [6]
amniote neuron-scaling history	300 Myr	66.64	A9 [3]
Next complex non-biomineralized eyes	~430 Ma	66.97	A6 [16] (computed)
Ordovician agnathans	450 Ma	67.01	A6 [17]
Age at which common vertebrate sleep signatures “may have emerged”	over 450 Myr	67.01	A7 [11] (inferred)
Cnidarian Cav genes conserved, at least	500 Myr	67.10	A1 [3]
Emu Bay Shale compound eyes	~515 Ma	67.13	A6 [15, 16] (fossil)
vertebrate origin, stated as before	520 Ma	67.14	A9 [4]
Conservation of Caspr / neurexin IV	>750 Myr	67.47	A5 [1]

C5 Lifetimes

All LIFETIMES rows of the ten data files, sorted by position, smallest first. Positions are computed here with `pos.py` time for every printed duration, in the order printed; a frequency is placed as its period $1/f$. A row with several positions is placed by its smallest.

Rows whose duration is given only in words carry no position and stand at the end.

structure or event	species	lifetime	position	chapter [ref]
ion passage through channel	KcsA (bacterial K ⁺ channel)	up to 10^8 ions s ⁻¹ (10 ns per ion, computed)	16.39	A1 [31]
ion passage through channel	general comparison value	about 0.1 μ s at 10^7 ions s ⁻¹	18.48	A1 [36]
Hair-cell receptor potential	human	~10 μ s	22.67	A6 [2]
Cole-Moore shift (gating)	NaChBac (<i>Bacillus halodurans</i>)	533 μ s	26.29	A1 [38]
Motor giant action potential (half amplitude)	<i>Aglantha digitale</i>	1.2-1.4 ms	27.03-27.17	A3 [7]
Escape reaction, myelinated copepod	<i>Undinula vulgaris</i> ; <i>Neocalanus gracilis</i>	1.5 ms; 1.6 ms	27.23; 27.29	A5 [5]
Ring giant action	<i>Aglantha digitale</i>	~1.6 ms	27.29	A3 [7]

potential				
Synaptic delay ring giant → motor giant	<i>Aglantha digitale</i>	1.6–1.8 ms	27.29–27.40	A3 [7]
Synaptic delay motor giant → myoepithelium	<i>Aglantha digitale</i>	~1.6 ms	27.29	A3 [7]
action potential	neuron (human)	about 2 ms	27.50	A1 [27]
Escape-burst impulse	<i>Aglantha digitale</i>	2–3 ms	27.50–27.87	A3 [7]
One spike plus downstream events	rodent (model)	2.5 ms interval	27.70	A5 [9]
Cone inactivation time constants	human	~3 and ~10 ms	27.87 and 28.96	A6 [27]
Escape reaction, non-myelinated copepod	<i>Pleuromamma xiphias</i> ; <i>Labidocera madurae</i>	6.6 ms; 3.1 ms	28.58; 27.90	A5 [5]
reversal latency	<i>Paramecium caudatum</i>	30 to ≤4 ms	29.96–28.13	A1 [11]
Response to hydrodynamic disturbance	<i>Acartia</i> spp.	within 4 ms	28.13	A5 [5]
Interval between kicks	copepods	5 ms	28.33	A5 [5]
ChR2-driven spike trains	neurons expressing ChR2	millisecond precision; not followed above ~40 Hz; ChETA ≥200 Hz	29.80 (25 ms, computed); 28.33 (5 ms, computed)	A6 [29]
recovery from inactivation, τ	<i>Odontella sinensis</i>	5.1 ± 0.4 ms	28.35	A1 [29]
Stroke and recovery	<i>Acartia</i> spp.	~7 ms	28.64	A5 [5]
Membrane time constant of neurons	not named (review)	10 to 30 msec	28.96–29.96	A7 [2]
Myoepithelial impulse	<i>Aglantha digitale</i>	15–70 ms	29.33–30.73	A3 [7]
Proteorhodopsin photocycle	SAR86 bacteria	15 ms	29.33	A6 [3]
Cone integration time	<i>Macaca fascicularis</i>	19–28 ms	29.55–29.90	A6 [26]
Transport rhodopsin photocycle	microbes	typically <20 ms	29.59	A6 [3]
Cone dim-flash time to peak	human	~20 ms	29.59	A6 [27]
Spike-timing window for LTP /	rat (cultured hippocampal	20 msec after / before	29.59	A8 [4]

LTD	neurons)			
Cycle of a 40-Hz oscillation	not named (review)	25 ms	29.80	A7 [2]
phototransduction delay	<i>Chlamydomonas reinhardtii</i>	28 ± 11 ms; 38 ± 5 ms	29.90; 30.18	A1 [34]
electrotonic time constant	<i>Paramecium caudatum</i>	40–50 ms	30.22–30.43	A1 [28]
Nerve-net absolute refractory period	<i>Pennatula phosphorea</i>	40–50 ms	30.22–30.43	A3 [6]
Activated rhodopsin	mouse rod	40–45 ms	30.22–30.33	A6 [13]
Cone flash response time to peak	<i>Macaca fascicularis</i>	47–55 ms	30.37–30.51	A6 [26]
action potential	<i>Odontella sinensis</i>	50–100 ms	30.43–31.06	A1 [29]
ciliary reversal	<i>Paramecium caudatum</i>	50 ms to 2.4 s or more	30.43–33.95	A1 [11]
Sharp-wave ripple event	not named (review)	80–150 ms	30.85–31.43	A7 [2]
Sharp-wave ripple event	not named (review)	80–150 ms	30.85–31.43	A8 [21]
Population OFF period in NREM	rat	85.8 ± 5.9 ms	30.92	A7 [26]
photoresponse time to peak	<i>Chlamydomonas reinhardtii</i>	97 ± 18 ms	31.03	A1 [34]
Escape contraction	<i>Aglantha digitale</i>	~100 ms	31.06	A3 [7]
Rod small-response decay time constant	mouse	258 ms (wild type); 122 ms (GNAT2C)	31.92; 31.24	A6 [13]
visual response latency of NCL neurons	carion crow (<i>Corvus corone corone</i>)	144 ms (average)	31.39	A9 [21]
refractoriness	<i>Paramecium caudatum</i>	up to 200 ms	31.69	A1 [28]
action potential	human ventricular muscle cell	250–300 ms	31.89–32.06	A1 [27]
Swim beat interval (shortest)	<i>Aurelia aurita</i>	~0.25 s (small) to 0.75 s (larger)	31.89–32.89	A3 [27]
SS1 absolute refractory period	<i>Calliactis parasitica</i>	~300 ms	32.06	A3 [5]
Sensory rhodopsin photocycle	microbes	≥300 ms	32.06	A6 [3]
Absolute refractory period	<i>Aurelia aurita</i>	0.7 s (Bullock 1943, cited in [27])	32.83	A3 [27]
adaptation time τ_a	<i>Chlamydomonas reinhardtii</i>	0.764 ± 0.190 s	32.91	A1 [34]
Population ON period in NREM	rat	815.5 ± 119.9 ms	32.97	A7 [26]
electrical spiking	<i>Escherichia coli</i>	up to 1 Hz	33.15 (1 s,	A1 [40]

			computed)	
action potential	<i>Chara corallina</i>	about 1 s (40 °C) to about 30 s (3.5 °C)	33.15–36.25	A1 [30]
Phototransduction cascade	vertebrate	~1 s	33.15	A6 [2]
Quiet-sleep oscillatory event	octopus	up to 1 s	33.15	A7 [12]
Whole-brain volume imaging	larval zebrafish	0.8 Hz volume rate	33.36 (1.25 s, computed)	A4 [26]
SS1 relative refractory period	<i>Calliactis parasitica</i>	~1,400 ms	33.46	A3 [5]
action potential	<i>Dionaea muscipula</i>	2 s	33.78	A1 [15]
action potential, half-amplitude duration	<i>Chara</i>	about 2–3 s	33.78–34.15	A1 [18]
absolute / relative refractory period	<i>Chara</i>	2–10 s / up to 90 s	33.78–35.25 / 37.25	A1 [18]
Geotaxis response before decapitation	<i>Symsagittifera roscoffensis</i>	8.6 s (mean, N = 69)	35.11	A4 [6]
SWS episode in flight	bird (species not read)	10.89 ± 0.81 s	35.33	A7 [21]
trap closing by two action potentials	<i>Dionaea muscipula</i>	within 15–20 s; within about 30 s	35.62–35.88; 36.25	A1 [14]
SWS episode on land	bird (species not read)	28.25 ± 1.75 s	36.19	A7 [21]
absolute / relative refractory period	<i>Rhabdocalyptus dawsoni</i> (glass sponge)	29 s / further 95–100 s	36.22 / 37.30–37.34	A1 [20]
absolute / relative refractory period of impulse	<i>Rhabdocalyptus dawsoni</i> (glass sponge)	29 s / further 95–100 s	36.22 / 37.30–37.34	A2 [22]
onset of feeding pause after peptide pulse	<i>Trichoplax adhaerens</i>	about 30 s	36.25	A2 [23]
Infraslow sleep rhythm, NREM	rat	47 s	36.66	A7 [10]
Infraslow sleep rhythm, NREM	pigeon	49 s	36.70	A7 [10]
Infraslow cerebral-blood-volume rhythm	mouse	50 s	36.71	A7 [10]
delay of gratification sustained	cuttlefish	up to 50–130 s	36.71–37.58	A9 [19]
Infraslow sleep rhythm, N2	human	51 s	36.73	A7 [10]
Active-sleep bout	octopus	75 ± 28 s	37.08	A7 [12]

SW-REM cycle	<i>Pogona vitticeps</i>	~80 s	37.14	A7 [9]
Infraslow sleep rhythm (beta power)	7 lizard species	84–134.5 s; mean 113.2 ± 6.8 s	37.19–37.61; mean 37.46	A7 [10]
Infraslow cerebral-blood-volume rhythm	bearded dragon	100 s	37.34	A7 [10]
Early memory minimum, colour learning	honeybee	roughly 2–3 min	37.51–37.88	A8 [24]
Skin-brightness rhythm in sleep	panther chameleon	175.7 ± 18.3 s	37.86	A7 [10]
single feeding pause	<i>Trichoplax adhaerens</i>	2.97 ± 0.96 min (n = 64)	37.87	A2 [23]
group pause	<i>Trichoplax adhaerens</i>	4.13 min every 12.9 ± 2.0 min (n = 38)	38.17; 39.21	A2 [23]
Sleep cycle	short-tailed shrew	about 8 minutes	38.77	A7 [22]
repeat of pause under continuous peptide	<i>Trichoplax adhaerens</i>	9.11 ± 4.22 min (n = 33)	38.89	A2 [23]
PWN peptide effect	<i>Trichoplax adhaerens</i>	about 10 min	38.98	A2 [24]
First REM period	human	about 10 min	38.98	A7 [24]
Recovery from habituation (90 % of cells)	<i>Stentor coeruleus</i>	within 15 minutes	39.34	A8 [8]
motile-cell lag after biofilm electrical peak	<i>Bacillus subtilis</i> ; <i>Pseudomonas aeruginosa</i>	26 ± 9 min; 22 ± 13 min	39.85; 39.69	A1 [10]
Rapid memory decay in mutants (<i>amnesiac</i> , <i>rutabaga</i> , <i>dunce</i>)	<i>Drosophila melanogaster</i>	first 30 min; measurable at least 3 h	39.98; 41.61	A8 [15]
Daily sleep in flight	bird (species not read)	0.69 h d ⁻¹	40.27	A7 [21]
Quiet-sleep bout	octopus	50.5 ± 16.43 min	40.45	A7 [12]
Interval between active-sleep bouts	octopus	roughly every 60 min	40.61	A7 [12]
Last REM period	human	up to an hour	40.61	A7 [24]
Cell death after amputation (peak)	<i>Nematostella vectensis</i>	1.5–12 h	40.98–42.87	A3 [25]
Sleep cycle	human	90–110 min	40.98–41.16	A7 [24]
Sleep cycle	Asiatic elephant	1.8 hours	41.14	A7 [22]
Daily sleep, wild	African elephant (2 matriarchs)	2.3 and 1.8 h/day	41.36 and 41.14	A7 [23]
S phase to mitosis, gastrula	<i>Nematostella vectensis</i>	about 2–4 h	41.24–41.87	A2 [31]
biofilm mean peak interval	<i>Pseudomonas aeruginosa</i>	2.1 h	41.28	A1 [10]

Longest immobility (rest bout)	<i>Drosophila melanogaster</i>	up to 157 min	41.48	A7 [13]
Daily sleep	elephant, giraffe	3–4 hours	41.61–41.87	A7 [22]
Early LTP	rat	less than three hours	41.61	A8 [5]
Synaptic tag	rat	decays in less than three hours	41.61	A8 [5]
Ultradian rhythm in the sleep-like state	<i>Hydra vulgaris</i>	4 h	41.87	A7 [8]
Neoblast G2 phase	planarian	median about 6 h	42.24	A3 [23]
Continuous SW-REM oscillation per night	<i>Pogona vitticeps</i>	6 to 10 hours	42.24–42.70	A7 [9]
Wild-type olfactory memory	<i>Drosophila melanogaster</i>	gradual decay over 7 hours; present 24 h	42.38; 43.50	A8 [15]
Labelling to nematoblast	<i>Hydra attenuata</i>	12 h	42.87	A3 [16]
LTP decay τ (5 / 20 / 4 $\times$ 5 trains)	rat	0.7 d / 1.0 d / 3.3 d	43.17 / 43.50 / 44.59	A8 [17]
planning delay tolerated	raven	up to 17 hours	43.19	A9 [20]
Labelling to visible nerve cell	<i>Hydra attenuata</i>	~18 h	43.24	A3 [16]
Daily sleep	bats, opossums	18–20 hours	43.24–43.33	A7 [22]
egg to hatching after spawning	<i>Mnemiopsis leidyi</i>	22–26 h	43.42–43.57	A2 [29]
nerve differentiation from interstitial stem cells	<i>Hydra attenuata</i>	about 1 day	43.50	A2 [32]
interstitial stem cell cycle	<i>Hydra attenuata</i>	24 h	43.50	A2 [32]
Interstitial stem-cell cycle	<i>Hydra attenuata</i>	24 h	43.50	A3 [16]
Interstitial stem-cell cycle	<i>Hydra</i>	about 24–30 hours	43.50–43.70	A3 [17]
Reconstructed cydippid (age)	<i>Mnemiopsis leidyi</i>	1 day	43.50	A3 [4]
Locomotion test after decapitation	<i>Symsagittifera roscoffensis</i>	one day	43.50	A4 [6]
New hippocampal neurons	human	~700 per day per hippocampus; turnover 1.75 % per year	43.50; 48.87	A5 [37]
KaiC phosphorylation cycle	cyanobacteria (KaiC CII domains)	24 h period	43.50	A7 [27]

Backscatter oscillation	<i>Synechocystis</i> sp. PCC 6803	approximately 24 h	43.50	A7 [18]
Long-term tap-habituation memory	<i>C. elegans</i>	tested 24 h	43.50	A8 [13]
Synaptic decrement after rapid long-term habituation	<i>Aplysia</i>	still present 24 h later	43.50	A8 [23]
eLTM	honeybee	1–2 d	43.50–44.13	A8 [16]
Intermediate colour memory without reinforcement	honeybee	fades within 1 or a few days	43.50	A8 [24]
Contextual fear memory dependence on hippocampus	rat	abolished by lesion at 1 day; spared at 7, 14, 28 days	43.50; 45.27, 45.90, 46.53	A8 [18]
Intrinsic circadian period	human	24.18 h	43.51	A7 [28]
Luminescence rhythm in vivo, 30 °C	<i>Synechococcus elongatus</i>	25.6 ± 0.1 h	43.56	A7 [27]
Longest time without sleep, wild	African elephant	up to 46 h	44.09	A7 [23]
appearance of neurons after muscle in development	ctenophore (<i>Pleurobrachia</i>)	about 2 days	44.13	A2 [2]
Neurite extension of new nerve cells in grafts	<i>Hydra</i>	by days 2 and 3	44.13 and 44.50	A3 [1]
Habituation, until spontaneous recovery	<i>Physarum polycephalum</i>	stimulus withheld 2 days	44.13	A8 [1]
cydippid reaching 3–5 mm	<i>Mnemiopsis leidyi</i>	3–5 days	44.50–44.96	A2 [29]
Stem-cell population doubling	<i>Hydra</i>	about 3–4 days	44.50–44.76	A3 [17]
Labelling to nematocyte	<i>Hydra attenuata</i>	72–96 h	44.50–44.76	A3 [16]
Larva at whole-body connectome	<i>Platynereis dumerilii</i>	72 h	44.50	A4 [20]
Cortical neuron after forced cycle re-entry	mouse (culture)	viability unchanged 3 days; progressive death through day 7	44.50; 45.27	A5 [17]
ILTM	honeybee	≥3 d	44.50	A8 [16]
atypical mirror-directed behaviour	cleaner wrasse (<i>Labroides dimidiatus</i>)	peak days 3–5; nearly ended by day 10	44.50–44.96; 45.60	A9 [18]

Tentacle tissue (renewal)	<i>Hydra</i>	4–5 days	44.76–44.96	A3 [1]
Rb-TKO cortical neuron division	mouse (culture)	2.02 % in M phase at 4 days	44.76	A5 [18]
Nematocyte differentiation	<i>Hydra attenuata</i>	5–7 days	44.96–45.27	A3 [16]
Phototaxis after decapitation	<i>Symsagittifera roscoffensis</i>	not restored at 5 days	44.96	A4 [6]
Observational learning, correct choice	<i>Octopus vulgaris</i>	5 days	44.96	A8 [14]
organism (adult lifespan)	<i>Megaphragma mymaripenne</i>	5 days at 25 °C	44.96	A9 [15]
Oral regeneration	<i>Nematostella vectensis</i>	by 7 days (82 of 83)	45.27	A3 [25]
FMRFamide giant neurons doubling 7 → 14	<i>Tripedalia cystophora</i>	~1 week	45.27	A3 [28]
Rapid long-term habituation	<i>Aplysia</i>	more than 1 week	45.27	A8 [23]
Dendritic spine, mean lifetime	mouse (CA1)	approximately 1–2 weeks	45.27–45.90	A8 [27]
mouth fighting at the mirror	cleaner wrasse (<i>Labroides dimidiatus</i>)	fell to zero by day 7	45.27	A9 [18]
organism (adult lifespan)	<i>Megaphragma mymaripenne</i>	8.8 days at 15 °C	45.48	A9 [15]
Longest flight recorded	bird (species not read)	10.02 days	45.60	A7 [21]
Whole tissue including nerve net (renewal)	<i>Hydra</i>	every 2–3 weeks	45.90–46.27	A3 [1]
Rhopalial neural elements (regrowth)	<i>Tripedalia cystophora</i>	within two weeks	45.90	A3 [28]
Familiarisation memory	planarian	at least 14 days	45.90	A8 [12]
Long-term habituation	<i>Aplysia</i>	at least 3 weeks	46.27	A8 [25]
Learned leaf-folding response	<i>Mimosa pudica</i>	a month	46.60 (30 d taken, as in A8 Times)	A8 [9]
Stable dendritic spines (about 50 %)	mouse (barrel cortex)	at least a month	46.60 (30 d taken, as in A8 Times)	A8 [28]
Dendritic spines stable over one month	mouse (cortex)	~73 % young; ~96 % adult	46.60 (30 d taken, as in A8 Times)	A8 [29]
Ebbinghaus savings	human	0.0410 at 31 days	46.63	A8 [26]
LTP decay τ (50	rat	32 d / 42 d / 127 d	46.65 / 46.90 /	A8 [17]

trains short baseline / lateral path / one-year animal)			47.91	
Stable LTP, recording span	rat	42-119 days (mean 68)	46.90-47.85 (47.34)	A8 [17]
Brain neuropil regeneration (~70 % of animals)	<i>Symsagittifera roscoffensis</i>	by 50 days	47.06	A4 [6]
synapse density peak, auditory cortex	human	near 3 months after birth	47.61	A10 [14]
synaptogenesis in cerebral cortex	human	begins before 27 weeks of gestation	48.27	A10 [14]
heart muscle cell renewal	human	1 % per year at age 25; 0.45 % at 75; fewer than half replaced in a lifetime	48.87 (per year)	A1 [43]
LTP, longest record	rat	369 days; “up to at least 1 year”	48.88; 48.87	A8 [17]
hippocampal neuron population (adult turnover)	human	1.75 % per year; turns over in 57 years (computed)	48.87; 52.55	A10 [30]
Dendritic spine half-life, adult	mouse (cortex)	greater than 13 months	48.93 (390 d taken, as in A8 Times)	A8 [29]
synapse density peak, frontal cortex	human	after 15 months	49.07	A10 [14]
cortical thickness (peak)	human	1.7 years	49.35	A10 [28]
School Spanish, exponential loss	human	first 3-6 years	49.87-50.50	A8 [30]
grey matter volume (peak)	human	5.9 years	50.49	A10 [28]
School Spanish, response life spans	human	0-6 years and 6-25 years	50.50 (upper of 0-6 y); 50.50-51.80	A8 [30]
New hippocampal neurons	human	none detected in adults aged 18-77; a few at 7 and 13 years	51.50-52.82; 50.64 and 51.21	A5 [19]
young hippocampal neurons	human	a few at 7 and 13 years; none detected at 18-77 years	50.64 and 51.21; 51.50-52.82	A10 [31]
net synapse elimination, auditory cortex	human	ended by 12 years	51.13	A10 [14]
Myelinated fibre length	human	falls 45 % from age 20 to age 80	51.60 and 52.86	A5 [14]

myelinated fibre length	human	falls 45 % between 20 and 80 years, about 10 % per decade	51.60 and 52.86	A10 [25]
white matter volume (peak)	human	28.7 years	51.93	A10 [28]
School Spanish, stable retention	human	up to 30 years	51.97	A8 [30]
Cambrian radiation	—	as little as 25 Myr	64.38	A6 [17]
gene movement between chromosomes	animals and relatives	about 1 % of genes every ~40 Myr	64.80	A2 [4]
Absence of complex non-biomineralized eyes from the record	—	~85 Myr	65.49	A6 [16]
metazoan stem	animals	about 150–200 Myr	66.01–66.27	A2 [5]
differentiated nerve cells	<i>Hydra attenuata</i>	2n post-mitotic DNA content (no duration given)	—	A2 [32]
Brain geometry from birth to adulthood	<i>Caenorhabditis elegans</i>	preserved (no duration given)	—	A4 [29]
Cortical neuron	human	dates from around birth; not made in adulthood at detectable levels	—	A5 [7]
Non-neuronal cortical cells	human	replaced (no duration given)	—	A5 [7]
Polyploid neuron in Alzheimer's disease	human	"hundreds of days" ("many months") before death	—	A5 [20]
Neuron in cell-cycle arrest	vertebrate (review)	"many months" without completing the cycle or dying	—	A5 [21]
Retinal 11-cis to all-trans isomerization	vertebrate	femtosecond time scale	—	A6 [2]
Photoreceptor flash response	fly	typically hundreds of ms	—	A6 [31]
Patch to focused lens eye	model	a few hundred thousand years; $<5 \times 10^5$ generations	—	A6 [28, 17]
eSTM	honeybee	seconds range	—	A8 [16]
lSTM	honeybee	lasting minutes	—	A8 [16]
MTM	honeybee	decays after several hours	—	A8 [16]

Colour memory after 3 trials	honeybee	life-long	—	A8 [24]
Transient dendritic spines	mouse (barrel cortex)	a few days or less	—	A8 [28]
Dendritic spines formed by novel experience (small fraction)	mouse	throughout the entire life	—	A8 [32]
dendritic spine overproduction and remodelling, prefrontal cortex	human	decline from puberty; continues into the third decade of life	—	A10 [29]
myelination of neocortex	human	extends past late adolescence	—	A10 [19]
myelination of neocortex	chimpanzee	adult-like around sexual maturity	—	A10 [19]

C6 Neuron numbers

Every count of neurons or nerve cells printed in the chapter texts, sorted by count, smallest first; a range is placed by its lower value. Counts of nuclei or cells in a nervous system are entered where the chapter prints them in place of a neuron count. Counts listed only under “Not verified”, rates per day and densities are not entered.

species or structure	neurons	chapter [ref]
choanoflagellates	none	A2 [19, 33]
sponges (<i>Amphimedon</i> , <i>Spongilla</i>)	none	A2 [5, 21]
<i>Trichoplax</i> (placozoan)	none	A2 [23, 12]
<i>Spongilla</i> (sponge)	no nerve cells	A3 [22]
<i>Mnemiopsis</i> cydippid, 1 day: nerve net; mesogleal neurons (22 putative sensory cells beside)	5 net + 6 mesogleal	A2 [28]
<i>Mnemiopsis</i> cydippid, 1 day, main block: nerve net; mesogleal neurons (22 putative sensory cells beside)	5 nerve-net + 6 mesogleal	A3 [4]
<i>Tripedalia</i> , regenerating rhopalium, FMRFamide-positive giant neurons	7 → 14 in about one week	A3 [28]
<i>Tripedalia</i> , regenerating rhopalium, RFamide-positive neurons	8 (day 8) → 16 (day 14)	A3 [28]
<i>Hydra</i> , hypostome sample	20–30 nerve cells	A3 [1]
<i>Hydra oligactis</i> , nerve ring around the hypostome	20–30 nerve cells	A3 [1]
<i>Nematostella</i> , small animals, longitudinal neurons	20–40	A3 [25]
<i>Ciona</i> larva, peripheral nervous	28	A4 [21]

system (8 left, 6 centre, 14 right)		
<i>Drosophila</i> , hemilineages (10th to 90th percentile)	60-282 neurons each	A4 [23]
<i>Hydra</i> , body-column or peduncle sample	80-400 nerve cells	A3 [1]
<i>Hydra</i> , tissue bands of about 4 % of the body column (57 ectodermal, 76 endodermal)	133 nerve cells	A3 [1]
<i>Ciona</i> larva, CNS neurons with axons and presynaptic sites (CNS about 330 cells, 301 imaged)	177	A4 [21]
<i>Megaphragma mymaripenne</i> , adult brain	179-253 nuclei (mean 215)	A9 [15]
<i>C. elegans</i> hermaphrodite (118 classes)	302	A4 [22]
<i>C. elegans</i>	302	A8 [13]
<i>Megaphragma mymaripenne</i> , adult CNS	339-372 nuclei (mean 361)	A9 [15]
<i>Symsagittifera roscoffensis</i> (acoel), brain	about 700 ("about 700 cells" in [5])	A4 [6], [5]
<i>Platynereis</i> 72-h larva, classified neurons (180 neuronal types)	892	A4 [20]
<i>Drosophila</i> (adult), descending neurons	1,303	A4 [23]
<i>Drosophila</i> hemibrain, Kenyon cells	1,917	A4 [23]
<i>Drosophila</i> male nerve cord, descending plus motor neurons	2,065	A4 [24]
<i>Drosophila</i> (adult), ascending neurons	2,362	A4 [23]
<i>Drosophila</i> FlyWire, Kenyon cells, left; right	2,580; 2,597	A4 [23]
<i>Drosophila</i> larva, whole brain	3,016	A4 [30]
<i>Hydra</i> , body column, scaled from 133 / 0.04	3,325 nerve cells (computed; not a value the paper gives)	A3 [1]
<i>Drosophila</i> (adult), sensory neurons projecting into the central brain	5,512	A4 [23]
<i>Megaphragma mymaripenne</i> , pupal CNS	about 7,199-7,593 cells (mean 7,396)	A9 [15]
<i>Aurelia</i> , motor nerve net of a jellyfish about 4 cm across	of the order of 10,000	A3 [26] (modelled)
<i>Drosophila</i> hemibrain, traced to cell bodies	15,912	A4 [25]
<i>Drosophila</i> male nerve cord, intrinsic neurons other than motor neurons	21,683	A4 [24]
<i>Drosophila</i> hemibrain, typed and named	22,594	A4 [25]

<i>Drosophila</i> male nerve cord	roughly 23,000 traced	A4 [24]
<i>Drosophila</i> male nerve cord, intrinsic plus descending and motor neurons	23,748 (computed)	A4 [24]
<i>Drosophila</i> hemibrain	around 25,000	A4 [25]
<i>Drosophila</i> FlyWire, intrinsic neurons wholly in the central brain	32,388	A4 [27]
<i>Drosophila</i> FlyWire, intrinsic neurons in optic lobes and ocellar ganglia	77,536	A4 [27]
<i>Drosophila</i> , whole brain (hemibrain paper)	approximately 100,000	A4 [25]
<i>Drosophila</i> FlyWire, intrinsic neurons	118,501	A4 [27]
<i>Drosophila</i> FlyWire, identified neurons in connections of ≥ 5 synapses	134,181	A4 [27]
<i>Drosophila</i> , whole brain (FlyWire), proofread	139,255	A4 [27]
<i>Drosophila</i> , adult CNS, brain plus nerve cord (different animals and sexes)	162,255 (computed)	A4 [27, 24]
honeybee brain (1 μ L)	950,000	A8 [16]
honeybee brain (about 1 mm ³)	about 960,000	A9 [16, 17]
Algerian sand gecko	just under 2 million	A5 [11]
Sumatran flying dragon	barely more than 5 million	A5 [11]
41 mammals, rest of brain, lowest	6 million	A5 [29]
human olfactory receptor neurons (about 5 cm ²)	6–20 million	A6 [2]
mouse lemur, olfactory bulb	7.6 million	A5 [29]
smoky shrew, cortex (lowest of 41 mammals)	9.8 million	A5 [29]
human, olfactory bulb	15–16 million	A5 [29]
smoky shrew, cerebellum (lowest of 41 mammals)	21 million	A5 [29]
rat, cortex (40 % of its cells)	about 30 million	A5 [16]
rhesus macaque, prefrontal cortex, one hemisphere	68 million	A9 [31]
baboon, prefrontal cortex, one hemisphere	115 million	A9 [31]
rat, whole brain (about 60 % of 330 million cells)	about 200 million (200.13 $\pm$ 21.17 million)	A5 [16]
ostrich, telencephalon, per hemisphere (pallium 208.1 million; mesopallium 41 million); text gives 282 million	228.3 million	A9 [31]
human, hippocampus plus	about 250 million	A5 [28]

amygdala		
chimpanzee, per hemisphere (prediction, not a measurement)	fewer than 300 million	A9 [31]
hooded crow, telencephalon, per hemisphere (pallium 301.8 million; mesopallium 81.1 million; nidopallium 156.9 million)	352.7 million	A9 [31]
carrion crow, telencephalon, per hemisphere (pallium 336.1 million; mesopallium 89.4 million; nidopallium 182.7 million)	409.9 million	A9 [31]
rook, telencephalon, per hemisphere (pallium 408.7 million; mesopallium 116.0 million; nidopallium 214.2 million)	483.0 million	A9 [31]
41 mammals, rest of brain, highest	690 million	A5 [29]
human, rest of brain outside cortex and cerebellum	about 1 billion (computed)	A10 [32]
African elephant, cerebral cortex	5.6 billion	A5 [28]
African elephant, cerebral cortex	5.6 billion	A9 [33]
African elephant, cerebral cortex	5.6 billion	A10 [34]
human, cerebral cortex (1,233 g)	16 billion	A5 [27]
human, cortex (highest of 41 mammals)	16 billion	A5 [29]
human, cerebral cortex	16 billion	A10 [32]
human, cortex	16.3 billion	A5 [28]
human, cerebral cortex (as cited in the elephant paper)	16.3 billion	A9 [33]
human, cerebral cortex (as cited in the elephant paper)	16.3 billion	A10 [34]
long-finned pilot whale, neocortex	about 37.2×10^9 ($29.1\text{--}46.3 \times 10^9$)	A9 [34]
long-finned pilot whale, neocortex	37.2×10^9	A10 [35]
human, cerebellum (154 g)	69 billion	A5 [27]
human, cerebellum (highest of 41 mammals)	69 billion	A5 [29]
human, cerebellum (154 g)	69 billion	A10 [32]
human, whole brain	86 billion	A5 [27]
human, whole brain (adult male, NeuN-positive)	86.1 ± 8.1 billion	A10 [1]
African elephant, cerebellum (97.5 %)	250.7 billion	A5 [28]
African elephant, cerebellum (97.5 %)	251 billion	A9 [33]

African elephant, whole brain	257.0 billion	A5 [28]
African elephant	257 billion	A5 [11]
African elephant, whole brain (4,618.6 g)	257 billion	A9 [33]
African elephant, whole brain (97.5 % in the cerebellum)	257 billion	A10 [34]

C7 Present-day quantities

Totals printed in the chapters: energy use, synapse and connection counts, gene counts, cell counts, brain masses and lengths, species counts and global totals. Values from one source printed in several chapters are given once, with every chapter listed. Single-event physiology (potentials, speeds, frequencies), correlation coefficients, test statistics and values listed only under “Not verified” are not entered; durations stand in C4 and C5.

quantity	value	chapter [ref]
Energy and metabolism		
human brain, share of body mass; share of resting O ₂ consumption	only 2 %; ~20 %	A5 [9]
nervous system, share of the body's resting metabolic budget	20 %	A5 [1]
adult brain, share of resting metabolism	20 %	A10 [36]
adult brain, resting energy at body-mass share	about 20 % at about 2 %	A10 [36, 2]
brain glucose use at birth, share of resting metabolic rate, males; females	52.5 %; 59.8 %	A5 [25]; A10 [37]
brain glucose use at birth, share of daily energy expenditure, males; females	35.4 %; 38.7 %	A5 [25]; A10 [37]
brain glucose use, childhood peak, share of resting metabolic rate, males; females	66.3 %; 65.0 %	A5 [25]; A10 [37]
brain glucose use, childhood peak, share of daily energy expenditure, males; females	43.3 %; 43.8 %	A5 [25]; A10 [37]
glucose per neuron, whole-brain average (six species)	$5.79 \times 10^{-9} \mu\text{mol/min}$ ($\pm 0.76 \times 10^{-9}$ in A10)	A5 [26]; A10 [2]
glucose per neuron, cerebral cortex	$1.50 \times 10^{-8} \pm 0.49 \times 10^{-8} \mu\text{mol/min}$	A5 [26]; A10 [2]
glucose per neuron, cerebellum	$0.87 \times 10^{-9} \pm 0.36 \times 10^{-9} \mu\text{mol/min}$	A5 [26]; A10 [2]
glucose per neuron, variation across six species	40 % (A5); about 0.4-fold (A10)	A5 [26]; A10 [2]
brain of 1 billion neurons; of 100	5.79 μmol glucose/min; 579	A5 [26]; A10 [2]

billion neurons (model)	$\mu\text{mol/min}$	
human brain, glucose ($86 \times 10^9 \times 5.79 \times 10^{-9}$)	498 $\mu\text{mol/min}$ (computed)	A5 [26]; A10 [2]
human brain, glucose per day	129 g (computed)	A10 [2]
brain O_2 use per mass	3.5 mL O_2 per 100 g per min	A10 [36]
brain of about 1,400 g, O_2 use	about 49 mL O_2/min , close to one fifth of basal body O_2 use	A10 [36]
brain O_2 use per day	70.6 L (computed)	A10 [36]
Na^+ per action potential; ATP per action potential	11.5×10^8 ; 3.84×10^8 (modelled)	A5 [22]
rodent signalling at 4 Hz, ATP per neuron per second; with resting potential	2.85×10^9 ; 3.29×10^9 (modelled)	A5 [22]
energy budget: action potentials; postsynaptic glutamate effects; resting potential; glutamate recycling	47 %; 34 %; 13 %; 3 % (modelled)	A5 [22]
energy budget, second split: postsynaptic receptors; action potentials; resting potential; glutamate recycling; presynaptic Ca^{2+}	50 %; 22 %; 20 %; 4 %; 4 % (modelled)	A5 [9]
synaptic transmission at 4 Hz, share of signalling ATP; of total cortical ATP	55 %; 41 % (modelled)	A5 [9]
ATP per vesicle released; per bit	1.64×10^5 ; about 24,000 (20,500 at release probability 1) (modelled)	A5 [9]
one spike plus downstream events per 2.5 ms; resting and housekeeping	4.5×10^8 ATP; 3×10^6 ATP (modelled)	A5 [9]
Na^+ influx and energy per action potential, rat mossy fibres	1.3 times the theoretical minimum	A5 [23]
one extra action potential per cortical neuron per second	+145 mL O_2 per 100 g grey matter per hour (modelled)	A5 [22]
white matter against grey matter, energy use	3-fold less (modelled)	A5 [9]
fly retina, share of resting ATP consumption	10 %	A5 [9]
ATP from mitochondria; from glycolysis	about 93 %; about 7 %	A5 [9]
myelin, metabolic efficiency	several hundred-fold improvement	A5 [1]
KaiC, ATP per day per subunit; KaiC-AA null mutant	15; 27	A7 [27]
Synapses and connections		
<i>Mnemiopsis</i> nerve net	no synapses between net cells	A2 [28]
mammalian post-synaptic density	about one thousand proteins	A2 [6]
<i>Platynereis</i> larva connectome,	25,509; 11,437 (graph density	A4 [20]

synapses; edges	0.0015)	
<i>Platynereis</i> larva, presynaptic; postsynaptic sites	27,943; 26,433	A4 [20]
<i>Ciona</i> larva, synapses	6,618 (abstract); 8,768 (Results); 8,617 (Table 1)	A4 [21]
<i>Ciona</i> larva, gap junctions	1,206 (abstract); 2,105 (Results); 3,205 (Table 1)	A4 [21]
<i>Ciona</i> larva, neuromuscular junctions	1,772	A4 [21]
<i>Ciona</i> larva, per neuron: presynaptic sites; gap junctions	37; 7	A4 [21]
<i>C. elegans</i> , chemical synapses; neuromuscular junctions; gap junctions	about 5,000; 2,000; 600	A4 [22]
<i>C. elegans</i> , chemical synapses	about 5,000	A8 [13]
<i>C. elegans</i> non-pharyngeal neuron: synapses; gap junctions	28; 3.2	A4 [21]
mouse somatosensory cortex neuron, synapses	about 8,200	A4 [21]
<i>Drosophila</i> larva, synapses	about 548,000	A4 [30]
<i>Drosophila</i> hemibrain, chemical synapses; T-bars; PSDs	about 20 million; 9.5 million; 64 million	A4 [25]
<i>Drosophila</i> hemibrain graph, edges	3 million	A4 [25]
<i>Drosophila</i> FlyWire, chemical synapses	about 5×10^7 (abstract); 54.5 million between reconstructed neurons; about 130 million in the whole volume	A4 [27]
<i>Drosophila</i> FlyWire, connections of at least five synapses	2,700,513	A4 [27]
<i>Drosophila</i> male nerve cord, T-bars; PSDs	10 million; 74 million	A4 [24]
chemical synapses per neuron: worm; <i>Platynereis</i> ; fly larva; FlyWire brain; hemibrain	16.6; 28.6; 182; 391; 800 (computed)	A4 [22, 20, 30, 27, 25]
human cortex, synapses per mm ³	about 10 ⁹	A10 [33]
human brain, synapses	10 ¹³ –10 ¹⁵	A10 [33]
human cortex, synapses per cortical neuron (5.2×10^{14} / 1.6×10^{10})	about 33,000 (32,500, computed)	A10 [33, 32]
white matter against grey matter, synapse density	80-fold lower	A5 [9]
neocortical presynaptic terminals, mitochondria each	0.3–1.4	A5 [9]
octopus brain, connections between 32 regions	more than 350 (abstract); 249 directed edges (results); 439 (discussion); 2,178 literature hits (methods)	A9 [25]
Genes		

<i>Bacillus subtilis</i> , characterised K ⁺ channels	1 (YugO)	A1 [8]
prokaryotes (survey), channel sequences	2 Na ⁺ and 1 Ca ²⁺	A1 [45]
<i>Monosiga brevicollis</i> , channels	1 T-type Cav + 1 high-voltage Cav; Nav-like; putative Kv	A1 [3]
<i>Paramecium tetraurelia</i>	~40,000 genes; 34 Ca ²⁺ -release channel genes in 6 groups; K ⁺ channel multigene family (Pak1, Pak2 complete; three fragments)	A1 [46, 47, 48]
<i>Thalassiosira pseudonana</i> , channels	1 putative four-domain Na ⁺ /Ca ²⁺ channel + single-domain channels	A1 [29]
<i>Phaeodactylum tricornutum</i> , channels	0 four-domain channels; EukCatA single-domain	A1 [29, 7]
<i>Karenia brevis</i> , four-domain channels	7 (transcriptome)	A1 [29]
<i>Arabidopsis thaliana</i>	9 Shaker-type + 6 KCO K ⁺ channels; 20 CNGC; ~880 transporters in 46 families; about 5 % of the genome for membrane transport	A1 [49]
<i>Amphimedon queenslandica</i> , channels	two-TM Kir only; 0 Kv; 0 Nav	A1 [3]
<i>Trichoplax</i> , <i>Mnemiopsis</i> , channels	putative Kv; all Nav with DEEA filter	A1 [3]
<i>Nematostella vectensis</i> , channels	44 Kv (18 Shaker, 14 intron-less); 5 Nav2 (3 DEEA, 1 DEET, 1 DKEA)	A1 [3]
sea anemones and corals, Cav	6	A1 [3]
<i>Hydra magnipapillata</i> , Kv	35	A1 [3]
<i>Caenorhabditis elegans</i> , channels	38 K ⁺ + 2 CNG subunit genes in 8 families (1996); ≥80 K ⁺ channels, no voltage-gated Na ⁺ channel (1998)	A1 [50, 51]
<i>Drosophila melanogaster</i> , channels	5 Kv; 1 Nav1 + 1 Nav2	A1 [3]
most invertebrate bilaterians, Cav	3	A1 [3]
<i>Homo sapiens</i> , channels	27 Kv (or 35); 10 Nav (Nav1.1–1.9 and Nax); 8 Shaker (7 intron-less); 10 Cav	A1 [3, 45]
human, non-redundant K ⁺ channel proteins (23 with two pore signatures); CNG channels; pore-forming K ⁺ subfamilies	123; 7 (6 in an earlier count); 18	A1 [45]
human voltage-gated-like ion channel superfamily	143 members in eight families	A1 [53]
human genes encoding ion channels; encoding pore-forming parts of plasma-membrane	more than 400; at least 232	A1 [54, 55]

channels		
<i>Monosiga brevicollis</i> , genome; genes	~41.6 Mb; ~9,200 (9,196 models)	A2 [19]
<i>Salpingoeca rosetta</i> , genome; genes	~55 Mb; 11,629	A2 [33]
<i>Trichoplax adhaerens</i> , genome; genes	~98 Mb; 11,514	A2 [12]
<i>Pleurobrachia bachei</i> , genome; genes	156,146,497 bp draft (estimated 160–180 Mb); 19,523 (44 % with orthologues in other animals, 8,590 computed)	A2 [2]
<i>Amphimedon queenslandica</i> , genome; loci	~167 Mb; ~30,000 loci (called an overestimate); 18,693 (63 %) with Swiss-Prot homologues	A2 [5]
pan-metazoan gene families; metazoan-specific	4,670; 1,286 (27 %)	A2 [5]
placozoan branch, genes lost	4,952 (modelled)	A2 [2]
human opsin genes; <i>Drosophila</i> ; amphioxus; <i>C. elegans</i>	9 (in 6 of 7 subfamilies); 7; at least 6; 0	A6 [1]
opsins identified	more than a thousand, in seven subfamilies	A6 [1]
13 placental mammals, intact OR genes	more than 10,000, in 781 orthologous gene groups (about 769 per species, computed)	A6 [4]
African elephant, functional OR genes	~2,000	A6 [4]
OR genes: human; mouse; platypus; cow; macaque; most other species	about 800 (about 50 % pseudogenes); about 1,400; fewer than 400 functional; nearly 1,000 functional; fewer than 400 functional; 800–1,200 functional	A6 [5]
OR genes: dog; rat	1,094; 1,493	A6 [5]
human OR genes (Malnic, Godfrey and Buck 2004); working genes (Gilad and Lancet 2003)	339 intact and 297 broken; 400	A6 [2]
insect odorant receptors: <i>D. melanogaster</i> ; <i>A. gambiae</i> ; honey bee	62; 79; 170 (7 pseudogenes)	A6 [6]
insect gustatory receptors: bee; <i>D. melanogaster</i> ; <i>A. gambiae</i>	10; 68; 76	A6 [6]
SRGAP2, human-specific copies	3 (B, C, D)	A10 [5]
NOTCH2NL paralogs highly expressed in radial glia	3	A10 [16]
human radial-glia genes without mouse orthologs; hominid-specific duplicated genes	56; 35	A10 [6, 15]
Cells and cell types		
cell types: non-bilaterian animals; invertebrate bilaterians;	about 5–15; about 50–100; about 225	A2 [5]

vertebrates		
<i>Spongilla</i> , cell types	18	A2 [21]; A3 [22]
<i>Trichoplax</i> , cell types	6 (four, possibly five, in 2008)	A2 [23, 12]
<i>Trichoplax</i> , secretory cells around a 500 µm animal	about 1,500 (4 % of the total)	A2 [23]
<i>Hydra</i> , stem cells	3,000–6,000	A2 [32]; A3 [16]
<i>Hydra</i> , nerve cells differentiating per day	about 900	A2 [32]; A3 [16]
<i>Hydra</i> , nerve cells per epithelial cell	0.12	A3 [1]
<i>Hydra</i> , neuronal subtypes (single-cell atlas); sensory and ganglion populations	12; 3 + 5	A3 [3, 1]
<i>Platynereis</i> 72-h larva, cells with a soma; in the final connectome	8,852; 2,728	A4 [20]
<i>Platynereis</i> larva, non-neuronal cells; unclassified cells	2,905 in 90 types; 5,230	A4 [20]
<i>Platynereis</i> larva, neuronal; all cell types (preprint); later version	180; 270; 202 neuronal and 92 non-neuronal in over 9,000 cells	A4 [20, 28]
<i>Ciona</i> larva, cells; CNS cells; neuron types	~2,600; about 330; at least 25 types, 52 subtypes	A4 [21]
<i>C. elegans</i> , cells of the adult hermaphrodite	959	A8 [13]
<i>C. elegans</i> , neuron classes	118	A4 [22]
<i>Drosophila</i> hemibrain, morphology types; connectivity types	5,229; 5,609	A4 [25]
<i>Drosophila</i> FlyWire, cell types; neuropils	8,453; 78	A4 [23, 27]
rat brain, cells; cortex; cerebellum	about 330 million; about 80 million; about 170 million	A5 [16]
non-neuronal cell density, mammals, birds and reptiles	50,000–120,000 cells/mg	A5 [11]
human brain, non-neuronal cells	85 billion	A5 [27]
human brain, non-neuronal cells (adult male)	84.6 ± 9.8 billion	A10 [1]
pilot whale neocortex, glial cells	127 × 10 ⁹ (99.9–183 × 10 ⁹)	A9 [34]
teleost total brain cells: wrasses; cichlids; outgroup	45.7–185.08 million (one large <i>C. anchorago</i> 301.9 million); 37.54–61.78 million; 6.66–100.84 million	A9 [13]
human ear: inner hair cells; outer hair cells	about 3,500; about 12,000	A6 [2]
human utricle; saccule, hair cells	about 30,000; about 16,000	A6 [2]
human taste buds	2,000–4,000, with 10–50 cells each	A6 [2]
<i>Dionaea</i> trap, glands	about 37,000	A1 [14]
SAR86 cell, proteorhodopsin	24,000; more than 100,000	A6 [3, 24]

orange cone, proteorhodopsin molecules; purple membrane, rhodopsins per cell	43,000, more than 100,000	A9 [9, 43]
Brain mass and length		
human brain at autopsy: men; women	1,407 g (1,070–1,767); 1,233 g (1,000–1,618)	A10 [40]
human cerebral cortex	1,233 g, 82 % of brain mass	A5 [27]; A10 [32, 1]
human cerebellum	154 g	A5 [27]; A10 [32]
human cortex surface, per hemisphere	973 cm ²	A10 [24]
human myelinated fibre at age 20: men; women	176,000 km; 149,000 km	A5 [14]; A10 [25]
human myelinated fibre at age 80: men; women	97,200 km; 82,000 km	A5 [14]; A10 [25]
African elephant brain (without olfactory bulb)	4,618.6 g	A5 [28]; A9 [33]
long-finned pilot whale, total brain weight	3,062–4,618 g	A9 [34]
honeybee brain	1 µL	A8 [16]
<i>Drosophila</i> brain, neuronal path length	~149 m	A4 [27]
<i>Drosophila</i> male nerve cord, neuronal cable	44 m	A4 [24]
Species, individuals and global totals		
ctenophore species described	about 200	A2 [15]
living cephalopod species	about 750	A9 [26]
living decapod species	about 15,000	A9 [26]
fish species with passive electroreception; with electric organs	about 16 %; about 1.5 %	A6 [23]
proteorhodopsin-expressing bacteria in the oceans	about 10 ²⁸	A6 [24]
ants on Earth, individuals; ground-dwelling	almost 20 × 10 ¹⁵ (19.8 ± 5 × 10 ¹⁵); over 3 × 10 ¹⁵	A10 [38]
ants on Earth, dry biomass	about 12 Mt C (12.3 ± 3.1 Mt C); about 20 % of human dry biomass	A10 [38]
named ant species and subspecies	more than 15,700	A10 [38]
known ant species; subfamilies	roughly 5,000–6,000 circa 1940 to > 14,000 today; 6 to about 20	A10 [3]
Argentine ant main supercolony, extent	more than 6,000 km	A10 [26]
internet users, 2025; growth in 2025	about 6 billion (about three quarters of the world population); more than 240 million	A10 [39]
internet users, 2024	revised from 5.5 to 5.8 billion (71	A10 [39]

	%)	
offline, 2025; 2024	2.2 billion; 2.3 billion (revised from 2.6 billion, 29 %)	A10 [39]
offline living in low- and middle-income countries	96 %	A10 [39]
internet use: high-income; low-income; men; women; urban; rural	94 %; 23 %; 77 %; 71 %; 85 %; 58 %	A10 [39]
5G subscriptions	about 3 billion, about one third of mobile broadband	A10 [39]
New York Declaration on Animal Consciousness, signatures on 14 Oct 2026	611	A9 [36]
LSE sentence review: studies; criteria	over 300; 8	A9 [26]
LSE criteria at high or very high confidence: octopods; true crabs; squid and cuttlefish; anomuran crabs; astacid lobsters and crayfish; spiny lobsters; caridean shrimps; penaeid shrimps	7 (medium for the 8th); 5; 4; 3; 3; 2; 2; 1	A9 [26]

Row counts

C1: 95 rows (62 with an age in Ma, 33 without). C2: 33 rows. C3: 145 rows.

C4: 395 rows. C5: 201 rows (183 with a position, 18 without). C6: 89 rows.

C7: 153 rows in 6 groups.

Layer B — The Mind Set Beside the Net

B1 Method

The data of this layer are the ten chapters of Layer A, their Pattern paragraphs and the seven tables of Part C. The other side is what the Vacuum.Net texts state, quoted in B2. A pairing sets one statement from each side together where both have the same form.

A pairing is a read. A read is a hypothesis until a test decides it. No statement about the net is added, and where nothing pairs the entry says none.

For this book the texts say more than for the earlier ones. They name the membrane, the nerve cell, synchrony, deep sleep, seizure, memory and consciousness. Three tests were therefore fixed from the texts before any dossier was written (B13).

One alternative was known when they were fixed: a published claim that brain rhythms step by e.

B2 What the texts say that can be set beside Layer A

Quoted as fetched from constable.blog on 14 October 2026 (text).

1. **The rungs.** "1. Closure: every ring whose windows close, including chemistry." "2. Life: closure that holds while its content changes." "3. Representation: closure over the phases of closures." "4. Consciousness: representation that counts itself." (*Life and Consciousness from One Rule*, §7.)
2. **Reading.** "The reading ring is therefore not a copy of what lies below. It is a homomorphic image: it keeps the relations and drops the rest." (Same, §6.) "Each handover is its own window." (*One Window*, §4.)
3. **The membrane.** "The correspondence is the cell membrane, where the largest potential step of the cell is found." "The inside of the ring carries none." (*Life and Consciousness*, §4.)
4. **The nerve cell.** "At this depth the nerve cell adds nothing new." "It is a cell whose edge tension travels along its length." (*One Window*, §5.) "De zenuwcel als ring die zich niet deelt." (*Three Chains, One Standstill*.)
5. **Synchrony.** "The living form measures $R = 0$. The crystal form measures $R = 1$." "Clinically, a brain in which all cells fire together is a brain in seizure." (*One Window*, §9.) "Diepe slaap is de staat waarin de schorscellen samen draaien." (*Three Chains*.)
6. **Clock and layer.** "Elke gesloten ring heeft dus een eigen klok met periode 3." (*Life and Consciousness*, Dutch version.) "Elke laag is een factor drie." (*Three Chains*.)
7. **Memory.** "Heredity is memory in form with reach two." "Direct inheritance reaches two rings; further only by chaining." "Ring n remembers ring $n-2$ directly and nothing earlier directly." "Forgetting is impossible; immediate access is also impossible." (*Balanced Tree*, §8, §10, §11.)
8. **Body.** "The net permits self-referential closure without life, and so without a body." "A body is one carrier of consciousness. It is not its condition." (*Life and Consciousness*, §8.)
9. **Scale and classes.** "N5, Scale. The same winding appears at every depth." "The closed class persists and holds form." "The unclosed class decays, and while it lasts it carries tension from one closure to the next." (As quoted in the earlier books.)
10. **The eye.** "The eye of the animal built a chain on top of it and became fifty times slower, and far more sensitive." (*One Window*, §13.)

The texts make no statement on neuron numbers, brain size, energy use, gene counts, sense-organ counts or the dates of any step. These absences are recorded so that they are not filled.

B3 The order of the rungs

Measured (A1-A4, A9, A10). Every cell measured carries a negative inside: plants -116 to -250 mV, bacteria -105 to -150 mV, protists and animals -30 to -95 mV (A1). Electrical events run in bacteria, diatoms, plants and protists without neurons (A1). Nerve nets appear in animals dated by clock at 741 Ma (686-819 Ma; modelled, A3).

Fossil brains appear at about 520 Ma (A4). Complex brains arise in seven named groups across three bilaterian lineages (A9). The human brain grows from about 450 cc to 1,297–1,460 cc (A10).

Text. Statement 1: closure, life, representation, consciousness.

Read. The membrane potential sits at the second rung: it is found in every living cell measured. The nerve net and the brain are the third rung: their cells read the phases of other cells. The fourth rung, a reading that counts itself, has no measured counterpart in Layer A. What Layer A holds there are positions taken by named authors.

They widen by date: mammals, birds and octopuses in 2012; insects in 2016; cephalopods and decapods in 2021–2022; all vertebrates and at least cephalopods, decapods and insects as a “realistic possibility” in 2024 (A9).

Status. Rungs 2 and 3: read, untested. Rung 4: none measured. Read: the order in time follows the order of the rungs; no text gives dates, and no test was set.

B4 The membrane and the step

Measured (A1). All resting potentials read are negative inside, from -30 to -250 mV. The neuron reference rests at -70 mV. Bacterial channels already carry the fourfold pore, with a filter $4.6 \text{ \AA}$ wide in the bacterial Na^+ channel.

Text. Statement 3: the largest potential step of the cell is at the membrane; the inside of the ring carries none.

Read. A potential that sits across the boundary is the form named. The sign is the same in every group read. Read; consistent; not discriminating, since this is the textbook account of the membrane.

B5 The nerve cell adds nothing new

Measured (A1, A2). The unicellular sister of animals holds the post-synaptic scaffold backbone, the presynaptic secretion complex and all voltage-gated channel families (A2). The Na^+ -channel family is older than animals (A1). The sponge lacks neurons and synapses, yet keeps scaffold genes in one larval cell type.

The placozoan coordinates feeding by peptides without synapses (A2). Action potentials run in diatoms (50–100 ms) and plants (2–3 s) as well as in neurons (2 ms) (A1).

Text. Statement 4: at this depth the nerve cell adds nothing new; it is a cell whose edge tension travels along its length.

Read. Every part the neuron uses is in place before the neuron. What the neuron changes is speed and reach. Its event lasts 2 ms against 50 ms to 3 s in other cells, and its signal travels along an axon.

That is the form of the statement: the same edge, now running along the length. Read; consistent with the toolkit data; untested.

B6 The nerve cell that does not divide

Measured (A2, A3, A5). In cnidarians and flatworms the dividing cells are progenitors. *Hydra* nerve cells carry post-mitotic DNA content, and the whole *Hydra* nerve net is renewed in 2–3 weeks from a stem pool (A2, A3). Human cortical neurons date from around birth (A5).

In Alzheimer's disease about 4 per cent of at-risk neurons copy their DNA, and none has been seen in mitosis (A5). Completed division of differentiated neurons is recorded after loss of Rb-family genes or added DNA damage (A5). In Rb-deficient mouse cortical neurons in culture, 2 per cent are in mitosis.

After added DNA damage, such neurons divide with daughters that keep their neuronal marker (A5).

Text. Statement 4: the nerve cell as a ring that does not divide.

Tested. Test M1 required that no differentiated neuron be documented completing division. One is documented with status V. **Fail** (B13).

Read after the test. In every case recorded with the cell-cycle brakes intact, the neuron does not divide. Division appears when those genes are removed or DNA is damaged. The text as fixed made no such exception, and the test does not grant one afterwards.

What survives is a description: the neuron does not divide unless its brakes are taken away or its DNA is damaged. That is a read made after the data; it is not a pass.

Status. Failed as fixed; read after the test; untested in that form.

B7 The spacing of the rhythms

Measured (A7). One group publishes ten classes, from 15–40 s to 200–600 Hz. Computed centres step by 2.58–2.90, geometric mean 2.73. The authors state a constant ratio on the natural-logarithm scale, and drew the classes on an axis ticked at powers of e.

Frequencies vary 30–100 per cent across mammals while brain size varies hundreds- to thousands-fold.

Text. Statement 6: each layer a factor three; each closed ring a clock with period three.

Tested. Test M2 required a mean step within 2.85–3.15. Found: 2.73. The value $e = 2.718$ lies 0.5 per cent from it; three lies 9.8 per cent above it.

Fail (B13). The mean step depends only on the two end classes of a published scheme. A test on measured spectral peaks would not depend on that scheme; none was fixed.

Read after the test. The brain's rhythm classes step by a nearly constant factor, as statement 9 (the same winding at every depth) would have it. That factor is not three. The conservation across brain sizes is the stronger fact: frequencies vary 30–100 per cent while brains differ hundreds- to thousandsfold.

Read, after the test.

Status. Factor three: failed. Constant step and conservation across size: read, untested.

B8 Synchrony, sleep and seizure

Measured (A7). Nine of thirteen awake spike-count means lie below 0.1; the others are 0.10, 0.11, 0.12 and 0.20. In slow-wave sleep three of five comparisons show more co-activity, one shows less (the correlation between excitatory and inhibitory ensembles) and one is mixed. In seizures two comparisons show higher synchrony and three lower, not higher or disrupted.

Synchrony rises toward the end of a seizure in two of five.

Text. Statement 5. The living form measures $R = 0$, the crystal form $R = 1$. A brain in which all cells fire together is in seizure.

Deep sleep is the state in which the cortical cells turn together.

Tested. Test M3 required at least 80 per cent of awake means below 0.1, and synchrony higher in every sleep and seizure comparison. Found: 69 per cent; one sleep comparison lower; seizures in both directions. **Fail** (B13).

Read after the test. The direction holds in most of the data. Awake correlations are low, with a median below 0.1. Slow-wave sleep is more co-active in three of five comparisons, less in one.

The seizure is not one state: in rat slices it is desynchronised, in some human recordings hypersynchronous, and toward its end more homogeneous. Statement 5 names one crystal form for the seizure; the measurements show more than one.

Status. Failed as fixed; the waking and sleep halves are consistent in direction.

B9 The eye and the chain

Measured (A6). Microbial rhodopsin cycles fall in two bands: pumps at or under 20 ms, sensory rhodopsins at or over 300 ms. Cone time to peak is about 20 ms in human and 47–55 ms in macaque; mouse rod decay takes 122–258 ms. Eyes or photoreceptors arose at least 40 times, up to 65 or more.

The first dated compound eyes, at about 515 Ma, hold 3,000 and 16,000 lenses.

Text. Statement 10: the animal eye built a chain on top of the light-gated channel and became fifty times slower. Statement 2: each handover is its own window.

Read. The ratio of fifty asks for the response time of channelrhodopsin. Layer A holds its conductance and its precision but its kinetics only in a secondary source (A6, Not verified). The ratio cannot be formed from Layer A. None.

B10 Memory with reach two

Measured (A8). Spaced training gives memory of days to weeks in *Aplysia*, worm and bee; massed training does not. The phase lasting beyond hours needs protein synthesis in rat, *Aplysia*, worm and bee. Two forgetting curves show breaks, at 24 hours and at 3–6 years.

Habituation with recovery is recorded in a ciliate, a slime mould and a plant.

Text. Statement 7: memory reaches two rings directly; further only by chaining; forgetting is impossible, immediate access also impossible.

Read. Two phases of memory, a short one without new protein and a long one with it, recur in four animal groups. The texts speak of a reach of two rings, not of two phases in time. The pairing would equate them, and nothing in the texts does.

None.

B11 Fast carriers, slow forms

Measured (Table C5; A1, A3, A5, A8). A neuronal spike lasts 2 ms (A1). Adult cortical spines are 50 or 96 per cent stable over a month; CA1 spines live 1–2 weeks (A8). Human cortical neurons date from around birth (A5).

In *Hydra*, the nerve net as a whole persists while every nerve cell is replaced within 2–3 weeks (A3).

Text. Statement 9: the closed class persists; the carriers decay while they carry.

Read. In the human cortex the neuron is the slow form and its spikes and spines are the carriers. In *Hydra* the nerve cell itself is a carrier, and the net is the slow form. The division runs between event and form at each scale, as in *The Weaving of Life*, B7.

Read; untested.

B12 Where nothing pairs

- **Counts.** Neuron numbers run from 177 (*Ciona* nervous system) to 257 billion (elephant) (A4, A5). Cell types number 5–15, 50–100 and 225 by grade; peptides 11 to 129 per group (A2). Opsin genes run from 0 to 9, olfactory receptor genes from about 400 to 2,000 (A6). Rhopalia come in multiples of 4 (A3). The texts set no count beside a biological count, and this book does not. None.
- **Energy.** One action potential costs 3.84×10^8 ATP; one spike with its downstream events 4.5×10^8 (A5). The adult human brain takes 20 per cent of resting energy at 2 per cent of body mass; in childhood its share reaches 65–66 per cent of resting metabolic rate (A5, A10). None.
- **Brain size and dates.** Cranial volume 426 to 1,460 cc; steps in its rate of increase at 2.10 Ma and at 1.49 or 1.97 Ma; SRGAP2 copies at 3.4, 2.4 and 1 Ma (A10). None.
- **Consciousness without a body.** Statement 8 names consciousness without life. Layer A measures bodies only. None.
- **The ladder.** Tables C1, C3, C4 and C5 give their rows positions. No clustering test

was run. No claim.

B13 The tests, fixed first and then run

Fixed on 14 October 2026 from the texts, before any dossier was written. Run by Claude Code on the dossiers M1-M10 the same day. The attestation is the author's.

Protocol, rows and arithmetic are in the file TM-tests.md that accompanies this book.

M1, the nerve cell does not divide. Required: no documented completed division of a differentiated neuron. Found: Rb-deficient mouse cortical neurons in culture divide, with daughters that keep their neuronal marker (status V). **Fail.**

M2, the rhythm step is three. Required: mean step 2.85–3.15. Found: 2.73 over ten published classes; e lies 0.5 per cent from it. **Fail.**

M3, the living form is not synchronous. Required: ≥ 80 per cent of awake means below 0.1, and higher synchrony in every sleep and seizure comparison. Found: 69 per cent; one sleep comparison lower and one mixed; seizures in both directions. **Fail.**

Across the four books the theory has now been set against biological data twelve times with the outcome fixed first. One passed: the nesting depth in *The Weaving of Life*. Six failed outright: the count list, the retention rule, the partner-age rule, and the three tests here.

One failed on its own rule, which was ill-posed, while confirming its measured half. Four could not be completed on the data reachable. That is the state.

B14 The answer to the question of this book

The question: how excitable cells, nerve nets, brains and minds evolved, and how that evolution can be described in the Vacuum.Net model.

Layer A gives the history. A negative inside in every cell measured. Channels with the fourfold pore in bacteria. Electrical events in protists, diatoms and plants.

The synaptic parts in the unicellular sister of animals, before any neuron. Nerve nets dated by clock at 741 Ma, brains in the fossil record at about 520 Ma. Myelin in five groups, eyes or photoreceptors arising at least 40 times, complex brains in seven groups.

Ten rhythm classes held across a thousandfold range of brain size. Two phases of memory in four animal groups. A human brain about three times the volume of an australopith's, taking a fifth of resting energy.

Layer B gives three reads and three failed tests. 1. The neuron adds no new part; it adds speed and reach to an edge every cell has (statement 4). Read. 2. Membrane, nerve net and brain follow the rungs of life and representation (statement 1). Read; the fourth rung has no measured counterpart. 3. The carriers are fast and the forms slow at each scale, and in *Hydra* the net is the form while its neurons are carriers (statement 9). Read.

What does not hold, as fixed: the neuron that never divides (M1), the factor three between rhythms (M2), and the synchrony of sleep and seizure in every case (M3). In M1 and M3 the direction of the text is in much of the data, and the strict form fails. The neuron does not divide unless its brakes are removed or its DNA damaged.

Sleep is more co-active than waking in three of five comparisons; seizures go both ways. In M2 the published classes step by 2.73, close to e and not three (read, after the test).

Read, as a whole. In these terms the mind is the third rung built on the second. Its parts are older than the neuron. Its rhythm classes keep nearly one spacing, and nearly the same frequencies across brain sizes.

Its cells are carriers or forms depending on the scale. The texts give the form of that description. Where they gave a number, three times, the number failed.

Part D — Left Out, by Rule

- Facts that the dossiers marked as read only in a secondary page, or whose citation alone was verified, do not enter Layer A. Each chapter lists them under “Not verified”.
 - Where two sources disagree, both numbers stand in Layer A. This book does not choose.
 - Blog texts on consciousness from before the Vacuum.Net derivation (2025 and early 2026) use other frameworks. They are not quoted in Layer B.
 - Numbers from background books are not used; their figures are replaced by the primaries.
 - No count of neurons, cell types, genes or sense organs is set beside a sequence of the theory unless a text sets it there. None does.
 - Statements on consciousness in Layer A are positions of named authors, with dates. Layer B pairs no measurement with the fourth rung.
-

Annotated references for Layer B

The texts

Konstapel, J. (2026). *Life and Consciousness from One Rule: Closure in the Net*. Constable Research, Leiden, 29 September 2026. Dutch version: *Leven en bewustzijn uit één rekenregel in een driewaardig net*. constable.blog. Why read?

The four rungs: closure, life, representation, consciousness. The reading ring as homomorphic image, the membrane as the place of the largest potential step, and the coherence values $R = 1$ and $R = 0$.

Reading advice: §4, §6 and §7.

Konstapel, J. (2026). *One Window: Light-Gated Channels, the 2026 Nobel Prize in Medicine, and the Closure Rule of the Vacuum.Net*. Constable Research, Leiden, 10 October 2026. Why read? The channel as a window with one free place; the nerve cell that adds nothing new; synchrony as the crystal form and the seizure; the eye that became fifty times slower.

Konstapel, J. (2026). *Three Chains, One Standstill: Dementia and Parkinson's Disease on the Ladder of the Vacuum.Net*. Constable Research, Leiden, 10 October 2026. Why read? The nerve cell as a ring that does not divide, each layer a factor three, deep sleep as the state in which cortical cells turn together. The source of tests M1 and M3, and with *Life and Consciousness* of M2.

Konstapel, J. (2026). *The Balanced Three, the Balanced Tree and the Vacuum.Net Theory*. Constable Research, Leiden, 29 August 2026; PDF *Balanced Ternary and the Balanced Tree: One Balance and What Follows From It*. Why read? Memory with reach two (§8), the impossibility of forgetting (§10), and heredity as memory in form (§11).

Konstapel, J. (2026). *The Climate on the Ladder of Three*. Constable Research, Leiden, 3 October 2026. Why read? Depth as layer, $3^n \cdot S_0$, the definition behind every position in this book.

Konstapel, J. (2026). *Plants on the Ladder; The Company of Plants; The Weaving of Life*. Constable Research, Leiden, 12-13 October 2026. Why read? The three books this one follows, and the nine earlier tests that B13 counts with these three.

Background books

Godfrey-Smith's *Other Minds*, Buzsáki's *Rhythms of the Brain*, Herculano-Houzel's *The Human Advantage*, Striedter's *Principles of Brain Evolution*, and Feinberg and Mallatt's *The Ancient Origins of Consciousness* framed the choice of topics. No number is taken from them.