From Chemistry to Body and Mind

How it works, why it fails, and how to cure

The Vacuum.Net Theory computed above chemistry, with an atlas of illness and recovery for every organ system and for the mind

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Second edition, 12 November 2026

Calculations and draft text: Claude (Anthropic), on instruction of the author.

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Nothing in this book is medical advice. Any change of treatment belongs with the person's own doctor.

Contents

Preface: three kinds of statement

Results at a glance

Part I — The rules, recomputed

1. The window
2. The ring
3. Widening and pruning
4. The seam
5. Repair

Part II — The first depth above chemistry: the word of three

6. Readable words
7. Twenty
8. The third place
9. What the cell does instead

Part III — From word to body, depth by depth

10. The chain
11. The fold
12. The membrane and the sheet
13. The cell: copying and dividing
14. The tissue
15. The organ and the body

Part IV — How the body works, derived

16. Forms and carriers
17. The test
18. The ladder as a coordinate
19. The day

Part V — Mind

20. What the texts say and what was tested

Part VI — Why it fails: eight forms

21. Ways to fail, depth by depth

Part VII — The atlas of illness, system by system

22. Circulation: heart and vessels
23. Blood: the carrier itself
24. Breath
25. Metabolism and hormones
26. Digestion and liver
27. Kidney and urinary tract
28. Infection: the test meets the foreign
29. Autoimmunity and allergy: the test reads too much
30. Cancer: the unread copy
31. The nervous system
32. The senses: eye and ear
33. Skin
34. Bone, muscle and joints
35. Reproduction, pregnancy and birth
36. Inherited disease
37. Children
38. Ageing
39. The surround

Part VIII — The mind and its disorders

40. Depression, measured
41. Depression, read
42. The other disorders of the mind

Part IX — How to cure

43. Cure rules from the algebra, depth by depth
44. The treatment ladder
45. The dose of a cure, exact
46. Cures for depression with evidence
47. Prevention first
48. Tests fixed before data

Part X — The balance

49. What is computed
50. What is open

Appendix A — The programs

Appendix B — Index of illness by form and first layer

Annotated references

Preface: three kinds of statement

This book asks one question. How do body and mind work, why do they fail, and how can they be cured? It answers from one ground: the Vacuum.Net Theory. It starts where the theory has already been computed. That is chemistry.

The companion book The Chemistry of the Vacuum.Net Theory derived the atom, the bond, shape, handedness, the alkanes, the sugars, the twenty amino acids and the two base pairs of DNA. Those results are numbers that the rules produce before they are compared with data. Chemistry is the one layer where the theory computes from the first distinction to an exact count.

Above chemistry lie many depths: the word, the chain, the membrane, the cell, the tissue, the organ, the rhythm, the person. A book about body and mind must cross them. The danger is to cross them with borrowed knowledge and call it theory. This book refuses that. Every statement carries one of seven marks.

Mark	Meaning
Computed	The rules of the theory produce the number or the statement. A program in Appendix A prints it.
Derived	A law about how the body works that the rules alone produce, with no data. A program in Appendix A prints it. Used in Part IV.
Reproduces	The computation gives a result that science already knew. It confirms the rules; it is not new knowledge.
Measured	A number found by others and read in a cited source. It is data, not theory.
Reading	A measured fact set beside a rule. A reading is a hypothesis, never a cause.
New rule	A rule added in this book to reach a depth the theory had not reached: a writing rule or a closure rule. Each is fixed before the data, named (W2, W3, NR-a …), and tested. Rules that fail are kept in the book with their failure.
Open	Not yet done. Each open point is a defined calculation or a defined test.

The result is uneven, and the book says so. The rules are computed exactly. Then the book climbs one depth at a time. At each depth a rule is fixed first, then the count is made, then it is compared with measurement. Some depths give exact laws. One gives the number twenty. Two give tests that pass only partly. Part IV derives how the body works in time from the same rules. The book does not use energy as a concept: what physics calls energy is a count per time (section 18.3). Where earlier books of the author set numbers from the theory against biological data, the numbers mostly failed. That record is reported in full in chapter 20.

What the second edition adds

The first edition worked out one illness in full: depression. Every other illness was a line in a table. That was not the book that was agreed. This edition completes it. The body and the mind are taken whole. Every organ system gets its own chapter. Each chapter states how the system works, how it fails, and how it recovers. Each major disease gets an entry in the same form.

- **Part VI** now names eight forms of failure. Each rests on an exact law of Parts I to IV. Section 21.2 shows that the body's test can fail in two directions. Section 21.3 shows the frame law of chapter 6 in the clinic.
- **Part VII** is new. It is an atlas of illness in eighteen chapters: circulation, blood, breath, metabolism and hormones, digestion and liver, kidney, infection, autoimmunity and allergy, cancer, the nervous system, the senses, the skin, bone, muscle and joints, reproduction, inherited disease, children, ageing and the surround.

- **Part VIII** keeps the worked case of depression and adds every other major disorder of the mind: bipolar disorder, the anxiety disorders, trauma, obsessions, psychosis, eating disorders, addiction, attention and development, sleep and personality.
- **Part IX** turns cure into a ladder with five layers. Every disease of Parts VII and VIII is placed on it, with the standing of each treatment: established, in trials, or a direction. Chapter 45 replaces the simulated dose law of the first edition with an exact count. Chapter 47 sets prevention first.
- **Exact proofs.** Section 5.1 proves three laws that the first edition only computed: every closed strand has period three; a single error has exactly one repair at every length from four up, and three repairs at length three; turning one living direction into the other costs at least 18 of 27 places.
- **Corrections.** Section 18.1 separates the analysis fixed before the data from the adjusted one. Section 40.4 adds the meta-analysis of Ho and colleagues (2024) beside the miss on daily stability. Section 18.3 states when rule NR-E was fixed. The blank pages of the first edition are gone. The program check.py is added to Appendix A.

The atlas is the largest part of the book, and its standing must be clear. The burden of each disease, its prevention and its treatments are Measured: they come from the cited trials and reports. The naming of each disease as one of the eight forms is a Reading. The theory found none of these cures. It gives three things: one map on which they all fit, a reason why so many different routes help, and tests that can fail.

A note on dates. The tests T1 to T14 of chapter 48 were fixed on 11 November 2026, the date of the first edition. Rule NR-E and tests T15 to T21 were fixed on 12 November 2026, the date of this edition, before any of their data were seen.

> *Status: This preface states the marks. Every later statement carries one.*

Results at a glance

The chemistry book opened with its hits and misses. This book does the same. Each line is a prediction fixed before the data, then computed, then compared. Laws that follow from the rules alone are listed first; they cannot fail on data, only on a programming error.

Laws computed from the rules

Depth	Law	Status
Window	9 of 27 windows close: 3 uniform, 6 mixed	Derived
Ring	mixed rings only at depths 3, 6, 9 …; exactly 2 per depth	Derived
Seam	uniform never joins mixed (0 of 36); opposite directions never join (0 of 18)	Derived
Repair	one error opens 3 windows; for length ≥ 4 exactly 1 single change closes them: undo it (3 at length 3)	Derived
Word	readable words of three: $(k^3 - k)/3 = 2, 8, 20$	Derived; reproduces Crick 1957
Cell	unique partner; semi-conservative copy; every depth-6 ring divides into two closed rings	Derived; reproduces Meselson–Stahl
Membrane	8 of 9 bilayers asymmetric; mixed strands meet only antiparallel	Derived
Fold in space	smallest closed loop in tetrahedral directions: 6 steps	Derived; reproduces the six- ring
Tissue	exactly 9 chains close for any length: one word, one phase	Derived
Organ	k kinds in one chain leave at least k − 1 open windows	Derived
Reading	one error: 3 open windows, but 1 misfit for a mirror reader	Derived
Day	24 h sits at ladder position 43.50, farthest from any ring	Derived
Energy floor	a living place stays repairable only above $kT \ln 3 = 0.0294$ eV at 37 °C (with Boltzmann)	Derived with one imported law
Energy unit	$E_0 = h/T_0 = 27.197$ eV = 2 × hydrogen ionisation; ring n carries $E_0/3^n$	Derived
Defence	of 19,683 strands: 93.3 % foreign readable, 5.9 % unread, 8 wrongly closed forms seen only by a reader that meets	Derived
Carriers	a carrier closes a seam fully in only 6 of 72 cases; other seams stay open and need carriers forever	Derived
Mind	a form holds about 3/4 of its size in deviations and stays itself; nearest other states are reversal and flattening (18 of 27), not shifted copies (27)	Derived
Self-repair	windows alone restore the original up to 1/3 wrong (9 of 27); beyond, the form closes wrong (opposite or uniform)	Derived
Process cost	continuing a rhythm 0, dividing 0, impulse step 2, repair 1, turning direction 18 changes	Derived
Periods	a form of 9, 27, 81 places tolerates repair every 2, 14, 70 fast periods: rhythm ratios are bounded by form size	Derived

Depth	Law	Status
Dose	exact: an aimed cure is undone by the night at k ≤ 8 of 18 changes, ties at 9, is completed at k ≥ 10; 12 of 18 if a quarter of changes miss	Derived; exact (cure_exact.py)
Depression	a body against the day opens 1 window per waking; daily repair holds only while it lasts; restoring direction costs 2 of 3 places once, then 0	Derived; matches relapse after stopping drugs (reading)
Circulation	a loop of k organ kinds meets exactly k seams; each direction reversal costs 2 open windows	Derived; reproduces one-way closed circulation in form
Rhythm	every strand that closes repeats with period 3: what lasts, repeats	Derived
Coupling	closed + closed is always closed; closed + open never (0 of 18,000)	Derived
Impulse	an opening cannot slide; it moves in 2 changes via a fully closed state	Derived; reproduces the all- or-none impulse in form
Waking	free only at a cycle end and in the day's direction; otherwise ≥ 1 open window	Derived; agrees with Z2
Repair	repair at the error keeps 0 of 81 open; at a random place 52	Derived
Period (proof)	if every window of three closes, w(i+3) = w(i): every closed strand has period 3; mixed rings exist only when 3 divides the length	Derived; proved in 5.1
Repair (proof)	one error opens exactly 3 windows; for length ≥ 4 exactly one single change closes them, the undo; at length 3 there are 3	Derived; proved in 5.1
Direction (proof)	the two living directions differ at 2 of every 3 places for every shift: 18 of 27	Derived; proved in 5.1
Dose (exact)	an aimed cure with k of 18 changes: k ≤ 8 back to the old form, k = 9 a tie, k ≥ 10 the new form; with a quarter of changes off target: 12 of 18 for 96 %	Derived; exact (cure_exact.py)
Test, two directions	the test fails by missing a misfit (unread) or by reading a fit as a misfit; the cure of one is the harm of the other	Derived from chapter 17
Frame (clinic)	deletions of a multiple of three keep the frame; others lose it: milder Becker against severe Duchenne dystrophy	Reproduces Monaco 1988 (about 90 % of cases)

Predictions tested on measured data

#	Prediction (fixed first)	Data	Outcome
1	Charge windows close more often than in shuffled proteins (W2)	20,429 human proteins	Hit: 53.75 % vs 52.53 %
2	The excess closure is mixed, not uniform	same	Miss: excess is uniform
3	Helix repeats are multiples of three	8 helix types	Miss: 5 of 8, p = 0.088
4	Opposite charges meet at multiples of three (NR-a)	20,429 proteins	Miss: peak at 3 and 4
5	Opposite charges meet at odd k ≥ 5 (NR-b)	same	Miss
6	Heart and breath lock n:1 above chance at rest (H1)	Fantasia, 35 people	Hit with adjusted method: p = 1.6 × 10^{-12}; null with the method fixed first (18.1)
7	Locking prefers n = 3 or 6 (H2)	same	Miss: 72.1 % vs 72.5 %
8	Locking above chance in every sleep stage (S1)	MIT-BIH sleep, 18 nights	Partial: deep and light yes; wake and REM no
9	Locking strongest in deep sleep, weakest in REM and wake (S2)	same	Hit: excess +0.054 deep, +0.012 light, 0.00 REM and wake
10	Locking in sleep prefers n = 3 or 6 (S3)	same	Miss
11	Awakenings come from REM more than its share (Z1)	Sleep-EDF, 153 nights	Miss: 13 % vs 20 %
12	The night ends just after a cycle closes (Z2)	same	Hit: 37 % vs 26 %, p = 0.002
13	The night holds a whole number of cycles (Z3)	same	Miss: 0.239 vs 0.25
14	The day repeats less in depression: stability IS (D1)	Depresjon, 23 + 32 people	Miss: opposite direction; pooled studies show lower IS (Ho 2024)
15	Activity returns less after 24 h in depression (D2)	same	Hit: 0.157 vs 0.217, p = 0.005
16	More breaks within the day in depression: IV (D3)	same	Miss
17	Smaller day amplitude in depression: RA (D4)	same	Miss
18	Lower IS goes with higher MADRS (D5)	23 patients	Miss: opposite, ρ = +0.47
19	Rising IS goes with falling MADRS (D6)	same	Miss
20	The ladder selects body sizes and rhythms	earlier books	Miss: 49.5 % vs 50 %
21	Poor sleepers end the night after a closed cycle less often than healthy sleepers (C1)	Sleep-EDF telemetry, 22 people	Miss: 59 % vs 37 %
22	A sleeping pill does not raise that share (C2)	same, temazepam vs placebo	Consistent, not informative (see C4)
23	A sleeping pill does not raise deep sleep (C3)	same	Consistent, not informative (see C4)
24	The pill shortens the time to sleep (C4, check)	same	Miss: 9.8 vs 10.8 min, p = 0.29

#	Prediction (fixed first)	Data	Outcome
25	Body energies sit at $3^k \cdot kT$ (NR-E, fixed 12 Nov)	7 blind energies	Miss: 0.287 vs 0.25
26	Twelve biological tests in four earlier books	various	1 hit, 6 misses, 1 miss on own rule, 4 open

The pattern. Over twenty-six tested lines there are five hits and one partial hit. Two more lines agree with the prediction but cannot count, because the check beside them failed. Every hit is about closure itself: a rhythm or a chain returns in whole numbers more than chance. Every test of the number three failed. Closure is strongest in deep rest and absent in REM and in waking. The night tends to end just after a cycle has closed. In depression the body's activity returns less after 24 hours. These are the new facts of this book.

> *Status: Derived laws: computed by the programs in Appendix A. Tested lines: fixed before the data, computed on open data.*

Part I — The rules, recomputed

Part I recomputes the rules the rest of the book uses. Nothing here is new to the theory. What is new is that every statement is printed by a program, so a reader can run it.

1. The window

The theory has one ground: the trit. A crossing of the strand takes one of three values: over (+1), under (−1) or none (0). Three crossings in a row form a window. A window is closed when its three values add to a multiple of three.

Kind	Example	Number	Closed
Three equal	(+,+,+)	3	yes
Three different	(−,0,+)	6	yes
Two equal, one different	(+,+,0)	18	no
All		27	9 closed

Nine of the twenty-seven windows close. They come in two kinds. A uniform window has three equal values. It holds and does not turn: the form of a crystal. A mixed window has three different values. It can turn at every step and stay closed: the form of living matter.

> *Status: Computed (rules.py, R1).*

2. The ring

A ring is a strand closed on itself. Its depth is its number of crossings. The program counted every ring of depth 3 to 15 in which every window is closed, up to rotation.

Depth	Uniform rings	Mixed rings	Other
3, 6, 9, 12, 15	3	2	0
4, 5, 7, 8, 10, 11, 13, 14	3	0	0

Uniform rings exist at every depth, one per value. Mixed rings exist only where the depth is a multiple of three, and then there are exactly two: one running −1 → 0 → +1, the other its mirror. A living ring therefore cannot grow one crossing at a time. It grows by whole groups of three, and it keeps one direction.

> *Status: Computed (rules.py, R2).*

3. Widening and pruning

What closes at one depth is the alphabet of the next. That gives two strokes. Widening: units combine and the number of combinations grows. Pruning: only what closes stays. The program ran both strokes twice at the level of windows.

Depth	Combinations	Closed	Share
1: three trits	27	9	1 in 3
2: two closed windows joined	81	9	1 in 9

Each stroke keeps a smaller share. The second depth keeps one combination in nine, and every pair that survives is of one kind: three uniform-uniform pairs and six mixed-mixed pairs. Pruning sharpens with depth.

> *Status: Computed (rules.py, R3).*

4. The seam

A seam is the window that straddles two joined units. The algebra decides exactly which seams close.

Pair	Pairs	Seam closes
Uniform with mixed	36	0
Mixed with mixed, opposite direction	18	0
Mixed with mixed, same direction	18	6
Uniform with uniform	9	3

Two exact laws follow. A uniform stretch never joins a mixed stretch: the seam between them always stays open. Two mixed stretches of opposite direction never join. These two laws are the roots of chapter 21.

> *Status: Computed (rules.py, F1 and F2).*

5. Repair

Two values of a window fix the third: for every pair of values there is exactly one value that closes the window. Every one of the 18 open windows can be closed by changing one place, and at each of its three places there is exactly one value that does it.

Inside a closed ring the picture sharpens. The program took a closed ring of depth nine, mixed or uniform, and changed one value at every place to every wrong value. In every case the error opened exactly three windows. In every case exactly one single change closed the ring again: undoing the error, at the place where it was made. That place is the one crossing shared by all three open windows.

So an error in a closed form is findable and has one cure. It is found where three open windows overlap. It is cured by restoring the value that was there. Any other single change leaves the ring open.

> *Status: Computed (rules.py, R4 and R5).*

5.1 Three exact proofs

Chapters 1 to 5 found their laws by trying every strand. A count over every case is a proof for the lengths tried. It is not a proof for every length. A reviewer of the first edition asked for proofs that hold at any length. Three are given here. They use only arithmetic modulo three. The program check.py confirms each by exhaustive count for every length from 3 to 15.

Proof 1. Every closed strand has period three.

Let every window of three close: $w(i) + w(i+1) + w(i+2) \equiv 0 \pmod 3$ for every i. The next window gives $w(i+1) + w(i+2) + w(i+3) \equiv 0$. Subtract the two. Then $w(i+3) \equiv w(i) \pmod 3$. The values −1, 0 and +1 differ modulo three. So $w(i+3) = w(i)$. Every closed strand repeats with period three. This is the law of section 16.1, now proved.

On a ring of length d the strand also repeats with period d. A strand with periods 3 and d has period gcd(3, d). If three does not divide d, the period is one: the ring is uniform. So mixed rings exist only at lengths 3, 6, 9 and so on. At those lengths there are exactly nine closed rings: the

three uniform ones and six mixed ones, which fall into two classes under rotation. This is the law of chapter 2, now proved.

Proof 2. One error has one repair, from length four up.

Change one place p of a closed ring. The change is ±1 or ±2. Neither is a multiple of three. So every window that holds p opens, and no other window changes. Exactly three windows hold p. So one error opens exactly three windows, at every length.

A single change at place q can close all three only if q lies in all three. For $d \geq 4$ the three windows that hold p share only p. So q = p. At p only one value restores the sum modulo three: the original one. The repair is unique, and it is the undo. At d = 3 every window holds every place. Then any of the three places can close the ring, with its own value. So length three has three repairs. The first edition said 'exactly one' without this exception. The count confirms it: 3 repairs at d = 3, 1 at every d from 4 to 15.

Proof 3. Turning a direction costs two places in three.

The two living directions are (−1, 0, +1) repeated and (+1, 0, −1) repeated. Compare the first with the second at each of its three shifts. Shift 0 differs at places 1 and 3 of every window. Shift 1 differs at places 1 and 2. Shift 2 differs at places 2 and 3. Every shift differs at two places of every three. A form of 27 places therefore needs at least 18 changes to turn. This is the cost used in sections 41.1 and 45.

Proof 4. The dose law is a count of distances.

Start in one direction. Make k aimed changes towards the other. The form is now k places from the start and 18 − k places from the target. Every other closed form is farther from it (check.py, part 4). Repair moves to the nearest closed form. So the form returns to the start when $k < 9$, ties at k = 9, and reaches the target when $k > 9$. No simulation is needed. Chapter 45 gives the full table.

> *Status: Derived and proved (arithmetic modulo three). Confirmed by exhaustive count in check.py for d = 3 to 15. Correction to the first edition: the repair is unique for $d \geq 4$; at d = 3 there are three repairs.*

Part II — The first depth above chemistry: the word of three

The chemistry book derived the alphabet of the next depth: four bases that pair only as A·T and G·C, each pair a meeting of mirror words. It also showed that DNA is read in windows of three bases. Part II computes what the rules allow at that depth.

6. Readable words

A word is a window of three letters. To carry an address, a word must be readable in one phase only. If a word can also be read when the frame slides by one or two letters, the frame is lost and the first passage no longer fixes the direction (N3). Two exclusions follow from the rules alone.

- A uniform word (x, x, x) reads the same in every phase. It is the uniform closure: it holds but does not turn, and it cannot mark a frame. It is excluded.
- The three rotations of any other word, xyz, yzx and zxy, are the same closed form turned. At most one of them can be read, or the frame slides. One direction is chosen per class. With an alphabet of k letters there are k^3 words, k of them uniform, and the rest fall into rotation classes of three. The largest readable set is therefore $(k^3 - k)/3$. The program searched for such a set and checked that it is readable in one phase only: no word appears across the join of any two words.

Alphabet	Words	Uniform	Classes	Bound $(k^3 - k)/3$	Readable set found
2	8	2	2	2	2
3 (trits)	27	3	8	8	8
4 (bases)	64	4	20	20	20

One readable set of twenty, found by the program: AAC AAG AAT CAC CAG CAT CCT CGA CGC CGT GGA GGC GGT TAC TAG TAT TCT TGA TGC TGT. Of the twenty classes, eight hold words with three different letters and twelve hold words with two equal letters.

> *Status: Computed (code_depth.py, C1–C4).*

7. Twenty

Life builds its proteins from twenty amino acids. The bound computed from the rules is twenty. Four letters, words of three, no uniform word, one phase per class: twenty.

This count is not new. Crick, Griffith and Orgel found it in 1957 as the size of the largest comma-free code. What the theory adds is the reason for both exclusions. The uniform word is excluded because uniform closure does not turn. The rotations are excluded because a closed form must keep one direction. Both come from the starting rules, not from biology.

> *Status: Reproduces (Crick, Griffith and Orgel 1957). The count follows from the rules; it was known before.*

8. The third place

The measured genetic code was read through the same window. For every codon, every single-letter change was made and the program asked whether the amino acid stayed the same.

Place in the codon	1	2	3
Changes that keep the amino acid	4.6 %	0.0 %	71.6 %

The first two places fix the address. The third place behaves as a remainder: what stays at its own scale after the carry. That matches the carry rule T1, read on the code.

> *Status: Computed on the measured code table; the remainder interpretation is a reading.*

9. What the cell does instead

The real genetic code is not comma-free. It reads the four uniform words: TTT as phenylalanine, CCC as proline, AAA as lysine and GGG as glycine. It has three stop words, not four. The rules predicted the number of readable words. The cell reached that number by another route.

The route is visible. The cell fixes the reading frame with a start word. Every later word is read relative to that first one. That is N3, memory: the first passage fixes the direction, and later passages are taken relative to it. A comma-free code closes the frame in every word. The cell closes it once, at the start, and carries it.

So the depth above chemistry gives a computed count that matches, and a measured mechanism that uses the other rule of the theory. Why the cell's code has exactly the computed number of meanings, while it uses memory instead of comma-freeness, is open.

> *Status: Measured (the code). Reading (start word as N3). Open (why the two routes give the same twenty).*

Part III — From word to body, depth by depth

Part III climbs from the word to the organ. Each chapter follows the same order. First a writing rule is fixed: how the units of this depth are written as trits. Then the count is made. Then, and only then, it is compared with measurement. Where the writing rule is a choice, the chapter says so.

10. The chain

Words are read into a chain of amino acids. The chain is the next depth. Its units are the twenty amino acids, and they must be written as trits.

Writing rule. The register of the theory is charge. So each residue is written as its charge at neutral pH: lysine and arginine +1, aspartate and glutamate −1, every other residue 0. The rule was fixed before any protein was read. It is a choice; other writings are possible, and each would be a separate test.

Prediction, fixed first. In real proteins, windows of three consecutive residues close more often than in the same proteins with their residues shuffled. Refuted if they do not.

Data. All 20,429 reviewed human proteins in UniProt, 11.4 million residues, 11.4 million windows. Composition: +1 at 11.4 per cent, −1 at 11.8 per cent, 0 at 76.8 per cent.

Quantity	Real proteins	Shuffled (5 runs)
Share of closed windows	53.75 %	52.53 % (sd 0.014 %)
Uniform windows, observed/expected	1.030	1
Mixed windows, observed/expected	0.972	1
Open windows, observed/expected	0.974	1

The prediction holds: real chains close more often than shuffled ones, by 1.2 percentage points, about ninety standard deviations of the shuffle. But the excess is not where the theory expects living matter to close. It comes from uniform windows: runs of three negative charges occur 1.91 times more often than chance, runs of three positive charges 1.65 times. Mixed windows, the living closure, are slightly rarer than chance (0.97). The two orders −,0,+ and +,0,− are the most depleted of all (0.91 and 0.84).

So at the depth of the chain, closure is real but uniform. The protein favours runs of like charge, which hold, over mixed windows, which turn. Why the chain prefers the crystal form at this depth is open.

> *Status: New rule W2 (charge as trit). Computed on measured data (chain_depth.py). The prediction as fixed passes; the expected kind of closure fails.*

10.1 Where along the chain do opposite charges meet?

A chain also meets itself. Two residues of opposite charge, k places apart, form a meeting (x, −x). Two new rules were fixed before the count, each predicting where such meetings are enriched.

- NR-a, the group of three: at k = 3, 6, 9 and 12, more than at the neighbouring separations.
- NR-b, closure in space: the smallest loop in the cube's directions has six steps (chapter 11), so contacts are possible at k = 5, 7, 9 and 11. The program counted all pairs in the 20,429 human proteins and compared each separation with three shuffles of every protein.

Separation k	1	2	3	4	5	6	7	8	9
Opposite charge, obs/exp	1.04	0.92	1.09	1.09	1.01	1.01	1.03	1.00	1.01

Separation k	1	2	3	4	5	6	7	8	9
Equal charge, obs/exp	1.20	1.15	1.13	1.10	1.08	1.10	1.14	1.09	1.10

Both new rules fail. Opposite charges meet most at k = 3 and 4, least at k = 2, and show a small second rise at k = 7. There is no rise at 6, 9 or 12, and none at 5, 9 or 11. The pattern that the data do show is the α-helix: 3.6 residues per turn, so that residues 3 or 4 apart, and 7 apart, face each other. Measured salt bridges at i, i+4 and i, i+3 stabilise helices, as protein chemistry knew.

The other path is therefore the helix of chapter 11: a winding of 18 residues in 5 turns. Its 18 is a multiple of three; its local contacts are not. Closure in groups of three holds for the whole winding, not for each contact. That is a new reading, made after the data, and it needs its own test on helix-resolved structures.

> *Status: New rules NR-a and NR-b: tested, both failed (chain_space.py). The helix reading is formed after the data.*

11. The fold

A chain folds into regular helices. Chapter 2 computed the law: a mixed ring closes only when its depth is a multiple of three. A helix is a winding that returns in step after a whole number of units.

Writing rule. The repeat of a helix is the smallest whole number of units after which it returns in whole turns: the numerator of units per turn written as a reduced fraction. The α-helix has 3.6 residues per turn, which is 18 residues in 5 turns: repeat 18.

Prediction. Helix repeats are multiples of three more often than the one in three expected by chance.

Helix	Units per turn	Repeat	Multiple of 3
α-helix	3.6	18 in 5 turns	yes
3_{10} helix	3.0	3 in 1 turn	yes
π-helix	4.4	22 in 5 turns	no
Polyproline I	about 3.3	10 in 3 turns	no
Polyproline II	3	3 in 1 turn	yes
A-DNA	11	11 in 1 turn	no
B-DNA	10.5	21 in 2 turns	yes
Z-DNA	12	12 in 1 turn	yes

Five of eight repeats are multiples of three; chance predicts 2.7. The one-sided binomial probability is 0.088. The two forms that dominate living matter, the α-helix of proteins and B-DNA, both obey the law. The π-helix, which is rare in proteins, does not. A-DNA, the common form of double-stranded RNA, does not either.

The test was not blind: the chemistry book had already named 18 and 21. It is reported as suggestive, not as a finding.

> *Status: New rule W3 (helix repeat). Computed on measured values (fold_depth.py). Suggestive (p = 0.088), not significant; not blind.*

The fold in space. The chemistry book placed the four bonds of a carbon on the alternate corners of the cube, and the next atom on the mirror tetrahedron. A chain that steps in these directions lives on the diamond lattice. The program counted every closed loop without self-crossing that returns to its starting atom.

Loop length (steps)	3	4	5	6	7	8	10
Closed loops through one atom	0	0	0	24	0	48	480

No loop of three, four or five steps can close in the cube's directions. The smallest closed loop has six steps: a ring of two groups of three. Each atom lies on twelve such rings, counted once in each direction.

Measured: rings smaller than six atoms are strained. The ring strain of cyclopropane is about 27.5 kcal/mol, of cyclobutane 26.3, of cyclopentane 6.2, of cyclohexane 0.1: the six-ring is strain-free. Six-rings are the rings of diamond, of ice and of the sugars in their ring form. The computed smallest closure in space is the measured strain-free ring.

> *Status: Computed (space_depth.py). Reproduces the strain-free six-ring (Baeyer strain; Wikipedia, Ring strain).*

12. The membrane and the sheet

Closed strands also meet side by side. Two such meetings build much of a cell: the two leaflets of a membrane, and the strands of a folded sheet. The algebra of meeting decides both.

The leaflet. By the tissue law of chapter 14, a leaflet that closes as one strand is one word repeated. There are nine. The program confirmed that exactly nine closed strands of length nine exist, and that each is one word repeated.

The bilayer. Two leaflets meet face to face, position by position. A meeting closes only as (x, −x). For every leaflet the program counted the partners that meet it at every position.

Leaflet	Only partner	Same as the leaflet	Directions
(−,−,−)	(+,+,+)	no	none
(0,0,0)	(0,0,0)	yes	none
(−,0,+) and its rotations	(+,0,−) and its rotations	no	opposite
(+,+,+)	(−,−,−)	no	none

Every leaflet has exactly one partner. In eight of the nine cases the partner differs from the leaflet. Only the neutral leaflet faces itself. So a closed bilayer is asymmetric unless it is neutral: its inside differs from its outside.

Measured: the plasma membranes of mammalian cells are asymmetric. The inner leaflet holds about twice as many unsaturated phospholipids as the outer one; the outer leaflet is packed more tightly. The authors report that these asymmetries are conserved across eukaryotes (Lorent and colleagues, Nature Chemical Biology, 2020).

The sheet. The program took every closed mixed strand of depth 3, 6 and 9 and paired it side by side with every other one. It counted the pairs that meet at every position, and whether the two strands run the same way or opposite ways.

Pairing of mixed strands	Pairs that meet at every position
Parallel (same direction)	0
Antiparallel (opposite direction)	18

The law is strict: a mixed strand meets its partner only antiparallel. Here the seam law of chapter 4 and the meeting law work together. Opposite directions never join end to end, and they are the only way to meet side by side.

Measured: the two strands of DNA always run antiparallel. In protein β-sheets the antiparallel arrangement gives the strongest inter-strand stability; parallel sheets are harder to form and may be slightly less stable; strands with a parallel neighbour on one side and an antiparallel one on the other are rarer than chance (Wikipedia, Beta sheet, read 11 November 2026). The law holds strictly for DNA. For proteins it holds as a preference, not as a rule: parallel sheets exist.

> *Status: Computed (membrane_depth.py). Measured: membrane asymmetry (agrees), DNA antiparallel (agrees), β-sheets (partly: preference, not exclusion).*

13. The cell: copying and dividing

A cell copies its chain and divides. The algebra of meeting and of rings computes both steps exactly.

Pairing. A value x meets only −x: for every value the partner is unique. The mirror of every closed ring is closed and runs the opposite direction. So a closed strand and its mirror form a double whose two strands run in opposite directions.

Copying. Separate the double. Each strand takes its unique partner again. The result is two doubles that are identical, and each holds one old strand and one new one. That is semi-conservative copying, found by Meselson and Stahl in 1958 and implied by the pairing of Watson and Crick. Here it follows from one fact: the partner is unique.

Dividing. The program cut every closed ring of depth six at every one of its six places into two rings of depth three. Every cut of every ring gives two closed rings, and every half keeps the parent's direction. A closed ring of three, written twice, is a closed ring of six. So copy and divide close at every step: $3 \rightarrow 6 \rightarrow 3 + 3$.

> *Status: Computed (cell_depth.py). Reproduces semi-conservative copying (Meselson and Stahl 1958).*

14. The tissue

A tissue joins many units. The program wrote chains of n closed windows, one after another, and counted every chain in which every window of the whole strand is closed.

Units joined	Chains	Closing	Share
1	9	9	1
2	81	9	1 in 9
3	729	9	1 in 81
4	6,561	9	1 in 729
5	59,049	9	1 in 6,561
6	531,441	9	1 in 59,049

The law is exact and simple. However many units are joined, exactly nine chains close: those that repeat one closed word, in one phase. A chain that holds two different words never closes. So a tissue that closes as one strand is made of identical units, in step.

Read on the body, a tissue is many cells of one kind, kept in register. Where two kinds meet, the seam stays open. The author's earlier book found most deviations at such seams.

> *Status: Computed (tissue_depth.py). The reading for tissues is a hypothesis.*

15. The organ and the body

An organ is made of several tissues. Chapter 14 computed that a strand holding two different words never closes. An organ therefore cannot close as one strand. Its seams stay open.

The theory has one class that crosses open seams: the carriers, the unclosed class of chapter 16. So the algebra implies a statement about every organ: it is held together by carriers across its seams. In a body these are the blood, the nerves and the hormones. Every organ has a blood supply and a nerve supply.

The algebra also counts the seams. The program joined k different closed words in every order and counted the open windows.

Different kinds joined	Fewest open windows	Most open windows
2	1	2
3	2	4
4	3	6

With k kinds there are at least k − 1 open windows: exactly one per seam in the best order. So an organ of k tissue kinds needs at least k − 1 carriers to hold it, one across each seam. A badly ordered organ needs twice as many.

The same holds one depth up. A body is many organs. It too cannot close as one strand. It is a set of closed forms held together by carriers. Health, read this way, is carriers that arrive and are read. The leading causes of death fit this reading: ischaemic heart disease and stroke are failures of the blood as a carrier. Chapter 22 takes them in full.

Above the organ no further count was made. The rhythm and the person are treated in chapters 18 and 19 as coordinates, and the mind in chapter 20.

> *Status: Computed (no chain of different words closes). Reading (organs held by carriers; body as forms and carriers).*

15.1 Circulation, derived

Organs of different kinds leave open seams between them. A carrier must cross each seam. A carrier that is to last must itself close, so its path must return to where it started (section 16.1). The program counted what such a returning path costs.

Organs of different kinds	In a row: open seams	In a loop: open seams
2	1	2
3	2	3
4	3	4
5	4	5

A loop through k kinds of organ meets exactly k seams: one carrier crossing per organ. That is the minimum; no order of the organs does better.

The program then built loops of 6 and 9 living units and let the direction reverse at r places.

Direction reversals in the loop	Minimum open windows
0	0
2	4
4	8

Each reversal costs two open windows, at any length. A loop that carries without new openings runs one way only. So a lasting circulation is a closed loop, it visits every organ kind once per round, and it flows in one direction.

Measured anatomy: blood runs in closed loops, and valves in the heart and veins keep the flow one way. The law reproduces that form. It does not say why there are two loops (lungs and body), nor give pressure or flow. Those need the count of changes per period at this depth (section 18.4).

> *Status: Derived (organ_derive.py, O1 and O2). Reproduces in form: closed one-way circulation with valves. Open: the two loops, pressure and flow.*

15.2 The organ systems, one by one

The chemistry book went through every element. This section goes through every organ system. For each it names the derived law that governs it, what the law fixes, the failure the law names, and the cure rule that follows. The laws are derived in this book; their assignment to a system is a reading, and the last column says what remains open. This table is the summary. Part VII takes each system in full, disease by disease.

System	Governing law (derived)	Failure the law names	Cure rule	Open
Circulation	Closed one-way loop; k seams for k organ kinds (15.1)	Reversal or blockage: a seam left open	Restore the carrier across the seam	Pressure, flow, two loops
Respiration	Coupling keeps closure; heart and breath lock in whole numbers at rest (16.2, 18.1)	Loss of locking; breathing broken (apnea)	Restore rest and the rhythm, not add a new one	Breathing rate
Nervous system	An opening moves only via a closed state (16.3); a reader fits one strand (20.1)	Signals that cannot close behind them; unread errors	Read at the place; undo there	Speed, voltage
Endocrine (hormones)	Carriers must decay to deliver (16)	A carrier that does not end, or does not arrive	Restore the missing carrier at its seam	Which hormone at which seam
Immune system	The test: fit +1, misfit −1, unread 0 (17); repair unique below 1/3 wrong (19.0a)	Unread misfits remain; wrong closure is read as self	Make the misfit readable; outside reader for wrong closure	Rates and doses
Digestion	Unclosed forms are taken apart and their parts re-used (16, 17)	Parts that do not close again	Restore the closing step, not add parts	Energies of bonds
Skin and barriers	Bilayers are asymmetric; mixed strands meet only antiparallel (12)	Seams between kinds: where deviations start (14)	Return units to one word and phase	Thickness, turnover
Muscle and movement	What persists repeats (16.1); acting opens, rest repairs (19.0a)	Errors past one third: fixed or reversed state	Repair before the limit; rest	Force
Bone and connective tissue	Uniform (fixed) never joins mixed (living) (4)	Seam between fixed and living stays open: scar, deposit	Prefer living-with-living cures	Mineral amounts
Kidney and excretion	Only what ends can be passed on; open forms must leave (16)	Open forms that are kept	Restore the removing carrier	Filtration rates
Reproduction and growth	Unique partner; every depth-6 ring splits into two closed rings (13)	Copy errors carried into both daughters	Copy through the partner; proofread	Timing of division
Sleep and the day	Waking free only at a cycle end in the day's direction (19.0); repair before 1/3 (19.0a)	Body against the day; wrong closure	Restore direction once; repair at the place	Lengths of cycles

System	Governing law (derived)	Failure the law names	Cure rule	Open
Mind	Holds about 3/4 of its size as deviation; nearest slips are reversal and flattening (20.2)	Wrong closure read as healthy	An outside reader with the right form	Any number for experience

> *Status: Derived laws, cited by section. Reading: their assignment to each organ system.*

Part IV — How the body works, derived

Part III built the body from units that close. Part IV derives how those units work together in time: why a body is made of rhythms, how rhythms couple, how a signal moves, and how the body leaves sleep. Every law in this part is printed by a program that uses the rules alone (body_derive.py). Data come only after the law, and the order is stated each time.

16. Forms and carriers

Closure is all or nothing. So at every depth there are two classes. The closed class holds its form: molecules, cells, organs, bodies. The unclosed class decays. While it lasts it carries tension from one closed form to the next: light between atoms, signal molecules between cells, the nerve impulse and the hormone within a body, speech between people.

Only what ends can deliver. A closed form returns its tension to itself and can hand nothing over. That the carriers decay is what keeps a body readable: each message is erased after it is read.

> *Status: Rule of the theory (closed and unclosed classes). Its application to nerve impulse and hormone is a reading.*

16.1 What persists repeats

Take any strand of trits and ask that every window of three closes. The program tried every strand of length 4, 6, 9 and 12. The answer is the same at each length: exactly 9 strands close, and every one of them repeats with period 3.

The reason is short. If x + y + z and y + z + w both close, then w equals x. So a closed strand is fixed by its first three values and repeats them forever.

This is the first law of the living body in time. Whatever lasts, repeats. A form that persists is a rhythm; a form that does not repeat is open and decays. So a body that lasts must be built from rhythms: the cell cycle, the heartbeat, the breath, the sleep cycle, the day. Chapter 14 found the same 9 strands in space as the tissue; here they appear in time as the rhythm.

> *Status: Derived (body_derive.py, B1). Reading: that body rhythms are this law at work.*

16.2 Coupling keeps closure but cannot create it

Two rhythms that act on one another add their tensions, place by place. The program added every pair of closed strands of length 9: the sum is always closed. It then added each closed strand to 2,000 open strands: none of the 18,000 sums closed.

So coupling is safe for what is closed. Two healthy rhythms can lock together without breaking. Section 18.1 found exactly that between heart and breath. But coupling cannot repair. A broken rhythm coupled to a healthy one stays broken. Repair needs the one change at the place of the error (chapter 5).

For cure this is exact. An outside rhythm, such as light or a fixed meal time, can hold a body rhythm that is already closed. It cannot close one that is open.

> *Status: Derived (B2). Agrees with section 18.1 (coupling found at rest). Reading: light as a coupling, not a repair.*

16.3 How an opening moves: the impulse

A signal is an opening that travels. Can an opening move along a closed ring? The program put one error at place i in a closed ring of 9 and searched every path of single changes to an error at place i + 1.

Question	Answer (computed)
Can the opening jump one place in a single change?	No

Question	Answer (computed)
Shortest path	2 changes
Open windows along the path	3, then 0, then 3
Number of shortest paths	2

An opening never slides. It moves only by closing where it is and opening at the next place. In between the ring is fully closed. So a moving signal is all or nothing at each step, and it leaves its old place restored.

Measured biology: the nerve impulse is all-or-none, and the membrane behind it returns to rest before it can fire again. The law reproduces that form. It does not give the speed or the voltage. Those need the count of changes per period at the membrane (section 18.4).

> *Status: Derived (B4). Reproduces in form: the all-or-none impulse that leaves rest behind. Open: speed and voltage.*

16.4 Carriers at a seam: why hormones never stop

Between two organs of different kinds lies an open seam (15.1). Can a carrier placed in the seam close it? The program took all 72 ordered pairs of different closed words and tried every carrier strand of length 0 to 3 between them.

Carrier length	Seams closed completely (of 72)	Open windows left, mean
0 (no carrier)	0	1.50
1	6	1.08
2	6	1.08
3	0	1.25

A carrier of the right length lowers the open windows at a seam by about a quarter. It closes a seam fully only in 6 of 72 cases: where the two sides are the same living word at a different phase. Every other seam stays open whatever is put in it.

So the seams between organ kinds are permanent. The body cannot close them once and for all; it can only carry tension across them, again and again, with carriers that end after delivery (chapter 16). That is the form of hormones and other signals: produced all the time, broken down all the time, never finished. Their failure is a seam left without its carrier.

> *Status: Derived (immune_hormone_derive.py, H1). Reading: hormones and signals as the permanent carriers at open seams.*

17. The test

When one form reads another there are three outcomes, the three values of the register. It fits (+1): the form stays. It does not fit (−1): its tension is discharged and it is taken apart. It is not read (0): nothing happens.

The third outcome is the important one. A form that is never read is neither kept nor removed. It simply remains. Chapter 5 adds the exact part. An error opens three windows, and the place where they overlap is the place to read. A test that reads finds it. A test that does not read leaves it.

> *Status: Rule of the theory (the test). The link to chapter 5 is computed; its use for cells and bodies is a reading.*

17.1 The test counted: what the body's defence can see

The program read every one of the 19,683 strands of 9 places against one self form and sorted them by what the test can do with them.

Class	Strands	Share	What the test does
Self	1	0.01 %	fits (+1): kept
Damaged self (1 or 2 places wrong)	162	0.82 %	repaired by windows to self (19.0a)
Foreign, with at least one closed window	18,360	93.28 %	readable: misfit (−1), taken apart
Foreign, no closed window anywhere	1,152	5.85 %	nothing to grip: unread (0), stays
Wrong closure: closed but not self	8	0.04 %	windows find no error; only a reader that meets sees it

Three laws follow. Almost all that is foreign can be read and removed. About one in seventeen foreign strands has no closed window and cannot be gripped at all: it stays unread. And a few forms are closed but not self. A test by windows reads them as healthy. Only a reader that carries the self form and meets the strand place by place (20.1) finds them.

Measured biology shows the same three kinds of trouble: pathogens that are cleared, pathogens that hide from detection, and the body's own wrongly closed forms, such as misfolded proteins that the immune system does not attack. The match is a reading.

> *Status: Derived (immune_hormone_derive.py, I1). Reading: the match with clearance, hiding and wrong closure.*

18. The ladder as a coordinate

The theory fixes a length and a time from hydrogen alone: $S_0 = 1/(2R_H) = 45.59$ nm and $T_0 = S_0/c = 1.52066 \times 10^{-16}$ s. Any size or duration then has a position: the number of factors of three between it and the unit. Ring n has period $3^n \cdot T_0$.

The ladder orders. It does not select. In the companion book on the body, 192 of 388 measured body sizes lay within a quarter step of a ladder mark: 49.5 per cent, against 50 per cent by chance. In Rhythms Out of Tune, nine healthy body rhythms lay at a mean distance of 0.216 from the nearest ring, against 0.25 by chance ($p = 0.24$). Seven proven treatment frequencies lay at 0.285 ($p = 0.74$). In From Cell to Mind, the published classes of brain rhythm stepped by a factor of 2.73, not 3.

So no body part and no body rhythm is assigned to a ring in this book. Positions are given as coordinates only.

> *Status: Measured and tested in the author's earlier books. The ladder as a selector is not supported by those tests.*

18.1 A test on the living body: heart and breath

The rule of closure can be tested on the body itself. If two body rhythms close on each other, the heart should fit a whole number of beats into a breath more often than chance: n:1 locking.

Data. The open Fantasia recordings on PhysioNet: 40 healthy people, 20 young and 20 old, two hours at rest, with respiration and every heartbeat recorded. In 35 recordings the breathing signal could be read.

Tests fixed before the analysis. H1: windows of breathing show n:1 locking more often than surrogates in which the breathing is shifted 10 to 50 minutes against the heartbeats, which keeps both rhythms and breaks their coupling. H2: among locked windows, n = 3 or 6 is more frequent than in the surrogates.

Analysis fixed before the data. Windows of 30 breaths and a strict threshold ($\gamma \geq 0.8$). It found no locked window in real or in surrogate data. The test as preregistered is therefore null: it could not separate real from surrogate. Adjusted analysis. The method was then changed once, and the change is reported: windows of 8 breaths, with the strength of the best n:1 locking compared directly. The adjusted analysis is exploratory for this dataset. It was then fixed without change for section 18.2, where it served as a method fixed before the data.

Quantity	Real	Surrogate
Mean strength of the best n:1 locking (γ)	0.351	0.334
Windows above the surrogate's 95th percentile	8.1 % (681 of 8,377)	5.0 % (by construction)
Share of those windows locked at n = 3 or 6	72.1 %	72.5 %

In the adjusted analysis H1 holds: heart and breath lock in whole numbers more often than chance, about 60 per cent more often in the strongest windows (Mann–Whitney $p = 1.6 \times 10^{-12}$). The body closes these two rhythms on each other in short stretches. H2 fails: the preference for 3:1 is fully explained by the heart and breathing rates of these people; the surrogates show it equally.

Measured before this book: cardiorespiratory synchronisation is known in athletes, in sleep and at rest (Schäfer and colleagues, 1998; Bartsch and colleagues, 2007). The test here reproduces it from open data and adds that whole-number closure, not the number three, is what the body shows at rest.

> *Status: Measured data, computed test (body_lock.py). Preregistered analysis (30 breaths): null. Adjusted analysis (8 breaths, reported change): H1 passes; H2 fails. The adjusted method was fixed before the data of section 18.2.*

18.2 Heart and breath through the night

If closure is the rule, it should be strongest where the body acts least. The theory gives an order. Deep sleep is the most closed state. REM sleep is reading: the form is open to its own contents. Waking is acting on the world.

Data. The MIT-BIH Polysomnographic Database on PhysioNet: 18 night recordings of 16 men, with ECG beats, respiration and a sleep stage for every 30 seconds. These men were tested for sleep apnea, which breaks breathing; that lowers locking in every stage.

Tests fixed before the analysis. S1: locking is above surrogate in every stage group. S2: the excess is largest in deep sleep (stages 3 and 4), then light sleep (1 and 2), smallest in REM and wake. S3: locked windows prefer n = 3 or 6. The method is that of section 18.1 without change.

Stage	Windows	γ real	γ surrogate	Excess	p	Above 95th pct (real / sur)
Deep (3+4)	480	0.336	0.281	+0.054	1.3×10^{-8}	21.5 % / 8.4 %
Light (1+2)	3,911	0.263	0.252	+0.012	0.002	7.8 % / 4.6 %
REM	484	0.275	0.275	−0.001	0.40	6.4 % / 6.6 %
Wake	2,109	0.254	0.253	+0.001	0.65	5.5 % / 4.7 %

S2 holds. In deep sleep heart and breath lock in whole numbers two and a half times as often as chance. In light sleep the effect is smaller. In REM sleep and in waking it is gone. S1 therefore holds only for the two NREM stages. S3 fails: in deep sleep only 10.7 per cent of locked windows were at 3 or 6, against 18.4 per cent in the surrogates.

Measured before this book: Bartsch and colleagues (2012) found more cardiorespiratory phase synchronisation in deep sleep and less in REM, in healthy sleepers. The test here reproduces that

order in a different group, from open data. The new part is the reading. Closure is the property of rest; reading (REM) and acting (wake) open it.

> *Status: Measured data, computed test (sleep_lock.py). S2 passes and reproduces Bartsch 2012. S1 passes for deep and light sleep only. S3 fails.*

18.3 Energy is a count per time

Energy is a concept from the age of the steam engine. It treats energy as a substance that is set free by destroying matter: burn this, split that. The author described that paradigm and its successor, the oscillatory paradigm, in 'De Energietransitie die Geen Transitie Is' (constable.blog, 24 May 2026). This book does not need the old concept. In the theory the quantity that matters is a count: how many places a process closes or restores, how many windows stay open, and on which ring of the ladder it runs. What physics calls an energy is that count per unit of time, multiplied by Planck's constant. The section below shows this for the body, and it is the reason why the rest of the book speaks of changes, open windows and periods, not of energy.

The ladder fixes its unit from hydrogen. The same unit gives an energy: one passage per time unit T_0 carries $E_0 = h/T_0 = 2hcR_H = 27.197$ eV. That is twice the ionisation energy of hydrogen, 13.598 eV. The chemistry book derives the energy ratios of the atom: $1/n^2$ over the shells and Z^2 over the nucleus (its chapter 11). With E_0 these ratios become absolute energies. So the theory does have energies. Ring n of the ladder carries $E_0/3^n$.

The program placed seven measured energies of the body on this ladder.

Energy (measured)	eV	Ring position	Distance to nearest ring
Hydrogen ionisation (½ E_0, derived)	13.598	0.63	0.37
Carbon–carbon bond	3.6	1.84	0.16
Photon seen by the eye, 550 nm	2.25	2.27	0.27
ATP hydrolysis in the cell, about 50 kJ/mol	0.52	3.60	0.40
Hydrogen bond, about 20 kJ/mol	0.21	4.44	0.44
One charge across the nerve membrane, 70 mV	0.070	5.43	0.43
Thermal energy kT at 37 °C	0.027	6.30	0.30

The body's energies run from ring 2 (light) to ring 6 (heat). Their mean distance to the nearest ring is 0.34, more than the 0.25 of chance. As with sizes and rhythms (section 18), the ladder orders the body's energies but does not select them.

Read as counts per time, these energies are rings on the ladder: the body works between ring 2 and ring 6 above the unit T_0. The ladder orders them; it does not select them. What is missing is therefore not energy. It is a count: how many places a process must close or restore, and on which ring it runs.

> *Status: Derived (E_0 from the ladder's unit; energy_ladder.py). Measured (the body's energies). Computed: positions; no selection.*

18.4 How many changes a body process needs: two attempts

Section 18.3 left one gap: a law that says which energy a body process takes. This section tries to fill it.

Attempt 1: a ladder anchored at heat (new rule NR-E). Four energies were seen first: heat kT at 37 °C (0.027 eV), the resting membrane (0.070), the hydrogen bond (0.21) and ATP (0.52). Each step is close to a factor three. The rule was then fixed: the body's energies sit at $3^k \cdot kT$. Heat is the unclosed carrier at body depth, so it is the body's ring 0. Seven other energies were then

computed blind. Rule NR-E was fixed on 12 November 2026, before the seven blind energies were computed. The first edition carried the date 11 November, the day its main tests were fixed; NR-E was added the next day.

Energy (blind)	eV	$\log_3$(E/kT)	Distance
Kinesin step, 6 pN × 8.2 nm	0.307	2.22	0.22
Mitochondrial proton-motive force, per proton	0.200	1.83	0.17
NADH to oxygen, per electron	1.14	3.42	0.42
Rhodopsin photon, 500 nm	2.48	4.12	0.12
Action potential amplitude	0.100	1.20	0.20
Na^+ entering at rest	0.130	1.44	0.44
Creatine phosphate hydrolysis	0.446	2.56	0.44

Mean distance 0.287 against 0.25 by chance (p = 0.77). NR-E fails. The four energies that suggested it fit by coincidence. Covalent bonds, checked apart, do not fit either (0.317).

Attempt 2: the price of one trit. Section 19.0a derived that self-repair works only while less than one third of a form is wrong. If heat opens a place with the Boltzmann weight e^(−E/kT), that place stays repairable only when e^(−E/kT) < 1/3, that is E > kT ln 3. At 37 °C that is 0.0294 eV. It is also the least energy needed to choose one value among three. So kT ln 3 is the price of one trit in a living body, and no working energy of a body can lie below it.

Every energy in the two tables lies above that floor. Measured in this price, the membrane is worth 2.4 trits, a hydrogen bond 7.0, the proton-motive force 6.8, a kinesin step 10.5, creatine phosphate 15.2 and ATP 17.6. ATP is close to 18 trits. Restoring the direction of a living form of 27 places costs 18 changes (section 41.1). That coincidence is noted, not claimed: it was seen after the count.

The result is a floor, not a value. The rules, with the Boltzmann weight added, fix the least that a living place can cost: one trit, kT ln 3, below which heat opens more than a third of a form. They do not yet fix how many changes a given process needs. That count is the next calculation: for each process, the number of places it must close or restore, and the ring on which it runs. It needs no energy and no new constant.

> *Status: NR-E: new rule, failed blind (energy_law.py). Derived with one imported law (Boltzmann): the floor kT ln 3 per trit. Fitted, not claimed: ATP ≈ 18 trits. Open: the trit count per process.*

18.5 What body processes cost, counted

Section 18.3 replaced energy by a count. This section makes the count. The rule was fixed before any comparison: the cost of a process is the number of single-place changes in the smallest form that carries it, from the closed state before to the closed state after, plus the changes needed to undo the openings that arise on the way. Staying closed costs nothing.

Process	Form that carries it	Changes (computed)
A rhythm continuing one step (heartbeat, breath)	closed living strand (16.1)	0
Cell division	closed ring of 6 into two closed rings of 3 (13)	0 changes, 2 cuts
Copying a strand of n places	unique partner per place (13)	n new places, no choice
Impulse, one step	one opening on a closed ring (16.3)	2
Repair of one opening	one error on a closed ring (5)	1
Turning a form to the other direction	living ring of 27 (23.1)	18

The law is plain. Living in a closed rhythm is free; so is dividing a closed form. What costs is opening and repair. This is the oscillatory paradigm of section 18.3, now derived for the body: a body is not a machine that burns fuel to run its rhythms; its rhythms run by closing, and only what opens must be paid for. A body at rest should therefore spend its turnover on repairing what opens, not on keeping its rhythms going.

Measured physiology fits this reading. At rest most of the cell's turnover goes to pumps that restore ion gradients after they leak, about a fifth to a quarter of the whole body's turnover and more in the brain. The heartbeat and breath themselves are cheap compared with that repair. The match is a reading. Which ring each process runs on, and so its rate, is still open: section 19.0b bounds the ratios between rhythms but does not select them.

> *Status: Derived (process_counts.py, with B4, 13 and 23.1). Reading: the match with the cost of ion pumping. Open: the ring, and so the rate, of each process.*

19. The day

One position stands out by construction. The solar day of 24 hours sits at position 43.50. That is exactly between rings 43 (13.87 h) and 44 (41.60 h); their geometric middle is 24.02 h. The day is the rhythm farthest from any ring.

The rest–activity cycle of about 90 minutes lies near ring 41 (92.4 min). A day holds 15.58 of those cycles, which is 3 to the power 2.499. The day does not divide into whole cycles. The body cannot close the day on its own cycle; it must place its sleep in the day.

The day is imposed from outside by the turning of the Earth. In the theory's terms it is an open remainder that every living body must temper. Circadian disruption carries the broadest disease link of any rhythm imbalance: night shift work involving circadian disruption is classified as probably carcinogenic (IARC Group 2A).

> *Status: Computed (positions, depressie_ladder.py). Measured (IARC). Reading (the day as the open remainder the body must temper).*

19.0 The seam to waking

Sleep is a living, mixed rhythm. Waking joins it to the day, which the body does not make. The program cut a living strand after every possible step and joined it to a fixed closed strand: a day of the same direction, a day of the opposite direction, or a uniform day. It counted the open windows at the seam.

The day joined to	Cut at the end of a whole cycle	Cut one or two steps into a cycle
Mixed, same direction	0 open windows	2 open windows
Mixed, opposite direction	2	1
Uniform	2	1

Two laws follow. Waking is free only at the end of a whole cycle, and only when the body runs in the day's direction. A body that runs against the day, or meets a fixed day, has no free moment to wake: every waking leaves at least one open window.

The first law was tested before it was derived. Section 19.1 found that the night ends after a closed cycle more often than chance. The second law is new. It predicts that in a body out of step with the day, waking does not cluster at cycle ends, and each waking leaves something open. That is a candidate for the unrefreshing early waking of depression (chapter 41). It is test T13.

> *Status: Derived (B3). The first law agrees with test Z2 (section 19.1), which came first. The second law is a prediction (T13).*

19.0a The limit of self-repair, and why rest is needed

A body tests itself by windows only. It has no copy of how it should be. Can it still find its way back? The program put errors at random places on a living ring of 27 places and let the windows guide the repair: the fewest changes that close every window. Only 9 closed rings exist, so repair always ends in one of them.

Wrong places (of 27)	Back to the original	Closes in the opposite direction	Closes uniform	Tie or other
3	100 %	0	0	0
6	100 %	0	0	0
9	100 %	0	0	0
12	92.8 %	1.0 %	1.0 %	5.2 %
15	29.3 %	20.9 %	19.9 %	29.9 %
18	0 %	31.8 %	31.4 %	36.8 %

Two laws follow. Up to one third of the places wrong, self-repair always finds the original. With a few windows' tests and no template, the body is exact. Beyond that limit it starts to close onto a wrong form: a ring of the opposite direction, or a uniform ring. Both are closed. The body's own test then finds no error at all.

So repair cannot wait. Errors arise while the body acts (section 21). They must be read and undone before a third of a form is wrong. That sets a limit on how long acting can go on without a phase of repair. Sleep is the measured phase in which the body acts least and repairs most. The law gives the need for it, not its length; that needs the rate of errors, which the theory does not give.

> *Status: Derived (sleep_derive.py, Q1–Q3). Reading: sleep as the repair phase that the limit requires.*

19.0b How far apart a rhythm and its repair may lie

Section 19.0a gave the limit of self-repair. It also fixes how long a repair phase may wait. Suppose a fast rhythm opens one place per period, at random, and a slower rhythm repairs every R periods. The program found the largest R at which a form of N places still returns to itself in 95 per cent of repair phases.

Form size N	Largest repair interval R (fast periods)	R / N
9	2	0.22
27	14	0.52
81	70	0.86

This is the first law that limits periods. The ratio between a repair rhythm and the rhythm whose openings it repairs cannot exceed a bound set by the size of the form it keeps. A small form needs repair almost every period. A large form can wait much longer, more than in proportion to its size.

Read the other way, a measured ratio of two body rhythms gives the least size of the form the slower one keeps. A breath holds about four heartbeats: a form between 9 and 27 places. The night's sleep cycle holds about 1,350 breaths: a form far larger than 81 places. The day holds about 16 sleep cycles: a form of roughly 27 places. These sizes are readings. The law itself is derived, and it is the first rule in this book that says which periods can follow which.

> *Status: Derived (period_derive.py). Reading: the form sizes implied by measured rhythm ratios. Open: the exact bound for large N.*

19.1 Does the night end where a cycle closes?

A night is a chain of sleep cycles. Each cycle ends with a REM period. In the theory a cycle closes at that end. Leaving sleep is a seam, and chapter 4 says a seam costs least where a form has closed. So the body should prefer to wake at the end of a cycle.

Data. Sleep-EDF Expanded on PhysioNet: 153 nights of 78 healthy people aged 25 to 101, scored every 30 seconds.

Tests fixed before the analysis. Z1: brief awakenings inside the night come directly from REM more often than REM's share of sleep. Z2: the final awakening falls within 30 minutes after the end of a REM period more often than a random time in the last three hours of sleep. Z3: the length of the night, divided by the person's own cycle length, lies closer to a whole number than chance.

Test	Measured	Chance	p	Outcome
Z1 awakenings from REM	452 of 3,388 = 13.3 %	19.9 % (REM share)	1.0	Miss
Z2 final awakening ≤ 30 min after REM end	57 of 153 = 37.3 %	26.3 %	0.002	Hit
Z3 distance to a whole number of cycles	0.239 (143 nights)	0.25	0.18	Miss

The night does end where a cycle has closed, more often than chance. But the brief awakenings inside the night do not. They come mostly from light sleep. And the night as a whole is not a whole number of cycles. Closure decides how the night ends, not how it is built.

> *Status: Measured data, computed test (cycle_close.py). Z2 passes; Z1 and Z3 fail.*

Part V — Mind

20. What the texts say and what was tested

The theory's texts describe four rungs: closure, life, representation and consciousness. The mind is read as the third rung built on the second. Its parts are older than the neuron. The neuron adds no new part; it adds speed and reach to an edge every cell has. At every scale the carriers are fast and the forms slow.

The author's book From Cell to Mind set this description beside measured biology in two strictly separated layers. Three tests were fixed from the texts before any data were gathered. All three failed in their strict form:

- The nerve cell does not divide: failed. Mouse cortical neurons without the Rb brake divide in culture.
- The rhythm step is three: failed. The ten published classes of brain rhythm step by 2.73.
- The living form is not synchronous: failed. 69 per cent of awake measures lay below the threshold where 80 per cent was required. Across four books the theory has now been set against biological data twelve times with the outcome fixed first. One test passed: the nesting depth in The Weaving of Life. Six failed outright. One failed on its own rule. Four could not be completed on the data at hand.

That is the state of the mind in this theory. The texts give the form of a description. Where they gave a number, the number failed. This book adds no new claim about the mind. It adds the depths where the rules do compute at the level of the body's own information: the word of three in Part II and the chain, fold, cell, tissue and organ in Part III. Section 20.1 computes what the rules say about reading. None of it gives a number for the mind.

> *Status: Text and measured (From Cell to Mind, B13–B14).*

20.1 What the rules compute about reading

The theory places mind in the act of reading: one form tests another. That act can be computed. The program took every closed strand of depth nine and every single error, and read the damaged strand in two ways.

Way of reading	What one error shows
By windows of three	exactly 3 open windows
By meeting a mirror reader, position by position	exactly 1 misfit, at the place of the error
Strands that fit one reader everywhere	exactly 1 of the 9 closed strands

Two exact laws follow. A reader that meets is specific: it fits one strand and no other. And it is precise: it finds an error at the one place where it sits, while a window shows only that something nearby is open.

A third count concerns images. A closed mixed ring of depth 3k maps onto the ring of depth 3 in exactly one way that keeps every value. The ring of depth 3 fits into the ring of depth 3k in exactly k places. A small reader recognises a large form once as a whole, and counts it k times as parts.

These are laws of reading, not a theory of mind. They say what any reader built from closed strands can and cannot do: it is specific, it locates, and it needs carriers to pass on what it read, because a closed form cannot deliver (chapter 16). They do not say what it is like to read, and they give no number for a mind. That number is still missing.

> *Status: Computed (mind_depth.py). Reading: that minds read this way. Open: any number for mind.*

20.2 What a mind can hold, and where it slips

Section 19.0a found that a living form returns to itself as long as less than one third of it is wrong. Inside that limit it can carry deviations and still be itself. The program counted how many.

Form of n places	States that still return to the form	Information held
9	163	4.6 trits
27	7.0×10^{8}	18.5 trits
81	9.8×10^{28}	60.8 trits

A large form can hold about three quarters of its own size in deviations without losing itself. That is the room for memory and experience inside a stable identity. It grows with the size of the form.

The program then measured how far each closed form lies from a given living form of 27 places.

Target form	Changes needed (of 27)
The same form	0
Opposite direction (3 forms)	18
Uniform (3 forms)	18
Same direction, other phase (2 forms)	27

The nearest other states are not shifted copies of the form. They are its reversal and its flattening. A living form that is pushed too far slips first into running backwards or into standing still. That is the same pair of wrong closures found in section 19.0a. In the reading of chapter 41 these are the two faces of depression: the rhythm against the day, and the flat, fixed state.

> *Status: Derived (mind_derive.py, M1 and M2). Reading: memory as held deviation; reversal and flattening as the nearest failures of a mind.*

Part VI — Why it fails: eight forms

21. Ways to fail, depth by depth

Chapters 4 and 5 give exact laws about seams and errors. Each becomes a form of failure. The laws are computed. Their naming in the body is a reading.

Failure	Exact law (computed)	Reading in a body
1. The seam	A uniform stretch never joins a mixed stretch (0 of 36 seams close).	Where something fixed meets something living, tension stays: scar, deposit, plaque, a rigid habit in a changing life.
2. The direction	Mixed stretches of opposite direction never join (0 of 18).	Two living rhythms that run against each other cannot couple: a body clock against the day, a meal rhythm against the sleep rhythm.
3. The unread form	An error opens three windows and stays until it is read and undone (chapter 5).	A misfit that no test reads remains: neither kept nor removed. Chronic disease as unread error.
4. Drift	A living ring grows only by groups of three and keeps one direction (chapter 2).	A rhythm that leaves its own phase and does not land on another. Read in Rhythms Out of Tune; not supported at group level.

The four failures share one feature. Each is an open window that persists. Health is not the absence of open windows. Open windows arise every day. Health is a test that reads them and closes them fast enough.

That last sentence can be counted. The program placed one error per round on a living ring of 81 places for 200 rounds, under three regimes.

Repair	Open windows after 200 rounds (of 81)
None	64
One change per round, at a random place	52
One change per round, at the place of the error	0

Repair at the same rate but at the wrong place barely helps. Repair at the right place keeps the body fully closed. Illness, in this count, is not too many errors. It is errors that are not read where they are.

> *Status: Derived (body_derive.py, B5). Reading: illness as unread error.*

Part III adds one exact law per depth. Each law names a way to fail at that depth. The third column gives a measured process that matches; the match is a reading.

Depth	Exact law and the failure it names	Measured process that matches (reading)
Word	A word readable in two phases loses the frame (chapter 6).	Frameshift mutations destroy the protein; transcripts with a premature stop are removed (nonsense-mediated decay).
Chain	One error opens three windows and stays until undone (chapter 5).	Point mutations; mismatches left after copying.
Fold	A winding closes only in whole groups of three units (chapter 11).	Misfolding; rare helix forms such as the π-helix.
Cell	A copy is exact only through the unique partner (chapter 13).	Copying errors carried into both daughters.

Depth	Exact law and the failure it names	Measured process that matches (reading)
Tissue	Two different words in one chain never close (chapter 14).	Seams between tissue kinds, where many deviations start.
Organ and body	No organ closes as one strand; it depends on carriers (chapter 15).	Failure of a carrier: ischaemia, stroke, nerve damage, hormone failure.
Rhythm	The day is the open remainder (chapter 19).	Circadian disruption; depression (chapters 40 and 41).

Status: Computed (the laws). Reading (their naming in the body).

21.1 Eight forms of failure

The four failures above come from the seam and the error. Parts III and IV add four more. The carrier law of chapter 15 adds failure of the carrier. The test of chapter 17 can fail by reading too much. Section 19.0a adds the wrong closure: a form that closes on the wrong shape and is read as healthy. Chapter 6 and chapter 13 add the error of frame and copy. Together they give eight forms. Each rests on an exact law. Every disease in Parts VII and VIII is named by one or more of them.

Code	Form	Exact law it rests on	What it looks like in a body (reading)
S	Seam	Uniform never joins mixed: 0 of 36 seams close (ch. 4).	Something fixed lodged in something living: plaque, stone, crystal, scar, fibrosis, deposit.
D	Direction	Opposite directions never join: 0 of 18 (ch. 4); waking free only in the day's direction (19.0).	Rhythms that run against each other or against the day: shift work, mistimed sleep, lost cycles, arrhythmia.
U	Unread	An error opens three windows and stays until read (ch. 5); 5.9 % of strands go unread (17.1).	A misfit that the test does not see: cancer, latent and chronic infection, a deposit no one clears.
O	Over-read	The test gives +1, −1 or 0 (ch. 17); a fit read as −1 is attacked.	The body's test attacks its own fit forms or harmless ones: autoimmunity, allergy, asthma.
C	Carrier	No organ closes as one strand; most seams need carriers for ever: 66 of 72 (15, 16.4).	A carrier that does not arrive or is not read: ischaemia, hormone loss, conduction block, anaemia, failed filtration.
W	Wrong closure	Past one third of a form wrong, self-repair closes onto the reverse or the uniform form (19.0a).	A stable, closed, wrong state that the body reads as healthy: depression, addiction, chronic pain, seizure.
F	Frame and copy	A word must be read in one phase (ch. 6); a copy is exact only through its partner (ch. 13).	Inherited and acquired mutation, frameshift, repeat expansion, wrong chromosome number.
R	Drift	Repair must come within a bound set by form size (19.0b); windows alone restore only below one third (19.0a).	Repair that falls behind: ageing, frailty, slow loss of rhythm and amplitude.

The forms combine. A heart attack is S then C: a plaque breaks and the carrier stops. Type 1 diabetes is O then C: the test removes the cells that make the carrier. Dementia is U, S and R together. The code is a reading. It does not replace a diagnosis. It says which law a disease breaks, and so which kind of repair can work.

Status: Derived (each law, cited by chapter). Reading (the naming of each form in a body).

21.2 The test fails in two directions

Chapter 17 gave the test three answers. A form that fits the reader is +1. A misfit is −1. A form the reader cannot read is 0. A healthy test gives each form its right answer. It can go wrong in two ways that mirror each other.

- **Too little.** A misfit is read as 0 or as +1. It stays. This is form U. Cancer works this way: a cell that carries errors also carries the signal that reads 'self'. Chronic infection works this way: the microbe hides inside the reader or changes its face.
- **Too much.** A fit form, or a harmless one, is read as −1. The test attacks it. This is form O. Autoimmunity and allergy work this way.

One law follows directly. A cure that raises reading helps the first failure and can cause the second. A cure that lowers reading helps the second and can cause the first. Measured medicine shows both sides of this law. Checkpoint medicines release the brake on reading. They cure some cancers. Their main harm is autoimmune inflammation of healthy organs. Drugs that dampen reading treat autoimmune disease. Their main harm is infection and, over years, some cancers. The law is exact in the algebra and the match is a reading. It gives a rule for cure: read the direction of the failure first, then move the test only in the other direction (rule 1 of chapter 43).

> *Status: Derived (the three answers of the test, chapter 17). Reading: the mirror between cancer and infection on one side and autoimmunity and allergy on the other; the side effects of checkpoint medicines and immune suppressants.*

21.3 The frame law in the clinic

Chapter 6 derived that a word of three must be read in one phase only. A deletion of one or two letters shifts every later word. A deletion of three letters, or of any multiple of three, removes whole words and keeps the frame. The rule is exact. It predicts that the same gene, hit at the same place, gives two kinds of disease: a severe one when the frame is lost, and a milder one when it is kept.

Measured: Duchenne and Becker muscular dystrophy are two diseases of one gene, dystrophin. Monaco and colleagues (1988) found that deletions which keep the frame give the milder Becker form and deletions which shift it give the severe Duchenne form. In a register of more than four thousand patients the rule held for about nine in ten (Aartsma-Rus and colleagues, 2006). The frame law reproduces this. It also gives the shape of the cure: restore the frame. Exon skipping does this. It removes a further piece so that the remaining loss is a multiple of three. Drugs of this kind have conditional approval. Their measured benefit is still small (chapter 36).

Chapter 2 adds a second law: a living ring grows only by whole groups of three. Measured: a family of inherited diseases is caused by words of three that repeat too often. Huntington's disease, fragile X syndrome, myotonic dystrophy and Friedreich's ataxia are the best known. The repeats grow from parent to child by whole words. In Huntington's disease the repeat sits inside the gene and keeps the frame. It writes a long uniform run of one amino acid. Chapter 4 says that a uniform stretch never joins a mixed one. The long uniform run is read as a seam, and the protein clumps. That last step is a reading.

> *Status: Derived (frame law, chapter 6; growth by threes, chapter 2). Reproduces: the reading-frame rule of Duchenne and Becker dystrophy (Monaco 1988; about 90 % of cases). Reading: repeat expansion as a uniform seam.*

21.4 Where in a life the forms strike

The forms are not spread evenly over a life. The laws say where each should cluster. Copying is fastest in the child, and the test is still learning. So forms F and U should dominate early: inherited disease and the cancers of growth. The test learns by meeting. A child who meets too little has a test that has not learned what is harmless. So form O should rise where early meeting falls. In midlife the rhythms of work, food and light meet the day. So form D should rise with shift work and late nights. Seams accumulate with use. So form S should rise with age. Repair falls behind its bound with time. So form R rises last.

Measured patterns match this order. Childhood cancers are cancers of growing tissue, unlike the adult cancers of worn epithelia. Allergy and asthma are rarer in children raised on traditional farms. Night shift work is classed as probably carcinogenic by IARC, and it raises the risk of diabetes. Atherosclerosis, stones and arthritis rise with age. Frailty comes last. Chapters 37 and 38 take this in full.

> *Status: Reading. The order of forms over a life is a hypothesis built from the laws; the matching facts are measured and cited in chapters 37 to 39.*

Part VII — The atlas of illness, system by system

This part goes through the body one system at a time, as the chemistry book went through the elements. Each chapter opens with how the system works, from the laws of Parts III and IV. It then names how the system fails, using the eight forms of chapter 21. Each major disease follows in the same form: what it is, where it fails, how it is prevented, and how it is treated.

The facts in every entry are Measured and cited. The naming of the form is a Reading. The cure ladder in each entry uses five layers (chapter 44). **Mesh**: remove, rebuild or replace tissue. **Chain**: close one molecular step with a drug or a gene. **Reading**: correct the body's test. **Phase**: restore rhythm and step. **Surround**: change what everyone is exposed to. The standing of each treatment is **established**, **in trials**, or a **direction** the map points to.

22. Circulation: heart and vessels

How it works. Section 15.1 derived the form of circulation. Organs of different kinds leave open seams. A carrier must cross each seam. A carrier that lasts must return, so its path is a loop. A loop through k organ kinds meets exactly k seams. Each reversal of direction costs two open windows. So a lasting circulation is a closed loop that runs one way. The heart is the place where the loop is driven. Its beat is a rhythm that closes on itself (16.1) and couples to breath in whole numbers at rest (18.1).

How it fails. The laws name three failures. A seam can fill with something fixed: form S. That is plaque in the wall of an artery. The carrier can stop at a seam: form C. That is the blocked artery of a heart attack or a stroke. The rhythm can lose its closure: form D. That is atrial fibrillation. Circulation fails mostly by S followed by C. The order of cure follows: open the seam at once, then remove what fills it, then keep the rhythm.

22.1 Coronary heart disease and heart attack

What it is. Fatty plaque narrows the arteries of the heart. When a plaque breaks, a clot closes the artery and heart muscle dies. Ischaemic heart disease is the leading cause of death in the world (WHO Global Health Estimates). Cardiovascular disease as a whole causes about 18 million deaths a year (WHO).

Where it fails (form S, C). Lipid lodges in the living wall and stays: a uniform form at a mixed seam, which never joins (S). When it breaks, the carrier stops (C). Inflammation in the plaque is the test reading a misfit it cannot remove.

Prevention. In the INTERHEART study nine modifiable factors explained about 90 % of the risk of a first heart attack (Yusuf, 2004). Each mmol/L fall in LDL cholesterol lowers major vascular events by about a fifth (CTT Collaboration, 2010). A Mediterranean diet with olive oil or nuts lowered major events by about 30 % (PREDIMED, Estruch, 2018). Smoke-free laws lower hospital admissions for heart attack (Frazer, Cochrane, 2016).

Layer	Treatment	Standing and evidence
Mesh	Primary angioplasty to reopen the artery; bypass surgery	Established. Primary angioplasty beats clot-dissolving drugs on death and re-infarction (Keeley, 2003).
Chain	Statins, antiplatelet drugs, beta-blockers, ACE inhibitors	Established. Statin benefit scales with LDL lowered (CTT, 2010).
Chain	Semaglutide in people with obesity and heart disease, without diabetes	Established. 20 % fewer major events (SELECT, Lincoff, 2023).
Reading	Low-dose colchicine to calm inflammation in the plaque	Established. 31 % fewer events in stable disease (LoDoCo2, Nidorf, 2020).
Phase	Exercise-based cardiac rehabilitation	Established. Fewer heart attacks and hospital stays (Dibben, Cochrane, 2021).
Surround	Tobacco control, salt and trans-fat policy	Established.

22.2 High blood pressure

What it is. Pressure in the arteries stays too high. About 1.4 billion adults have it, and about one in five has it under control (WHO Global report on hypertension, 2025). It is the largest single risk factor for death in the world.

Where it fails (form S, C). The vessel wall stiffens: a fixed form at a living seam (S). The carrier must push harder to cross it (C). Raised pressure then damages new seams in kidney, brain and eye.

Prevention. Less salt, less weight, more movement and less alcohol each lower pressure. Replacing salt with a potassium-rich substitute lowered stroke by 14 % in 21,000 villagers (SSaSS, Neal, 2021).

Layer	Treatment	Standing and evidence
Chain	Blood-pressure drugs; a target of 120 mmHg in people at high risk	Established. Intensive control lowered major events by 25 % (SPRINT, 2015).
Phase	Regular exercise, including isometric training	Established. Exercise lowers systolic pressure by several mmHg (Edwards, 2023).
Phase	Taking pills at bedtime instead of the morning	Tested and failed: no difference in outcomes (TIME, Mackenzie, 2022). The direction rule of chapter 43 does not hold for this case.
Surround	Population salt reduction	Established.

22.3 Heart failure

What it is. The heart cannot pump enough blood for the body's needs. About 64 million people live with it (GBD 2017). Half die within five years of diagnosis without modern treatment.

Where it fails (form C, R). The driver of the loop fails as a carrier (C). The body answers with hormones that hold salt and raise pressure. Those carriers do not end, as section 16.4 predicts for open seams, and they worsen the load. Repair falls behind (R).

Prevention. Control of blood pressure, diabetes and coronary disease prevents most heart failure.

Layer	Treatment	Standing and evidence
Chain	Four drug classes together: ARNI, beta-blocker, MRA, SGLT2 inhibitor	Established. SGLT2 inhibitors alone cut worsening and death by 26 % (DAPA-HF, McMurray, 2019).
Mesh	Implanted defibrillator, resynchronisation device, transplant	Established for selected patients.
Phase	Exercise training	Established. Better quality of life (HF-ACTION, 2009).

22.4 Atrial fibrillation

What it is. The upper chambers of the heart lose their beat and quiver. About 60 million people have it (GBD 2019). It raises the risk of stroke about five times.

Where it fails (form D). The atria lose closure. Section 16.3 derived that an opening moves only through a closed state. In fibrillation many openings circle without closing behind them. Clots form where blood stands still (C).

Prevention. Weight loss and stopping alcohol lower recurrence. In one trial, abstinence from alcohol lowered recurrence from 73 % to 53 % (Voskoboinik, 2020).

Layer	Treatment	Standing and evidence
Chain	Anticoagulation	Established. Warfarin lowers stroke by about 64 % (Hart, 2007).
Mesh	Catheter ablation; early rhythm control	Established. Early rhythm control lowered cardiovascular outcomes (EAST-AFNET 4, Kirchhof, 2020).
Phase	Weight loss and treatment of sleep apnoea	Established as part of care.

22.5 Stroke

What it is. A brain artery is blocked or bursts. About 12 million strokes occur each year and about 7 million people die of stroke (GBD 2021, published 2024). It is the second cause of death and a leading cause of disability.

Where it fails (form C, S). The carrier stops at the seam to the brain (C). Most strokes come from plaque or from a clot formed in a fibrillating heart (S, D).

Prevention. Ten modifiable factors explain about 90 % of stroke risk; blood pressure is the largest (INTERSTROKE, O'Donnell, 2016).

Layer	Treatment	Standing and evidence
Mesh	Removal of the clot by catheter (thrombectomy)	Established. One of every 2.6 patients treated has less disability (HERMES, Goyal, 2016).
Chain	Clot-dissolving drug within 4.5 hours	Established.
Mesh	Care in a stroke unit	Established. Fewer deaths and less dependency (Cochrane).
Phase	Rehabilitation that repeats the lost movement	Established.

> *Status: Derived (the laws of 15.1, 16.1, 16.3, 16.4). Measured (burden, prevention and treatment; sources in the references). Reading (the failure forms). One test of the direction rule failed: bedtime dosing of blood-pressure drugs.*

23. Blood: the carrier itself

How it works. Blood is the main carrier of the body. Chapter 15 derived that organs need carriers across their seams. Section 16.4 derived that a carrier must decay to deliver: it must give up what it carries. Red cells carry oxygen. Clotting proteins close a breach. White cells carry the test. Each part of the blood is made, used and removed in a cycle.

How it fails. Blood fails when the carrier is missing (C) or wrongly written (F). Anaemia is a missing carrier. Sickle cell disease and thalassaemia are errors in the word that writes the carrier. Haemophilia is a missing step in closing a breach. Blood cancers are taken in chapter 30.

23.1 Anaemia

What it is. Too little haemoglobin to carry oxygen. About 1.9 billion people had anaemia in 2021, one in four (GBD 2021, Lancet Haematology 2023). Iron deficiency is the main cause.

Where it fails (form C). The carrier is too scarce (C). Its causes lie in other forms: blood loss, worms, malaria (U), poor diet (surround).

Prevention. Iron fortification of food, treatment of worms and malaria, and later clamping of the cord at birth.

Layer	Treatment	Standing and evidence
Chain	Iron by mouth or by vein	Established.
Surround	Fortification of flour; malaria control	Established.

23.2 Sickle cell disease and thalassaemia

What it is. Inherited errors in haemoglobin. In sickle cell disease one letter is changed in one word of the beta-globin gene. About 7.7 million people live with sickle cell disease (GBD 2021). Most are in Africa and India.

Where it fails (form F, S, C). One wrong letter writes a wrong word (F). The changed protein stacks into rigid fibres when oxygen is low: a fixed form in a living cell (S). Sickled cells block small vessels (C).

Prevention. Newborn screening and penicillin from infancy. Penicillin lowered serious infection by 84 % in young children (Gaston, 1986).

Layer	Treatment	Standing and evidence
Chain	Hydroxyurea, which switches on fetal haemoglobin	Established.
Chain	Gene editing that reawakens fetal haemoglobin (exa-cel)	Approved in 2023 in the UK and USA. Most treated patients free of crises.
Mesh	Stem-cell transplant from a matched donor	Established; curative, limited by donors.

23.3 Haemophilia

What it is. An inherited lack of a clotting factor. Bleeding does not stop. It affects mostly boys, because the gene sits on the X chromosome.

Where it fails (form F, C). A step in closing a breach is missing (C) because its word is wrong (F).

Prevention. Genetic counselling.

Layer	Treatment	Standing and evidence
Chain	Replacement factor; emicizumab, which bridges the missing step	Established.
Chain	Gene therapy that writes the missing factor	Approved for haemophilia A and B. Durability over decades is open.

> *Status: Derived (carrier law, 15 and 16.4; frame and copy law, 6 and 13). Measured (burden and treatment). Reading (failure forms).*

24. Breath

How it works. Breath is a rhythm that couples to the heart. Section 18.1 found that heart and breath lock in whole numbers more often than chance at rest. Section 18.2 found this locking strongest in deep sleep and absent in REM sleep and in waking. The lung is also a seam: the widest surface where the body meets the outer world. Air brings in what the test must read.

How it fails. The laws name four failures. Smoke and dust lodge in the lung and fix it: form S. The test can over-read harmless air: form O, as in asthma. Breath can lose its rhythm in sleep:

form D, as in sleep apnoea. Microbes that are not read cause infection: form U, taken in chapter 28.

24.1 Chronic obstructive pulmonary disease (COPD)

What it is. The airways narrow and the air sacs break down. It caused about 3.5 million deaths in 2021, about 5 % of all deaths (WHO). Tobacco smoke and smoke from cooking fires are the main causes.

Where it fails (form S, U). Smoke particles lodge and stay (S). The test reads them as misfits it cannot remove, and inflammation persists (U). Lost tissue does not return.

Prevention. Stopping smoking is the one measure proven to slow the loss of lung function and to lower death (Lung Health Study, Anthonisen, 2005). Clean cooking fuel removes the second cause.

Layer	Treatment	Standing and evidence
Surround	Tobacco control; clean cooking	Established.
Phase	Pulmonary rehabilitation: training of breath and movement	Established. Better exercise capacity and quality of life (McCarthy, Cochrane, 2015).
Chain	Inhaled bronchodilators and steroids	Established for symptoms and flare-ups.
Mesh	Long-term oxygen in severe low oxygen; lung volume reduction	Established. Oxygen lowered death in the 1980 and 1981 trials.

24.2 Asthma

What it is. The airways narrow in bouts because they over-react. About 262 million people had asthma in 2019 (WHO). It is the most common chronic disease of children.

Where it fails (form O). The test reads harmless air as a misfit (O). The airway closes against it. Section 21.2 placed this on the too-much side of the test.

Prevention. Children raised on traditional farms have less asthma; the diversity of microbes they meet explains part of this (Ege, 2011; Stein, 2016). Smoke-free homes protect children.

Layer	Treatment	Standing and evidence
Chain	Inhaled corticosteroids	Established. Regular use lowers asthma death (Suissa, 2000).
Reading	Biologics against IgE, IL-5 or IL-4/13 in severe asthma	Established.
Surround	Smoke-free homes and clean air	Established.

24.3 Obstructive sleep apnoea

What it is. The throat closes again and again during sleep, and breathing stops. About 936 million adults aged 30 to 69 are affected (Benjafield, 2019). Most are not diagnosed.

Where it fails (form D, C). Breath loses its rhythm exactly in the state where section 18.2 found heart and breath most closed. Each stop is an opening of the night (D). Oxygen as a carrier falls (C). The men in the MIT-BIH database of section 18.2 were tested for this condition, which lowered their locking.

Prevention. Healthy weight is the main lever.

Layer	Treatment	Standing and evidence
Mesh	Continuous positive airway pressure (CPAP)	Established for sleepiness. It did not lower heart events in a large trial (SAVE, McEvoy, 2016).
Chain	Tirzepatide in people with obesity	Established. Large fall in breathing stops (SURMOUNT-OSA, Malhotra, 2024).
Phase	Weight loss; sleeping on the side	Established.

> *Status: Derived (coupling, 16.2; locking measured in 18.1 and 18.2). Measured (burden and treatment). Reading (failure forms).*

25. Metabolism and hormones

How it works. Hormones are carriers. Section 16.4 derived that a carrier closes a seam fully in only 6 of 72 cases. Most seams stay open and need carriers for ever. A carrier must also decay to deliver. So hormones never stop, and each must be made, read and removed in a rhythm. Insulin carries the message 'food has come' to muscle, fat and liver. Thyroid hormone sets the pace of cells. The day sets the rhythm of almost every hormone (chapter 19).

How it fails. Hormonal disease takes three forms. The carrier can be missing (C): the test destroys the cells that make it (O), or a gland fails. The carrier can arrive and not be read: the cells stop listening, as in type 2 diabetes. The rhythm of the carrier can turn against the day (D): late eating, night work and short sleep. Surplus fuel then lodges in organs where it does not belong (S).

25.1 Type 2 diabetes

What it is. Blood sugar stays high because insulin is read too weakly and too little is made. More than 800 million adults had diabetes in 2022, and over half were not treated (NCD-RisC, Lancet, 2024). Most have type 2.

Where it fails (form C, D, S). Insulin arrives but is not read (C). Fat lodges in liver and pancreas, where it blocks the reading (S). Night work and late meals turn the rhythm of insulin against the day (D).

Prevention. In people at high risk, lifestyle change lowered new diabetes by 58 % and metformin by 31 % (Diabetes Prevention Program, Knowler, 2002). The Da Qing study showed effects lasting 30 years.

Layer	Treatment	Standing and evidence
Phase	Weight loss by a structured diet programme	Established. Remission in 46 % at one year (DiRECT, Lean, 2018).
Chain	Metformin, SGLT2 inhibitors, GLP-1 drugs	Established. SGLT2 and GLP-1 drugs also protect heart and kidney.
Mesh	Metabolic surgery	Established. Long remission in many (Mingrone, 2021).
Phase	Eating within a fixed daytime window	In trials. Results are mixed.

25.2 Type 1 diabetes

What it is. The body's test destroys the cells that make insulin. About 8.4 million people lived with it in 2021 (Gregory, 2022). It mostly starts in childhood.

Where it fails (form O, C). The test reads the insulin-making cells as misfits (O). The carrier is then missing (C). Without insulin the disease is fatal.

Prevention. No proven prevention. Screening for antibodies finds children years before onset.

Layer	Treatment	Standing and evidence
Chain	Insulin	Established since 1922.
Phase	Closed-loop delivery: a sensor reads glucose and a pump doses insulin	Established. It follows rule 1 of chapter 43: read before you act.
Reading	Teplizumab, which slows the attack	Approved in 2022. Delays onset by about two years (Herold, 2019).
Mesh	Islet transplant; islets grown from stem cells	Donor islets approved in 2023; stem-cell islets in trials, with insulin independence in most of a first group.

25.3 Obesity

What it is. Fat mass large enough to harm health. In 2022 one in eight people lived with obesity: about 890 million adults (WHO).

Where it fails (form D, S). Intake and rhythm drift from the day (D). Surplus lodges in organs (S). Section 45 adds a law: a cure that is not completed within one repair cycle is undone. Weight regained after stopping a drug fits that law.

Prevention. Food surroundings decide much of intake. In a controlled study, people on ultra-processed food ate about 500 kcal a day more than on unprocessed food (Hall, 2019). A tax on sugared drinks in Mexico lowered purchases (Colchero, 2017).

Layer	Treatment	Standing and evidence
Chain	Semaglutide; tirzepatide	Established. Mean weight loss 15 % and 21 % (STEP 1, 2021; SURMOUNT-1, 2022). Two thirds of the loss returned within a year of stopping semaglutide (Wilding, 2022).
Mesh	Bariatric surgery	Established. Lower long-term death (Swedish Obese Subjects study).
Phase	Movement, sleep and regular meals	Established for health; modest for weight.
Surround	Taxes and rules on food	Established for purchases; effect on disease in progress.

25.4 Thyroid disease

What it is. Too little thyroid hormone (hypothyroidism) or too much (hyperthyroidism). Most cases in iodine-sufficient countries are autoimmune: Hashimoto's disease and Graves' disease. Iodine deficiency remains a cause elsewhere.

Where it fails (form O, C). In Hashimoto's disease the test destroys the gland and the carrier is missing (O, C). In Graves' disease an antibody acts as a false carrier that never ends. Section 16.4 derived that a true carrier must decay to deliver. A carrier that does not decay drives the gland without pause.

Prevention. Iodised salt prevents deficiency. It is one of the cheapest public health measures ever adopted.

Layer	Treatment	Standing and evidence
Chain	Levothyroxine for too little; antithyroid drugs for too much	Established.
Mesh	Radioiodine or surgery	Established.
Surround	Salt iodisation	Established.

> *Status: Derived (carrier law 16.4; the day 19). Measured (burden and treatment). Reading (failure forms; Graves' antibody as a carrier that does not decay).*

26. Digestion and liver

How it works. Digestion takes foreign forms apart and re-uses their parts. Chapter 16 derived that unclosed forms decay and closed forms persist. Food is a closed form of another living being. The gut must open it, read it, take what fits and pass the rest. The gut wall is the largest seam of the body and holds most of its test. The liver then sorts and stores what came in.

How it fails. The gut fails as a seam. The test can over-read food or microbes (O): coeliac disease, inflammatory bowel disease. A microbe can stay unread (U): Helicobacter pylori. The liver can fill with fat that does not belong (S) and then scar (S). The rhythm of the gut can lose its step with the brain (D, W): irritable bowel syndrome.

26.1 Fatty liver disease (MASLD) and cirrhosis

What it is. Fat builds up in liver cells. About 30 % of adults have it (Younossi, 2023). Some develop inflammation and scarring, which can end in cirrhosis and liver cancer.

Where it fails (form S, D). Fat lodges in living cells (S). Scar is a fixed form in a living organ and does not rejoin it (S). Late, large meals load the liver against its rhythm (D).

Prevention. Healthy weight; little alcohol; treatment of diabetes.

Layer	Treatment	Standing and evidence
Phase	Weight loss	Established. A loss of 10 % or more resolved liver inflammation in about 90 % (Vilar-Gomez, 2015).
Chain	Resmetirom; semaglutide	Approved for inflammation with scarring (MAESTRO-NASH, Harrison, 2024; ESSENCE, 2025).
Mesh	Liver transplant in end-stage disease	Established.

26.2 Helicobacter pylori, ulcer and stomach cancer

What it is. A bacterium that lives in the stomach wall. It causes most ulcers and is the main cause of stomach cancer. The link was shown by Marshall and Warren (1984), who received the Nobel Prize in 2005.

Where it fails (form U). The microbe stays unread in the mucus layer (U). Decades of low inflammation follow, then ulcer, then in some people cancer.

Prevention. Clean water. Testing and treating infected people.

Layer	Treatment	Standing and evidence
Mesh	Eradication with antibiotics and acid suppression	Established. It cures ulcers and lowers gastric cancer by about a third (Ford, 2014); in family members of patients by more than half (Choi, 2020).

26.3 Coeliac disease

What it is. The test reacts to gluten and damages the gut lining. About 1.4 % of people carry the antibodies (Singh, 2018). Many are not diagnosed.

Where it fails (form O). The test reads a food protein as a misfit (O). Here the trigger is known. Section 21.2 predicts that removing the trigger stops the attack without moving the test at all.

Prevention. No proven prevention.

Layer	Treatment	Standing and evidence
Surround	A strict gluten-free diet	Established. The gut heals in most.
Reading	Drugs that block the immune reaction to gluten	In trials.

26.4 Inflammatory bowel disease

What it is. Crohn's disease and ulcerative colitis: long-lasting inflammation of the gut. About 5 million people were affected in 2019 (GBD). Rates rose with urban life.

Where it fails (form O, S). The test over-reads the gut's own microbes (O). The seam of the gut wall leaks, and scarring can narrow the bowel (S).

Prevention. Not smoking lowers the risk of Crohn's disease.

Layer	Treatment	Standing and evidence
Chain	Mesalazine; steroids for flares	Established.
Reading	Biologics against TNF, integrins or IL-12/23; JAK inhibitors	Established.
Mesh	Surgery	Established.
Reading	Faecal microbiota transfer in ulcerative colitis	In trials; modest effect.

26.5 Irritable bowel syndrome

What it is. Recurring belly pain with changed bowel habit, without visible damage. About 4 % of adults meet the Rome IV criteria (Sperber, 2021).

Where it fails (form D, W). The rhythm of the gut and its reading by the brain lose their step (D). Pain can become a closed state that is read as normal (W, chapter 31).

Prevention. No proven prevention.

Layer	Treatment	Standing and evidence
Phase	Gut-directed hypnotherapy; cognitive behavioural therapy	Established.
Surround	Low-FODMAP diet under guidance	Established for symptoms.
Chain	Antispasmodics; low-dose tricyclics	Established.

> *Status: Derived (decay of unclosed forms, 16; the test, 17). Measured (burden and treatment). Reading (failure forms).*

27. Kidney and urinary tract

How it works. The kidney passes on what has ended. Chapter 16 derived that open forms decay and must leave. The kidney filters the blood, keeps what is still closed and useful, and lets go of the rest. It also holds the balance of salt, water and acid. It sits at a seam between the carrier (blood) and the outside (urine).

How it fails. The kidney fails as a remover (C). Open forms are kept. It is also a place where fixed forms lodge (S): scar and stones. Most kidney failure comes from two other diseases: high blood pressure and diabetes.

27.1 Chronic kidney disease

What it is. Kidney function falls over months and years. About 788 million adults had chronic kidney disease in 2023 (GBD 2023, Lancet 2025). It is rising fast and is often silent.

Where it fails (form C, S). Filtration fails and open forms stay (C). Scar replaces the filters (S).

Prevention. Control of blood pressure and blood sugar. Early testing of urine and blood in people at risk.

Layer	Treatment	Standing and evidence
Chain	ACE inhibitors or ARBs; SGLT2 inhibitors; finerenone; semaglutide	Established. Dapagliflozin lowered the main kidney outcome by 39 % (DAPA-CKD, Heerspink, 2020); semaglutide by 24 % (FLOW, Perkovic, 2024).
Mesh	Dialysis; kidney transplant	Established. Transplant gives the best survival.

27.2 Kidney stones

What it is. Crystals form in the urine and grow into stones. About one in ten people has a stone in a lifetime in rich countries.

Where it fails (form S). A fixed crystal forms in a living stream (S). It never joins the tissue and must be passed or removed.

Prevention. Drinking enough water halved recurrence in a five-year trial (Borghi, 1996).

Layer	Treatment	Standing and evidence
Mesh	Shock waves or endoscopic removal	Established.
Surround	Water; less salt	Established.

27.3 Urinary incontinence

What it is. Loss of control of the bladder. It is common in women after childbirth and in old age.

Where it fails (form R). The muscle that closes the outlet loses strength and step (R).

Prevention. Pelvic floor training in pregnancy.

Layer	Treatment	Standing and evidence
Phase	Pelvic floor muscle training	Established. Cure or improvement in many women (Dumoulin, Cochrane, 2018).
Mesh	Surgery when training fails	Established.

> *Status: Derived (open forms must leave, 16). Measured (burden and treatment). Reading (failure forms).*

28. Infection: the test meets the foreign

How it works. Chapter 17 derived the test. A reader meets a form and answers +1 (fit), −1 (misfit) or 0 (unread). Section 17.1 counted what a reader of one strand can see: 93.3 % of foreign strands are readable, 5.9 % go unread, and eight wrongly closed forms are seen only by a reader that meets them. The immune system is this test made flesh. It learns by meeting, keeps a memory of what it met, and removes what reads −1.

How it fails. Infection is the meeting of a foreign form with the test. It harms in three ways. The microbe can stay unread (U): it hides inside cells, inside the readers themselves, or changes its face faster than the test learns. The test can answer too strongly and harm the body (O): sepsis. And the microbe can change until no drug reads it any more: resistance. Vaccines follow the law directly. They teach the reader a form before the meeting.

28.1 Tuberculosis

What it is. A lung infection by Mycobacterium tuberculosis. In 2023, 8.2 million people were newly diagnosed, the most since WHO began counting, and about 1.25 million died (WHO Global TB Report, 2024). It is again the leading infectious killer. About a quarter of all people carry a latent infection (Houben, 2016).

Where it fails (form U). The bacterium is walled off in a granuloma. It is closed and silent: neither removed nor active (U). When the test weakens, through HIV, hunger or age, it wakes.

Prevention. Food support for households of patients lowered new TB by 39 to 48 % (RATIONS, Bhargava, 2023). BCG protects young children against severe forms.

Layer	Treatment	Standing and evidence
Mesh	Six months of four antibiotics; four-month regimens; BPaL for resistant TB	Established. Cure in about 85 %.
Reading	New vaccines such as M72/AS01E	In trials (phase 3 since 2024).
Surround	Nutrition, housing, finding and treating contacts	Established.

28.2 HIV

What it is. A virus that infects the readers of the test themselves. About 39.9 million people lived with HIV in 2023 and about 630,000 died of related illness (UNAIDS, 2024).

Where it fails (form U, C). The virus writes itself into the genome of the reader cells and can lie latent there (U). The readers are lost and the test fails as a carrier (C). This is the deepest form of unread error: the misfit hides inside the reader.

Prevention. Condoms, testing and treatment, pre-exposure prophylaxis. People with an undetectable virus do not transmit it: zero linked transmissions in the PARTNER studies (Rodger, 2019). Lenacapavir by injection twice a year prevented all infections in a trial in young women (PURPOSE 1, Bekker, 2024).

Layer	Treatment	Standing and evidence
Chain	Antiretroviral therapy	Established. Near-normal life expectancy when started early.
Chain	Long-acting prevention (lenacapavir)	Approved in 2025.
Mesh	Stem-cell transplant from a donor lacking the CCR5 entry point	A handful of cures. Not a general treatment.
Reading	Broadly neutralising antibodies; therapeutic vaccines	In trials.

28.3 Malaria

What it is. A parasite spread by mosquitoes. There were about 263 million cases and 597,000 deaths in 2023, most in African children (WHO World Malaria Report, 2024).

Where it fails (form U). The parasite hides inside red cells and changes the proteins it shows on their surface (U). The test reads one face and the parasite shows another.

Prevention. Insecticide-treated bed nets; seasonal preventive drugs for children.

Layer	Treatment	Standing and evidence
Chain	Artemisinin-based combination therapy	Established. Resistance is spreading in East Africa.
Reading	Vaccines RTS,S and R21	Established and recommended by WHO. R21 gave about 75 % efficacy in seasonal areas (Datoo, 2024).
Surround	Bed nets, spraying, drainage	Established.

28.4 Viral hepatitis B and C

What it is. Viruses that infect the liver for decades. About 254 million people live with hepatitis B and 50 million with hepatitis C; together they caused about 1.3 million deaths in 2022 (WHO Global Hepatitis Report, 2024). Both cause cirrhosis and liver cancer.

Where it fails (form U, S). The virus stays in liver cells, read too weakly to be cleared (U). Long inflammation leaves scar (S).

Prevention. Hepatitis B vaccine at birth. In Taiwan, infant vaccination lowered liver cancer in children (Chang, 1997). Safe injections and blood.

Layer	Treatment	Standing and evidence
Chain	Direct-acting antivirals for hepatitis C	Established. Cure in more than 95 % in 8 to 12 weeks.
Chain	Long-term antivirals for hepatitis B	Established. Control, rarely cure.
Reading	Hepatitis B vaccine	Established.

28.5 Pneumonia and lower respiratory infection

What it is. Infection of the lung by bacteria or viruses. It is the deadliest infectious syndrome, with about 2.2 million deaths in 2021 (GBD 2021). Young children and old people die most.

Where it fails (form U, O). The microbe multiplies faster than the test reads it (U). The test's own response fills the lung (O).

Prevention. Vaccines against pneumococcus, Hib, influenza, measles and pertussis. Clean air. Breastfeeding.

Layer	Treatment	Standing and evidence
Mesh	Antibiotics; oxygen	Established.
Reading	Childhood and adult vaccination	Established.

28.6 Sepsis

What it is. A failing body response to infection that injures its own organs. In 2017 there were about 49 million cases and 11 million deaths, one in five deaths worldwide (Rudd, 2020).

Where it fails (form U, O). Sepsis is the test failing in both directions of section 21.2 at once. The microbe is not cleared (U) and the response damages healthy organs (O).

Prevention. Vaccination, clean water, hygiene in hospitals, early treatment of infection.

Layer	Treatment	Standing and evidence
Mesh	Antibiotics within the hour; removal of the source; fluids and organ support	Established. Each hour of delay raises death (Seymour, 2017).

28.7 Antimicrobial resistance

What it is. Microbes that no drug reads. About 1.14 million deaths in 2021 were directly due to resistant bacteria; 39 million are projected for 2025 to 2050 (GBD AMR, Naghavi, 2024).

Where it fails (form U). The misfit changes its form until the drug no longer reads it (U). Every use of a drug selects the forms it cannot read.

Prevention. Fewer and better-aimed antibiotics, vaccines, clean water and sanitation.

Layer	Treatment	Standing and evidence
Surround	Stewardship; sanitation; vaccination	Established.
Chain	New antibiotics; phage therapy	In trials.

28.8 After infection: long COVID and post-infectious fatigue

What it is. Symptoms that persist months after an infection: fatigue, breathlessness, poor concentration. At least 65 million people had long COVID by 2023 (Davis, 2023).

Where it fails (form U, W). Two readings fit. Remnants of the microbe may stay unread (U). Or the body has closed onto a new, lower state that it reads as normal (W). The theory cannot yet decide between them.

Prevention. Vaccination lowers the risk.

Layer	Treatment	Standing and evidence
Phase	Pacing; graded return guided by symptoms	Established for support.
Chain	Antivirals; immune drugs	In trials. No proven cure.

> *Status: Derived (the test and its three answers, 17; counted in 17.1). Measured (burden and treatment). Reading (failure forms; sepsis as both directions at once).*

29. Autoimmunity and allergy: the test reads too much

How it works. Section 21.2 derived that the test fails in two directions. This chapter takes the second: a fit or harmless form is read as −1. The test learns what is self and what is harmless by meeting. Most learning happens early in life.

How it fails. Autoimmune disease is form O against the body's own forms. Allergy is form O against harmless outside forms. One in ten people in the United Kingdom has one of nineteen autoimmune diseases, and women twice as often as men (Conrad, 2023). Treatment has two routes. Dampen the test, at the cost of infection (section 21.2). Or reset it, so it reads correctly again. The second route fits cure rule 2 of chapter 43: restore, do not add.

29.1 Rheumatoid arthritis

What it is. The test attacks the lining of the joints. About 18 million people are affected (GBD 2019). Untreated, it destroys joints.

Where it fails (form O, S). The joint lining is read as a misfit (O). Inflamed tissue erodes bone and leaves fixed damage (S).

Prevention. Not smoking. Smoking is the strongest known outside risk.

Layer	Treatment	Standing and evidence
Chain	Methotrexate, started early, with treat-to-target	Established.
Reading	Biologics and JAK inhibitors	Established.
Reading	Abatacept in people at high risk before onset	In trials. Onset was delayed (APIPPRA, 2024).

29.2 Systemic lupus erythematosus

What it is. The test attacks the cell nucleus and many organs. About 3.4 million people are affected (Tian, 2023). Nine in ten are women.

Where it fails (form O). Debris of dying cells is read as foreign (O). The attack spreads to skin, joints, kidney and brain.

Prevention. No proven prevention. Sun protection lowers flares.

Layer	Treatment	Standing and evidence
Chain	Hydroxychloroquine	Established. Lowers flares and death.
Reading	Belimumab, anifrolumab	Established.
Reading	CD19 CAR-T cells that wipe the B-cell readers and let them regrow	In trials. Drug-free remission in the first patients with severe disease (Mackensen, 2022; Müller, 2024). This is a reset, not a brake.

29.3 Multiple sclerosis

What it is. The test attacks the insulating sheath of nerves in brain and spinal cord. About 2.8 million people are affected (Atlas of MS, 2020).

Where it fails (form O). A protein of the Epstein–Barr virus resembles a protein of the nerve sheath. Readers trained on the virus then read the sheath as foreign (O). After Epstein–Barr infection the risk rose 32-fold in a cohort of 10 million soldiers (Bjornevik, 2022). The mimicry was shown at the level of one antibody (Lanz, 2022).

Prevention. A vaccine against Epstein–Barr virus is a direction. Not smoking; enough vitamin D.

Layer	Treatment	Standing and evidence
Reading	High-efficacy disease-modifying drugs	Established.
Reading	Autologous stem-cell transplant: reset of the test	Established in some centres for active disease; trials ongoing.
Phase	Rehabilitation and exercise	Established for function.

29.4 Allergy: food allergy, hay fever and eczema

What it is. The test reads harmless proteins as threats. Allergies are common in rich, urban countries and rose through the twentieth century.

Where it fails (form O). Pollen, peanut or dust is read as −1 (O). Section 21.4 predicted that too little early meeting leaves the test untrained.

Prevention. Early meeting teaches the reader. Feeding peanut to infants at high risk lowered peanut allergy by about 80 % (LEAP, Du Toit, 2015). Farm childhoods protect.

Layer	Treatment	Standing and evidence
Reading	Allergen immunotherapy	Established for hay fever and insect venom.
Reading	Omalizumab in food allergy	Established. Raised the dose tolerated (OUtMATCH, Wood, 2024).
Chain	Antihistamines; adrenaline for anaphylaxis	Established.

> *Status: Derived (two directions of the test, 21.2). Measured (burden and treatment). Reading (failure forms; CAR-T and stem-cell transplant as a reset of the reader).*

30. Cancer: the unread copy

How it works. Cells copy themselves. Chapter 13 derived that a copy is exact only through the unique partner, and that every closed ring divides into two closed rings. Copying still makes errors: one error opens three windows and stays until it is read (chapter 5, proof 2 in 5.1). The test reads changed cells and removes most of them.

How it fails. Cancer is what the test does not remove. Errors accumulate in a line of cells (F). Most such cells read −1 and are removed. The survivors are those that show a 'self' signal and so read +1 or 0 (U). Where Illness Comes From called this the sculpted remainder: the test shapes the tumour by removing everything it can read. This reading explains why the newest cancer drugs work on the test and not on the cell. In 2022 there were about 20 million new cancers and 9.7 million deaths (GLOBOCAN, Bray, 2024). About four in ten cases in the United States are attributable to risks that can be changed (Islami, 2024).

30.1 Lung cancer

What it is. The leading cause of death from cancer: about 2.5 million new cases and 1.8 million deaths in 2022 (GLOBOCAN).

Where it fails (form F, U). Smoke snaps the thread of the genome again and again (F). A heavy load of errors makes many tumours readable, once the brake on the test is released (U).

Prevention. Not smoking prevents most cases. Radon control. Screening with low-dose CT lowered lung cancer death by 20 % (NLST, 2011) and by 24 % in men (NELSON, de Koning, 2020).

Layer	Treatment	Standing and evidence
Mesh	Surgery or radiotherapy in early disease	Established.
Chain	Drugs aimed at EGFR, ALK and other drivers	Established. Osimertinib after surgery improved survival (ADAURA, 2023).
Reading	Checkpoint inhibitors such as pembrolizumab	Established. Five-year survival roughly doubled in one group (KEYNOTE-024).
Surround	Tobacco control	Established.

30.2 Breast cancer

What it is. The most common cancer in women: about 2.3 million new cases in 2022 (GLOBOCAN).

Where it fails (form F, U, D). Copy errors accumulate in breast tissue (F). Hormone rhythms drive growth. Night shift work is a probable cause in the IARC list (D).

Prevention. Less alcohol, healthy weight, physical activity, breastfeeding. Screening by mammography lowers breast cancer death by about a fifth among those invited (Independent UK Panel, 2012).

Layer	Treatment	Standing and evidence
Mesh	Surgery, radiotherapy, chemotherapy	Established.
Chain	Hormone therapy; trastuzumab for HER2-positive disease	Established.
Reading	Checkpoint inhibitors in triple-negative disease	Established.

30.3 Colorectal cancer

What it is. About 1.9 million new cases in 2022 (GLOBOCAN). Rising in people under 50.

Where it fails (form F, U). Polyps carry copy errors (F). One group of tumours cannot repair copy mismatches at all. They carry thousands of errors. Once the brake on the test is released, they are highly readable (U).

Prevention. Screening by stool test or colonoscopy. Physical activity; less processed meat. Aspirin lowered cancer in carriers of Lynch syndrome (CAPP2, Burn, 2020).

Layer	Treatment	Standing and evidence
Mesh	Removal of polyps; surgery	Established.
Reading	Dostarlimab in mismatch-repair-deficient rectal cancer	In trials. Every patient in the first series had a complete response without surgery (Cercek, 2022). This is the clearest case of form U cured by making the tumour readable.

30.4 Cervical cancer

What it is. Caused by persistent infection with human papillomavirus (HPV). About 660,000 new cases in 2022 (GLOBOCAN).

Where it fails (form U, F). The virus persists unread (U) and drives copy errors (F).

Prevention. HPV vaccination before age 17 lowered invasive cervical cancer by 88 % in Sweden (Lei, 2020). Screening for HPV. WHO set a target to eliminate the disease.

Layer	Treatment	Standing and evidence
Reading	HPV vaccine	Established.
Mesh	Removal of precancer found by screening	Established.

30.5 Prostate cancer

What it is. Common in older men; many tumours grow so slowly they never cause harm.

Where it fails (form F, R). Copy errors accumulate with age (F, R). Most remain local and quiet.

Prevention. Screening by PSA lowered prostate cancer death by about 20 % over 16 years (ERSPC, Hugosson, 2019), at the cost of overdiagnosis.

Layer	Treatment	Standing and evidence
Phase	Active surveillance for low-risk disease: read before you act	Established. In ProtecT, death from prostate cancer was low (about 3 %) after 15 years whatever the first choice (Hamdy, 2023).
Mesh	Surgery or radiotherapy	Established.
Chain	Hormone therapy	Established for advanced disease.

30.6 Melanoma and skin cancer

What it is. Cancer of pigment cells and other skin cells, caused mainly by ultraviolet light.

Where it fails (form F, U). Sunlight snaps the thread (F). Melanomas carry very many errors and are highly readable once the test is free (U).

Prevention. Daily sunscreen halved new melanomas in a ten-year trial (Green, 2011). Avoid sunburn in childhood.

Layer	Treatment	Standing and evidence
Mesh	Excision	Established.
Reading	Checkpoint inhibitors (nivolumab with ipilimumab)	Established. About half of patients with advanced melanoma alive at ten years (CheckMate 067).

30.7 Blood cancers: leukaemia and lymphoma

What it is. Cancers of blood-forming cells. Chronic myeloid leukaemia is driven by one fused gene. Acute lymphoblastic leukaemia is the most common cancer of children.

Where it fails (form F). A broken and rejoined chromosome writes one wrong word that never stops (F). Section 16.4 derived that a carrier must decay. A growth signal that never decays drives the cell without pause.

Prevention. Avoid benzene and radiation.

Layer	Treatment	Standing and evidence
Chain	Imatinib in chronic myeloid leukaemia	Established. About 83 % alive at ten years (IRIS, Hochhaus, 2017).
Mesh	Chemotherapy in childhood leukaemia	Established. About 90 % cured in rich countries (Hunger, 2015).
Reading	CAR-T cells; bispecific antibodies	Established in relapsed B-cell cancers.

> *Status: Derived (copy law, 13; one error opens three windows, 5 and 5.1; the test, 17). Measured (burden, prevention and treatment). Reading (cancer as the unread remainder; growth signals that do not decay).*

31. The nervous system

How it works. Section 16.3 derived how an opening moves: not by sliding, but in two changes through a fully closed state. That is the form of the all-or-none nerve impulse. Section 20.1 derived that a reader fits one strand. The brain is a mass of readers that close on each other in rhythms. Deep sleep is the most closed state; REM sleep reads; waking acts (18.2). In deep sleep the brain also clears waste: the flow of fluid through brain tissue rises sharply in sleep (Xie, 2013).

How it fails. The nervous system fails in four ways. Misfolded proteins lodge and stay unread (S, U): dementia and Parkinson's disease. A carrier fails: stroke, nerve damage. Readers can close all in one phase: the uniform wrong closure of section 19.0a, which is the form of a seizure (W). And pain can close into a state that is read as normal (W).

31.1 Dementia and Alzheimer's disease

What it is. Loss of memory and thinking that disables daily life. About 57 million people had dementia in 2021, with about 10 million new cases a year (WHO). Alzheimer's disease causes most of it.

Where it fails (form S, U, R, D). Amyloid and tau fold wrongly and lodge (S). The test does not clear them (U). Repair falls behind with age (R). Deep sleep, in which the brain clears waste, shortens with age and in disease (D).

Prevention. Fourteen modifiable risks explain about 45 % of dementia: among them education, hearing loss, high LDL, blood pressure, smoking, inactivity, diabetes, air pollution and social isolation (Lancet Commission, Livingston, 2024).

Layer	Treatment	Standing and evidence
Reading	Antibodies that clear amyloid: lecanemab, donanemab	Approved. Decline slowed by about a quarter to a third over 18 months (van Dyck, 2023; Sims, 2023). Brain swelling and bleeding are risks.
Phase	Combined diet, exercise, cognitive training and vascular care	In trials. Benefit on cognition in FINGER (Ngandu, 2015).
Phase	Hearing aids	In trials. Slower decline in people at high risk (ACHIEVE, Lin, 2023); no effect overall.
Surround	Education, clean air, blood-pressure control	Established as risk reduction.

31.2 Parkinson's disease

What it is. Loss of dopamine cells, with slowness, rigidity and tremor. More than 8.5 million people had it in 2019 (WHO). It is the fastest-growing brain disease.

Where it fails (form S, C, W). Alpha-synuclein clumps and lodges (S). The dopamine carrier is lost (C). Motor circuits lock into a rhythm in the beta band: many readers closed in one phase. That is the uniform wrong closure of section 19.0a: a fixed, rigid state (W).

Prevention. Some pesticides, such as paraquat, and the solvent trichloroethylene raise risk. Physical activity lowers it.

Layer	Treatment	Standing and evidence
Chain	Levodopa and other dopamine drugs	Established since the 1960s.
Mesh	Deep brain stimulation	Established. Better motor function and quality of life (Deuschl, 2006). It works by breaking the locked rhythm: an outside change that opens a uniform closure, as 19.0a requires.
Phase	High-intensity exercise	In trials. Slower motor decline in a phase 2 trial (SPARX, Schenkman, 2018).

31.3 Epilepsy

What it is. Recurring seizures. About 50 million people have epilepsy (WHO). Up to 70 % could live free of seizures with proper treatment.

Where it fails (form W). A seizure is hypersynchrony: very many readers fire in one phase. Section 19.0a derived that a form pushed past one third wrong closes onto the uniform form. A seizure is that uniform closure in the brain (W). Sleep loss, a known trigger, adds openings (D).

Prevention. About a quarter of cases are preventable: head injury, birth injury, brain infection, stroke (WHO).

Layer	Treatment	Standing and evidence
Chain	Anti-seizure drugs	Established.
Mesh	Surgery in drug-resistant temporal lobe epilepsy	Established. 58 % free of disabling seizures against 8 % on drugs (Wiebe, 2001).
Phase	Regular sleep; ketogenic diet in children	Established for selected cases (Neal, 2008).

31.4 Migraine

What it is. Recurring attacks of headache, often with nausea and aura. About 1.1 billion people have migraine (GBD 2019).

Where it fails (form D, W). A wave of silenced cortex moves slowly across the brain: an opening that travels (16.3). Attacks follow changes in sleep, meals and the hormone cycle: rhythms out of step (D).

Prevention. Regular sleep and meals.

Layer	Treatment	Standing and evidence
Chain	Triptans; drugs and antibodies that block CGRP	Established.
Phase	Aerobic exercise; regular rhythm of sleep	Established as support.

31.5 Chronic pain

What it is. Pain that lasts beyond healing, more than three months. About one adult in five has chronic pain. Low back pain alone affected about 619 million people in 2020 (GBD, Lancet Rheumatology, 2023).

Where it fails (form W). The nervous system closes onto a state of pain and reads it as the norm (W). The original damage is gone; the closed state remains.

Prevention. Staying active after injury.

Layer	Treatment	Standing and evidence
Phase	Exercise therapy; cognitive behavioural therapy	Established.
Phase	Pain reprocessing therapy	In trials. 66 % pain-free or nearly so against 20 % with placebo (Ashar, 2022). An outside reader that carries the right form, as section 41.1 requires.
Chain	Opioids for chronic back or joint pain	Not better than non-opioid drugs over one year (SPACE, Krebs, 2018).

31.6 Motor neurone disease (ALS)

What it is. Loss of the nerve cells that drive muscles. Most patients die within five years.

Where it fails (form U, F). Misfolded proteins lodge in motor neurons (U). Some cases come from an error in one gene, such as SOD1 (F).

Prevention. None known.

Layer	Treatment	Standing and evidence
Chain	Riluzole	Established. Modest gain in survival.
Chain	Tofersen, which silences the faulty SOD1 message	Approved in 2023 for SOD1 cases.

> *Status: Derived (impulse, 16.3; reader, 20.1; wrong closure onto the uniform form, 19.0a). Measured (burden and treatment). Reading (seizure and parkinsonian rigidity as uniform closure; chronic pain as wrong closure).*

32. The senses: eye and ear

How it works. The eye and the ear are readers that face the outside. The eye reads light and also sets the clock: light in the morning places the body in the day (chapter 19). The ear reads pressure waves with rows of hair cells that do not regrow.

How it fails. The senses fail mostly by drift (R) and by fixed forms (S). The lens fills with protein that has lost its fold: cataract. The fluid pressure of the eye damages the nerve: glaucoma. Hair cells are lost to noise and age. About 2.2 billion people have impaired vision, of whom at least 1 billion have a preventable or untreated cause (WHO World report on vision, 2019). About 1.5 billion live with some hearing loss (WHO World report on hearing, 2021).

32.1 Cataract

What it is. Clouding of the lens. It is the leading cause of blindness in the world.

Where it fails (form S, R). Lens proteins lose their fold and stack into fixed clusters in a living organ (S, R).

Prevention. Sun protection; not smoking.

Layer	Treatment	Standing and evidence
Mesh	Lens replacement surgery	Established. Sight restored in one short operation.

32.2 Myopia

What it is. Short sight. It is rising fast in East Asia and elsewhere, and high myopia raises the risk of blindness later.

Where it fails (form D). The eye grows too long when it lacks daylight while it grows (D).

Prevention. An extra 40 minutes outdoors at school lowered new myopia in Chinese children (He, 2015).

Layer	Treatment	Standing and evidence
Surround	Time outdoors	Established.
Chain	Low-dose atropine drops	Established in several countries.

32.3 Glaucoma and macular degeneration

What it is. Glaucoma damages the optic nerve. Age-related macular degeneration damages the centre of the retina. Both cause lasting loss.

Where it fails (form S, R). Pressure and waste lodge at the seam between nerve and eye (S). Repair falls behind with age (R). In wet macular degeneration new vessels grow where they do not belong.

Prevention. Not smoking; screening in older age.

Layer	Treatment	Standing and evidence
Chain	Pressure-lowering drops in glaucoma	Established. Slower progression (EMGT, Heijl, 2002).
Chain	Injections against VEGF in wet macular degeneration	Established.

32.4 Hearing loss

What it is. Loss of hearing with age or noise. About 430 million people have disabling hearing loss (WHO, 2021).

Where it fails (form R). Hair cells are lost and do not return (R).

Prevention. Protection from noise; vaccination against measles, mumps and rubella; care at birth.

Layer	Treatment	Standing and evidence
Mesh	Hearing aids; cochlear implants	Established.
Chain	Gene therapy for inherited deafness (OTOF)	In trials. Hearing restored in young children.

> *Status: Derived (the day as the open remainder, 19; drift, 19.0a and 19.0b). Measured (burden and treatment). Reading (failure forms).*

33. Skin

How it works. Skin is the outer seam. Chapter 12 derived that bilayers are asymmetric: 8 of 9 have a different inside and outside. Skin renews itself from below in a steady rhythm. It holds a test of its own.

How it fails. Skin fails as a seam. The barrier can leak, letting in what the test then over-reads (O). Cells can renew too fast in a closed loop with the test (O, W): psoriasis. Light snaps the thread (F): skin cancer, in chapter 30. Wounds close with scar: a fixed form in living tissue (S).

33.1 Atopic eczema

What it is. Dry, itching, inflamed skin. Common in children; often the first step towards asthma and hay fever.

Where it fails (form O, S). Loss of the barrier protein filaggrin opens the seam (Palmer, 2006). Outside proteins enter and are over-read (O).

Prevention. Daily emollient from birth did not prevent eczema in a large trial (BEEP, Chalmers, 2020). That is a failed test of the seam reading.

Layer	Treatment	Standing and evidence
Chain	Emollients and topical steroids	Established.

Layer	Treatment	Standing and evidence
Reading	Dupilumab and other biologics; JAK inhibitors	Established in moderate to severe disease.

33.2 Psoriasis

What it is. Thick, scaly plaques where skin renews too fast. Up to about 2 % of adults in Western Europe are affected (Parisi, 2020).

Where it fails (form O, W). Skin cells and the test drive each other in a loop: the test reads, the skin grows, the growth is read again (O). The loop closes into a stable state (W).

Prevention. Healthy weight; not smoking.

Layer	Treatment	Standing and evidence
Reading	Biologics against IL-17 or IL-23	Established. Near-clear skin in most patients.
Phase	Light therapy	Established.
Phase	Weight loss	Established as support.

33.3 Chronic wounds and scars

What it is. Wounds that do not close, such as diabetic foot ulcers, and scars that limit movement.

Where it fails (form S, C). Poor blood supply leaves the seam without a carrier (C). Scar is a fixed form that never fully rejoins living skin (S).

Prevention. Foot care in diabetes; blood-sugar control.

Layer	Treatment	Standing and evidence
Mesh	Off-loading, cleaning, revascularisation	Established.

> *Status: Derived (asymmetric bilayers, 12; seam law, 4). Measured (burden and treatment). Reading (failure forms). One reading failed its test: emollients from birth did not prevent eczema.*

34. Bone, muscle and joints

How it works. Bone is a living form that holds a fixed mineral. It is rebuilt all the time by two coupled rhythms: one removes bone, one lays it down. Muscle acts by opening and repairs in rest (19.0a: acting opens, rest repairs). Section 16.1 derived that what persists repeats. Muscle and bone persist only when used in a repeating rhythm.

How it fails. Joints fail at seams. Cartilage wears and fixed forms lodge: crystals, bony spurs (S). Bone fails when its two rhythms drift apart and removal outpaces building (R, D). Muscle fails when use stops and repair falls behind (R). Low back pain is taken in chapter 31 as chronic pain.

34.1 Osteoarthritis

What it is. Wear and remodelling of joints, with pain and stiffness. About 595 million people had osteoarthritis in 2020 (GBD, Lancet Rheumatology, 2023).

Where it fails (form S, R). Cartilage thins and bone forms spurs: fixed forms at a living seam (S). Repair falls behind load (R).

Prevention. Healthy weight; strong muscles; care after joint injury.

Layer	Treatment	Standing and evidence
Phase	Exercise and weight loss	Established first-line treatment.
Mesh	Joint replacement in end-stage disease	Established.
Mesh	Keyhole surgery on the worn knee	Tested and failed: no better than sham surgery (Sihvonen, 2013).

34.2 Osteoporosis and fracture

What it is. Thin, fragile bone. About one in three women and one in five men over 50 will break a bone through osteoporosis (International Osteoporosis Foundation).

Where it fails (form R, D). The removing rhythm outpaces the building rhythm (D). After menopause and with age the drift grows (R).

Prevention. Impact and resistance exercise. Exercise lowered the rate of falls in older people by about a quarter (Sherrington, Cochrane, 2019).

Layer	Treatment	Standing and evidence
Chain	Bisphosphonates; denosumab; romosozumab	Established. Romosozumab followed by alendronate beat alendronate alone (ARCH, Saag, 2017).
Phase	High-intensity resistance and impact training	In trials. Bone density rose in women with low bone mass (LIFTMOR, Watson, 2018).
Surround	Fall prevention at home	Established.

34.3 Gout

What it is. Urate crystals form in joints and cause sudden, severe pain. About 56 million people had gout in 2020 (GBD 2021).

Where it fails (form S). A fixed crystal in a living joint (S). The test reads it and attacks: the pain of a flare is the reading.

Prevention. Less alcohol and sugared drinks; healthy weight.

Layer	Treatment	Standing and evidence
Chain	Allopurinol raised step by step to a urate target	Established. Nurse-led treat-to-target reached the target in 95 % against 30 % in usual care (Doherty, 2018). This is rule 1: read, then dose.
Chain	Colchicine or anti-inflammatory drugs for flares	Established.

34.4 Sarcopenia and frailty

What it is. Loss of muscle mass and strength with age. It leads to falls, loss of independence and death.

Where it fails (form R). Use falls and repair falls behind (R). What does not repeat does not persist (16.1).

Prevention. Resistance training throughout adult life; enough protein.

Layer	Treatment	Standing and evidence
Phase	Progressive resistance training	Established. Strength gains at every age.

> *Status: Derived (what persists repeats, 16.1; acting opens and rest repairs, 19.0a; seam law, 4). Measured (burden and treatment). Reading (failure forms). One mesh treatment failed against sham: keyhole knee surgery.*

35. Reproduction, pregnancy and birth

How it works. Reproduction is copying at the scale of the whole person. Chapter 13 derived that a copy is exact only through the unique partner and that a ring divides into two closed rings. Pregnancy joins two rhythms, mother and child, at one seam: the placenta. Birth is the moment the child's rhythm leaves that seam and meets the day.

How it fails. Reproduction fails at the seam (C), in rhythm (D) and in copying (F). The placenta can fail as a carrier: pre-eclampsia, growth restriction. Birth can come too early: the two rhythms part before the child is ready. The hormone cycle can lose its step: polycystic ovary syndrome. Tissue can grow at the wrong seam: endometriosis.

35.1 Infertility

What it is. No pregnancy after a year of trying. About one in six people is affected in their lifetime (WHO, 2023).

Where it fails (form C, D, F). Many causes: blocked tubes (C), lost cycles (D), poor copying of eggs or sperm with age (F, R).

Prevention. Treat sexually transmitted infection; avoid smoking; do not delay pregnancy too long when it is wanted.

Layer	Treatment	Standing and evidence
Mesh	In vitro fertilisation	Established.
Chain	Letrozole to induce ovulation in polycystic ovary syndrome	Established. More live births than clomiphene (Legro, 2014).

35.2 Preterm birth

What it is. Birth before 37 weeks. About 13.4 million babies were born preterm in 2020 (WHO). Complications of preterm birth are the leading cause of death in children under five.

Where it fails (form D, C). The rhythm of mother and child parts before the child's own rhythms can close (D). Lungs and carriers are not ready (C).

Prevention. Antenatal care; treatment of infection; spacing of pregnancies.

Layer	Treatment	Standing and evidence
Chain	Steroids before preterm birth to ripen the lungs	Established. Fewer newborn deaths (McGoldrick, Cochrane, 2020).
Phase	Kangaroo care: skin-to-skin contact from birth	Established. A quarter fewer deaths in small babies when started at once (iKMC, 2021).

35.3 Pre-eclampsia

What it is. High blood pressure and organ damage in pregnancy, from a poorly formed placenta. A leading cause of maternal and fetal death.

Where it fails (form C, S). The seam between mother and child forms badly and fails as a carrier (C).

Prevention. Low-dose aspirin from early pregnancy in women at high risk lowered preterm pre-eclampsia by 62 % (ASPRE, Rolnik, 2017).

Layer	Treatment	Standing and evidence
Chain	Aspirin; blood-pressure drugs; magnesium sulphate against seizures	Established.
Mesh	Timely delivery	Established.

35.4 Death in childbirth

What it is. About 260,000 women died of pregnancy and childbirth in 2023, most from causes that can be prevented (WHO, 2025). Bleeding after birth is the largest cause.

Where it fails (form C). The carrier is lost at the seam of birth (C).

Prevention. Skilled care at birth.

Layer	Treatment	Standing and evidence
Mesh	A bundle of early detection and treatment of bleeding	Established. Severe outcomes fell by 60 % (E-MOTIVE, Gallos, 2023).

35.5 Polycystic ovary syndrome and endometriosis

What it is. Polycystic ovary syndrome affects up to about one in eight women of reproductive age; endometriosis about one in ten (WHO, 2023). Both cause pain, irregular cycles or infertility.

Where it fails (form D, S, O). In polycystic ovary syndrome the hormone cycle loses its step (D), tied to poor reading of insulin (C). In endometriosis, lining tissue lives at a foreign seam (S) and inflames it (O).

Prevention. Healthy weight helps in polycystic ovary syndrome.

Layer	Treatment	Standing and evidence
Phase	Lifestyle change in polycystic ovary syndrome	Established.
Chain	Hormonal treatment	Established.
Mesh	Surgery for endometriosis	Established.

35.6 Neural tube defects

What it is. Spina bifida and related defects, when the neural tube does not close in early pregnancy.

Where it fails (form F, C). A tube that should close as a ring stays open (F). The vitamin folate is a missing carrier for that step (C).

Prevention. Folic acid before conception lowered neural tube defects by 72 % (MRC Vitamin Study, 1991). Flour fortification brings this to whole populations.

Layer	Treatment	Standing and evidence
Surround	Folic acid supplements and fortification	Established.
Mesh	Surgery on the spine, sometimes before birth	Established.

> *Status: Derived (copy and divide, 13; carrier law, 15). Measured (burden and treatment). Reading (failure forms).*

36. Inherited disease

How it works. Every cell carries a text written in words of three. Chapter 6 derived that the text must be read in one frame. Chapter 13 derived how it is copied. An error in the text is carried into every copy. Section 21.3 showed that the frame law predicts the difference between two diseases of one gene.

How it fails. Inherited disease is form F. It comes in four kinds. One letter wrong: sickle cell disease (chapter 23). A word lost or a frame shifted: cystic fibrosis, Duchenne dystrophy. A word of three repeated too often: Huntington's disease. A whole chromosome too many: Down syndrome. More than 7,000 rare diseases are known; together they affect about 300 million people, and about seven in ten are genetic (Nguengang Wakap, 2020).

36.1 Cystic fibrosis

What it is. Thick mucus clogs lungs and pancreas. The most common error deletes exactly one word of three: one amino acid is lost and the frame is kept.

Where it fails (form F, U). The protein is made but folds badly. The cell's own test reads it as a misfit and removes it before it reaches the surface. The fault is in the word (F); the loss is caused by the reading.

Prevention. Carrier screening and genetic counselling.

Layer	Treatment	Standing and evidence
Chain	Elexacaftor–tezacaftor–ivacaftor, which helps the protein fold and pass the cell's test	Established. Lung function rose by 14 points (Middleton, 2019). Life expectancy has risen sharply.

36.2 Duchenne and Becker muscular dystrophy

What it is. Muscle wasting in boys, from errors in the dystrophin gene. Duchenne is severe; Becker is milder.

Where it fails (form F). Deletions that shift the frame give Duchenne; deletions of a multiple of three keep the frame and give Becker (section 21.3). The frame law of chapter 6 reproduces the split.

Prevention. Genetic counselling.

Layer	Treatment	Standing and evidence
Chain	Corticosteroids	Established. Slower loss of strength.
Chain	Exon skipping to restore the frame	Conditional approval. Small measured gain in dystrophin; clinical benefit not yet shown.
Chain	Gene therapy with a shortened dystrophin	Approved in the USA; the confirmatory trial missed its main goal.

36.3 Huntington's disease and other repeat diseases

What it is. A repeat of the word CAG grows too long in the huntingtin gene. From about 40 repeats the disease is certain. It brings loss of movement, mood and thought in midlife.

Where it fails (form F, S). The ring grows by whole words, as chapter 2 requires. The long uniform run makes the protein clump (S, section 21.3). Longer repeats bring earlier onset.

Prevention. Predictive testing and counselling; preimplantation testing.

Layer	Treatment	Standing and evidence
Chain	Drugs that lower huntingtin; gene therapy	In trials. An antisense drug failed in 2021. A gene therapy reported slower decline in 2025; peer review is awaited.
Phase	Supportive care, exercise	Established for support.

36.4 Spinal muscular atrophy

What it is. Loss of motor neurons in infants from a missing gene, SMN1.

Where it fails (form F, C). The word for a needed protein is missing (F). A backup gene makes too little because of a reading error at a splice site (C).

Prevention. Newborn screening, so treatment starts before symptoms.

Layer	Treatment	Standing and evidence
Chain	Nusinersen and risdiplam, which correct the reading of the backup gene	Established (Finkel, 2017).
Chain	Gene therapy with a working SMN1	Established. Children treated before symptoms reach milestones.

36.5 Phenylketonuria

What it is. An enzyme that breaks down phenylalanine is missing. Untreated, the brain is harmed.

Where it fails (form F, C). A missing step (C) from an error in one gene (F).

Prevention. Newborn heel-prick screening since the 1960s.

Layer	Treatment	Standing and evidence
Surround	A diet low in phenylalanine from birth	Established. Normal development.
Chain	Enzyme substitution; sapropterin	Established in selected patients.

36.6 Down syndrome

What it is. A third copy of chromosome 21. About one in a thousand births. Life expectancy has risen to about sixty years with care.

Where it fails (form F). Chapter 13 derived that a closed ring divides into exactly two closed rings. A chromosome that fails to part in the egg breaks that law (F). Down syndrome is a different way of being, not a disease to cure. What needs care is the conditions that come with it: heart defects, thyroid disease, early dementia.

Prevention. Prenatal screening informs choice.

Layer	Treatment	Standing and evidence
Mesh	Heart surgery in infancy	Established.
Phase	Early support for development; inclusion	Established.

> *Status: Derived (frame law, 6; copy and divide, 13; growth by threes, 2). Reproduces: the Duchenne–Becker frame rule. Measured (burden and treatment). Reading (repeat expansion as uniform seam).*

37. Children

How it works. A child is a form in fast growth. Copying runs at its highest rate. The test is still learning by meeting. The rhythms of sleep and day are still closing. Where Illness Comes From called this the riddle of the children: why do children get cancers adults do not, and why do they survive them more often?

How it fails. Section 21.4 placed forms F and U early in life: copy errors in fast growth under a lenient test. Form O follows where early meeting is too thin. In poor settings the largest killers are infections (U) and carrier failures at birth (C). About 4.8 million children died before age five in 2023 (UN IGME, 2024). Most of these deaths are preventable.

37.1 Deaths before age five

What it is. The leading causes are complications of preterm birth, problems at birth, pneumonia, diarrhoea and malaria.

Where it fails (form U, C). Microbes that a young test cannot yet read (U). Carriers that fail at the seam of birth (C).

Prevention. Vaccines have saved about 154 million lives in fifty years, most of them infants (Shattock, 2024). Breastfeeding, clean water and oral rehydration salts with zinc for diarrhoea.

Layer	Treatment	Standing and evidence
Reading	Childhood vaccination	Established.
Chain	Oral rehydration salts and zinc	Established.
Surround	Clean water, sanitation, food	Established.

37.2 Childhood cancer

What it is. About 400,000 children get cancer each year. More than 80 % are cured in high-income countries; fewer than 30 % in low- and middle-income countries (WHO Global Initiative for Childhood Cancer).

Where it fails (form F, U). Copy errors in growing tissue (F), under a test that is lenient by design during growth (U). Few errors are needed, so the tumours are simple, and simple tumours respond well to treatment.

Prevention. Mostly not preventable. Access to diagnosis and treatment decides survival.

Layer	Treatment	Standing and evidence
Mesh	Chemotherapy, surgery, radiotherapy	Established.
Chain	Targeted drugs for single drivers	Established for some cancers.
Reading	CAR-T cells in relapsed leukaemia	Established.

37.3 Neurodevelopment, allergy and obesity in children

What it is. Attention and autism differences are taken in chapter 42. Allergy and asthma in chapters 24 and 29. Childhood obesity is rising in most countries.

Where it fails (form O, D). A test that met too little (O). Rhythms of sleep, screen light and food that turn against the day (D).

Prevention. Early meeting with foods and microbes; regular sleep; daylight; active play.

Layer	Treatment	Standing and evidence
Phase	Regular sleep and outdoor play	Established as health advice.

> *Status: Reading (forms of failure across the life course, 21.4). Measured (burden and treatment).*

38. Ageing

How it works. Section 19.0a derived that windows alone restore a form only while less than one third of it is wrong. Section 19.0b derived that a repair rhythm must stay within a bound set by the size of the form. Ageing is what happens when repair falls behind that bound for many forms at once.

How it fails. Ageing is form R: drift. Rhythms lose amplitude: deep sleep shortens, the daily swing of temperature and hormones flattens, heart-rate variability falls. Seams accumulate (S). The test thins and slows, so cancers and infections rise (U), and inflammation rises without a target (O). Most people over 65 have two or more chronic diseases (Barnett, 2012).

38.1 Healthy ageing

What it is. Ageing itself is not a disease. The aim is to keep repair within its bound for longer.

Where it fails (form R). Repair falls behind (R). The forms that fail first are those that are used least.

Prevention. In two large American cohorts, five low-risk habits (never smoking, healthy weight, regular activity, moderate alcohol, a healthy diet) added about 12 to 14 years of life expectancy at age 50 (Li, 2018).

Layer	Treatment	Standing and evidence
Phase	Exercise, sleep, social contact, hearing care	Established as risk reduction.
Chain	Metformin, rapamycin and drugs that remove senescent cells	In trials or a direction. No drug has yet been shown to slow human ageing.

38.2 Delirium

What it is. Acute confusion in older people in hospital. It raises the risk of death and dementia.

Where it fails (form D, W). The day is lost: no light, broken sleep, new drugs (D). The mind closes briefly onto a wrong state (W).

Prevention. Orientation, sleep, mobility, hearing and vision aids, hydration. These lowered delirium by about a third in hospital (Inouye, 1999).

Layer	Treatment	Standing and evidence
Phase	Restore the day: light, sleep, movement, familiar faces	Established.

> *Status: Derived (limits of self-repair, 19.0a and 19.0b). Measured (burden and prevention). Reading (ageing as drift).*

39. The surround

How it works. Every body hangs in a surround: air, water, food, light, heat, and other people. The surround is the one layer that acts on everyone at once. Where Illness Comes From called it the layer with the largest numbers and the smallest budgets.

How it fails. The surround snaps the thread (F), lodges fixed forms (S), turns rhythms against the day (D), and feeds the test too little or too much (O). It is a cause, not a form. That is why its cures are counted in whole populations.

39.1 Air pollution

What it is. Outdoor and household air pollution caused about 8.1 million deaths in 2021 (State of Global Air, 2024). It drives heart disease, stroke, COPD, lung cancer and dementia.

Where it fails (form S, U, F). Fine particles lodge in lungs and vessels (S). They keep the test reading (U) and snap the thread (F).

Prevention. Clean energy, clean cooking, traffic rules.

Layer	Treatment	Standing and evidence
Surround	Air quality rules; clean cooking	Established.

39.2 Tobacco

What it is. Tobacco kills more than 7 million users each year, and about 1.3 million non-smokers through second-hand smoke (WHO).

Where it fails (form S, F, U). Smoke lodges (S), snaps the thread (F) and inflames (U) in every organ it reaches.

Prevention. Stopping before age 40 avoids about 90 % of the excess risk of death (Jha, 2013).

Layer	Treatment	Standing and evidence
Surround	Taxes, smoke-free laws, plain packs, advertising bans	Established.
Chain	Varenicline; nicotine replacement	Established.

39.3 Alcohol

What it is. Alcohol caused about 2.6 million deaths in 2019 (WHO, 2024).

Where it fails (form S, F, W). Alcohol damages liver, heart and brain (S, F). Dependence is taken in chapter 42 (W).

Prevention. Price, availability and marketing rules.

Layer	Treatment	Standing and evidence
Surround	Minimum unit pricing; limits on sales	Established.

39.4 Light, night and shift work

What it is. Night shift work is classed as probably carcinogenic to humans (IARC, 2019). Light at night and irregular sleep are linked to diabetes, obesity and depression.

Where it fails (form D). Rhythms turned against the day (D). Opposite directions never join (chapter 4).

Prevention. Daylight in the morning; dark at night; forward-rotating shift rosters.

Layer	Treatment	Standing and evidence
Phase	Shift design; light and sleep hygiene	Established as advice; outcome trials are few.

39.5 Loneliness

What it is. Strong social ties raised the odds of survival by about 50 % in a meta-analysis of 148 studies (Holt-Lunstad, 2010).

Where it fails (form D, R). A person is a form among other forms. Contact is a carrier between them. Without it rhythms drift (D, R).

Prevention. Social contact through life.

Layer	Treatment	Standing and evidence
Surround	Community and social prescribing	In trials.

> *Status: Measured (burden and prevention). Reading (the surround as cause of each form).*

Part VIII — The mind and its disorders

Part V computed the laws of the mind: reading, holding and slipping. This part applies them to illness. Depression remains the worked case, with its own measured data and derivation (chapters 40 and 41). Chapter 42 then takes every other major disorder of the mind in the form of the atlas.

40. Depression, measured

Depression is the worked case of this book. It is a persistent instability of mood, energy, sleep and thought. Its global prevalence is 5.2 per cent of adults (WHO, 2026). This chapter holds only measured data. Most of it comes from a new re-analysis made for this book.

40.1 A re-analysis of the open trial data

The largest comparison of antidepressants (Cipriani and colleagues, Lancet, 2018) published its trial data openly as the GRISELDA dataset. For this book the data were re-analysed from the arm level with a random-effects network meta-analysis. It reproduces the published results closely: amitriptyline odds ratio 2.10 (published 2.13), reboxetine 1.34 (1.37); dropout for agomelatine 0.84 (0.84) and fluoxetine 0.88 (0.88).

Quantity	Value	Basis
Response without a drug (placebo)	35.9 % (34.7–37.0)	273 trials, 27,724 people
Response with a drug	52.6 % (51.4–53.7)	473 trials
Share of drug-arm response also reached on placebo	72 %	ratio of mean rates
Dropout on placebo	28.7 %	265 trials
Placebo response per extra week of trial	+0.056 logit (z 2.4)	independent of trial year
Placebo response per decade	+0.108 logit (z 2.7)	independent of duration
Drug–placebo difference per decade	−2.9 points (z −3.3)	216 trials
Drug–placebo difference per point of baseline severity	+0.6 points (z 1.9)	HAMD-17 trials only; borderline
Odds ratio range across 21 drugs	1.34 (reboxetine) to 2.10 (amitriptyline)	network meta-analysis
Share of between-drug spread that is real	31 % (efficacy), 23 % (dropout)	rest is sampling noise

Three facts stand out. Most recovery in drug trials happens without the drug. Recovery without the drug grows with time. The drugs differ from each other far less than from placebo.

Twenty features of the molecules and their binding were tested against efficacy and dropout, with a correction for the whole search. Nothing survived. With only 31 per cent of the spread real, no predictor could have reached significance with 21 drugs.

40.2 Sleep and heart

- Drug-free and comorbidity-free depressed patients have a shorter time from sleep onset to the first REM sleep (REM latency) and a higher REM density than controls: 46 REM-latency measurements (Arıkan and colleagues, Sleep Medicine Reviews, 2024).
- In one small study, REM latency was 60.9 minutes in 26 depressed inpatients against 73.9 in 8 controls (not significant), and the time to the first awakening was 122.8 against 304.1 minutes (significant) (Machowski and colleagues, 1989).

- Heart-rate variability is lower in unmedicated depression: HF-HRV g = −0.32, RMSSD g = −0.46, over 21 studies with 2,250 patients (Koch and colleagues, Psychological Medicine, 2019).
- SSRIs, SNRIs and activating tricyclics lengthen REM latency and suppress REM sleep. Sedating antidepressants such as mirtazapine and trazodone have little or no effect on REM sleep (Wichniak and colleagues, 2017). Both groups work about equally well.

40.3 Treatments that act on time

- One night of sleep deprivation brings rapid improvement in about 45 to 50 per cent of depressed patients, within 24 hours; 66 studies over 36 years (Boland and colleagues, 2017).
- Bright light: effect size 0.53 (0.18–0.89) in non-seasonal depression, three studies; 0.84 in seasonal depression (Golden and colleagues, 2005).
- Triple chronotherapy (36 hours awake, four days of advancing the sleep phase, six months of morning light), pilot trial with 82 outpatients: response 52 against 18 per cent at one week, 70 against 22 per cent at 26 weeks (BJPsych Open, 2021).
- Slow tapering of antidepressants with psychological support protects against relapse about as well as continuing: 76 trials, 17,379 adults (Zaccoletti and colleagues, Lancet Psychiatry, 2026).

> *Status: Measured. The re-analysis is computed on measured data with standard statistics, not with the theory.*

40.4 A new test: does the day close in depression?

Chapter 19 makes the day the one rhythm the body must close from outside. If depression is a failure of that closure, it should show in how the body's activity returns from one day to the next.

Data. The open Depresjon dataset (Garcia-Ceja and colleagues, 2018): wrist activity per minute for 23 people with depression, with MADRS scores at start and end, and 32 controls. Only whole days were used: a median of 14 days per patient and 18.5 per control.

Tests fixed before the analysis. D1: the stability of the day across days (IS) is lower in depression. D2: the correlation of minute activity with itself 24 hours later is lower. D3: breaks from hour to hour (IV) are more frequent. D4: the day's amplitude (RA) is smaller. D5: within the patients, lower IS goes with a higher MADRS. D6: patients whose IS rises over the recording improve more.

Test	Depressed (median)	Control (median)	p (one-sided)	Outcome
D1 stability IS	0.350	0.281	0.97	Miss (opposite)
D2 return after 24 h	0.157	0.217	0.005	Hit
D3 breaks IV	0.775	0.763	0.21	Miss
D4 amplitude RA	0.868	0.870	0.48	Miss
D5 IS against MADRS	ρ = +0.47		0.025 (wrong sign)	Miss (opposite)
D6 rise of IS against fall of MADRS	ρ = −0.15		0.50	Miss

One prediction holds. Minute by minute, a depressed person's activity returns less after exactly one day. The other five fail, and two fail in the opposite direction: the mean day of patients is more stable, and more so the more severe they are.

Pooled data point the other way on D1 and D4. A meta-analysis of 53 studies with 11,115 participants found lower interdaily stability in depression (standardised mean difference −0.17) and a smaller daily amplitude (−0.33) (Ho and colleagues, Journal of Affective Disorders, 2024).

The Depresjon sample is small and partly from a ward. Its misses on D1 and D4 should be read against that larger result. The hit on D2 agrees with its direction.

A check made after the tests, and marked as such: the more severe patients were mostly inpatients (median MADRS 27 against 22). Their mean day had IS 0.40 against 0.33 for outpatients. A ward imposes a fixed day. That would raise the stability of the mean day without restoring the return of the person's own activity. This is a reading and needs a dataset with only outpatients to test.

The two measures differ in what they read. IS asks whether the average day has a shape. The 24-hour return asks whether this minute's activity comes back at the same minute tomorrow. In depression the shape may be held from outside while the return from inside is weaker.

> *Status: Measured data, computed test (day_depth.py). D2 passes; D1, D3–D6 fail; D1 and D5 in the opposite direction. The inpatient account is a post-hoc reading. The pooled result of Ho and colleagues (2024) favours the direction of D1 and D4.*

41. Depression, read

This chapter sets the measured facts of chapter 40 beside the laws of chapter 21. Every sentence here is a reading.

The day as the place of failure. The day is the one rhythm without a ring (chapter 19). Sleep must be placed in it. Short REM latency and early first awakening say that the first sleep cycle starts and ends too early. On the ladder, REM latency moves from position 40.80 (73.9 min) to 40.62 (60.9 min), away from ring 41; the first awakening moves from 42.08, near ring 42, to 41.26. In the language of chapter 21 this is the failure of direction: the body's inner rhythm runs against the imposed day.

The body closes by itself. Thirty-six per cent recover without a drug, and more with every week. That is the test of chapter 17 doing its work, slowly. A drug adds about seventeen percentage points. In this reading drugs speed up a closure the body makes itself. They do not cause it. That would explain why twenty drugs with different entry points work about equally well.

Fast closure by skipping the day. Thirty-six hours awake sit at position 43.87, near ring 44: one full step above the untempered day. The improvement comes within a day. It is usually lost after recovery sleep, when the old placement returns. Holding the new placement with an advanced sleep phase and morning light keeps the gain in the one pilot trial.

What the new tests add. Three tests were run on the body for this book (sections 18.2, 19.1 and 40.4). Closure between heart and breath belongs to deep rest and is absent in REM. The night tends to end after a cycle has closed. And in depression the body's own activity returns less after one day. Read together: depression shortens the time to REM, so less of the first night is deep, closed rest; and the day returns less from inside. Both are failures of closure in time, not of any one number. This is a reading; it joins two tests on different people.

What the reading cannot do. It cannot say why an episode starts. It cannot compute the mood. It cannot explain why sedating drugs work as well as REM-suppressing ones. The sleep numbers rest on one small study. The ladder does not select at group level (chapter 18). Each of these is a limit, and chapter 48 turns the reading into tests.

> *Status: Reading throughout.*

41.1 Depression, derived

Section 19.0 computed the cost of waking. A body that runs in the day's direction can wake without leaving anything open. A body that runs against the day leaves at least one open window at every waking. The program followed both bodies for 60 days, with and without cure.

Course	Open windows day 10	Day 29	Day 60	Changes spent
Healthy: same direction	0	0	0	0
Against the day, untreated	10	29	60	0

Course	Open windows day 10	Day 29	Day 60	Changes spent
Against the day, repaired daily, repair stops on day 30	0	0	31	29
Against the day, direction restored once on day 10	9	9	9	18

Four laws follow from the count.

- A body against the day opens one window every day. Untreated, the openings pile up without limit. That is a persistent instability that grows with time.
- Daily repair at the seam keeps the body closed, but only while it lasts. It costs one change a day. When it stops, the openings start again from that day.
- Restoring the direction costs 18 changes once, for a living strand of 27 steps: two of every three places. After that no new openings arise, and nothing more needs to be spent. It does not undo the openings made before; those still need repair at their place.
- Coupling to the day alone cures nothing: a closed day strand added to an opened body leaves the same 3 open windows (section 16.2). The best course follows: repair the openings where they are, and restore the direction once. Then the body stays closed without further cost.

Section 19.0a adds the step that makes depression last. When unrepaired openings pass one third of a form, self-repair closes it onto the opposite direction or onto a uniform ring. That state is closed. The body's own test reads it as healthy, so nothing inside the body corrects it. In this count, a depressive episode is a wrong closure: stable because it is closed, and set off when openings pile up past the limit, for instance through lost sleep or long strain.

Three consequences follow. First, the body cannot leave a wrong closure by itself; it needs a reader from outside that carries the right form (section 20.1: a reader that meets finds what windows cannot). Second, the way out costs a fixed amount once: 18 of 27 places for the opposite direction. Third, the uniform wrong closure is a flat, fixed state, which is the form of the flat mood and the rigid day of severe depression; section 40.4 found the most severe patients with the most rigid mean day.

> *Status: Derived (sleep_derive.py Q3 with depression_derive.py). Reading: the episode as a wrong closure; the match with section 40.4.*

Measured treatment of depression shows the same shape. Antidepressants work while taken; relapse after stopping is common, and a slow taper with support protects about as well as continuing (chapter 46). Treatments that change how the person runs through the day, such as chronotherapy with a fixed wake time and morning light, or psychotherapy, keep their effect better after they end. Light alone helps only part of the patients. Each match is a reading. The count gives the number of changes a cure must make (18 of 27 to restore direction), and section 45 derives the period: more than half of them within one night's repair cycle.

> *Status: Derived (depression_derive.py, E0–E3). Reading: the match with maintenance, relapse and lasting treatments.*

42. The other disorders of the mind

How it works. Section 20.1 computed the laws of reading: one error gives three open windows but only one misfit for a mirror reader, and one reader fits one strand. Section 20.2 computed what a mind can hold: about three quarters of its own size in deviation while it stays itself. It also computed where a mind slips when it does not hold. The nearest other states are not shifted copies. They are the reversal and the flattening: 18 of 27 places away. Section 19.0a showed that a form pushed past one third wrong closes onto one of these and is read as healthy.

How it fails. This gives the disorders of the mind a short map. A flattening is a uniform wrong closure: the flat mood and fixed day of severe depression (chapter 41). A reversal is a closure

onto the opposite direction: the switch of bipolar disorder. A false alarm is the test reading a fit as a misfit (O): anxiety. A loop that cannot close keeps reopening its own window: obsession and trauma memory. A misattribution reads one's own signal as foreign: psychosis. A new closure built around an outside carrier is addiction. Each entry below is a reading. The treatments are measured. In this chapter more than any other the reading is a hypothesis. Mental disorders are counted in hundreds of millions: about one in eight people lived with a mental disorder in 2019 (WHO).

42.1 Bipolar disorder

What it is. Episodes of depression alternate with mania or hypomania. About 40 million people were affected in 2019 (WHO).

Where it fails (form W (reversal), D). Section 20.2 computed that the nearest other state of a form is its reversal. Mania is read here as the reversal; depression as the flattening. Sleep loss is a known trigger of mania (Wehr, 1987). That fits section 19.0a: openings pile past one third and the form closes onto a wrong state.

Prevention. Regular sleep and daily rhythm; early treatment of first episodes.

Layer	Treatment	Standing and evidence
Chain	Lithium	Established. Lowers relapse and suicide (Cipriani, 2013).
Chain	Mood stabilisers and some antipsychotics	Established.
Phase	Interpersonal and social rhythm therapy: fixed times for sleep, meals and contact	Established. Longer time well (Frank, 2005).
Phase	Protecting sleep in early mania	Established as clinical advice.

42.2 Anxiety disorders

What it is. Generalised anxiety, panic, social anxiety and phobias. About 301 million people were affected in 2019, the most common mental disorders (WHO).

Where it fails (form O, W). The test reads a safe form as a threat: a false alarm (O). Avoidance prevents the new reading that would correct it, so the alarm closes into a stable loop (W).

Prevention. Early help in childhood; exercise.

Layer	Treatment	Standing and evidence
Phase	Cognitive behavioural therapy with exposure	Established.
Phase	One-session treatment for specific phobia	Established. Two to three hours in one session work about as well as several sessions (Öst, 1989; Zlomke, 2008). This matches the dose law of chapter 45.
Chain	SSRIs and SNRIs	Established.

42.3 Post-traumatic stress disorder

What it is. After a terrifying event, the memory returns unbidden, with avoidance and constant alertness. About 3.9 % of people develop it in their lifetime across 24 countries (Koenen, 2017).

Where it fails (form U, W). The memory stays an open form that is not read and filed (U). It reopens by itself, in waking and in sleep. The alert state closes into a loop (W).

Prevention. Safety and support after trauma. Single-session debriefing does not prevent PTSD.

Layer	Treatment	Standing and evidence
Phase	Trauma-focused therapies: prolonged exposure, cognitive processing therapy, EMDR	Established.
Phase	Intensive delivery over one or two weeks	Established in several centres. Results about as good as weekly therapy, with fewer drop-outs.
Chain	SSRIs	Established, smaller effect.
Chain	Prazosin for nightmares	Tested and failed in a large trial (Raskind, 2018).

42.4 Obsessive-compulsive disorder

What it is. Unwanted thoughts and the acts that try to undo them. About 2 % of people are affected in their lifetime (Ruscio, 2010).

Where it fails (form W). Each check is a reading that never gives +1. The window reopens at once, so the loop never closes (W).

Prevention. None proven.

Layer	Treatment	Standing and evidence
Phase	Exposure and response prevention	Established.
Phase	Concentrated four-day treatment (the Bergen model)	In trials. About nine in ten responded and most stayed well (Hansen, 2019). This matches the dose law of chapter 45.
Chain	SSRIs	Established.
Mesh	Deep brain stimulation in severe, resistant cases	Established in specialist centres.

42.5 Schizophrenia and psychosis

What it is. Hallucinations, fixed false beliefs and disordered thought. About 24 million people are affected (WHO, 2022). Life is shortened by about fifteen years.

Where it fails (form O, U). One's own inner signals are read as coming from outside. A theory of self-monitoring proposed this decades ago (Frith, 1992). In the language of chapter 17, a fit form is read as foreign: the mind's own form of over-reading (O). Daily use of high-potency cannabis raises the risk (Di Forti, 2019).

Prevention. Avoiding high-potency cannabis in youth. Early detection services.

Layer	Treatment	Standing and evidence
Chain	Antipsychotic drugs	Established. Relapse at one year about 27 % on drug against 64 % on placebo (Leucht, 2012).
Chain	Clozapine when other drugs fail	Established.
Phase	Cognitive behavioural therapy for psychosis; family intervention; supported work	Established.

42.6 Eating disorders

What it is. Anorexia nervosa, bulimia nervosa and binge eating disorder. Anorexia has one of the highest death rates of any mental disorder (Arcelus, 2011).

Where it fails (form W). A rigid control loop closes and is read as right by the person (W). The body's own signals no longer correct it.

Prevention. Early recognition.

Layer	Treatment	Standing and evidence
Phase	Family-based treatment for adolescents	Established.
Phase	Enhanced cognitive behavioural therapy for adults	Established.

42.7 Addiction

What it is. About 400 million people live with alcohol use disorders (WHO, 2024). Opioid overdose deaths rose sharply in North America. Tobacco dependence is the deadliest addiction (chapter 39).

Where it fails (form W, C). A substance acts as a carrier from outside. The body rebuilds its rhythm around it and closes on that new form (W). Withdrawal is the open window of the old form. Section 16.4 says a carrier must decay to deliver: a drug taken again and again is a carrier that does not decay.

Prevention. Price, availability and marketing rules; prescribing control of opioids.

Layer	Treatment	Standing and evidence
Chain	Methadone or buprenorphine for opioid dependence	Established. Death during treatment is much lower than out of it (Sordo, 2017).
Chain	Naltrexone, acamprosate for alcohol; varenicline for tobacco	Established.
Phase	Contingency management; mutual-help groups	Established.
Surround	Naloxone in the community	Established. Reverses overdose.

42.8 ADHD

What it is. Lasting inattention, restlessness or impulsivity. About 5 % of children and 2 to 3 % of adults.

Where it fails (form D). Read here as a difference of timing: the reader closes on its strand for shorter stretches (D). It is a difference that becomes a disorder when the surround demands long closure.

Prevention. Not applicable as a disease. Support in school and work.

Layer	Treatment	Standing and evidence
Chain	Stimulants (methylphenidate in children, amphetamines in adults)	Established (Cortese, 2018).
Phase	Parent training; structure; sleep	Established.

42.9 Autism

What it is. A different way of perceiving and relating, present from early childhood. About one child in a hundred worldwide (WHO).

Where it fails (form None: a way of reading). Autism is not read here as a failure. Section 20.1 found that one reader fits one strand. A reader that fits fewer strands more exactly is a style of reading. Care is needed for conditions that often come with it: anxiety, epilepsy, poor sleep.

Prevention. Not applicable.

Layer	Treatment	Standing and evidence
Phase	Early communication support; adapted surroundings	Established.
Chain	Melatonin for sleep problems	Established in children (Gringras, 2017).

42.10 Insomnia and other sleep disorders

What it is. Chronic insomnia affects about one adult in ten. Narcolepsy type 1 follows the loss of orexin-making cells.

Where it fails (form D; O and C in narcolepsy). Insomnia is a rhythm that will not close at night (D). In narcolepsy the test destroys the cells that make the waking carrier orexin (O, C). Cases rose after one 2009 flu vaccine in some countries (Partinen, 2012).

Prevention. Regular sleep times; morning light; dark nights.

Layer	Treatment	Standing and evidence
Phase	Cognitive behavioural therapy for insomnia	Established first-line treatment (American College of Physicians, 2016).
Chain	Sleep medicines	Short-term use only. Section 46.1 found no gain in closure.
Chain	Sodium oxybate; orexin-receptor agonists in narcolepsy	Oxybate established; orexin agonists in trials with large effects.

42.11 Personality disorders

What it is. Lasting patterns of feeling and relating that cause suffering. Borderline personality disorder brings unstable mood and self-harm.

Where it fails (form W, D). Unstable closure: the form swings between states without settling (W, D).

Prevention. Early support for young people at risk.

Layer	Treatment	Standing and evidence
Phase	Dialectical behaviour therapy	Established. Fewer suicide attempts and less self-harm (Linehan, 2006).

> *Status: Derived (reading, holding and slipping, 20.1 and 20.2; wrong closure, 19.0a). Measured (burden and treatment). Reading (every naming of a disorder as a form). The reading of the mind is the least tested part of this book.*

Part IX — How to cure

43. Cure rules from the algebra, depth by depth

Chapter 5 computed that an error in a closed form opens exactly three windows, and that exactly one single change closes them again. Chapter 4 computed that uniform and mixed never join, and that opposite directions never join. Four design rules follow. The rules are derived. Their use on a body is a reading, and each is matched to a measured practice where one exists.

Rule	From the algebra	Body practice (measured where cited)
1. Read before you act	The error sits where three open windows overlap; only there does a single change close it.	Measure the person's state before treatment: sleep timing, rhythm, mood course. The author's device rule 'read the state first'.
2. Restore, do not add	The one closing change restores the original value. Any other single change leaves the form open.	Treatments that return a lost rhythm (sleep regularity, behavioural activation) rather than add a foreign one.
3. Match the direction	Opposite directions never join.	Time the cure to the person's phase: morning light, a fixed wake time, dosing at a fixed hour.
4. Living with living	Uniform never joins mixed.	Prefer cures that move with the body (activity, rhythm, contact) over fixed inputs alone; taper slowly rather than stop abruptly.

The same algebra gives one cure rule per depth. The rule is computed. The matching repair process in living matter is measured; the match is a reading.

Depth	Cure computed from the rules	Measured repair that matches (reading)
Word	Fix the frame once, at the first word, and read every later word relative to it (N3).	The start codon sets the reading frame for the whole protein.
Chain	Undo the error at the one place where three open windows overlap; use the original value.	Mismatch repair restores the original base, using the old strand as the template.
Cell	Copy through the unique partner, keep one old strand in each copy.	Semi-conservative replication with proofreading.
Tissue	Return every unit to the one word and phase of its neighbours.	Renewal of a tissue from its own stem cells, in register.
Organ and body	Restore the carrier across the seam.	Restoring blood flow, nerve conduction or a missing hormone.
Rhythm	Re-place the body in the day; match the direction.	Fixed wake time, morning light, chronotherapy (chapter 46).

> *Status: Derived (the algebra). Reading (the translation to practice).*

44. The treatment ladder

Chapter 43 gave four cure rules from the algebra. Parts VII and VIII placed every disease under one or more of eight forms of failure. This chapter joins the two. It orders cure by layer, as Where Illness Comes From did. Each layer acts at one depth of the body. Each fits some forms of failure and not others.

Layer	What it does	Forms it fits	Cure rule (ch. 43)	Examples from Parts VII and VIII
Mesh	Remove, rebuild, replace tissue	S, C, U	Read before you act	Angioplasty, thrombectomy, surgery, transplant, cataract surgery, antibiotics
Chain	Close or restore one molecular step	C, F, U	Restore, do not add	Insulin, thyroxine, statins, imatinib, CFTR modulators, antivirals, gene therapy
Reading	Correct the body's test in the right direction	U, O	Read the direction first (21.2)	Vaccines, checkpoint inhibitors, biologics, CAR-T reset, immunotherapy for allergy
Phase	Restore rhythm and step; let the body close itself	D, W, R	Match the direction; living with living	Exercise, sleep, light, chronotherapy, rehabilitation, psychotherapy, pacing
Surround	Change what everyone is exposed to	All, as cause	Prevent the opening	Tobacco control, clean air, vaccines for all, fortification, water, salt policy

Three laws follow from the table. Each is derived. Each is matched to measured medicine as a reading.

- **A layer cures only the forms it fits.** A mesh cure applied to a phase failure does nothing. Keyhole surgery on a worn knee did no better than sham surgery (chapter 34). Opioids did no better than simpler drugs for chronic pain, a wrong closure (chapter 31). A chain cure for a phase failure helps only while it is given: weight returns after semaglutide is stopped (chapter 25).
- **A reading cure works in one direction only.** Raising the test helps cancer and infection and can cause autoimmunity. Lowering it helps autoimmunity and allergy and can cause infection (section 21.2). The direction must be read before the dose is given.
- **A wrong closure needs a reader from outside.** Section 41.1 derived that the body cannot leave a closed wrong state by itself, because its own test reads it as healthy. Every effective treatment of a W-form brings an outside reader that carries the right form: a therapist in exposure, a fixed schedule in chronotherapy, a stimulator in deep brain stimulation, a family in family-based treatment. The outside reader must then make enough change within one repair cycle (chapter 45).

The ladder also gives an order of trust. A patient today is treated with what stands. In the atlas each treatment carries its standing. Established means proven in controlled trials and in use. In trials means a result exists that is not yet settled. A direction means the map points there and no trial has tested it.

Counted over the atlas, the five layers are not used evenly. Of the established treatments listed in Parts VII and VIII, most are mesh and chain. The largest effects on whole populations are surround measures: vaccines, tobacco control, clean water, iodised salt, folic acid. The phase layer is the least used, yet it is the only layer that fits the forms D, W and R. Those are the forms of ageing, of most mental disorders, and of the chronic diseases of rhythm. This is where Where Illness Comes From placed the frontier of medicine. The map of this book places it there too.

> *Status: Derived (the cure rules, 43; the two directions of the test, 21.2; the need for an outside reader, 41.1). Reading (the assignment of layers to forms and the examples). Measured (the trials cited in Parts VII and VIII).*

45. The dose of a cure, exact

Section 41.1 counted what a cure must change: 18 of 27 places to turn a form back to the right direction. Section 5.1 proved that this is the minimum. Section 19.0a showed that the body repairs itself by moving to the nearest closed form. So a cure works against the body's own repair. That repair takes place once in every repair phase: once a night. The question is what happens when a cure has made k of the 18 changes and the repair phase comes.

The first edition answered by simulation, with 3,000 random trials per line. A reviewer asked for an exact answer. Proof 4 of section 5.1 gives it for an aimed cure. After k aimed changes the form is k places from the old closure and 18 − k from the new one. Every other closed form is farther. Repair goes to the nearest. The program cure_exact.py adds the case of a cure in which a quarter of the changes miss their target and set the third value. It sums over every case with exact fractions. No sampling is used.

Changes made before the repair phase (of 18)	Aimed cure: ends at the new form	Aimed: back to the old form	75 % aimed: ends new	75 % aimed: back to old	75 % aimed: other closed form
0 to 8	0	1	0	1	0
9 (half)	½ (tie)	½ (tie)	0.038	0.962	0
10	1	0	0.385	0.615	0
11	1	0	0.799	0.196	0.004
12 (two thirds)	1	0	0.959	0.013	0.028
13 to 14	1	0	0.976	0	0.024
15 to 16	1	0	0.983	0	0.017
17 to 18	1	0	0.988	0	0.012

The law is sharp and now exact. An aimed cure with fewer than half of its changes made when the repair phase comes is undone completely. At exactly half the outcome is a tie. Past half, the body's own repair completes the cure. An imprecise cure must go further. With a quarter of its changes off target it needs two thirds of the changes (12 of 18) for a 96 % chance. A small share of imprecise cures lands on a third closed form, neither old nor new. The first edition's simulation gave 51 % at the half; the exact value is a tie of one half.

This gives the dose and the period without the concept of energy. The period of a cure is the body's repair cycle, one day. The dose is the share of needed changes made within one such cycle: more than half for a precise cure, about two thirds for an imprecise one. A cure that spreads its changes thinly over many days is undone every night. It helps only while it is renewed, and the old form returns when it stops.

45.1 The dose law across the atlas

Measured treatment shows this form in several places. Each match is a reading.

- **Depression.** One night of sleep deprivation improves about half of patients within a day. The gain is usually lost after the next sleep. Holding the new placement with phase advance and morning light keeps it (chapter 40). Antidepressants help while taken; relapse after stopping is common (chapter 46).
- **Specific phobia.** One session of two to three hours works about as well as several weekly sessions (chapter 42).
- **Obsessive-compulsive disorder and PTSD.** Concentrated treatment over four days or two weeks gives results at least as good as weekly therapy (chapter 42).
- **Obesity.** A drug that changes intake only while it is given is undone when it stops: two thirds of the weight returned within a year (chapter 25).
- **Type 2 diabetes.** A large, fast weight loss in a few months brought remission in nearly half of patients (DiRECT, chapter 25). Slow, small losses rarely do.

The law also predicts something not yet measured. A cure is lasting when the change made before one night passes a threshold, and not when the same change is spread out. That is test T14 for depression, and T21 for the other W-forms.

> *Status: Derived and exact (cure_exact.py; proof 4 in 5.1). Replaces the simulation of the first edition. Reading: the matches with sleep deprivation, one-session and concentrated therapy, drug withdrawal and rapid weight loss. Predicted: T14, T21.*

46. Cures for depression with evidence

The list below is ordered by strength of measured evidence. It is drawn from the depression entry of Where Illness Comes From and from the sources of chapter 40. The last column gives the cure rule of chapter 43 that each treatment fits. That column is a reading. Chapter 45 adds the exact dose law that fits the time course of these treatments.

Treatment	Measured evidence	Fits rule
Antidepressants	All 21 beat placebo; pooled odds ratio about 1.66; differences between drugs small (Cipriani 2018; re-analysis in chapter 40).	Speeds the body's own closure
Exercise	Walking or jogging g = −0.62; yoga −0.55; strength −0.49 (Noetel 2024, BMJ).	2, 4
Behavioural activation	Non-inferior to CBT in 440 patients, about 21 % cheaper (Richards 2016, Lancet).	2
Cognitive behavioural therapy	Effect sizes comparable to drugs; effects persist better after stopping.	1, 2
Treating insomnia (digital CBT-I)	Reduces incident depression in randomised trials.	3
Fixed sleep and wake times, morning light	Light: 0.53 non-seasonal, 0.84 seasonal (Golden 2005).	3
Sleep deprivation with phase advance and light	52 % vs 18 % at one week, 70 % vs 22 % at 26 weeks, pilot n = 82.	1, 3
Slow taper with support	About equal to continuing (Zaccoletti 2026).	4
Electroconvulsive therapy	Largest effect in severe and treatment-resistant depression.	—

No cure in this list was found by the theory. The theory supplies one thing: a reason why so many different routes help. All of them either speed the body's own closure or restore its placement in the day.

Nothing in this chapter is medical advice. Any change of treatment belongs with the person's own doctor.

> *Status: Measured (evidence). Reading (fit to the rules).*

46.1 A test of cure rule 2: does a sleeping pill restore closure?

Cure rule 2 says: restore, do not add. Chapter 5 computed that the one change that closes an open form gives back the original value. An added input closes nothing. A sleeping pill adds an input. So it should not restore the closure found in section 19.1.

Data. The telemetry part of Sleep-EDF: 22 people with mild difficulty falling asleep. Each slept one night on temazepam and one on placebo, in random order.

Tests fixed before the analysis. C1: on placebo the night ends just after a closed cycle less often than in healthy sleepers (37.3 per cent, section 19.1). C2: temazepam does not raise that share. C3: temazepam does not raise the share of deep sleep. C4, a check: temazepam shortens the time to sleep. Without C4 the test cannot show that the drug did anything at all.

Test	Placebo	Temazepam	p	Outcome
C1 night ends ≤ 30 min after a REM end	13 of 22 = 59 %		0.99 against 37 %	Miss (opposite)
C2 same share, drug against placebo	59 %	55 % (6 better, 7 worse)		Consistent
C3 share of deep sleep	0.174	0.182	0.79	Consistent
C4 time to first sleep (check)	10.8 min	9.8 min	0.29	Miss

C1 fails. These poor sleepers ended the night after a closed cycle more often than healthy sleepers, not less. One cause may be the setting: they slept in hospital, where waking time may have been set. C2 and C3 agree with the rule: the pill did not raise closure or deep sleep. But C4 also fails. In these hypnograms the pill did not even shorten the time to sleep. A test that cannot show the drug's own effect cannot show its absence either. So C2 and C3 are counted as consistent, not as hits. The rule needs a larger set with a clear drug effect.

> *Status: Measured data, computed test (st_cure.py). C1 fails; C2 and C3 consistent but not informative because the check C4 fails.*

47. Prevention first

Every entry of the atlas ended with prevention. Set side by side, the entries show one pattern. The largest effects at the lowest cost come before the first opening. The rules say why. Proof 2 of section 5.1 shows that one error has one repair: the undo at its own place. Chapter 21 counted that repair at the right place keeps a ring fully closed, while repair at a random place barely helps. Prevention is the limit of this law: no error, no repair needed. Section 19.0a adds that a form past one third wrong closes wrongly and cannot return by itself. Prevention keeps forms below that limit.

Measure	Effect (measured)	Forms prevented	Chapter
Vaccination of children	About 154 million lives saved in fifty years	U	28, 37
HPV vaccination before 17	88 % less invasive cervical cancer	U, F	30
Hepatitis B vaccination at birth	Less liver cancer in vaccinated children	U, S	28
Stopping smoking before 40	About 90 % of the excess risk of death avoided	S, F, U	39
Lifestyle change in people at risk of diabetes	58 % fewer new cases	C, D, S	25
Folic acid before conception	72 % fewer neural tube defects	F	35
Peanut in infancy for infants at risk	About 80 % less peanut allergy	O	29
Food support for households of TB patients	39 to 48 % less TB	U	28
Daily sunscreen	Half as many new melanomas	F	30
Salt substitute in villages	14 % fewer strokes	S, C	22
Low-dose aspirin in high-risk pregnancy	62 % less preterm pre-eclampsia	C	35
Time outdoors in school	Less new myopia	D	32
Fourteen risk factors for dementia	About 45 % of dementia attributable	S, U, R	31
Five healthy habits at 50	About 12 to 14 more years of life	R	38

Three rules for prevention follow from the laws. First, guard the seams: keep fixed forms out of living tissue (smoke, particles, excess fat and salt). Second, keep the direction: live with the day, not against it. Third, train the test by meeting: vaccines and an ordinary, varied early life. Each rule is a reading of a derived law. Each is matched by the measures in the table.

> *Status: Derived (repair at the place, 21 and 5.1; limit of self-repair, 19.0a). Measured (the table). Reading (the three rules for prevention).*

48. Tests fixed before data

Tests T1 to T14 were fixed on 11 November 2026 and tests T15 to T21 on 12 November 2026, before their data were looked at. Each names the measurement and the result that refutes it.

Test	Prediction	Refuted if
T1	In one person, REM latency moves towards about 92 minutes (ring 41) as the episode resolves.	Recovery without any shift of REM latency.
T2	Across treatments, response is better the closer REM latency ends to about 92 minutes; overshoot beyond about 160 minutes adds nothing.	No relation between response and distance to 92 minutes.
T3	The time to first awakening moves back towards about 4.6 hours (ring 42) on recovery.	No change in time to first awakening.
T4	Chronotherapy aimed at a first sleep cycle of about 92 minutes beats equally intensive chronotherapy without that target.	Equal outcomes.
T5	Heart–breath locking in deep sleep is weaker in depression than in healthy sleepers (revised after section 18.2 found no locking in REM).	Equal locking excess in deep sleep.
T6	Drugs taken as a single mirror form rank higher in long-term efficacy than racemates (van Haaren 2026 ranking).	Spearman not significant at 0.05/3.
T7	A lower share of tetrahedral atoms goes with better long- term efficacy.	As T6.
T8	Drugs with a closed ten-passage ring set rank higher in long- term efficacy.	As T6.
T9	In the cell, a misfit is removed only after it is read: blocking the reading step raises unread misfits, not removed ones.	Misfits fall when reading is blocked.
T11	In outpatients only, the 24-hour return of activity is lower in depression and rises on recovery.	No difference, or no rise on recovery.
T12	Waking at the end of a REM period (cycle closed) gives better mood that day than waking at a random time.	No difference in a within-person crossover.
T13	In depression, the final awakening does not cluster at the end of a sleep cycle, unlike in healthy sleepers (derived in 19.0).	Clustering at cycle ends equal to healthy sleepers.
T14	A depression cure has a lasting effect only when most of its change is made before one night of sleep; the same total spread over many days relapses when stopped.	Equal lasting effect for concentrated and spread delivery of the same treatment.
T10	Any code built by a living system on a four-letter alphabet with words of three carries at most twenty meanings plus stop signals.	A natural or evolved code of this form with more than twenty meanings.

Test	Prediction	Refuted if
T15	Heart–breath locking in deep sleep is lower in people with atrial fibrillation than in age-matched controls in sinus rhythm (form D).	Equal locking excess in deep sleep.
T16	Manic episodes in bipolar disorder follow a night with at least one third less sleep than the person's usual more often than chance (19.0a: past one third, a form closes onto its reversal).	No excess of short nights before manic onset in within-person sleep records.
T17	Drug-free remission after a reset of the test (CAR-T or stem-cell transplant) in autoimmune disease lasts without maintenance in at least two thirds of patients at two years (41.1: restoring the form once costs nothing afterwards).	Relapse in more than one third by two years.
T18	Backward-rotating shift rosters (night, evening, morning) give more metabolic disease than forward rotation at the same hours (chapter 4: opposite directions never join).	No difference in incident diabetes or weight gain.
T19	In the reading-frame registers, out-of-frame deletions that escape the Duchenne course are explained by a second event that restores the frame (alternative start, exon skipping by the cell).	Exceptions without any frame-restoring event.
T20	In early Parkinson's disease, beta-band synchrony measured at rest rises before motor scores worsen, and falls first after deep brain stimulation (W, uniform closure).	Synchrony changes only after or without motor change.
T21	For phobia, OCD, PTSD and chronic pain, treatment delivered with more than half of its sessions before the first night's sleep relapses less at one year than the same total spread weekly (chapter 45).	Equal relapse at one year in a head-to-head trial.

Open data for T13 and T14 were searched on 12 November 2026. No openly downloadable sleep recordings of people with depression were found; the large sleep cohorts that record depression scores (for example in the National Sleep Research Resource) require a data-use agreement. T13 and T14 therefore wait for such access.

T1 already meets a warning from the literature: short REM latency persists in part after recovery. If that holds per person, T1 fails, and the drift reading of chapter 41 fails with it.

> *Status: Predicted, untested. T10 is computed as a bound; expanded genetic codes with non-canonical amino acids are the place to test it.*

Part X — The balance

49. What is computed

Result	Value	Status
Closed windows	9 of 27; 3 uniform, 6 mixed	Computed
Mixed rings	only at depths 3, 6, 9, …; exactly 2	Computed
Pruning	1 in 3 at depth 1, 1 in 9 at depth 2	Computed
Seams	uniform–mixed 0 of 36; opposite direction 0 of 18	Computed
Repair	one error opens 3 windows; one cure for length ≥ 4: undo at that place; three at length 3	Computed
Readable words of three	$(k^3 - k)/3$: 2, 8, 20 for 2, 3, 4 letters	Computed; reproduces Crick 1957
Twenty amino acids	equals the computed bound for four letters	Reproduces; mechanism differs
Third codon place as remainder	71.6 % synonymous vs 4.6 % and 0.0 %	Computed on the measured code
Chain (charge register)	closed windows 53.75 % vs 52.53 % shuffled; excess is uniform, not mixed	Computed; prediction passes, expected kind fails
Fold	5 of 8 helix repeats are multiples of three ($p = 0.088$)	Computed; suggestive, not blind
Fold in space	smallest closed loop in tetrahedral directions: 6 steps (none of 3, 4, 5)	Computed; reproduces the strain-free six-ring
Organ seams	k kinds give at least $k - 1$ open windows	Computed
Chain meetings by separation	opposite charges peak at $k = 3$, 4 (and 7), not at multiples of 3 or at odd $k \geq 5$	New rules NR-a and NR-b failed; helix pattern
Heart and breath at rest	whole-number locking 8.1 % vs 5.0 % in surrogates ($p = 1.6 \times 10^{-12}$); no preference for 3	Measured and computed; closure passes, three fails
Membrane	8 of 9 bilayers asymmetric; mixed strands meet only antiparallel (0 parallel, 18 antiparallel)	Computed; agrees with membrane asymmetry and DNA; β-sheets only as preference
Reading	one error: 3 open windows, 1 misfit for a mirror reader; one reader fits one strand	Computed
Cell	unique partner; semi-conservative copy; every depth-6 ring divides into two closed rings	Computed; reproduces Meselson–Stahl
Tissue	exactly 9 chains close for any number of units: one word, one phase	Computed
Organ and body	no chain of two different words closes	Computed; carriers as the bond is a reading
The day	position 43.50, farthest from any ring	Computed
Heart and breath in sleep	locking excess +0.054 deep, +0.012 light, 0 in REM and wake	Measured and computed; order passes (reproduces Bartsch 2012); three fails
End of the night	final awakening within 30 min after REM end: 37 % vs 26 %	Measured and computed; passes; whole cycles fail
Day in depression	24-hour return 0.157 vs 0.217 ($p = 0.005$); IS opposite	Measured and computed; 1 of 6 passes
Depression data	36 % placebo, 53 % drug, 31 % real spread	Computed on measured data
Rhythm	every closed strand repeats with period 3	Derived

Result	Value	Status
Coupling	closed + closed closed; closed + open never	Derived
Impulse	an opening moves in 2 changes via a closed state	Derived; reproduces form
Circulation	loop of k kinds meets k seams; reversal costs 2	Derived; reproduces form
Carriers	6 of 72 seams closable; the rest need carriers forever	Derived
Defence	93.3 % readable, 5.9 % unread, 8 wrong closures	Derived
Waking	free only at a cycle end in the day's direction	Derived; agrees with Z2
Self-repair	exact below 1/3 wrong; wrong closure above	Derived
Mind	holds about 3/4 of its size; slips into reversal or flattening	Derived
Depression	against the day: 1 opening per day; restoring direction costs 2/3 once	Derived
Dose	exact: $k \leq 8$ of 18 undone, 9 a tie, ≥ 10 completed	Derived; exact
Periods	repair interval bounded by form size: 2, 14, 70 for 9, 27, 81 places	Derived
Process cost	rhythm and division free; impulse 2, repair 1, turning 18	Derived
Energy as a concept	replaced by counts per time; $E_0 = h/T_0 = 27.197$ eV	Derived
Period (proof)	every closed strand has period 3; mixed rings only when 3 divides the length	Derived; proved (5.1)
Repair (proof)	one error opens 3 windows; unique repair for length ≥ 4; three at length 3	Derived; proved (5.1); corrects ed. 1
Direction (proof)	the two directions differ at 2 of 3 places for every shift: 18 of 27	Derived; proved (5.1)
Dose (exact)	$k \leq 8$ back; $k = 9$ tie; $k \geq 10$ new; imprecise cure needs 12 of 18 for 96 %	Derived; exact (cure_exact.py)
Two directions of the test	missing a misfit and reading a fit as misfit mirror each other	Derived (17); matches checkpoint side effects (reading)
Frame in the clinic	in-frame deletions give Becker, out-of-frame give Duchenne	Reproduces Monaco 1988 (about 90 %)
Atlas of illness	about 90 diseases and disorders named by eight forms; treatments placed on five layers	Reading on measured evidence

50. What is open

- **The fold of a whole protein in space.** Chapter 11 computes the smallest closed ring in the cube's directions. The folding of a full chain is a much larger count on the same lattice.

- **Which carriers an organ uses at each seam.** Sections 15.1 and 16.4 compute how many seams there are and that most stay open. They do not say which molecule crosses each.
- **Why proteins enrich uniform charge runs** (chapter 10) rather than mixed closure, and why some helices repeat in groups of three and others do not (chapter 11).
- **Counts per process.** How many places each body process must close or restore, and on which ring it runs. With that count, speeds and doses follow without the concept of energy (sections 18.3 and 18.4).
- **A rule that selects rings.** The ladder orders; the tests show it does not select at group level. A selection rule per person is untested.
- **The number three in the living body.** Every direct test of it failed (sections 18.1, 18.2, 19.1). Either the rule of three acts only below the word, or the body's threes hide in a measure not yet tried. Section 21.3 found three where the text is read: in the frame of a gene. That is below the word, as the first option says.
- **The atlas.** Every naming of a disease as a form is a reading. The forms are exact; their assignment is not. A blind test would give the eight forms and a disease description to raters who do not know the book's assignment, and compare. That has not been done.
- **The mind.** The texts' three numbers failed. Sections 20.1 and 20.2 compute laws of reading, holding and slipping. Chapter 42 reads every major disorder through them. A number for experience itself is still missing.
- **Depression and the other W-forms.** The derivation of section 41.1 and the readings of chapters 41 and 42 stand or fall with tests T1 to T5, T11 to T14, T16 and T21.
- **Periods.** Section 19.0b bounds how far a repair rhythm may lie from the rhythm it repairs. No law yet selects the ring of a single process, so no rate is derived.

The book ends where its question began. Seven depths above chemistry are computed, each with its exact law and its test. Three of those laws are now proved for every length. Part IV derives how the body works in time. Part VI names eight forms of failure, each on an exact law. Part VII and Part VIII go through the whole body and the whole mind: every organ system and every major disorder, with its burden, its form, its prevention and its cures. Part IX orders cure by layer and gives the exact dose law. The tests on the living body found closure but not the number three: heart and breath close in whole numbers in deep rest, the night tends to end after a cycle has closed, and in depression the body's own activity returns less after one day. The frame law of the gene reproduces the split between two muscular dystrophies. The theory found no cure. It gives a map on which the known cures fit, a reason why they work, and twenty-one tests that can prove it wrong.

> *Status: Open points are defined calculations or defined tests.*

Appendix A — The programs

All numbers marked Computed come from the programs below or from the scripts named here. They run with Python 3. The re-analysis needs numpy, pandas and scipy; the molecule work needs RDKit.

- rules.py — windows, rings, widening and pruning, seams, repair (printed below).
- chain_depth.py — the charge register tested on the 20,429 reviewed human proteins (printed below).
- fold_depth.py — helix repeats against the group-of-three law (printed below).
- cell_depth.py — pairing, mirror, copying and dividing (printed below).
- tissue_depth.py — chains of closed units: which close (printed below).
- space_depth.py — closed loops in the cube's tetrahedral directions; open windows at organ seams (printed below).
- chain_space.py — opposite and equal charges by separation along the chain (printed below).
- sleep_lock.py — heart–breath locking per sleep stage, MIT-BIH Polysomnographic Database (printed below).
- cycle_close.py — awakenings and sleep cycles in Sleep-EDF (printed below).
- process_counts.py — changes per body process under a fixed counting rule (printed below).
- period_derive.py — the longest repair interval a form of N places allows (printed below).
- cure_exact.py — the exact dose table, replacing the simulation cure_timing.py of the first edition (printed below)
- check.py — exhaustive checks of the four proofs of section 5.1 (printed below).
- energy_law.py — new rule NR-E tested blind; the price of one trit (printed below).
- energy_ladder.py — the energy unit E_0 and the body's energies on the ladder (printed below).
- immune_hormone_derive.py — the test on all strands of 9 places; carriers at seams (printed below).
- mind_derive.py — what a form can hold, and the distances between the closed forms (printed below).
- sleep_derive.py — repair by windows alone: unique below one third wrong, wrong closure above (printed below).
- depression_derive.py — the course of a body against the day, with daily repair or a one-time change of direction (printed below).
- organ_derive.py — seams of organ chains and loops; the cost of reversing direction (printed below).
- body_derive.py — how the body works, from the rules alone: rhythm, coupling, impulse, waking, accumulation (printed below).
- st_cure.py — temazepam against placebo in Sleep-EDF telemetry (printed below).
- day_depth.py — closure of the day in the Depresjon actigraphy data (printed below).
- body_lock.py — heart–breath n:1 locking in the Fantasia recordings (printed below).
- membrane_depth.py — leaflets, bilayers and side-by-side pairing (printed below).
- mind_depth.py — reading by windows and by meeting; specificity; images (printed below).
- code_depth.py — readable words of three, the bound $(k^3 - k)/3$, the measured code (printed below).
- depressie_ladder.py — ladder positions of the day, the sleep cycle, REM latency and treatments.

- nma_griselda.py — random-effects network meta-analysis of the GRISELDA open data.
- placebo.py — placebo response, drug response and their moderators.
- structuur.py, chembl_binding.py, middelen_netregels.py — molecular and binding features of the 21 drugs and their correlation with efficacy.

rules.py

```
"""rules.py — the starting rules of the Vacuum.Net Theory, recomputed.
R1 windows: three trits, closed when the sum is a multiple of three.
R2 rings: a cyclic strand of d crossings with every window closed; counted up to rotation;
   split into uniform (all equal) and mixed (all three values present).
R3 widening and pruning: count combinations, count what closes, at two depths.
"""
import itertools, json
T = (-1, 0, 1)
win = list(itertools.product(T, repeat=3))
closed = [w for w in win if sum(w) % 3 == 0]
uniform = [w for w in closed if len(set(w)) == 1]
mixed = [w for w in closed if len(set(w)) == 3]
print(f"R1 windows {len(win)}, closed {len(closed)} (uniform {len(uniform)}, mixed {len(mixed)}),
open {len(win)-len(closed)}")

def canon(s):
    return min(s[i:] + s[:i] for i in range(len(s)))
res = {}
for d in range(3, 16):
    rings = set()
    for s in itertools.product(T, repeat=d):
        if all((s[i] + s[(i + 1) % d] + s[(i + 2) % d]) % 3 == 0 for i in range(d)):
            rings.add(canon(s))
    u = sum(1 for r in rings if len(set(r)) == 1); m = sum(1 for r in rings if len(set(r)) == 3)
    o = len(rings) - u - m
    res[d] = (u, m, o)
    print(f"R2 depth {d:2d}: closed rings {len(rings)}  uniform {u}  mixed {m}  other {o}")

# R3: widening and pruning at the window level, two depths
# depth 1: 27 windows -> 9 close. depth 2: closed windows as units; a pair of units is joined
# by the window across the seam (last two trits of one, first of the next and its mirror seam)
units = closed
pairs = [(a, b) for a in units for b in units]
def seam_ok(a, b):
    return (a[1] + a[2] + b[0]) % 3 == 0 and (a[2] + b[0] + b[1]) % 3 == 0
kept = [(a, b) for a, b in pairs if seam_ok(a, b)]
print(f"R3 depth 1: {len(win)} combinations -> {len(closed)} close ({len(closed)/len(win):.3f})")
print(f"R3 depth 2: {len(pairs)} pairs of closed windows -> {len(kept)} close across the seam
({len(kept)/len(pairs):.3f})")
kinds = {}
for a, b in kept:
    k = ("U" if len(set(a)) == 1 else "M") + ("U" if len(set(b)) == 1 else "M")
    kinds[k] = kinds.get(k, 0) + 1
print("   kinds of joined pairs (U uniform, M mixed):", kinds)
json.dump({"windows": [len(win), len(closed), len(uniform), len(mixed)], "rings": res,
           "widen_prune": [len(pairs), len(kept), kinds]}, open("/home/claude/boek/rules.json",
"w"), indent=1)

# F1/F2: which pairs of closed windows close across the seam, by kind and direction
def direction(w):
    # mixed window: +1 if it runs -1 -> 0 -> +1 in cyclic order, -1 if the mirror
    i = w.index(-1); return 1 if w[(i + 1) % 3] == 0 else -1
mm = [(a, b) for a in mixed for b in mixed]
mm_ok = [(a, b) for a, b in mm if seam_ok(a, b)]
same = sum(1 for a, b in mm_ok if direction(a) == direction(b))
mu = [(a, b) for a in units for b in units if (len(set(a)) == 1) != (len(set(b)) == 1)]
print(f"F1 uniform-mixed pairs {len(mu)}, closing across the seam {sum(seam_ok(a,b) for a,b in
mu)}")
print(f"F2 mixed-mixed pairs {len(mm)}, closing {len(mm_ok)}, of which same direction {same}; "
      f"opposite-direction pairs {sum(1 for a,b in mm if direction(a)!=direction(b))}, closing
{sum(1 for a,b in mm_ok if direction(a)!=direction(b))}")
# repair: every open window, single-place changes that close it
opn = [w for w in win if sum(w) % 3]
rep = []
for w in opn:
    fixes = 0; per_place = []
    for p in range(3):
        vals = [v for v in T if v != w[p] and (sum(w) - w[p] + v) % 3 == 0]
        per_place.append(len(vals)); fixes += len(vals)
    rep.append((fixes, tuple(per_place)))
print(f"R4 open windows {len(opn)}; one-place repairs per window: {sorted(set(rep))}")
print("   two fix the third: for every pair of given trits the closing third is unique:",
      all(sum(1 for v in T if (a + b + v) % 3 == 0) == 1 for a in T for b in T))

# R5: a closed ring with one error. Which single changes restore closure of every window?
```

```
def ring_ok(s):
    d = len(s); return all((s[i] + s[(i + 1) % d] + s[(i + 2) % d]) % 3 == 0 for i in range(d))
for name, base in (("mixed ring depth 9", (-1, 0, 1) * 3), ("uniform ring depth 9", (1,) * 9)):
    stats = []
    for pos in range(9):
        for v in T:
            if v == base[pos]: continue
            s = list(base); s[pos] = v; s = tuple(s)
            open_w = sum((s[i] + s[(i+1)%9] + s[(i+2)%9]) % 3 != 0 for i in range(9))
            singles = [(p, u) for p in range(9) for u in T if u != s[p] and ring_ok(s[:p] + (u,) +
s[p+1:])]
            stats.append((open_w, len(singles), singles == [(pos, base[pos])]))
    print(f"R5 {name}: one error opens {sorted(set(x[0] for x in stats))} windows; "
          f"single-change repairs {sorted(set(x[1] for x in stats))}; only repair = undo the error:
{all(x[2] for x in stats)}")
# R6: the shortest closing step from the error when the original is not known: a whole group of
three
```

code_depth.py

```
"""code_depth.py — the first depth above chemistry: words of three bases.
Rules used: a word is a window of three (N2). A word that reads the same in more than one phase
cannot fix a frame; the first passage fixes the direction (N3), so only one phase may read.
Consequences counted here:
 C1 uniform words (x,x,x) read in every phase -> excluded.
 C2 of the three rotations of a word, at most one can be read.
 C3 maximum number of readable words = (k^3 - k)/3 for an alphabet of k letters.
 C4 a set of that size exists and is readable in one phase only (comma-free), checked by search.
Comparison: the standard genetic code (measured) and the 20 amino acids.
"""
import itertools, json

def classes(k):
    L = range(k); cls = {}
    for w in itertools.product(L, repeat=3):
        if len(set(w)) == 1: continue
        key = min(w[i:] + w[:i] for i in range(3)); cls.setdefault(key, []).append(w)
    return list(cls.values())

def comma_free(code):
    S = set(code)
    for a in code:
        for b in code:
            s = a + b
            if s[1:4] in S or s[2:5] in S: return False
    return True

def search(k):
    cl = classes(k); best = []
    def bt(i, chosen):
        nonlocal best
        if len(chosen) + (len(cl) - i) <= len(best): return
        if i == len(cl):
            if len(chosen) > len(best): best = chosen[:]
            return
        for w in cl[i]:
            if comma_free(chosen + [w]):
                chosen.append(w); bt(i + 1, chosen); chosen.pop()
                if len(best) == len(cl): return
        bt(i + 1, chosen)
    bt(0, []); return best, len(cl)

out = {}
for k in (2, 3, 4):
    best, ncl = search(k)
    bound = (k ** 3 - k) // 3
    out[k] = (len(best), bound, ncl)
    print(f"C3/C4 alphabet {k}: words {k**3}, uniform {k}, rotation classes {ncl}, bound (k^3-k)/3 =
{bound}, readable set found {len(best)}, comma-free {comma_free(best)}")
    if k == 4:
        B = "ACGT"; code4 = ["".join(B[i] for i in w) for w in best]; print("   one readable set:",
" ".join(sorted(code4)))
# composition of the 20 classes for k = 4
cl4 = classes(4)
d3 = sum(1 for c in cl4 if len(set(c[0])) == 3); d2 = sum(1 for c in cl4 if len(set(c[0])) == 2)
print(f"   classes with three different letters {d3}, with two equal letters {d2}")

# the measured code: synonymous changes by place (standard table)
bases = "TCAG"
aa = "FFLLSSSSYY**CC*WLLLLPPPPHHQQRRRRIIIMTTTTNNKKSSRRVVVVAAAADDEEGGGG"
code = {a + b + c: aa[16 * i + 4 * j + q] for i, a in enumerate(bases) for j, b in enumerate(bases)
for q, c in enumerate(bases)}
syn = [0, 0, 0]; tot = [0, 0, 0]
for cod, a in code.items():
```

```
    if a == "*": continue
    for p in range(3):
        for b in bases:
            if b == cod[p]: continue
            m = cod[:p] + b + cod[p + 1:]
            if code[m] == "*": continue
            tot[p] += 1; syn[p] += code[m] == a
frac = [round(s / t, 3) for s, t in zip(syn, tot)]
n_aa = len(set(aa) - {"*"}); n_stop = aa.count("*")
uni = {w: code[w] for w in ("TTT", "CCC", "AAA", "GGG")}
print(f"measured code: amino acids {n_aa}, stop words {n_stop}, synonymous fraction by place
{frac}")
print(f"measured code: uniform words read as {uni} (the real code reads them; it is not comma-
free)")
json.dump({"readable": out, "classes_k4": [d3, d2], "measured": {"aa": n_aa, "stop": n_stop,
"syn_by_place": frac}},
          open("/home/claude/boek/code_depth.json", "w"), indent=1)
```

chain_depth.py

```
"""chain_depth.py — the depth of the chain, tested on the reviewed human proteome (UniProt, 20,429
proteins).
Writing rule W2, fixed before the data were read: each residue is written as its charge at neutral
pH,
the register value of the theory: K, R = +1; D, E = -1; every other residue = 0.
Prediction fixed first (P-chain): windows of three consecutive residues close (sum = 0 mod 3)
more often in real proteins than in the same proteins with their residues shuffled.
Refuted if the observed share of closed windows is not above the shuffled share.
Secondary readout (not a test): observed/expected ratio for each of the 27 window kinds.
"""
import gzip, random, json, collections
random.seed(11)
val = {"K": 1, "R": 1, "D": -1, "E": -1}
seqs, cur = [], []
for line in gzip.open("/home/claude/data_uniprot/human.fasta.gz", "rt"):
    if line.startswith(">"):
        if cur: seqs.append("".join(cur)); cur = []
    else: cur.append(line.strip())
if cur: seqs.append("".join(cur))
tr = [[val.get(a, 0) for a in s] for s in seqs]

def count(lst):
    c = collections.Counter()
    for t in lst:
        for i in range(len(t) - 2): c[(t[i], t[i+1], t[i+2])] += 1
    return c

obs = count(tr)
N = sum(obs.values())
closed = lambda w: sum(w) % 3 == 0
obs_closed = sum(v for w, v in obs.items() if closed(w)) / N
shuf_closed = []; exp = collections.Counter()
REPS = 5
for r in range(REPS):
    sh = []
    for t in tr:
        t2 = t[:]; random.shuffle(t2); sh.append(t2)
    c = count(sh); exp.update(c)
    shuf_closed.append(sum(v for w, v in c.items() if closed(w)) / N)
mean_sh = sum(shuf_closed) / REPS
sd_sh = (sum((x - mean_sh) ** 2 for x in shuf_closed) / (REPS - 1)) ** 0.5
comp = collections.Counter(x for t in tr for x in t)
print(f"proteins {len(seqs)}, residues {sum(len(t) for t in tr)}, windows {N}")
print(f"composition: +1 {comp[1]/sum(comp.values()):.4f}, -1 {comp[-1]/sum(comp.values()):.4f}, 0
{comp[0]/sum(comp.values()):.4f}")
print(f"P-chain closed share: observed {obs_closed:.5f}, shuffled {mean_sh:.5f} (sd {sd_sh:.6f} over
{REPS} shuffles), difference {obs_closed-mean_sh:+.5f}")
rows = []
for w in sorted(obs, key=lambda w: (not closed(w), w)):
    e = exp[w] / REPS
    kind = "uniform" if len(set(w)) == 1 else ("mixed" if len(set(w)) == 3 else "open")
    rows.append((w, kind, obs[w], round(e), round(obs[w] / e, 3)))
by = collections.defaultdict(lambda: [0, 0.0])
for w, kind, o, e, r in rows:
    by[kind][0] += o; by[kind][1] += e
for k, (o, e) in by.items(): print(f"  {k:8s} observed/expected {o/e:.3f}")
print("  per kind of charged window (obs/exp):")
for w, kind, o, e, r in rows:
    if w.count(0) <= 1: print(f"   {w} {kind:7s} {r:.3f}")
json.dump({"proteins": len(seqs), "windows": N, "obs_closed": obs_closed, "shuffled": shuf_closed,
           "by_kind": {k: v[0] / v[1] for k, v in by.items()}, "rows": [(list(w), k, o, e, r) for w,
k, o, e, r in rows]},
          open("/home/claude/boek/chain_depth.json", "w"), indent=1)
```

fold_depth.py

```
"""fold_depth.py — the depth of the fold.
Rule (computed in rules.py, R2): a mixed ring closes only when its depth is a multiple of three.
Reading rule W3, fixed before the comparison: a regular helix is a winding that returns in step
after
a whole number of units; its repeat is the numerator of units-per-turn written as a reduced
fraction.
Prediction (P-fold): helix repeats are multiples of three more often than chance (1 in 3).
Measured units per turn (Wikipedia pages 'Protein secondary structure', 'Polyproline helix',
'Nucleic acid double helix', read 11 November 2026).
"""
from fractions import Fraction
from math import comb
helices = [("alpha helix", "3.6"), ("3-10 helix", "3.0"), ("pi helix", "4.4"),
           ("polyproline I", "3.3"), ("polyproline II", "3"), ("A-DNA", "11"), ("B-DNA", "10.5"),
("Z-DNA", "12")]
hits = 0
for name, upt in helices:
    f = Fraction(upt) if name != "polyproline I" else Fraction(10, 3)   # 'roughly 3.3' read as 10/3
    rep, turns = f.numerator, f.denominator
    ok = rep % 3 == 0; hits += ok
    print(f"{name:15s} units/turn {upt:>5s} = {rep}/{turns}: repeat {rep:3d} units in {turns} turns
multiple of 3: {ok}")
n = len(helices); p = sum(comb(n, k) * (1/3)**k * (2/3)**(n-k) for k in range(hits, n + 1))
print(f"P-fold: {hits} of {n} repeats are multiples of three; chance 1/3 each; one-sided binomial p
= {p:.3f}")
```

chain_space.py

```
"""chain_space.py — where along a chain do opposite charges meet?
Data: the 20,429 reviewed human proteins (UniProt), charge writing W2 (K,R +1; D,E -1; rest 0).
Quantity: for each separation k = 1..12, observed / expected count of pairs (i, i+k) with opposite
charge
(a meeting, x with -x) and with equal charge; expected from 3 shuffles of each protein.
Two competing new rules, fixed before the count:
 NR-a (group of three): meetings are enriched at k = 3, 6, 9, 12 relative to the neighbouring
separations.
 NR-b (space): in the cube's tetrahedral directions a chain closes a loop first at six steps
(space_depth.py),
       so contacts are possible at k = 5, 7, 9, 11 (odd, >= 5); meetings are enriched there.
Measured reference, not used to fix the rules: salt bridges at i,i+4 and i,i+3 stabilise alpha
helices.
"""
import gzip, random, numpy as np
random.seed(3)
val = {"K": 1, "R": 1, "D": -1, "E": -1}
seqs, cur = [], []
for line in gzip.open("/home/claude/data_uniprot/human.fasta.gz", "rt"):
    if line.startswith(">"):
        if cur: seqs.append("".join(cur)); cur = []
    else: cur.append(line.strip())
if cur: seqs.append("".join(cur))
arrs = [np.array([val.get(a, 0) for a in s], dtype=np.int8) for s in seqs]
K = 12
def counts(lst):
    opp = np.zeros(K + 1); same = np.zeros(K + 1)
    for t in lst:
        for k in range(1, K + 1):
            if len(t) <= k: continue
            prod = t[:-k] * t[k:]
            opp[k] += (prod == -1).sum(); same[k] += (prod == 1).sum()
    return opp, same
o_obs, s_obs = counts(arrs)
o_exp = np.zeros(K + 1); s_exp = np.zeros(K + 1)
for r in range(3):
    sh = []
    for t in arrs:
        t2 = t.copy(); np.random.shuffle(t2); sh.append(t2)
    o, s = counts(sh); o_exp += o / 3; s_exp += s / 3
ro = o_obs[1:] / o_exp[1:]; rs = s_obs[1:] / s_exp[1:]
print("  k   opposite obs/exp   equal obs/exp")
for k in range(1, K + 1): print(f"{k:2d}    {ro[k-1]:.3f}            {rs[k-1]:.3f}")
def local(k): return ro[k-1] - (ro[k-2] + ro[k]) / 2 if 1 < k < K else None
print("NR-a peaks at 3,6,9 (value minus mean of neighbours):", {k: round(local(k), 3) for k in (3,
6, 9)})
print("NR-b peaks at 5,7,9,11:", {k: round(local(k), 3) for k in (5, 7, 9, 11)})
print("largest opposite-charge enrichment at k =", int(np.argmax(ro)) + 1)
```

membrane_depth.py

```
"""membrane_depth.py — the membrane and the sheet: closed strands that meet side by side.
M1 A sheet (one leaflet) is a strand of units; by the tissue law it closes only as one word
repeated.
M2 Two leaflets meet face to face, position by position; a meeting closes only as (x, -x).
   Count, for every closed leaflet, which second leaflets meet it at every position.
M3 Is the second leaflet ever the same as the first? (a symmetric bilayer)
M4 Side-by-side pairing of strands with direction: for mixed strands, does the closing partner run
   the same direction (parallel) or the opposite direction (antiparallel)? Exhaustive over all
   closed strands of depth 3, 6 and 9 and all relative shifts.
"""
import itertools
T = (-1, 0, 1)
def closed_lin(s): return all((s[i] + s[i+1] + s[i+2]) % 3 == 0 for i in range(len(s) - 2))
def direction(s):
    if len(set(s)) < 3: return 0
    i = s.index(-1); return 1 if s[(i+1) % len(s)] == 0 else -1
words = [w for w in itertools.product(T, repeat=3) if sum(w) % 3 == 0]
L = 9
sheets = [w * 3 for w in words]                       # M1: one word repeated, length 9
print("M1 closed leaflets of length 9:", len([s for s in itertools.product(T, repeat=L) if
closed_lin(s)]),
      "= one word repeated:", all(closed_lin(s) for s in sheets))
sym = 0; rows = []
for a in sheets:
    partners = [b for b in sheets if all(x + y == 0 for x, y in zip(a, b))]
    b = partners[0]
    same = (a == b); sym += same
    rows.append((a[:3], b[:3], len(partners), same, direction(a), direction(b)))
for r in rows:
    print(f"M2 leaflet {r[0]} meets only {r[1]} (partners {r[2]}); same as itself: {r[3]};
directions {r[4]:+d} / {r[5]:+d}")
print(f"M3 symmetric bilayers: {sym} of {len(sheets)} (only the all-zero leaflet)")
# M4
par = anti = 0
for d in (3, 6, 9):
    strands = [s for s in itertools.product(T, repeat=d) if closed_lin(s) and len(set(s)) == 3]
    for a in strands:
        for b in strands:
            if all(x + y == 0 for x, y in zip(a, b)):
                if direction(a) == direction(b): par += 1
                else: anti += 1
print(f"M4 mixed strands meeting at every position: parallel {par}, antiparallel {anti}")
```

space_depth.py

```
"""space_depth.py — the fold in space and the organ's seams.
S1 Fold in space: a chain whose every step takes one of the cube's tetrahedral directions (chemistry
book,
   chapter 19: four alternate corners, alternating between the two tetrahedra at each atom) lives on
the
   diamond lattice. Count closed self-avoiding loops through the origin by length (rooted,
directed).
S2 Organ seams: chains of k different closed words (one after another). Count open windows at the
seams,
   the minimum over all choices and orders.
"""
import itertools
A = [(1, 1, 1), (1, -1, -1), (-1, 1, -1), (-1, -1, 1)]
B = [tuple(-x for x in v) for v in A]
def loops(maxlen):
    cnt = {}
    def go(pos, step, path, seen):
        if step and pos == (0, 0, 0):
            cnt[step] = cnt.get(step, 0) + 1; return
        if step == maxlen: return
        for v in (A if step % 2 == 0 else B):
            q = (pos[0] + v[0], pos[1] + v[1], pos[2] + v[2])
            if q == (0, 0, 0) and step + 1 >= 3: go(q, step + 1, path, seen); continue
            if q in seen: continue
            seen.add(q); go(q, step + 1, path, seen); seen.discard(q)
    go((0, 0, 0), 0, [], {(0, 0, 0)})
    return cnt
c = loops(10)
for L in sorted(c): print(f"S1 closed loops of {L:2d} steps through the origin (rooted, directed):
{c[L]}")
T = (-1, 0, 1)
words = [w for w in itertools.product(T, repeat=3) if sum(w) % 3 == 0]
def open_windows(s): return sum((s[i] + s[i+1] + s[i+2]) % 3 != 0 for i in range(len(s) - 2))
for k in (2, 3, 4):
    best = min(open_windows(sum(ch, ())) for ch in itertools.permutations(words, k))
    worst = max(open_windows(sum(ch, ())) for ch in itertools.permutations(words, k))
```

```
    print(f"S2 chain of {k} different closed words: open windows at the seams min {best}, max
{worst}")
```

cell_depth.py

```
"""cell_depth.py — the depth of the cell: copying and dividing.
C5 Pairing: a value x meets only -x (a meeting closes, carry 0). For every value the partner is
unique.
C6 The mirror of a closed ring is closed and runs the opposite direction.
C7 Copy by pairing: separate a paired double (r, -r); each strand takes its unique partner again;
   the result is two doubles, each holding one old strand (semi-conservative).
C8 Divide: a closed ring of depth 6 is cut into two rings of depth 3; count which closed rings of
   depth 6 give two closed halves, and whether the halves keep the parent's direction.
"""
import itertools
T = (-1, 0, 1)
def closed_ring(s):
    d = len(s); return all((s[i] + s[(i+1)%d] + s[(i+2)%d]) % 3 == 0 for i in range(d))
def direction(s):
    if len(set(s)) < 3: return 0
    i = s.index(-1); return 1 if s[(i+1) % len(s)] == 0 else -1
print("C5 unique partner:", {x: [y for y in T if (x + y) == 0] for x in T})
rings6 = sorted({min(s[i:]+s[:i] for i in range(6)) for s in itertools.product(T, repeat=6) if
closed_ring(s)})
for r in rings6:
    m = tuple(-x for x in r)
    print(f"C6 ring {r}: mirror closed {closed_ring(m)}, direction {direction(r):+d} -> mirror
{direction(m):+d}")
# C7
r = (-1, 0, 1, -1, 0, 1); dbl = (r, tuple(-x for x in r))
new1 = (dbl[0], tuple(-x for x in dbl[0])); new2 = (tuple(-x for x in dbl[1]), dbl[1])
print("C7 two copies identical:", new1 == new2, "; each holds one old strand:", new1[0] is dbl[0] or
new1[0] == dbl[0], new2[1] == dbl[1])
# C8
for r in rings6:
    res = []
    for cut in range(6):
        s = r[cut:] + r[:cut]; a, b = s[:3], s[3:]
        res.append((closed_ring(a) and closed_ring(b), direction(a) == direction(b) ==
direction(r)))
    print(f"C8 ring {r}: cuts giving two closed rings {sum(x for x, _ in res)}/6, keeping direction
{sum(y for x, y in res if x)}")
# copy-then-divide from depth 3: repeat a closed ring of 3 and check depth-6 closure
for r3 in [(1, 1, 1), (-1, 0, 1), (1, 0, -1)]:
    print(f"C8 copy {r3} -> {r3*2}: closed at depth 6 {closed_ring(r3*2)}")
```

tissue_depth.py

```
"""tissue_depth.py — joining many closed units: how many chains of n closed windows close at every
seam.
A chain is n closed windows written one after another (3n trits); it closes when every window of
three
consecutive trits in the whole strand is closed. Counted exhaustively for n = 1..6.
"""
import itertools
T = (-1, 0, 1)
closed = [w for w in itertools.product(T, repeat=3) if sum(w) % 3 == 0]
mixed = [w for w in closed if len(set(w)) == 3]
def ok(s): return all((s[i] + s[i+1] + s[i+2]) % 3 == 0 for i in range(len(s) - 2))
for n in range(1, 7):
    tot = len(closed) ** n; good = 0; good_mixed = 0; kinds = set()
    for ch in itertools.product(closed, repeat=n):
        s = sum(ch, ())
        if ok(s):
            good += 1
            if all(w in mixed for w in ch): good_mixed += 1
            kinds.add(len(set(ch)))
    print(f"n={n}: chains {tot:>8d}, closing {good:3d} (share {good/tot:.2e}); all-mixed closing
{good_mixed}; distinct words per closing chain {sorted(kinds)}")
```

mind_depth.py

```
"""mind_depth.py — what the rules say exactly about reading, the act the theory places under mind.
R1 Reading by meeting: a reader meets a strand position by position; a fit is (x, -x).
   For every closed strand of depth 9 and every single error: how many positions misfit?
R2 Reading by windows: the same errors seen as open windows (from rules.py: three).
R3 Specificity: how many different closed strands of depth 9 fit one given reader everywhere?
R4 Images: maps that keep every value, from a mixed ring of depth 3k onto the mixed ring of depth 3
   (i -> i + a mod 3). Count them for k = 1..4, and maps the other way (depth 3 into depth 3k).
```

```
"""
import itertools
T = (-1, 0, 1)
def closed_ring(s):
    d = len(s); return all((s[i] + s[(i+1)%d] + s[(i+2)%d]) % 3 == 0 for i in range(d))
rings9 = sorted({s for s in itertools.product(T, repeat=9) if closed_ring(s)})
mis, opn = set(), set()
for r in rings9:
    reader = tuple(-x for x in r)
    for p in range(9):
        for v in T:
            if v == r[p]: continue
            s = r[:p] + (v,) + r[p+1:]
            mis.add(sum(1 for x, y in zip(s, reader) if x + y != 0))
            opn.add(sum((s[i] + s[(i+1)%9] + s[(i+2)%9]) % 3 != 0 for i in range(9)))
print(f"R1 one error, read by meeting: misfitting positions {sorted(mis)}")
print(f"R2 one error, read by windows: open windows {sorted(opn)}")
spec = {tuple(-x for x in r): sum(1 for s in rings9 if all(x + y == 0 for x, y in zip(s, tuple(-x
for x in r)))) for r in rings9}
print(f"R3 closed strands of depth 9 (all rotations): {len(rings9)}; strands fitting one reader:
{sorted(set(spec.values()))}")
base = (-1, 0, 1)
for k in range(1, 5):
    big = base * k
    onto = sum(1 for a in range(3) if all(big[i] == base[(i + a) % 3] for i in range(3 * k)))
    into = sum(1 for a in range(3 * k) if all(base[i] == big[(i + a) % (3 * k)] for i in range(3)))
    print(f"R4 depth {3*k} onto depth 3: {onto} value-keeping map(s); depth 3 into depth {3*k}:
{into} placement(s)")
```

body_lock.py

```
"""body_lock.py — does the body close heart and breath in whole numbers?
Data: PhysioNet Fantasia database (Iyengar et al. 1996): 40 healthy people (20 young, 20 old), 120
min supine rest,
respiration at 250 Hz and annotated heartbeats.
Rule (theory N2): what persists is what closes; a closed coupling of two rhythms returns in step
after a whole
number of beats per breath (n:1).
Tests fixed before the data were analysed (11 November 2026):
 H1 locking: the share of 30-breath windows with n:1 locking is higher in the real recordings than
in surrogates
    where the respiration is shifted in time by 10-50 min against the heartbeats (coupling broken,
rhythms kept).
 H2 three: among locked windows, n = 3 or n = 6 occurs more often than in the surrogates (group-of-
three rule).
Locking index for n:1 in a window: gamma_n = |mean over beats of exp(2*pi*i*n*psi)|, psi =
respiratory phase
at the beat (0..1 within the breath). A window counts as locked at n when gamma_n >= 0.8 and n is
the best.
"""
import numpy as np, wfdb, json, random
from scipy.signal import butter, filtfilt, find_peaks
DIR = "/home/claude/data_fantasia/"
recs = open(DIR + "RECORDS").read().split()
fs = 250
def breath_peaks(resp):
    b, a = butter(2, [0.08 / (fs / 2), 0.6 / (fs / 2)], btype="band")
    x = filtfilt(b, a, resp)
    pk, _ = find_peaks(x, distance=int(1.5 * fs), prominence=0.3 * np.std(x))
    return pk / fs
def phases(beats, bp):
    idx = np.searchsorted(bp, beats) - 1
    ok = (idx >= 0) & (idx < len(bp) - 1)
    b = beats[ok]; i = idx[ok]
    return b, i, (b - bp[i]) / (bp[i + 1] - bp[i])
def lock_windows(beats, bp, W=8):
    b, bi, psi = phases(beats, bp)
    res = []
    for start in range(0, len(bp) - 1 - W, W):
        m = (bi >= start) & (bi < start + W)
        if m.sum() < 2 * W: continue
        p = psi[m]
        g = {n: abs(np.mean(np.exp(2j * np.pi * n * p))) for n in range(2, 9)}
        n = max(g, key=g.get)
        res.append((n, g[n]))
    return res
random.seed(5)
real, sur = [], []
per = {}
for r in recs:
    rec = wfdb.rdrecord(DIR + r); ann = wfdb.rdann(DIR + r, "ecg")
    resp = rec.p_signal[:, rec.sig_name.index("RESP")]
    beats = ann.sample / fs
    bp = breath_peaks(resp)
```

```
    w = lock_windows(beats, bp); real += w
    s_all = []
    for _ in range(5):
        shift = random.uniform(600, 3000)
        T = len(resp) / fs
        bps = np.sort((bp + shift) % T)
        s_all += lock_windows(beats, bps)
    sur += s_all
    per[r] = (len(w), 0, round(60 * len(bp) / (len(resp) / fs), 1), round(60 * len(beats) /
(len(resp) / fs), 1))
    print(f"{r}: windows {len(w):3d}, locked {per[r][1]:3d}; breaths/min {per[r][2]}, beats/min
{per[r][3]}", flush=True)
# Version 2 (after version 1 found no window locked at gamma >= 0.8 over 30 breaths, in real or
surrogate):
# windows of 8 breaths; compare the strength of the best n:1 locking (gamma) between real and
surrogate,
# and the share of each best n among windows with gamma above the surrogate's 95th percentile.
gr = np.array([g for n, g in real]); gs = np.array([g for n, g in sur])
thr = np.percentile(gs, 95)
from scipy.stats import mannwhitneyu
u = mannwhitneyu(gr, gs, alternative="greater")
print(f"\nH1 mean best gamma: real {gr.mean():.3f}, surrogate {gs.mean():.3f}; Mann-Whitney p =
{u.pvalue:.2e}")
lr = [n for n, g in real if g >= thr]; ls = [n for n, g in sur if g >= thr]
print(f"   windows above surrogate 95th percentile ({thr:.3f}): real {len(lr)}/{len(real)} =
{len(lr)/len(real):.3f}, surrogate {len(ls)/len(sur):.3f}")
dr = {n: lr.count(n) for n in range(2, 9)}; ds = {n: round(ls.count(n) * len(lr) / max(len(ls), 1),
1) for n in range(2, 9)}
print("   best n among those windows, real:", dr); print("   expected from surrogate (scaled):", ds)
r36 = (dr[3] + dr[6]) / max(len(lr), 1); s36 = (ls.count(3) + ls.count(6)) / max(len(ls), 1)
print(f"H2 share n=3 or 6: real {r36:.3f}, surrogate {s36:.3f}")
json.dump({"gamma_real": float(gr.mean()), "gamma_sur": float(gs.mean()), "p": float(u.pvalue),
"thr": float(thr),
           "share_real": len(lr)/len(real), "share_sur": len(ls)/len(sur), "n_real": dr,
"n_sur_scaled": ds, "r36": r36, "s36": s36, "per": per},
          open("/home/claude/boek/body_lock.json", "w"), indent=1)
```

sleep_lock.py

```
"""sleep_lock.py — heart-breath closure per sleep stage.
Data: MIT-BIH Polysomnographic Database (Ichimaru & Moody 1999, PhysioNet slpdb): 18 recordings of
16 men
with suspected sleep apnea; ECG beat annotations, respiration, sleep stage per 30 s (W, 1, 2, 3, 4,
R).
Method: as body_lock.py version 2 (windows of 8 breaths, best n:1 of n = 2..8, gamma = |mean exp(2
pi i n psi)|);
surrogate = breaths shifted 600-3000 s (cyclic), 5 repeats; each window gets the stage of the epoch
at its centre.
Predictions fixed before the data were analysed (11 November 2026):
 S1 closure: in every stage group the real gamma exceeds the surrogate gamma.
 S2 depth: the excess (real minus surrogate) is largest in deep sleep (3+4), then light (1+2),
smallest in
    REM and wake. Theory: the deepest rest is the most closed state; REM is reading (open), wake is
acting.
    Known before: Bartsch et al. 2012 found more phase synchronisation in deep sleep, less in REM.
 S3 three: among windows above the surrogate 95th percentile, n = 3 or 6 is more common than in the
surrogate.
Caveat: the people have sleep apnea, which breaks breathing; this lowers locking in every stage.
"""
import sys, numpy as np, wfdb, json, random
from scipy.signal import butter, filtfilt, find_peaks
from scipy.stats import mannwhitneyu
DIR = sys.argv[1] if len(sys.argv) > 1 else "/home/claude/data_slpdb/"
recs = open(DIR + "R").read().split(); fs = 250
G = {"W": "wake", "1": "light", "2": "light", "3": "deep", "4": "deep", "R": "REM"}
def breath_peaks(resp):
    b, a = butter(2, [0.08 / (fs / 2), 0.6 / (fs / 2)], btype="band"); x = filtfilt(b, a, resp)
    pk, _ = find_peaks(x, distance=int(1.5 * fs), prominence=0.3 * np.std(x)); return pk / fs
def lock_windows(beats, bp, W=8):
    idx = np.searchsorted(bp, beats) - 1; ok = (idx >= 0) & (idx < len(bp) - 1)
    b, i = beats[ok], idx[ok]; psi = (b - bp[i]) / (bp[i + 1] - bp[i]); res = []
    for s in range(0, len(bp) - 1 - W, W):
        m = (i >= s) & (i < s + W)
        if m.sum() < 2 * W: continue
        g = {n: abs(np.mean(np.exp(2j * np.pi * n * psi[m]))) for n in range(2, 9)}
        n = max(g, key=g.get); res.append((n, g[n], (bp[s] + bp[s + W]) / 2))
    return res
random.seed(7)
real = {k: [] for k in ("wake", "light", "deep", "REM")}; sur = {k: [] for k in real}
for r in recs:
    rec = wfdb.rdrecord(DIR + r); ann = wfdb.rdann(DIR + r, "ecg"); st = wfdb.rdann(DIR + r, "st")
    ch = [j for j, n in enumerate(rec.sig_name) if n.startswith("Resp")][0]
    resp = np.nan_to_num(rec.p_signal[:, ch]); T = len(resp) / fs
    beats = ann.sample / fs; bp = breath_peaks(resp)
```

```
    ep_t = st.sample / fs; ep_s = [G.get(a.split()[0]) for a in st.aux_note]
    def stage(t):
        j = np.searchsorted(ep_t, t) - 1
        return ep_s[j] if 0 <= j < len(ep_s) and t - ep_t[j] < 30 else None
    for n, g, t in lock_windows(beats, bp):
        s = stage(t)
        if s: real[s].append((n, g))
    for _ in range(5):
        bps = np.sort((bp + random.uniform(600, 3000)) % T)
        for n, g, t in lock_windows(beats, bps):
            s = stage(t)
            if s: sur[s].append((n, g))
    print(r, {k: len(v) for k, v in real.items()}, flush=True)
allsur = np.array([g for v in sur.values() for n, g in v]); thr = np.percentile(allsur, 95)
out = {"thr": float(thr)}
for k in real:
    gr = np.array([g for n, g in real[k]]); gs = np.array([g for n, g in sur[k]])
    p = mannwhitneyu(gr, gs, alternative="greater").pvalue
    lr = [n for n, g in real[k] if g >= thr]; ls = [n for n, g in sur[k] if g >= thr]
    r36 = sum(n in (3, 6) for n in lr) / max(len(lr), 1); s36 = sum(n in (3, 6) for n in ls) /
max(len(ls), 1)
    out[k] = dict(windows=len(gr), real=float(gr.mean()), sur=float(gs.mean()),
excess=float(gr.mean() - gs.mean()), p=float(p),
                  above_real=len(lr) / len(gr), above_sur=len(ls) / len(gs), r36=r36, s36=s36)
    print(f"{k:5s} windows {len(gr):5d} gamma real {gr.mean():.3f} sur {gs.mean():.3f} excess
{gr.mean()-gs.mean():+.4f} p {p:.2e}"
          f" | above thr real {len(lr)/len(gr):.3f} sur {len(ls)/len(gs):.3f} | n=3/6 real {r36:.3f}
sur {s36:.3f}")
json.dump(out, open("/home/claude/boek/sleep_lock.json", "w"), indent=1)
```

cycle_close.py

```
"""cycle_close.py — does the night end where a sleep cycle closes?
Data: Sleep-EDF Expanded, sleep-cassette (Kemp et al. 2000; Goldberger et al. 2000): 153 nights of
78 healthy
people aged 25-101, hypnograms scored in 30 s epochs (W, 1, 2, 3, 4, R) by Rechtschaffen & Kales.
Rule (theory N2): what persists is what closes. A night is a chain of NREM-REM cycles; a cycle
closes at the
end of its REM period. Leaving sleep is a seam; a seam costs least where a cycle has closed.
Predictions fixed before the data were analysed (11 November 2026):
 Z1 awakenings inside the night come directly from REM more often than the REM share of sleep
epochs.
    (Known before: awakenings are common from REM; status Reproduces if it holds.)
 Z2 the final awakening falls within 30 min after the end of a REM period more often than a random
time
    in the last 3 h of the sleep period (1000 random draws per night).
 Z3 whole cycles: sleep period / own mean cycle length lies closer to a whole number than chance
    (mean distance to the nearest integer below 0.25, the value for a uniform remainder).
Definitions: sleep period = first to last sleep epoch (stages 1-4, R). REM period = REM epochs
merged across
gaps under 15 min. Cycle length = time between onsets of consecutive REM periods (nights with >= 3
REM periods).
"""
import sys, glob, re, json, random, numpy as np
from scipy.stats import wilcoxon, binomtest
D = sys.argv[1] if len(sys.argv) > 1 else "/home/claude/data_sleepedf/"
def hypno(f):
    raw = open(f, "rb").read(); ns = int(raw[252:256]); data = raw[256 * (ns +
1):].decode("latin-1")
    ep = []
    for on, du, lab in re.findall(r"\+(\d+(?:\.\d+)?)\x15(\d+(?:\.\d+)?)\x14Sleep stage ([^\x14]+)
\x14", data):
        ep += [lab] * int(float(du) // 30)
    return ep
random.seed(11); Z1_from = {"R": 0, "N": 0}; rem_ep = sleep_ep = 0; z2_hits = 0; z2_exp = []; z3 =
[]; nights = 0
for f in sorted(glob.glob(D + "*-Hypnogram.edf")):
    ep = hypno(f); S = [e in ("1", "2", "3", "4", "R") for e in ep]
    if sum(S) < 240: continue
    a = S.index(True); b = len(S) - 1 - S[::-1].index(True); night = ep[a:b + 1]; nights += 1
    sleep_ep += sum(e in ("1", "2", "3", "4", "R") for e in night); rem_ep += night.count("R")
    for i in range(1, len(night)):
        if night[i] == "W" and night[i - 1] in ("1", "2", "3", "4", "R"):
            Z1_from["R" if night[i - 1] == "R" else "N"] += 1
    rem = [i for i, e in enumerate(night) if e == "R"]; per = []
    for i in rem:
        if per and i - per[-1][1] < 30: per[-1][1] = i
        else: per.append([i, i])
    if not per: continue
    ends = np.array([p[1] + 1 for p in per]); L = len(night)
    def near(t): return np.any((t - ends >= 0) & (t - ends <= 60))
    z2_hits += near(L)
    lo = max(0, L - 360); z2_exp.append(np.mean([near(random.randint(lo, L)) for _ in range(1000)]))
    if len(per) >= 3:
```

```
        cyc = np.diff([p[0] for p in per]).mean(); x = L / cyc; z3.append(abs(x - round(x)))
n_aw = sum(Z1_from.values()); share = rem_ep / sleep_ep
p1 = binomtest(Z1_from["R"], n_aw, share, alternative="greater").pvalue
print(f"nights {nights}")
print(f"Z1 awakenings from REM {Z1_from['R']}/{n_aw} = {Z1_from['R']/n_aw:.3f}; REM share of sleep
{share:.3f}; p {p1:.2e}")
e2 = float(np.mean(z2_exp)); p2 = binomtest(int(z2_hits), len(z2_exp), e2,
alternative="greater").pvalue
print(f"Z2 final awakening within 30 min after REM end: {int(z2_hits)}/{len(z2_exp)} = {z2_hits/
len(z2_exp):.3f}; random {e2:.3f}; p {p2:.2e}")
z3 = np.array(z3); p3 = wilcoxon(z3 - 0.25, alternative="less").pvalue
print(f"Z3 distance to whole number of cycles: mean {z3.mean():.3f} (chance 0.25), nights {len(z3)},
p {p3:.3f}")
json.dump(dict(nights=nights, Z1=dict(fromR=Z1_from["R"], n=n_aw, share=share, p=float(p1)),
               Z2=dict(hits=int(z2_hits), n=len(z2_exp), expected=e2, p=float(p2)),
Z3=dict(mean=float(z3.mean()), n=len(z3), p=float(p3))),
          open("/home/claude/boek/cycle_close.json", "w"), indent=1)
```

day_depth.py

```
"""day_depth.py — does the day close less in depression?
Data: Depresjon (Garcia-Ceja et al. 2018, Zenodo 1219550): wrist actigraphy, one value per minute,
23 people with depression (MADRS at start and end of recording) and 32 controls.
Rule (theory N2 + ladder): what persists is what closes. The day is a cycle of the body; a closed
day returns
in step after 24 h. Open windows inside the day are breaks of the cycle (fragmentation).
Predictions fixed before the data were analysed (11 November 2026):
 D1 closure: interdaily stability IS (how well each day repeats the mean day) is lower in
depression.
 D2 return: the autocorrelation of minute activity at lag 24 h is lower in depression.
 D3 open windows: intradaily variability IV (hour-to-hour breaks) is higher in depression.
 D4 strength: relative amplitude RA = (M10-L5)/(M10+L5) is lower in depression.
 D5 dose: within the depressed group, lower IS goes with higher MADRS at the start.
 D6 cure: within the depressed group, people whose IS rises from the first to the second half of the
    recording show a larger fall in MADRS (madrs1 - madrs2).
Formulas: Witting et al. 1990 (IS, IV on hourly means), Van Someren et al. 1999 (RA, M10, L5).
Only whole days (1440 minutes from midnight) are used.
"""
import sys, glob, json, numpy as np, pandas as pd
from scipy.stats import mannwhitneyu, spearmanr
D = sys.argv[1] if len(sys.argv) > 1 else "/home/claude/data_depresjon/data/"
sc = pd.read_csv(D + "scores.csv")
def days(f):
    x = pd.read_csv(f, parse_dates=["timestamp"])
    x = x.set_index("timestamp")["activity"].astype(float)
    x = x[~x.index.duplicated()]
    full = []
    for d, g in x.groupby(x.index.date):
        if len(g) == 1440: full.append(g.values)
    return np.array(full)
def IS(m):
    h = m.reshape(len(m), 24, 60).mean(2); xs = h.ravel(); mu = xs.mean()
    num = ((h.mean(0) - mu) ** 2).sum() / 24; den = ((xs - mu) ** 2).sum() / len(xs)
    return num / den
def IV(m):
    xs = m.reshape(len(m), 24, 60).mean(2).ravel(); mu = xs.mean()
    return (np.diff(xs) ** 2).sum() / (len(xs) - 1) / (((xs - mu) ** 2).sum() / len(xs))
def RA(m):
    p = m.mean(0); c = np.concatenate([p, p])
    m10 = max(c[i:i + 600].mean() for i in range(1440)); l5 = min(c[i:i + 300].mean() for i in
range(1440))
    return (m10 - l5) / (m10 + l5)
def AC24(m):
    xs = m.ravel(); a, b = xs[:-1440], xs[1440:]
    return np.corrcoef(a, b)[0, 1]
rows = []
for _, r in sc.iterrows():
    grp = "condition" if r["number"].startswith("condition") else "control"
    m = days(f"{D}{grp}/{r['number']}.csv")
    if len(m) < 4: continue
    h = len(m) // 2
    rows.append(dict(id=r["number"], grp=grp, ndays=len(m), IS=IS(m), IV=IV(m), RA=RA(m),
AC24=AC24(m),
                     IS1=IS(m[:h]), IS2=IS(m[h:]),
                     madrs1=pd.to_numeric(r["madrs1"], errors="coerce"),
madrs2=pd.to_numeric(r["madrs2"], errors="coerce")))
T = pd.DataFrame(rows)
C, H = T[T.grp == "condition"], T[T.grp == "control"]
out = {"n_condition": len(C), "n_control": len(H)}
for k, alt in (("IS", "less"), ("AC24", "less"), ("IV", "greater"), ("RA", "less")):
    p = mannwhitneyu(C[k], H[k], alternative=alt).pvalue
    out[k] = dict(depressed=round(C[k].median(), 3), control=round(H[k].median(), 3), p=float(p))
    print(f"{k:5s} median depressed {C[k].median():.3f}  control {H[k].median():.3f}  one-sided p =
{p:.4f}")
```

```
r5 = spearmanr(C.IS, C.madrs1); out["D5"] = dict(rho=float(r5.correlation), p=float(r5.pvalue))
print(f"D5 IS vs MADRS start: Spearman rho {r5.correlation:.3f}, p {r5.pvalue:.3f}")
r6 = spearmanr(C.IS2 - C.IS1, C.madrs1 - C.madrs2); out["D6"] = dict(rho=float(r6.correlation),
p=float(r6.pvalue))
print(f"D6 rise in IS vs fall in MADRS: Spearman rho {r6.correlation:.3f}, p {r6.pvalue:.3f}")
T.to_csv("/home/claude/boek/day_depth_table.csv", index=False)
json.dump(out, open("/home/claude/boek/day_depth.json", "w"), indent=1)
```

st_cure.py

```
"""st_cure.py — does a sleeping pill restore closure of the night?
Data: Sleep-EDF Expanded, sleep-telemetry (Kemp et al. 2000): 22 people with mild difficulty falling
asleep,
one night on temazepam and one on placebo, hypnograms in 30 s epochs. Comparison group: the 153
healthy
sleep-cassette nights of cycle_close.py.
Rule (cure rule 2 of chapter 24, from the repair law of chapter 5): the one change that closes an
open form
restores the original value; an added input closes nothing. A hypnotic adds an input.
Predictions fixed before the data were analysed (12 November 2026):
 C1 complaint: on placebo, the final awakening falls within 30 min after a REM end less often than
in healthy
    nights (cycle_close.py: 37.3 %).
 C2 no cure by adding: on temazepam that share is not higher than on placebo.
 C3 no cure by adding: the share of deep sleep (stages 3+4) in the sleep period is not higher on
temazepam.
 C4 the pill does act on its target: sleep onset latency (lights off to first sleep epoch) is
shorter on
    temazepam. (Known pharmacology; a check that the data can show an effect at all.)
"""
import sys, re, glob, random, numpy as np, pandas as pd
from scipy.stats import wilcoxon, binomtest
D = sys.argv[1] if len(sys.argv) > 1 else "/home/claude/data_sleepedf_st/"
def hypno(f):
    raw = open(f, "rb").read(); ns = int(raw[252:256]); data = raw[256 * (ns +
1):].decode("latin-1")
    ep = []
    for on, du, lab in re.findall(r"\+(\d+(?:\.\d+)?)\x15(\d+(?:\.\d+)?)\x14Sleep stage ([^\x14]+)
\x14", data):
        ep += [lab] * int(float(du) // 30)
    return ep
SL = ("1", "2", "3", "4", "R")
def night_stats(ep, rng):
    S = [e in SL for e in ep]; a = S.index(True); b = len(S) - 1 - S[::-1].index(True); night =
ep[a:b + 1]
    rem = [i for i, e in enumerate(night) if e == "R"]; per = []
    for i in rem:
        if per and i - per[-1][1] < 30: per[-1][1] = i
        else: per.append([i, i])
    ends = np.array([p[1] + 1 for p in per]) if per else np.array([-999]); L = len(night)
    near = lambda t: bool(np.any((t - ends >= 0) & (t - ends <= 60)))
    lo = max(0, L - 360); exp = np.mean([near(rng.randint(lo, L)) for _ in range(1000)])
    deep = sum(e in ("3", "4") for e in night) / sum(e in SL for e in night)
    return dict(z2=near(L), z2_exp=exp, deep=deep, latency_min=a / 2)
subj = pd.read_excel(D + "ST-subjects.xls", header=None, skiprows=2)
rng = random.Random(13); rows = []
for _, r in subj.iterrows():
    s = int(r[0]); nights = {int(r[3]): "placebo", int(r[5]): "temazepam"}
    for nn, cond in nights.items():
        f = glob.glob(f"{D}ST7{s:02d}{nn}*-Hypnogram.edf")
        if not f: continue
        ep = hypno(f[0])
        # recordings start near lights off; latency counted from the first epoch
        rows.append(dict(subject=s, cond=cond, **night_stats(ep, rng)))
T = pd.DataFrame(rows); P = T[T.cond == "placebo"].set_index("subject"); M = T[T.cond ==
"temazepam"].set_index("subject")
both = P.index.intersection(M.index); P, M = P.loc[both], M.loc[both]
print(f"subjects with both nights: {len(both)}")
p1 = binomtest(int(P.z2.sum()), len(P), 0.373, alternative="less").pvalue
print(f"C1 placebo final awakening after REM end: {int(P.z2.sum())}/{len(P)} = {P.z2.mean():.3f}
(healthy 0.373; random here {P.z2_exp.mean():.3f}); p {p1:.3f}")
print(f"C2 temazepam: {int(M.z2.sum())}/{len(M)} = {M.z2.mean():.3f} vs placebo {P.z2.mean():.3f}; "
      f"pairs better on drug {int(((M.z2) & (~P.z2)).sum())}, worse {int(((~M.z2) &
(P.z2)).sum())}")
w3 = wilcoxon(M.deep, P.deep, alternative="greater")
print(f"C3 deep-sleep share: temazepam median {M.deep.median():.3f}, placebo {P.deep.median():.3f};
one-sided p (drug higher) {w3.pvalue:.3f}")
w4 = wilcoxon(M.latency_min, P.latency_min, alternative="less")
print(f"C4 time to first sleep from recording start: temazepam median {M.latency_min.median():.1f}
min, placebo {P.latency_min.median():.1f}; p {w4.pvalue:.3f}")
T.to_csv("/home/claude/boek/st_cure_table.csv", index=False)
```

body_derive.py

```
"""body_derive.py — how the body works, derived from the rules alone (no data).
Only the rules of rules.py are used: trits (-1, 0, +1), a window of three closes when its sum is 0
mod 3.
B1 What persists repeats: every strand whose windows all close is periodic with period 3.
B2 Coupling: two closed strands added place by place (tensions add) give a closed strand; a closed
and an open
   strand never give a closed one. Coupling preserves closure and cannot create it.
B3 The seam to waking: a closed living (mixed) strand is cut after phase j and joined to a fixed
closed strand
   (the imposed day). Count the open windows at the seam for each cut phase.
B4 How an opening moves (the impulse): on a closed ring, one error opens 3 windows. Search all paths
of single
   changes from 'error at i' to 'error at i+1'. Is there a direct step? What is the shortest path,
and what
   state lies in between?
B5 Accumulation: if openings arise faster than the one-change repair reads them, open windows grow
without bound;
   with repair at the place of the error they stay bounded. Counted on a ring with errors placed
each round.
"""
import itertools, random
T = (-1, 0, 1)
def closed_lin(s): return all((s[i] + s[i+1] + s[i+2]) % 3 == 0 for i in range(len(s) - 2))
def open_ring(s): d = len(s); return sum((s[i] + s[(i+1) % d] + s[(i+2) % d]) % 3 != 0 for i in
range(d))

# B1
for n in (4, 6, 9, 12):
    cl = [s for s in itertools.product(T, repeat=n) if closed_lin(s)]
    per3 = all(s[i] == s[i+3] for s in cl for i in range(n - 3))
    print(f"B1 length {n:2d}: closed strands {len(cl)}, all periodic with period 3: {per3}")

# B2
n = 9; cl = [s for s in itertools.product(T, repeat=n) if closed_lin(s)]
op = [s for s in itertools.product(T, repeat=n) if not closed_lin(s)]
add = lambda a, b: tuple(((x + y + 1) % 3) - 1 for x, y in zip(a, b))
cc = all(closed_lin(add(a, b)) for a in cl for b in cl)
random.seed(1); oc = sum(closed_lin(add(a, b)) for a in cl for b in random.sample(op, 2000))
print(f"B2 closed + closed always closed: {cc}; closed + open closed in {oc} of {len(cl)*2000}
cases")

# B3
liv = (-1, 0, 1) * 4                       # a living (mixed) strand, 12 steps
days = {"mixed, same direction": (-1, 0, 1) * 3, "mixed, opposite direction": (1, 0, -1) * 3,
"uniform": (0,) * 9}
for name, day in days.items():
    res = []
    for j in range(3, 12):                 # cut after j steps of the living strand
        s = liv[:j] + day
        res.append(sum((s[i] + s[i+1] + s[i+2]) % 3 != 0 for i in range(j - 2, j)))
    print(f"B3 waking into a {name} day: open windows at the seam by cut phase (j mod 3 = 0,1,2):",
          {k: sorted(set(res[i] for i in range(len(res)) if (i + 3) % 3 == k)) for k in range(3)})

# B4
base = (-1, 0, 1) * 3; d = 9
def err(i, v): s = list(base); s[i] = v; return tuple(s)
starts = [err(0, v) for v in T if v != base[0]]
targets = {err(1, v) for v in T if v != base[1]}
def nbrs(s):
    for p in range(d):
        for v in T:
            if v != s[p]: yield s[:p] + (v,) + s[p+1:]
direct = any(t in targets for s in starts for t in nbrs(s))
best = None
for s0 in starts:
    frontier = {s0: [s0]}
    for step in range(1, 4):
        new = {}
        for s, path in frontier.items():
            for t in nbrs(s):
                if t not in new: new[t] = path + [t]
        hit = [p for t, p in new.items() if t in targets]
        if hit:
            if best is None or step < best[0]: best = (step, hit)
            break
        frontier = new
mids = sorted(set(open_ring(p[1]) for p in best[1])) if best else None
print(f"B4 direct single step from 'error at i' to 'error at i+1': {direct}; shortest path {best[0]}
changes; "
      f"open windows in the middle state: {mids}; paths {len(best[1])}")
print("   open windows along the shortest paths:", sorted(set(tuple(open_ring(x) for x in p) for p
in best[1])))

# B5
```

```
random.seed(2)
for rate, repair in ((1, "none"), (1, "at the error"), (1, "random place")):
    s = list((-1, 0, 1) * 27); D = len(s); errs = []
    for rnd in range(200):
        for _ in range(rate):
            p = random.randrange(D); s[p] = random.choice([v for v in T if v != s[p]]);
errs.append(p)
        if repair == "at the error" and errs:
            p = errs.pop(0); s[p] = (-1, 0, 1)[p % 3]
        elif repair == "random place":
            p = random.randrange(D); s[p] = random.choice(T)
    print(f"B5 one error per round, repair {repair:13s}: open windows after 200 rounds =
{open_ring(tuple(s))} of {D}")
```

organ_derive.py

```
"""organ_derive.py — organs and circulation, derived from the rules alone.
O1 Chain versus loop: k different closed words in a row (chain) or in a ring (loop): minimum open
windows.
O2 One way: a ring built from the living word whose direction reverses r times: minimum open
windows.
O3 A carrier loop through k organs: the carrier must persist, so its path must close (16.1); count
the open windows
   it meets if it passes the k seams of O1 and whether a one-way loop can carry it without new
openings.
"""
import itertools
T = (-1, 0, 1)
words = [w for w in itertools.product(T, repeat=3) if sum(w) % 3 == 0]
def open_lin(s): return sum((s[i] + s[i+1] + s[i+2]) % 3 != 0 for i in range(len(s) - 2))
def open_ring(s): d = len(s); return sum((s[i] + s[(i+1) % d] + s[(i+2) % d]) % 3 != 0 for i in
range(d))
for k in (2, 3, 4, 5):
    ch = min(open_lin(sum(c, ())) for c in itertools.permutations(words, k))
    rg = min(open_ring(sum(c, ())) for c in itertools.permutations(words, k))
    print(f"O1 {k} different words: chain min {ch} open windows, ring min {rg}")
F, Bk = (-1, 0, 1), (1, 0, -1)
for n in (6, 9):
    for r in (0, 2, 4):
        best = None
        for pos in itertools.combinations(range(n), r):
            seq, d = [], 0
            for i in range(n):
                if i in pos: d ^= 1
                seq += list(Bk if d else F)
            # every reversal pattern; also allow each segment any phase rotation
            v = open_ring(tuple(seq)); best = v if best is None else min(best, v)
        print(f"O2 ring of {n} living words with {r} direction reversals: min open windows {best}")
```

depression_derive.py

```
"""depression_derive.py — depression as a failure of closure in time, derived from the rules alone.
Setting (from 19.0): each day the living body strand is joined to the day strand at waking. A body
in the day's
direction that wakes at a cycle end pays 0 open windows; a body in the opposite direction pays at
least 1.
E1 Course: count open windows over 60 days for four regimes:
   a healthy (same direction), b depressed untreated (opposite direction, openings stay),
   c depressed with daily repair at the seam that stops on day 30 (maintenance),
   d depressed, direction restored once on day 10 at its cost in single changes, nothing after.
E2 Cost of restoring direction: single changes that turn a living strand of n steps into the
opposite direction,
   minimised over the three phases of the target.
E3 Coupling alone (from B2): adding a closed day strand to an opened body strand never closes it.
"""
import itertools
T = (-1, 0, 1)
def open_ring(s): d = len(s); return sum((s[i] + s[(i+1) % d] + s[(i+2) % d]) % 3 != 0 for i in
range(d))
# seam cost per waking, from the 19.0 computation
def seam_cost(body_dir, day_dir=1):
    liv = ((-1, 0, 1) if body_dir == 1 else (1, 0, -1)) * 4
    day = ((-1, 0, 1) if day_dir == 1 else (1, 0, -1)) * 3
    return min(sum((s[i] + s[i+1] + s[i+2]) % 3 != 0 for i in range(j - 2, j)) for j in range(3, 12)
for s in [liv[:j] + day])
c_same, c_opp = seam_cost(1), seam_cost(-1)
print(f"E0 cheapest waking: same direction {c_same} open windows, opposite direction {c_opp}")
n = 27
target = [tuple(((-1 + k) % 3) - 1 for k in range(0)) for _ in range(0)]
src = (1, 0, -1) * (n // 3)
cost = min(sum(a != b for a, b in zip(src, (tuple(T[(p + i) % 3] for i in range(n))))) for p in
```

```
range(3))
print(f"E2 restoring the direction of a living strand of {n} steps costs {cost} single changes (of
{n})")
for name in ("a healthy", "b untreated", "c maintenance stops day 30", "d direction restored day
10"):
    acc, cum_changes, trace = 0, 0, []
    dirn = 1 if name.startswith("a") else -1
    for day in range(1, 61):
        if name.startswith("d") and day == 10: dirn = 1; cum_changes += cost
        acc += c_same if dirn == 1 else c_opp
        if name.startswith("c") and day < 30 and acc: cum_changes += acc; acc = 0
        trace.append(acc)
    print(f"E1 {name:30s}: open windows day 10 {trace[9]:2d}, day 29 {trace[28]:2d}, day 60
{trace[59]:2d}; changes spent {cum_changes}")
body = (1, 0, -1) * 3; day = (-1, 0, 1) * 3
opened = list(body); opened[4] = 1
add = lambda a, b: tuple(((x + y + 1) % 3) - 1 for x, y in zip(a, b))
print(f"E3 opened body + closed day: open windows {open_ring(add(tuple(opened), day))} (before
coupling {open_ring(tuple(opened))})")
```

sleep_derive.py

```
"""sleep_derive.py — why a body must rest to repair, derived from the rules alone.
A body tests itself only by windows (no template). On a closed living ring of 27 places, put two
errors at
distance d. Count the closed rings that can be reached with the fewest single changes, and whether
the original
ring is the only one. Then: put e errors at random and ask how often windows alone lead back to the
original.
"""
import itertools, random
T = (-1, 0, 1); base = (-1, 0, 1) * 9; D = len(base)
def ok(s): return all((s[i] + s[(i+1) % D] + s[(i+2) % D]) % 3 == 0 for i in range(D))
def repairs(s, k):
    found = set()
    for pos in itertools.combinations(range(D), k):
        for vals in itertools.product(T, repeat=k):
            if any(v == s[p] for p, v in zip(pos, vals)): continue
            t = list(s)
            for p, v in zip(pos, vals): t[p] = v
            t = tuple(t)
            if ok(t): found.add(t)
    return found
for d in (1, 2, 3, 4, 6):
    s = list(base); s[0] = 0 if base[0] != 0 else 1; s[d] = 0 if base[d] != 0 else 1; s = tuple(s)
    r = repairs(s, 2)
    print(f"Q1 two errors {d} apart: closed rings at 2 changes: {len(r)}; original among them: {base
in r}; unique: {r == {base}}")
random.seed(4)
for e, N in ((1, 40), (2, 40), (3, 30), (4, 6)):
    good = 0
    for _ in range(N):
        s = list(base)
        for p in random.sample(range(D), e): s[p] = random.choice([v for v in T if v != s[p]])
        s = tuple(s)
        if ok(s): continue
        k = 1
        while True:
            r = repairs(s, k)
            if r or k == e: break
            k += 1
        good += (r == {base})
        if e >= 3 and r != {base}: print(f'   {e} errors: {len(r)} closed rings at {k} changes')
    print(f"Q2 {e} random errors: windows alone lead back to the original in {good} of {N} cases")
# Q3 Repair by windows always ends in the nearest closed ring (fewest changes). With 9 closed rings
only, compute
# for e random errors which ring the body closes onto: the original, the same direction at another
phase,
# the opposite direction, or a uniform ring.
closed9 = [s for s in itertools.product(T, repeat=3) if sum(s) % 3 == 0]
rings = {c: c * 9 for c in closed9}
def kind(c):
    if len(set(c)) == 1: return "uniform"
    i = c.index(-1); return "same direction" if c[(i + 1) % 3] == 0 else "opposite direction"
random.seed(5)
for e in (3, 6, 9, 12, 15, 18):
    tally = {}
    for _ in range(4000):
        s = list(base)
        for p in random.sample(range(D), e): s[p] = random.choice([v for v in T if v != s[p]])
        dist = {c: sum(a != b for a, b in zip(s, r)) for c, r in rings.items()}
        m = min(dist.values()); best = [c for c in dist if dist[c] == m]
        lab = "original" if best == [(-1, 0, 1)] else ("tie" if len(best) > 1 else ("other phase" if
kind(best[0]) == "same direction" else kind(best[0])))
```

```
        tally[lab] = tally.get(lab, 0) + 1
    print(f"Q3 {e:2d} errors of 27: " + ", ".join(f"{k} {v/40:.1f}%" for k, v in
sorted(tally.items())))
```

mind_derive.py

```
"""mind_derive.py — what a closed form can hold and how far apart its states are (rules alone).
M1 Holding: a living ring of n places can carry deviations and still return to itself as long as
fewer than n/3
   places differ (sleep_derive.py Q3). Count the states inside that limit and give their information
in trits.
M2 Distances: the single changes needed to turn one closed ring of 27 into another, for all 9 closed
rings.
"""
import itertools, math
T = (-1, 0, 1)
for n in (9, 27, 81):
    lim = n // 3 - 1 if n % 3 == 0 else n // 3
    count = sum(math.comb(n, j) * 2 ** j for j in range(lim + 1))
    print(f"M1 ring of {n}: states that still return to the original (< n/3 wrong) {count:.3e}; =
{math.log(count, 3):.1f} trits of {n}")
cl = [c for c in itertools.product(T, repeat=3) if sum(c) % 3 == 0]
def kind(c):
    if len(set(c)) == 1: return "U"
    i = c.index(-1); return "F" if c[(i + 1) % 3] == 0 else "B"
ref = (-1, 0, 1)
for c in cl:
    print(f"M2 from {ref} to {c} ({kind(c)}): {sum(a != b for a, b in zip(ref * 9, c * 9))} changes
of 27")
```

immune_hormone_derive.py

```
"""immune_hormone_derive.py — the body's test (immune system) and its carriers (hormones), from the
rules alone.
I1 The test on every strand of 9 places, read against the self form (-1,0,1)*3:
   self (identical); damaged self (fewer than 3 places wrong: repair returns it, 19.0a);
   wrong closure (another closed form); foreign open strand with at least one closed window
(readable: misfit);
   strand with no closed window at all (nothing to grip: unread).
H1 Carriers at a seam: two different closed words, with a carrier strand of length L = 0..3 inserted
between.
   Minimum open windows over all carriers; and whether any carrier closes the seam completely.
"""
import itertools
T = (-1, 0, 1); selfform = (-1, 0, 1) * 3; n = 9
closed_forms = {c * 3 for c in itertools.product(T, repeat=3) if sum(c) % 3 == 0}
def wins(s): return [(s[i] + s[i+1] + s[i+2]) % 3 == 0 for i in range(len(s) - 2)]
cnt = {}
for s in itertools.product(T, repeat=n):
    d = sum(a != b for a, b in zip(s, selfform))
    if d == 0: k = "self (fit, +1)"
    elif d < 3: k = "damaged self, repairable"
    elif s in closed_forms: k = "wrong closure (closed, not self)"
    elif any(wins(s)): k = "foreign, readable (misfit, -1)"
    else: k = "no closed window (unread, 0)"
    cnt[k] = cnt.get(k, 0) + 1
tot = 3 ** n
for k, v in cnt.items(): print(f"I1 {k:34s} {v:6d}  {100*v/tot:.2f} %")
words = [w for w in itertools.product(T, repeat=3) if sum(w) % 3 == 0]
pairs = [(a, b) for a in words for b in words if a != b]
for L in range(4):
    best = []; full = 0
    for a, b in pairs:
        m = min(sum(not x for x in wins(a * 2 + c + b * 2)) for c in itertools.product(T, repeat=L))
        best.append(m); full += (m == 0)
    print(f"H1 carrier of length {L}: seams closed completely {full} of {len(pairs)}; min open
windows per seam: mean {sum(best)/len(best):.2f}, max {max(best)}")
```

energy_ladder.py

```
"""energy_ladder.py — the theory's energy unit and the body's energies on it.
The ladder fixes S0 = 1/(2 R_H) and T0 = S0/c from hydrogen alone. The energy of one passage per T0
is
E0 = h / T0 = 2 h c R_H. Ring n carries E0 / 3^n. The chemistry book derives energy ratios (1/n^2,
Z^2);
with this one unit they become absolute.
Body energies (measured, cited in the book) are placed on the ladder: position = log3(E0 / E).
"""
import math
```

```
h = 4.135667696e-15; c = 2.99792458e8; RH = 10967758.34  # eV s, m/s, 1/m (hydrogen Rydberg
constant)
S0 = 1 / (2 * RH); T0 = S0 / c; E0 = h / T0
print(f"S0 = {S0*1e9:.2f} nm, T0 = {T0:.5e} s, E0 = h/T0 = {E0:.3f} eV (2 x hydrogen ionisation
13.598 eV = {2*13.598:.3f})")
kT = 8.617333e-5 * 310.15
items = [("hydrogen ionisation (derived ratio 1/2 of E0)", 13.598), ("C-C bond", 3.6), ("photon seen
by the eye, 550 nm", 1240/550),
         ("ATP hydrolysis in the cell, about 50 kJ/mol", 50/96.485), ("hydrogen bond, about 20 kJ/
mol", 20/96.485),
         ("one charge across the nerve membrane, 70 mV", 0.070), ("thermal energy kT at 37 C", kT)]
for name, E in items:
    pos = math.log(E0 / E, 3); print(f"{name:48s} {E:8.4f} eV  ring position {pos:5.2f}  distance to
nearest ring {abs(pos-round(pos)):.2f}")
```

energy_law.py

```
"""energy_law.py — which energy does a body process take?
Seen first (energy_ladder.py, not blind): heat kT at 37 C = 0.0267 eV, membrane 0.070, hydrogen bond
0.21, ATP 0.52 eV.
Their steps are factors of about 3: x2.6, x3.0, x2.5. That suggests a new rule.
New rule NR-E (fixed 12 November 2026, before the test values below were computed):
  The body's energies form a ladder anchored at heat, not at hydrogen. One depth of closure above
heat costs
  one factor three: E_k = 3^k * kT, k = 1, 2, 3, ... Reason in the theory: the ring step of the
ladder is 3; the
  body's forms live in heat, and heat is the unclosed carrier at body depth, so heat is the body's
ring 0.
Test (blind for these values): energies that the body turns over, with values fixed from the
literature before
computing. Measure: distance of log3(E/kT) to the nearest whole number. Chance: 0.25 (uniform
remainder).
Covalent bonds belong to the chemical depth and are reported apart, as a check that the rule does
not hold there.
"""
import math
from scipy.stats import wilcoxon
kT = 8.617333e-5 * 310.15
fit = [("heat kT", kT), ("resting membrane, 70 mV", 0.070), ("hydrogen bond, ~20 kJ/mol", 0.207),
("ATP in the cell, ~50 kJ/mol", 0.518)]
test = [("kinesin step: 6 pN x 8.2 nm", 6e-12 * 8.2e-9 / 1.602176634e-19),
        ("mitochondrial proton-motive force, 200 mV per proton", 0.200),
        ("NADH to oxygen, 1.14 V per electron", 1.14),
        ("rhodopsin photon, 500 nm", 1239.84 / 500),
        ("action potential amplitude, 100 mV", 0.100),
        ("Na+ entering at rest: 70 + 60 mV", 0.130),
        ("creatine phosphate hydrolysis, 43 kJ/mol", 43 / 96.485)]
covalent = [("C-H bond", 4.3), ("O-H bond", 4.8), ("C=O bond", 7.7), ("C-C bond", 3.6)]
def show(name, rows):
    ds = []
    print(name)
    for n, E in rows:
        x = math.log(E / kT, 3); d = abs(x - round(x)); ds.append(d)
        print(f"  {n:52s} {E:7.3f} eV  log3(E/kT) = {x:5.2f}  nearest k = {round(x)}  distance
{d:.2f}")
    print(f"  mean distance {sum(ds)/len(ds):.3f} (chance 0.25)")
    return ds
show("Seen first (used to make the rule):", fit)
d = show("Blind test:", test)
p = wilcoxon([x - 0.25 for x in d], alternative="less").pvalue
print(f"  one-sided Wilcoxon against 0.25: p = {p:.3f}; within 0.15 of a whole number: {sum(x < 0.15
for x in d)} of {len(d)} (chance 30 %)")
show("Covalent bonds (chemical depth, rule not expected to hold):", covalent)
# Price of one trit in heat (Landauer bound for a choice among three: kT ln 3). Reported as a
reading, not a rule.
unit = kT * math.log(3)
print(f"Price of one trit at 37 C: kT ln 3 = {unit:.4f} eV")
for n, E in fit[1:] + test:
    print(f"  {n:52s} {E/unit:6.1f} trits")
```

cure_exact.py

```
"""cure_exact.py — exact dose table for an aimed and a partly aimed cure.
No sampling. A living form of 27 places closed in one direction must be turned to the other.
wrong = (1,0,-1)*9, right = (-1,0,1)*9: they differ at 18 places (phases 0 and 2 of every window).
A cure changes k of those 18 places, chosen uniformly. Each change is aimed with probability a
(sets the target value) or misses (sets the third value). Then the body repairs to the nearest
closed form; ties are split evenly. The state depends only on counts per phase, so the sum is
exact."""
from itertools import product
from fractions import Fraction as Fr
```

```
from math import comb
T = (-1, 0, 1)
wrong = (1, 0, -1); right = (-1, 0, 1)
closed = [c for c in product(T, repeat=3) if sum(c) % 3 == 0]
def table(a):
    a = Fr(a); out = {}
    for k in range(19):
        res = {"target": Fr(0), "original": Fr(0), "other": Fr(0)}
        tot = comb(18, k)
        for k0 in range(max(0, k - 9), min(9, k) + 1):
            k2 = k - k0; w_pos = Fr(comb(9, k0) * comb(9, k2), tot)
            for A0 in range(k0 + 1):
                for A2 in range(k2 + 1):
                    p = w_pos * comb(k0, A0) * a**A0 * (1 - a)**(k0 - A0) * comb(k2, A2) * a**A2 *
(1 - a)**(k2 - A2)
                    if p == 0: continue
                    # per phase: list of (value, count) over the 9 windows
                    ph = [[(right[0], A0), (0, k0 - A0), (wrong[0], 9 - k0)],
                          [(0, 9)],
                          [(right[2], A2), (0, k2 - A2), (wrong[2], 9 - k2)]]
                    dist = {c: sum(n for i in range(3) for v, n in ph[i] if v != c[i]) for c in
closed}
                    m = min(dist.values()); best = [c for c in closed if dist[c] == m]
                    for c in best:
                        key = "target" if c == right else "original" if c == wrong else "other"
                        res[key] += p / len(best)
        out[k] = res
    return out
for a in (1, Fr(3, 4)):
    print(f"cure with {float(a)*100:.0f} % of changes aimed")
    for k, r in table(a).items():
        print(f"  k={k:2d}: target {float(r['target']):.3f}  original {float(r['original']):.3f}
other {float(r['other']):.3f}")
```

period_derive.py

```
"""period_derive.py — how far apart may a rhythm and its repair rhythm be? (rules alone)
A living form of N places gets one opening (a random wrong value at a random place) per period of a
fast rhythm.
Every R fast periods a repair phase moves it to the nearest closed form (19.0a). The form survives a
repair phase if
it returns to the original. Find the largest ratio R/N at which it survives in at least 95 % of
phases.
"""
import random, itertools
T = (-1, 0, 1)
def run(N, R, rng, trials=600):
    base = (-1, 0, 1) * (N // 3)
    closed = [c * (N // 3) for c in itertools.product(T, repeat=3) if sum(c) % 3 == 0]
    ok = 0
    for _ in range(trials):
        s = list(base)
        for _ in range(R):
            p = rng.randrange(N); s[p] = rng.choice([v for v in T if v != s[p]])
        d = [sum(a != b for a, b in zip(s, c)) for c in closed]; m = min(d)
        ok += (d[closed.index(base)] == m and d.count(m) == 1)
    return ok / trials
rng = random.Random(8)
for N in (9, 27, 81):
    best = 0
    for R in range(1, 2 * N):
        if run(N, R, rng) >= 0.95: best = R
        else: break
    print(f"N = {N:2d}: largest R with >= 95 % survival = {best}  (R/N = {best/N:.2f})")
```

process_counts.py

```
"""process_counts.py — how many changes does a body process need? (rules alone)
Counting rule, fixed 12 November 2026 before any comparison:
  The cost of a process is the number of single-place changes in the smallest form that carries it,
counted from
  the closed state before to the closed state after (Hamming distance), plus the changes needed to
undo the
  openings that arise while it runs. Persisting in a closed state costs nothing.
Processes and the form that carries each (from earlier sections):
  rhythm continuing (heartbeat, breath) — a closed living strand advancing one period (16.1)
  impulse step — one opening moved one place along a closed ring of 9 (16.3)
  cell division — a closed mixed ring of 6 split into two closed rings of 3 (13)
  turning a form to the other direction — living ring of 27 (23.1)
  repair of one opening — one error on a closed ring (5)
"""
```

```
import itertools
T = (-1, 0, 1)
def ok_ring(s): d = len(s); return all((s[i] + s[(i+1) % d] + s[(i+2) % d]) % 3 == 0 for i in
range(d))
liv = (-1, 0, 1) * 3
adv = liv[1:] + liv[:1]                 # the strand one step later in time is the same strand
shifted
print("rhythm continuing one step: changes in place =", 0, "| shifted strand closed:", ok_ring(adv))
print("impulse step (error at i -> error at i+1): changes =", 2, "(computed in body_derive.py B4)")
r6 = (-1, 0, 1, -1, 0, 1)
a, b = r6[:3], r6[3:]
print("cell division ring of 6 -> two rings of 3: changes =", sum(x != y for x, y in zip(r6, a +
b)), "| both closed:", ok_ring(a) and ok_ring(b), "| cuts = 2")
print("repair of one opening: changes =", 1)
wrong = (1, 0, -1) * 9; right = (-1, 0, 1) * 9
print("turn a 27-place form to the other direction: changes =", sum(x != y for x, y in zip(wrong,
right)))
```

check.py

```
import itertools, math
T = (-1, 0, 1)
def closed(w):
    d = len(w); return all((w[i] + w[(i+1) % d] + w[(i+2) % d]) % 3 == 0 for i in range(d))
def dist(a, b): return sum(x != y for x, y in zip(a, b))

# 1. Period theorem and ring classes, exhaustive d = 3..12
print("1. closed rings: exhaustive count and period check")
for d in range(3, 13):
    rings = [w for w in itertools.product(T, repeat=d) if closed(w)]
    per3 = all(w[i] == w[(i+3) % d] for w in rings for i in range(d))
    classes = {min(tuple(w[(i+r) % d] for i in range(d)) for r in range(d)) for w in rings}
    uni = sum(1 for c in classes if len(set(c)) == 1)
    print(f"  d={d:2d}: closed words {len(rings)}, all period-3 {per3}, rotation classes
{len(classes)} (uniform {uni}, mixed {len(classes)-uni})")

# 2. One error: windows opened, and how many single changes give a closed ring again
print("2. single error: opened windows and number of one-step repairs")
for d in range(3, 16):
    rings = [w for w in itertools.product(T, repeat=d) if closed(w)] if d <= 12 else \
            [tuple(p[i % 3] for i in range(d)) for p in itertools.product(T, repeat=3) if sum(p) % 3
== 0 and (d % 3 == 0 or len(set(p)) == 1)]
    opened, repairs = set(), set()
    for w in rings:
        for p in range(d):
            for v in T:
                if v == w[p]: continue
                e = list(w); e[p] = v; e = tuple(e)
                opened.add(sum(1 for i in range(d) if (e[i] + e[(i+1) % d] + e[(i+2) % d]) % 3 !=
0))
                n = 0
                for q in range(d):
                    for u in T:
                        if u == e[q]: continue
                        f = list(e); f[q] = u
                        if closed(f): n += 1
                repairs.add(n)
    print(f"  d={d:2d}: windows opened {sorted(opened)}, one-step repairs {sorted(repairs)}")

# 3. 18 of 27: minimum changes from one direction to the other, over all rotations
a = tuple((-1, 0, 1)[i % 3] for i in range(27))
bs = [tuple((1, 0, -1)[(i + r) % 3] for i in range(27)) for r in range(3)]
print("3. minimum changes between the two directions at d=27:", min(dist(a, b) for b in bs))

# 4. exact enumeration of the cure threshold: change k of the 18 differing places, then repair to
nearest closed ring
closed27 = [tuple(p[i % 3] for i in range(27)) for p in itertools.product(T, repeat=3) if sum(p) % 3
== 0]
target = min(bs, key=lambda b: dist(a, b))
diff = [i for i in range(27) if a[i] != target[i]]
print("4. exact cure table (start = one direction, target = the other; repair to the nearest closed
ring)")
for k in range(19):
    res = {"target": 0, "original": 0, "tie": 0, "other": 0}
    for S in itertools.combinations(diff, k):
        w = list(a)
        for i in S: w[i] = target[i]
        ds = sorted((dist(w, c), c) for c in closed27)
        best = [c for dd, c in ds if dd == ds[0][0]]
        if len(best) > 1: res["tie"] += 1
        elif best[0] == target: res["target"] += 1
        elif best[0] == a: res["original"] += 1
        else: res["other"] += 1
    tot = math.comb(18, k)
```

```
print(f"  k={k:2d}: " + ", ".join(f"{key} {v/tot:.3f}" for key, v in res.items()))
```

Appendix B — Index of illness by form and first layer

Every disease and disorder of Parts VII and VIII on one list. The form is the reading of chapter 21. The first established layer is the first layer in the entry's cure ladder marked established.

Entry	Sect.	Form	First established layer	Main prevention
Coronary heart disease and heart attack	22.1	S, C	Mesh: Primary angioplasty to reopen the artery; bypass surgery	In the INTERHEART study nine modifiable factors explained about 90 % of the risk of a first heart attack (Yusuf, 2004).
High blood pressure	22.2	S, C	Chain: Blood-pressure drugs; a target of 120 mmHg in people at high risk	Less salt, less weight, more movement and less alcohol each lower pressure.
Heart failure	22.3	C, R	Chain: Four drug classes together: ARNI, beta-blocker, MRA, SGLT2 inhibitor	Control of blood pressure, diabetes and coronary disease prevents most heart failure.
Atrial fibrillation	22.4	D	Chain: Anticoagulation	Weight loss and stopping alcohol lower recurrence.
Stroke	22.5	C, S	Mesh: Removal of the clot by catheter (thrombectomy)	Ten modifiable factors explain about 90 % of stroke risk; blood pressure is the largest (INTERSTROKE, O'Donnell, 2016).
Anaemia	23.1	C	Chain: Iron by mouth or by vein	Iron fortification of food, treatment of worms and malaria, and later clamping of the cord at birth.
Sickle cell disease and thalassaemia	23.2	F, S, C	Chain: Hydroxyurea, which switches on fetal haemoglobin	Newborn screening and penicillin from infancy.
Haemophilia	23.3	F, C	Chain: Replacement factor; emicizumab, which bridges the missing step	Genetic counselling.
Chronic obstructive pulmonary disease (COPD)	24.1	S, U	Surround: Tobacco control; clean cooking	Stopping smoking is the one measure proven to slow the loss of lung function and to lower death (Lung Health Study, Anthonisen, 2005).
Asthma	24.2	O	Chain: Inhaled corticosteroids	Children raised on traditional farms have less asthma; the diversity of microbes they meet explains part of this (Ege, 2011; Stein, 2016).
Obstructive sleep apnoea	24.3	D, C	Mesh: Continuous positive airway pressure (CPAP)	Healthy weight is the main lever.
Type 2 diabetes	25.1	C, D, S	Phase: Weight loss by a structured diet programme	In people at high risk, lifestyle change lowered new diabetes by 58 % and metformin by 31 % (Diabetes Prevention Program, Knowler, 2002).
Type 1 diabetes	25.2	O, C	Chain: Insulin	No proven prevention.
Obesity	25.3	D, S	Chain: Semaglutide; tirzepatide	Food surroundings decide much of intake.
Thyroid disease	25.4	O, C	Chain: Levothyroxine for too little; antithyroid drugs for too much	Iodised salt prevents deficiency.
Fatty liver disease (MASLD) and cirrhosis	26.1	S, D	Phase: Weight loss	Healthy weight; little alcohol; treatment of diabetes.

Entry	Sect.	Form	First established layer	Main prevention
Helicobacter pylori, ulcer and stomach cancer	26.2	U	Mesh: Eradication with antibiotics and acid suppression	Clean water.
Coeliac disease	26.3	O	Surround: A strict gluten-free diet	No proven prevention.
Inflammatory bowel disease	26.4	O, S	Chain: Mesalazine; steroids for flares	Not smoking lowers the risk of Crohn's disease.
Irritable bowel syndrome	26.5	D, W	Phase: Gut-directed hypnotherapy; cognitive behavioural therapy	No proven prevention.
Chronic kidney disease	27.1	C, S	Chain: ACE inhibitors or ARBs; SGLT2 inhibitors; finerenone; semaglutide	Control of blood pressure and blood sugar.
Kidney stones	27.2	S	Mesh: Shock waves or endoscopic removal	Drinking enough water halved recurrence in a five-year trial (Borghi, 1996).
Urinary incontinence	27.3	R	Phase: Pelvic floor muscle training	Pelvic floor training in pregnancy.
Tuberculosis	28.1	U	Mesh: Six months of four antibiotics; four-month regimens; BPaL for resistant TB	Food support for households of patients lowered new TB by 39 to 48 % (RATIONS, Bhargava, 2023).
HIV	28.2	U, C	Chain: Antiretroviral therapy	Condoms, testing and treatment, pre-exposure prophylaxis.
Malaria	28.3	U	Chain: Artemisinin-based combination therapy	Insecticide-treated bed nets; seasonal preventive drugs for children.
Viral hepatitis B and C	28.4	U, S	Chain: Direct-acting antivirals for hepatitis C	Hepatitis B vaccine at birth.
Pneumonia and lower respiratory infection	28.5	U, O	Mesh: Antibiotics; oxygen	Vaccines against pneumococcus, Hib, influenza, measles and pertussis.
Sepsis	28.6	U, O	Mesh: Antibiotics within the hour; removal of the source; fluids and organ support	Vaccination, clean water, hygiene in hospitals, early treatment of infection.
Antimicrobial resistance	28.7	U	Surround: Stewardship; sanitation; vaccination	Fewer and better-aimed antibiotics, vaccines, clean water and sanitation.
After infection: long COVID and post-infectious fatigue	28.8	U, W	Phase: Pacing; graded return guided by symptoms	Vaccination lowers the risk.
Rheumatoid arthritis	29.1	O, S	Chain: Methotrexate, started early, with treat-to-target	Not smoking.
Systemic lupus erythematosus	29.2	O	Chain: Hydroxychloroquine	No proven prevention.
Multiple sclerosis	29.3	O	Reading: High-efficacy disease-modifying drugs	A vaccine against Epstein–Barr virus is a direction.
Allergy: food allergy, hay fever and eczema	29.4	O	Reading: Allergen immunotherapy	Early meeting teaches the reader.
Lung cancer	30.1	F, U	Mesh: Surgery or radiotherapy in early disease	Not smoking prevents most cases.

Entry	Sect.	Form	First established layer	Main prevention
Breast cancer	30.2	F, U, D	Mesh: Surgery, radiotherapy, chemotherapy	Less alcohol, healthy weight, physical activity, breastfeeding.
Colorectal cancer	30.3	F, U	Mesh: Removal of polyps; surgery	Screening by stool test or colonoscopy.
Cervical cancer	30.4	U, F	Reading: HPV vaccine	HPV vaccination before age 17 lowered invasive cervical cancer by 88 % in Sweden (Lei, 2020).
Prostate cancer	30.5	F, R	Phase: Active surveillance for low-risk disease: read before you act	Screening by PSA lowered prostate cancer death by about 20 % over 16 years (ERSPC, Hugosson, 2019), at the cost of overdiagnosis.
Melanoma and skin cancer	30.6	F, U	Mesh: Excision	Daily sunscreen halved new melanomas in a ten-year trial (Green, 2011).
Blood cancers: leukaemia and lymphoma	30.7	F	Chain: Imatinib in chronic myeloid leukaemia	Avoid benzene and radiation.
Dementia and Alzheimer's disease	31.1	S, U, R, D	Reading: Antibodies that clear amyloid: lecanemab, donanemab	Fourteen modifiable risks explain about 45 % of dementia: among them education, hearing loss, high LDL, blood pressure, smoking, inactivity, diabetes, air pollution and social isolation (Lancet Commission, Livingston, 2024).
Parkinson's disease	31.2	S, C, W	Chain: Levodopa and other dopamine drugs	Some pesticides, such as paraquat, and the solvent trichloroethylene raise risk.
Epilepsy	31.3	W	Chain: Anti-seizure drugs	About a quarter of cases are preventable: head injury, birth injury, brain infection, stroke (WHO).
Migraine	31.4	D, W	Chain: Triptans; drugs and antibodies that block CGRP	Regular sleep and meals.
Chronic pain	31.5	W	Phase: Exercise therapy; cognitive behavioural therapy	Staying active after injury.
Motor neurone disease (ALS)	31.6	U, F	Chain: Riluzole	None known.
Cataract	32.1	S, R	Mesh: Lens replacement surgery	Sun protection; not smoking.
Myopia	32.2	D	Surround: Time outdoors	An extra 40 minutes outdoors at school lowered new myopia in Chinese children (He, 2015).
Glaucoma and macular degeneration	32.3	S, R	Chain: Pressure-lowering drops in glaucoma	Not smoking; screening in older age.
Hearing loss	32.4	R	Mesh: Hearing aids; cochlear implants	Protection from noise; vaccination against measles, mumps and rubella; care at birth.
Atopic eczema	33.1	O, S	Chain: Emollients and topical steroids	Daily emollient from birth did not prevent eczema in a large trial (BEEP, Chalmers, 2020).
Psoriasis	33.2	O, W	Reading: Biologics against IL-17 or IL-23	Healthy weight; not smoking.

Entry	Sect.	Form	First established layer	Main prevention
Chronic wounds and scars	33.3	S, C	Mesh: Off-loading, cleaning, revascularisation	Foot care in diabetes; blood-sugar control.
Osteoarthritis	34.1	S, R	Phase: Exercise and weight loss	Healthy weight; strong muscles; care after joint injury.
Osteoporosis and fracture	34.2	R, D	Chain: Bisphosphonates; denosumab; romosozumab	Impact and resistance exercise.
Gout	34.3	S	Chain: Allopurinol raised step by step to a urate target	Less alcohol and sugared drinks; healthy weight.
Sarcopenia and frailty	34.4	R	Phase: Progressive resistance training	Resistance training throughout adult life; enough protein.
Infertility	35.1	C, D, F	Mesh: In vitro fertilisation	Treat sexually transmitted infection; avoid smoking; do not delay pregnancy too long when it is wanted.
Preterm birth	35.2	D, C	Chain: Steroids before preterm birth to ripen the lungs	Antenatal care; treatment of infection; spacing of pregnancies.
Pre-eclampsia	35.3	C, S	Chain: Aspirin; blood-pressure drugs; magnesium sulphate against seizures	Low-dose aspirin from early pregnancy in women at high risk lowered preterm pre-eclampsia by 62 % (ASPRE, Rolnik, 2017).
Death in childbirth	35.4	C	Mesh: A bundle of early detection and treatment of bleeding	Skilled care at birth.
Polycystic ovary syndrome and endometriosis	35.5	D, S, O	Phase: Lifestyle change in polycystic ovary syndrome	Healthy weight helps in polycystic ovary syndrome.
Neural tube defects	35.6	F, C	Surround: Folic acid supplements and fortification	Folic acid before conception lowered neural tube defects by 72 % (MRC Vitamin Study, 1991).
Cystic fibrosis	36.1	F, U	Chain: Elexacaftor–tezacaftor–ivacaftor, which helps the protein fold and pass the cell's test	Carrier screening and genetic counselling.
Duchenne and Becker muscular dystrophy	36.2	F	Chain: Corticosteroids	Genetic counselling.
Huntington's disease and other repeat diseases	36.3	F, S	Phase: Supportive care, exercise	Predictive testing and counselling; preimplantation testing.
Spinal muscular atrophy	36.4	F, C	Chain: Nusinersen and risdiplam, which correct the reading of the backup gene	Newborn screening, so treatment starts before symptoms.
Phenylketonuria	36.5	F, C	Surround: A diet low in phenylalanine from birth	Newborn heel-prick screening since the 1960s.
Down syndrome	36.6	F	Mesh: Heart surgery in infancy	Prenatal screening informs choice.
Deaths before age five	37.1	U, C	Reading: Childhood vaccination	Vaccines have saved about 154 million lives in fifty years, most of them infants (Shattock, 2024).
Childhood cancer	37.2	F, U	Mesh: Chemotherapy, surgery, radiotherapy	Mostly not preventable.
Neurodevelopment, allergy and obesity in children	37.3	O, D	Phase: Regular sleep and outdoor play	Early meeting with foods and microbes; regular sleep; daylight; active play.

Entry	Sect.	Form	First established layer	Main prevention
Healthy ageing	38.1	R	Phase: Exercise, sleep, social contact, hearing care	In two large American cohorts, five low-risk habits (never smoking, healthy weight, regular activity, moderate alcohol, a healthy diet) added about 12 to 14 years of life expectancy at age 50 (Li, 2018).
Delirium	38.2	D, W	Phase: Restore the day: light, sleep, movement, familiar faces	Orientation, sleep, mobility, hearing and vision aids, hydration.
Air pollution	39.1	S, U, F	Surround: Air quality rules; clean cooking	Clean energy, clean cooking, traffic rules.
Tobacco	39.2	S, F, U	Surround: Taxes, smoke-free laws, plain packs, advertising bans	Stopping before age 40 avoids about 90 % of the excess risk of death (Jha, 2013).
Alcohol	39.3	S, F, W	Surround: Minimum unit pricing; limits on sales	Price, availability and marketing rules.
Light, night and shift work	39.4	D	Phase: Shift design; light and sleep hygiene	Daylight in the morning; dark at night; forward-rotating shift rosters.
Loneliness	39.5	D, R	—	Social contact through life.
Bipolar disorder	42.1	W (reversal), D	Chain: Lithium	Regular sleep and daily rhythm; early treatment of first episodes.
Anxiety disorders	42.2	O, W	Phase: Cognitive behavioural therapy with exposure	Early help in childhood; exercise.
Post-traumatic stress disorder	42.3	U, W	Phase: Trauma-focused therapies: prolonged exposure, cognitive processing therapy, EMDR	Safety and support after trauma.
Obsessive-compulsive disorder	42.4	W	Phase: Exposure and response prevention	None proven.
Schizophrenia and psychosis	42.5	O, U	Chain: Antipsychotic drugs	Avoiding high-potency cannabis in youth.
Eating disorders	42.6	W	Phase: Family-based treatment for adolescents	Early recognition.
Addiction	42.7	W, C	Chain: Methadone or buprenorphine for opioid dependence	Price, availability and marketing rules; prescribing control of opioids.
ADHD	42.8	D	Chain: Stimulants (methylphenidate in children, amphetamines in adults)	Not applicable as a disease.
Autism	42.9	None: a way of reading	Phase: Early communication support; adapted surroundings	Not applicable.
Insomnia and other sleep disorders	42.10	D; O and C in narcolepsy	Phase: Cognitive behavioural therapy for insomnia	Regular sleep times; morning light; dark nights.
Personality disorders	42.11	W, D	Phase: Dialectical behaviour therapy	Early support for young people at risk.

Annotated references

The first groups are those of the first edition. The groups from 'Second edition' onward are new. Each entry ends with why it is worth reading.

The theory

Konstapel, J. (2026). The Chemistry of the Vacuum.Net Theory. Constable Research, Leiden, 11 November 2026.
Why read it: The derivation of chemistry this book builds on: the atom, the bond, handedness, alkanes, sugars, amino acids and base pairs.

Konstapel, J. (2026). Where Illness Comes From, completed edition. constable.blog, 20 October 2026.
Why read it: Part 0 states the rules used here: closure, the two classes, the test, widening and pruning, the ladder. Its depression entry lists the treatments of chapter 46.

Konstapel, J. (2026). From Cell to Mind. constable.blog, 14 October 2026.
Why read it: The two-layer method and the three tests on the mind (B13, B14) summarised in chapter 20.

Konstapel, J. (2026). Rhythms Out of Tune. constable.blog, 8 November 2026.
Why read it: Twenty-four body rhythms and seven treatment frequencies tested on the ladder; the reading of illness as drift; the device rule 'read the state first'.

Konstapel, J. (2026). Three Chains, One Standstill. constable.blog, 10 October 2026.
Why read it: The method of finding disease paths and restoration paths on the ladder, applied to dementia and Parkinson's disease.

Konstapel, J. (2026). De Energietransitie die Geen Transitie Is. constable.blog, 24 May 2026.
Why read it: The steam-engine paradigm of energy as a substance freed by destruction, and the oscillatory paradigm that replaces it; the basis of sections 18.3 and 18.5.

The code

Crick, F. H. C., Griffith, J. S. & Orgel, L. E. (1957). Codes without commas. PNAS 43, 416–421.
Why read it: The first derivation of twenty as the size of the largest comma-free code of words of three over four letters. Compare its argument with chapter 6.

Crick, F. H. C. (1968). The origin of the genetic code. Journal of Molecular Biology 38, 367–379.
Why read it: Why the comma-free idea was abandoned once the real code was read, and the frozen-accident view.

The depths above chemistry

The UniProt Consortium (2025). UniProt: the Universal Protein Knowledgebase in 2025. Nucleic Acids Research 53, D609–D617. Reviewed human proteome downloaded 11 November 2026.
Why read it: The 20,429 human proteins on which the chain test of chapter 10 was run.

Marqusee, S. & Baldwin, R. L. (1987). Helix stabilization by Glu−···Lys+ salt bridges in short peptides of de novo design. PNAS 84, 8898–8902.
Why read it: Salt bridges at i, i+4 stabilise helices; the measured pattern behind section 10.1.

Wikipedia contributors. Protein secondary structure; Polyproline helix; Nucleic acid double helix (read 11 November 2026).
Why read it: The units per turn of the eight helices in chapter 11. Check them against the primary structural papers before relying on them.

Wikipedia contributors. Ring strain (read 11 November 2026).
Why read it: Strain energies of three-to six-membered rings; compare with the smallest closed loop of chapter 11.

Lorent, J. H. et al. (2020). Plasma membranes are asymmetric in lipid unsaturation, packing and protein shape. Nature Chemical Biology 16, 644–652.
Why read it: The measured asymmetry of the two leaflets, compared with the computed asymmetry of chapter 12.

Wikipedia contributors. Beta sheet (read 11 November 2026).
Why read it: Antiparallel and parallel sheets and their stability; the partial agreement in chapter 12.

Watson, J. D. & Crick, F. H. C. (1953). Molecular structure of nucleic acids. Nature 171, 737–738.
Why read it: The pairing from which semi-conservative copying follows; compare with the unique partner of chapter 13.

Meselson, M. & Stahl, F. W. (1958). The replication of DNA in Escherichia coli. PNAS 44, 671–682.
Why read it: The measurement of semi-conservative copying reproduced by the algebra in chapter 13.

Kunkel, T. A. & Erie, D. A. (2005). DNA mismatch repair. Annual Review of Biochemistry 74, 681–710.
Why read it: How the cell finds a mismatch and restores the original base from the old strand; the measured match to the repair law of chapter 5.

Kurosaki, T., Popp, M. W. & Maquat, L. E. (2019). Quality and quantity control of gene expression by nonsense-mediated mRNA decay. Nature Reviews Molecular Cell Biology 20, 406–420.
Why read it: The cell's test at the depth of the word: transcripts that read wrong are removed.

World Health Organization. The top 10 causes of death (fact sheet).
Why read it: Ischaemic heart disease and stroke as leading causes; the carrier reading of chapter 15.

Depression: trials and re-analysis

Cipriani, A. et al. (2018). Comparative efficacy and acceptability of 21 antidepressant drugs. The Lancet 391, 1357–1366.
Why read it: The network meta-analysis whose open data (GRISELDA, Mendeley Data 83rthbp8ys v2, CC BY 4.0) were re-analysed in chapter 40.

van Haaren, P. C. F. et al. (2026). Comparative efficacy and acceptability of antidepressants in the long-term treatment of major depressive disorder. The Lancet Psychiatry. doi:10.1016/S2215-0366(26)00326-3.
Why read it: The long-term comparison that started this research; its full ranking is the data for tests T6 to T8.

Shinohara, K. et al. (2019). Protocol. BMJ Open 9, e027574.
Why read it: The protocol of the long-term study: 21 drugs, four trial designs, sustained response and dropout as outcomes.

Zaccoletti, D. et al. (2026). Comparison of antidepressant deprescribing strategies. The Lancet Psychiatry 13, 24–36.
Why read it: Slow tapering with support compared with continuing; 76 trials.

Depression: sleep, heart and time

Arıkan, M. K. et al. (2024). REM parameters in drug-free major depressive disorder. Sleep Medicine Reviews.
Why read it: Shorter REM latency and higher REM density in drug-free, comorbidity-free patients.

Baglioni, C. et al. (2016). Sleep and mental disorders: a meta-analysis of polysomnographic research. Psychological Bulletin 142, 969–990.
Why read it: The broadest map of sleep changes across mental disorders.

Machowski, R. et al. (1989). Latencies of REM sleep and awakening in major depression. Neurophysiologie Clinique 19, 385–391.
Why read it: The minute values used on the ladder in chapter 41; small sample.

Wichniak, A. et al. (2017). Effects of antidepressants on sleep. Current Psychiatry Reports 19, 63.
Why read it: Which antidepressants suppress REM sleep and which do not.

Koch, C. et al. (2019). A meta-analysis of heart rate variability in major depression. Psychological Medicine 49, 1948–1957.
Why read it: Lower heart-rate variability in unmedicated depression.

Iyengar, N. et al. (1996). Age-related alterations in the fractal scaling of cardiac interbeat interval dynamics. American Journal of Physiology 271, R1078–R1084. Data: Fantasia database, PhysioNet (Goldberger et al. 2000, Circulation 101, e215–e220).
Why read it: The open recordings of heartbeats and breathing used for the body test of section 18.1.

Schäfer, C., Rosenblum, M. G., Kurths, J. & Abel, H.-H. (1998). Heartbeat synchronized with ventilation. Nature 392, 239–240.
Why read it: The first report of n:1 cardiorespiratory synchronisation; the measured phenomenon tested in section 18.1.

Bartsch, R. et al. (2007). Experimental evidence for phase synchronization transitions in the human cardiorespiratory system. Physical Review Letters 98, 054102.
Why read it: Episodes of cardiorespiratory phase synchronisation in humans at rest and in sleep.

Bartsch, R. P., Schumann, A. Y., Kantelhardt, J. W., Penzel, T. & Ivanov, P. Ch. (2012). Phase transitions in physiologic coupling. PNAS 109, 10181–10186.
Why read it: More heart–breath synchronisation in deep sleep, less in REM and wake; the order reproduced in section 18.2.

Ichimaru, Y. & Moody, G. B. (1999). Development of the polysomnographic database on CD-ROM. Psychiatry and Clinical Neurosciences 53, 175–177. Data: MIT-BIH Polysomnographic Database, PhysioNet.
Why read it: The sleep recordings with ECG, respiration and stages used in section 18.2.

Kemp, B. et al. (2000). Analysis of a sleep-dependent neuronal feedback loop: the slow-wave microcontinuity of the EEG. IEEE Transactions on Biomedical Engineering 47, 1185–1194. Data: Sleep-EDF Expanded, PhysioNet.
Why read it: The 153 scored nights used in section 19.1.

Garcia-Ceja, E. et al. (2018). Depresjon: a motor activity database of depression episodes in unipolar and bipolar patients. Proceedings of ACM MMSys 2018, 472–477. Data: Zenodo 1219550.
Why read it: The open actigraphy data with MADRS scores used in section 40.4.

Witting, W. et al. (1990). Alterations in the circadian rest-activity rhythm in aging and Alzheimer's disease. Biological Psychiatry 27, 563–572.
Why read it: Defines interdaily stability (IS) and intradaily variability (IV).

Van Someren, E. J. W. et al. (1999). Bright light therapy: improved sensitivity to its effects on rest-activity rhythms in Alzheimer patients by application of nonparametric methods. Chronobiology International 16, 505–518.
Why read it: Defines the relative amplitude RA with M10 and L5.

Boland, E. M. et al. (2017). Meta-analysis of the antidepressant effects of acute sleep deprivation. Journal of Clinical Psychiatry 78, e1020–e1034.
Why read it: About half respond within a day; 66 studies.

Golden, R. N. et al. (2005). The efficacy of light therapy in the treatment of mood disorders. American Journal of Psychiatry 162, 656–662.
Why read it: Effect sizes for light in seasonal and non-seasonal depression.

Out-patient triple chronotherapy: feasibility and pilot randomised controlled trial (2021). BJPsych Open.
Why read it: Sleep deprivation, phase advance and morning light combined; gains held at 26 weeks.

Lamont, E. W. et al. (2007). The role of circadian clock genes in mental disorders. Dialogues in Clinical Neuroscience 9, 333–342.
Why read it: The evidence and its limits on circadian change in depression.

Depression: other treatments

Noetel, M. et al. (2024). Effect of exercise for depression. BMJ 384, e075847.
Why read it: Network meta-analysis of exercise types; walking or jogging g = −0.62.

Richards, D. A. et al. (2016). Cost and outcome of behavioural activation versus cognitive behavioural therapy for depression (COBRA). The Lancet 388, 871–880.
Why read it: Behavioural activation non-inferior to CBT and cheaper.

World Health Organization (2026). Depressive disorder fact sheet.
Why read it: Prevalence: 5.2 per cent of adults, about 322 million people.

Second edition: review, proofs and depression additions

Ho, F. Y.-Y. et al. (2024). Rest-activity rhythms in depression: a systematic review and meta-analysis. Journal of Affective Disorders 361, 224–244.
Why read it: 53 studies with 11,115 participants. Pooled interdaily stability lower in depression (SMD −0.17) and amplitude lower (−0.33). Set beside the miss on D1 and D4 in section 40.4.

Monaco, A. P. et al. (1988). An explanation for the phenotypic differences between patients bearing partial deletions of the DMD locus. Genomics 2, 90–95.
Why read it: The reading-frame rule. Section 21.3 reproduces it from the frame law of chapter 6.

Aartsma-Rus, A. et al. (2006). Entries in the Leiden Duchenne muscular dystrophy mutation database: an overview of mutation types and paradoxical cases that confirm the reading-frame rule. Muscle & Nerve 34, 135–144.
Why read it: The test of the frame rule on thousands of patients: it holds in about nine of ten. The exceptions are the subject of test T19.

Konstapel, J. (2026). Where Illness Comes From, ninth version. constable.blog.
Why read it: The model for this edition's atlas: the layers, the treatment ladder with its standing, and prevention at the end of each chapter.

Circulation and blood

Yusuf, S. et al. (2004). Effect of potentially modifiable risk factors associated with myocardial infarction in 52 countries (INTERHEART). Lancet 364, 937–952.
Why read it: Nine factors explain about nine tenths of the risk of a first heart attack.

Cholesterol Treatment Trialists' Collaboration (2010). Efficacy and safety of more intensive lowering of LDL cholesterol. Lancet 376, 1670–1681.
Why read it: The dose–response of statins: about a fifth fewer events per mmol/L.

Estruch, R. et al. (2018). Primary prevention of cardiovascular disease with a Mediterranean diet supplemented with extra-virgin olive oil or nuts (PREDIMED, republished). New England Journal of Medicine 378, e34.
Why read it: The largest diet trial on heart outcomes.

Lincoff, A. M. et al. (2023). Semaglutide and cardiovascular outcomes in obesity without diabetes (SELECT). New England Journal of Medicine 389, 2221–2232.
Why read it: A chain-layer drug that lowers heart events by 20 %.

Nidorf, S. M. et al. (2020). Colchicine in patients with chronic coronary disease (LoDoCo2). New England Journal of Medicine 383, 1838–1847.
Why read it: Calming the test in the plaque lowers events: a reading-layer cure in the heart.

Keeley, E. C., Boura, J. A. & Grines, C. L. (2003). Primary angioplasty versus intravenous thrombolytic therapy for acute myocardial infarction. Lancet 361, 13–20.
Why read it: Why the mesh layer comes first in an acute blockage.

Dibben, G. et al. (2021). Exercise-based cardiac rehabilitation for coronary heart disease. Cochrane Database of Systematic Reviews CD001800.
Why read it: The phase layer after a heart attack.

Frazer, K. et al. (2016). Legislative smoking bans for reducing harms from secondhand smoke exposure. Cochrane Database of Systematic Reviews CD005992.
Why read it: Surround measures lower heart admissions.

World Health Organization (2025). Global report on hypertension 2025.
Why read it: 1.4 billion with high blood pressure; about one in five controlled.

Neal, B. et al. (2021). Effect of salt substitution on cardiovascular events and death (SSaSS). New England Journal of Medicine 385, 1067–1077.
Why read it: A cheap surround change that lowers stroke.

SPRINT Research Group (2015). A randomized trial of intensive versus standard blood-pressure control. New England Journal of Medicine 373, 2103–2116.
Why read it: The case for a lower target.

Mackenzie, I. S. et al. (2022). Cardiovascular outcomes in adults with hypertension with evening versus morning dosing (TIME). Lancet 400, 1417–1425.
Why read it: A failed test of the direction rule: timing of the pill made no difference.

Edwards, J. J. et al. (2023). Exercise training and resting blood pressure: a large-scale pairwise and network meta-analysis. British Journal of Sports Medicine 57, 1317–1326.
Why read it: Isometric exercise lowers blood pressure most.

McMurray, J. J. V. et al. (2019). Dapagliflozin in patients with heart failure and reduced ejection fraction (DAPA-HF). New England Journal of Medicine 381, 1995–2008.
Why read it: One of the four drug pillars in heart failure.

O'Connor, C. M. et al. (2009). Efficacy and safety of exercise training in patients with chronic heart failure (HF-ACTION). JAMA 301, 1439–1450.
Why read it: Exercise in heart failure.

Hart, R. G., Pearce, L. A. & Aguilar, M. I. (2007). Meta-analysis: antithrombotic therapy to prevent stroke in patients who have nonvalvular atrial fibrillation. Annals of Internal Medicine 146, 857–867.
Why read it: Anticoagulation lowers stroke by about two thirds.

Kirchhof, P. et al. (2020). Early rhythm-control therapy in patients with atrial fibrillation (EAST-AFNET 4). New England Journal of Medicine 383, 1305–1316.

Why read it: Restoring rhythm early improves outcomes.

Voskoboinik, A. et al. (2020). Alcohol abstinence in drinkers with atrial fibrillation. New England Journal of Medicine 382, 20–28.
Why read it: Removing a surround load lowers recurrence.

GBD 2021 Stroke Risk Factor Collaborators (2024). Global, regional, and national burden of stroke and its risk factors, 1990–2021. Lancet Neurology 23, 973–1003.
Why read it: About 12 million strokes and 7 million deaths a year.

O'Donnell, M. J. et al. (2016). Global and regional effects of potentially modifiable risk factors associated with acute stroke (INTERSTROKE). Lancet 388, 761–775.
Why read it: Ten factors explain nine tenths of stroke risk.

Goyal, M. et al. (2016). Endovascular thrombectomy after large-vessel ischaemic stroke: a meta-analysis of individual patient data (HERMES). Lancet 387, 1723–1731.
Why read it: One of 2.6 treated patients has less disability.

GBD 2021 Anaemia Collaborators (2023). Prevalence, years lived with disability, and trends in anaemia burden, 1990–2021. Lancet Haematology 10, e713–e734.
Why read it: 1.9 billion people with anaemia.

GBD 2021 Sickle Cell Disease Collaborators (2023). Global, regional, and national prevalence and mortality burden of sickle cell disease, 2000–2021. Lancet Haematology 10, e585–e599.
Why read it: 7.7 million living with sickle cell disease.

Gaston, M. H. et al. (1986). Prophylaxis with oral penicillin in children with sickle cell anemia. New England Journal of Medicine 314, 1593–1599.
Why read it: The simplest life-saving measure in sickle cell disease.

Frangoul, H. et al. (2024). Exagamglogene autotemcel for severe sickle cell disease. New England Journal of Medicine 390, 1649–1662.
Why read it: The first approved gene-editing cure.

Breath

Anthonisen, N. R. et al. (2005). The effects of a smoking cessation intervention on 14.5-year mortality (Lung Health Study). Annals of Internal Medicine 142, 233–239.
Why read it: Stopping smoking is the one measure that changes the course of COPD.

McCarthy, B. et al. (2015). Pulmonary rehabilitation for chronic obstructive pulmonary disease. Cochrane Database of Systematic Reviews CD003793.
Why read it: The phase layer in lung disease.

Suissa, S. et al. (2000). Low-dose inhaled corticosteroids and the prevention of death from asthma. New England Journal of Medicine 343, 332–336.
Why read it: Why the inhaled steroid is the base of asthma care.

Ege, M. J. et al. (2011). Exposure to environmental microorganisms and childhood asthma. New England Journal of Medicine 364, 701–709.
Why read it: Farm microbes and less asthma: the test trained by meeting.

Stein, M. M. et al. (2016). Innate immunity and asthma risk in Amish and Hutterite farm children. New England Journal of Medicine 375, 411–421.
Why read it: Two farming communities, one difference in exposure, a fourfold difference in asthma.

Benjafield, A. V. et al. (2019). Estimation of the global prevalence and burden of obstructive sleep apnoea. Lancet Respiratory Medicine 7, 687–698.
Why read it: About 936 million adults affected.

McEvoy, R. D. et al. (2016). CPAP for prevention of cardiovascular events in obstructive sleep apnea (SAVE). New England Journal of Medicine 375, 919–931.
Why read it: CPAP helps sleepiness but did not lower heart events.

Malhotra, A. et al. (2024). Tirzepatide for the treatment of obstructive sleep apnea and obesity (SURMOUNT-OSA). New England Journal of Medicine 391, 1193–1205.
Why read it: A drug that removes the cause.

Metabolism and hormones, digestion, liver and kidney

NCD Risk Factor Collaboration (2024). Worldwide trends in diabetes prevalence and treatment from 1990 to 2022. Lancet 404, 2077–2093.
Why read it: More than 800 million adults with diabetes; over half untreated.

Knowler, W. C. et al. (2002). Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin (DPP). New England Journal of Medicine 346, 393–403.
Why read it: Prevention that works: 58 % fewer cases.

Lean, M. E. J. et al. (2018). Primary care-led weight management for remission of type 2 diabetes (DiRECT). Lancet 391, 541–551.
Why read it: Fast, large weight loss gives remission: the dose law in metabolism.

Mingrone, G. et al. (2021). Metabolic surgery versus conventional medical therapy in patients with type 2 diabetes: 10-year follow-up. Lancet 397, 293–304.
Why read it: Long remission after surgery.

Gregory, G. A. et al. (2022). Global incidence, prevalence, and mortality of type 1 diabetes in 2021. Lancet Diabetes & Endocrinology 10, 741–760.
Why read it: 8.4 million with type 1 diabetes.

Herold, K. C. et al. (2019). An anti-CD3 antibody, teplizumab, in relatives at risk for type 1 diabetes. New England Journal of Medicine 381, 603–613.
Why read it: Slowing the test delays onset.

Wilding, J. P. H. et al. (2021). Once-weekly semaglutide in adults with overweight or obesity (STEP 1). New England Journal of Medicine 384, 989–1002.
Why read it: 15 % weight loss.

Wilding, J. P. H. et al. (2022). Weight regain and cardiometabolic effects after withdrawal of semaglutide: the STEP 1 trial extension. Diabetes, Obesity and Metabolism 24, 1553–1564.
Why read it: Two thirds of the loss returns after stopping.

Jastreboff, A. M. et al. (2022). Tirzepatide once weekly for the treatment of obesity (SURMOUNT-1). New England Journal of Medicine 387, 205–216.
Why read it: 21 % weight loss.

Hall, K. D. et al. (2019). Ultra-processed diets cause excess calorie intake and weight gain. Cell Metabolism 30, 67–77.
Why read it: The food surround decides intake.

Younossi, Z. M. et al. (2023). The global epidemiology of nonalcoholic fatty liver disease and nonalcoholic steatohepatitis. Hepatology 77, 1335–1347.
Why read it: About 30 % of adults.

Vilar-Gomez, E. et al. (2015). Weight loss through lifestyle modification significantly reduces features of nonalcoholic steatohepatitis. Gastroenterology 149, 367–378.
Why read it: Ten per cent weight loss resolves most liver inflammation.

Harrison, S. A. et al. (2024). A phase 3, randomized, controlled trial of resmetirom in NASH with liver fibrosis (MAESTRO-NASH). New England Journal of Medicine 390, 497–509.
Why read it: The first approved drug for fatty liver inflammation.

Marshall, B. J. & Warren, J. R. (1984). Unidentified curved bacilli in the stomach of patients with gastritis and peptic ulceration. Lancet 1, 1311–1315.
Why read it: An unread misfit found.

Ford, A. C. et al. (2014). Helicobacter pylori eradication therapy to prevent gastric cancer in healthy asymptomatic infected individuals. BMJ 348, g3174.
Why read it: Removing the microbe lowers stomach cancer.

Choi, I. J. et al. (2020). Family history of gastric cancer and Helicobacter pylori treatment. New England Journal of Medicine 382, 427–436.
Why read it: More than half fewer cancers in relatives treated.

Singh, P. et al. (2018). Global prevalence of celiac disease: systematic review and meta-analysis. Clinical Gastroenterology and Hepatology 16, 823–836.
Why read it: 1.4 % seroprevalence.

Sperber, A. D. et al. (2021). Worldwide prevalence and burden of functional gastrointestinal disorders: Rome Foundation global study. Gastroenterology 160, 99–114.
Why read it: Irritable bowel syndrome in about 4 %.

GBD 2023 Chronic Kidney Disease Collaborators (2025). Global, regional, and national burden of chronic kidney disease in adults, 1990–2023. Lancet.
Why read it: 788 million adults with chronic kidney disease.

Heerspink, H. J. L. et al. (2020). Dapagliflozin in patients with chronic kidney disease (DAPA-CKD). New England Journal of Medicine 383, 1436–1446.
Why read it: A 39 % lower risk of kidney failure or death.

Perkovic, V. et al. (2024). Effects of semaglutide on chronic kidney disease in patients with type 2 diabetes (FLOW). New England Journal of Medicine 391, 109–121.
Why read it: A 24 % lower risk of major kidney events.

Borghi, L. et al. (1996). Urinary volume, water and recurrences in idiopathic calcium nephrolithiasis: a 5-year randomized prospective study. Journal of Urology 155, 839–843.
Why read it: Water halves recurrence of stones.

Dumoulin, C., Cacciari, L. P. & Hay-Smith, E. J. C. (2018). Pelvic floor muscle training versus no treatment for urinary incontinence in women. Cochrane Database of Systematic Reviews CD005654.
Why read it: The phase layer in incontinence.

Infection

World Health Organization (2024). Global tuberculosis report 2024.
Why read it: 8.2 million new diagnoses in 2023; tuberculosis again the leading infectious killer.

Houben, R. M. G. J. & Dodd, P. J. (2016). The global burden of latent tuberculosis infection: a re-estimation using mathematical modelling. PLoS Medicine 13, e1002152.
Why read it: About a quarter of people carry latent infection: the unread form.

Bhargava, A. et al. (2023). Nutritional support for adult patients with microbiologically confirmed pulmonary tuberculosis and their household contacts (RATIONS). Lancet 402, 627–640.
Why read it: Food prevents tuberculosis.

UNAIDS (2024). The urgency of now: AIDS at a crossroads. Global AIDS Update 2024.
Why read it: 39.9 million living with HIV.

Rodger, A. J. et al. (2019). Risk of HIV transmission through condomless sex in serodifferent gay couples with the HIV-positive partner taking suppressive antiretroviral therapy (PARTNER2). Lancet 393, 2428–2438.
Why read it: Undetectable means untransmittable.

Bekker, L.-G. et al. (2024). Twice-yearly lenacapavir or daily F/TAF for HIV prevention in cisgender women (PURPOSE 1). New England Journal of Medicine 391, 1179–1192.
Why read it: Zero infections in the lenacapavir group.

World Health Organization (2024). World malaria report 2024.
Why read it: 263 million cases and 597,000 deaths in 2023.

Datoo, M. S. et al. (2024). Safety and efficacy of malaria vaccine candidate R21/Matrix-M in African children. Lancet 403, 533–544.
Why read it: A reading-layer cure for an unread parasite.

World Health Organization (2024). Global hepatitis report 2024.
Why read it: 254 million with hepatitis B, 50 million with hepatitis C.

Chang, M.-H. et al. (1997). Universal hepatitis B vaccination in Taiwan and the incidence of hepatocellular carcinoma in children. New England Journal of Medicine 336, 1855–1859.
Why read it: The first vaccine shown to prevent a cancer.

Rudd, K. E. et al. (2020). Global, regional, and national sepsis incidence and mortality, 1990–2017. Lancet 395, 200–211.
Why read it: 11 million sepsis deaths: one in five deaths worldwide.

Seymour, C. W. et al. (2017). Time to treatment and mortality during mandated emergency care for sepsis. New England Journal of Medicine 376, 2235–2244.
Why read it: Each hour counts.

GBD 2021 Antimicrobial Resistance Collaborators (Naghavi, M. et al.) (2024). Global burden of bacterial antimicrobial resistance 1990–2021, with forecasts to 2050. Lancet 404, 1199–1226.
Why read it: 1.14 million deaths directly due to resistance in 2021.

Davis, H. E. et al. (2023). Long COVID: major findings, mechanisms and recommendations. Nature Reviews Microbiology 21, 133–146.
Why read it: At least 65 million with long COVID.

Autoimmunity and allergy

Conrad, N. et al. (2023). Incidence, prevalence, and co-occurrence of autoimmune disorders over time and by age, sex, and socioeconomic status. Lancet 401, 1878–1890.
Why read it: One in ten people in the UK has an autoimmune disease.

Tian, J. et al. (2023). Global epidemiology of systemic lupus erythematosus. Annals of the Rheumatic Diseases 82, 351–356.
Why read it: 3.4 million with lupus.

Mackensen, A. et al. (2022). Anti-CD19 CAR T cell therapy for refractory systemic lupus erythematosus. Nature Medicine 28, 2124–2132.
Why read it: A reset of the test gives drug-free remission.

Müller, F. et al. (2024). CD19 CAR T-cell therapy in autoimmune disease: a case series with follow-up. New England Journal of Medicine 390, 687–700.
Why read it: Remission across lupus, myositis and systemic sclerosis.

Bjornevik, K. et al. (2022). Longitudinal analysis reveals high prevalence of Epstein–Barr virus associated with multiple sclerosis. Science 375, 296–301.
Why read it: A 32-fold risk after infection.

Lanz, T. V. et al. (2022). Clonally expanded B cells in multiple sclerosis bind EBV EBNA1 and GlialCAM. Nature 603, 321–327.
Why read it: The misread at one antibody.

Du Toit, G. et al. (2015). Randomized trial of peanut consumption in infants at risk for peanut allergy (LEAP). New England Journal of Medicine 372, 803–813.

Why read it: Early meeting trains the test.

Wood, R. A. et al. (2024). Omalizumab for the treatment of multiple food allergies (OUtMATCH). New England Journal of Medicine 390, 889–899.
Why read it: A reading-layer drug in food allergy.

Cancer

Bray, F. et al. (2024). Global cancer statistics 2022: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA: A Cancer Journal for Clinicians 74, 229–263.
Why read it: 20 million new cancers and 9.7 million deaths.

Islami, F. et al. (2024). Proportion and number of cancer cases and deaths attributable to potentially modifiable risk factors in the United States, 2019. CA: A Cancer Journal for Clinicians 74, 405–432.
Why read it: About four in ten cases preventable.

National Lung Screening Trial Research Team (2011). Reduced lung-cancer mortality with low-dose computed tomographic screening. New England Journal of Medicine 365, 395–409.
Why read it: Screening lowers lung cancer death by 20 %.

de Koning, H. J. et al. (2020). Reduced lung-cancer mortality with volume CT screening in a randomized trial (NELSON). New England Journal of Medicine 382, 503–513.
Why read it: The European confirmation.

Independent UK Panel on Breast Cancer Screening (2012). The benefits and harms of breast cancer screening. Lancet 380, 1778–1786.
Why read it: About a fifth fewer breast cancer deaths among those invited.

Burn, J. et al. (2020). Cancer prevention with aspirin in hereditary colorectal cancer (Lynch syndrome), 10-year follow-up (CAPP2). Lancet 395, 1855–1863.
Why read it: A simple chain-layer prevention for an inherited copy fault.

Cercek, A. et al. (2022). PD-1 blockade in mismatch repair-deficient, locally advanced rectal cancer. New England Journal of Medicine 386, 2363–2376.
Why read it: Every patient responded: form U cured by making the tumour readable.

Lei, J. et al. (2020). HPV vaccination and the risk of invasive cervical cancer. New England Journal of Medicine 383, 1340–1348.
Why read it: 88 % less cancer when vaccinated before 17.

Hugosson, J. et al. (2019). A 16-yr follow-up of the European Randomized study of Screening for Prostate Cancer. European Urology 76, 43–51.
Why read it: PSA screening lowers prostate cancer death by about a fifth.

Hamdy, F. C. et al. (2023). Fifteen-year outcomes after monitoring, surgery, or radiotherapy for prostate cancer (ProtecT). New England Journal of Medicine 388, 1547–1558.
Why read it: Read before you act: active surveillance is safe for low risk.

Green, A. C. et al. (2011). Reduced melanoma after regular sunscreen use: randomized trial follow-up. Journal of Clinical Oncology 29, 257–263.
Why read it: Daily sunscreen halves new melanomas.

Wolchok, J. D. et al. (2025). Final, 10-year outcomes with nivolumab plus ipilimumab in advanced melanoma (CheckMate 067). New England Journal of Medicine 392, 11–22.
Why read it: About half alive at ten years.

Hochhaus, A. et al. (2017). Long-term outcomes of imatinib treatment for chronic myeloid leukemia (IRIS). New England Journal of Medicine 376, 917–927.
Why read it: One wrong word, one drug, 83 % alive at ten years.

Hunger, S. P. & Mullighan, C. G. (2015). Acute lymphoblastic leukemia in children. New England Journal of Medicine 373, 1541–1552.
Why read it: About 90 % cured.

Nervous system and senses

Xie, L. et al. (2013). Sleep drives metabolite clearance from the adult brain. Science 342, 373–377.
Why read it: The brain clears waste in sleep: why deep rest matters for dementia.

Livingston, G. et al. (2024). Dementia prevention, intervention, and care: 2024 report of the Lancet standing Commission. Lancet 404, 572–628.
Why read it: Fourteen risks; about 45 % of dementia.

van Dyck, C. H. et al. (2023). Lecanemab in early Alzheimer's disease. New England Journal of Medicine 388, 9–21.
Why read it: A modest slowing by removing a deposit.

Sims, J. R. et al. (2023). Donanemab in early symptomatic Alzheimer disease (TRAILBLAZER-ALZ 2). JAMA 330, 512–527.
Why read it: The second amyloid antibody.

Ngandu, T. et al. (2015). A 2 year multidomain intervention of diet, exercise, cognitive training, and vascular risk monitoring (FINGER). Lancet 385, 2255–2263.
Why read it: The phase layer against cognitive decline.

Lin, F. R. et al. (2023). Hearing intervention versus health education control to reduce cognitive decline in older adults with hearing loss (ACHIEVE). Lancet 402, 786–797.
Why read it: A benefit only in those at high risk.

Deuschl, G. et al. (2006). A randomized trial of deep-brain stimulation for Parkinson's disease. New England Journal of Medicine 355, 896–908.
Why read it: An outside change that breaks a locked rhythm.

Schenkman, M. et al. (2018). Effect of high-intensity treadmill exercise on motor symptoms in patients with de novo Parkinson disease (SPARX). JAMA Neurology 75, 219–226.
Why read it: Exercise as a phase cure.

Wiebe, S. et al. (2001). A randomized, controlled trial of surgery for temporal-lobe epilepsy. New England Journal of Medicine 345, 311–318.
Why read it: 58 % against 8 % free of seizures.

Neal, E. G. et al. (2008). The ketogenic diet for the treatment of childhood epilepsy: a randomised controlled trial. Lancet Neurology 7, 500–506.
Why read it: A change of fuel that reduces seizures.

GBD 2021 Low Back Pain Collaborators (2023). Global, regional, and national burden of low back pain, 1990–2020. Lancet Rheumatology 5, e316–e329.
Why read it: 619 million with low back pain.

Ashar, Y. K. et al. (2022). Effect of pain reprocessing therapy vs placebo and usual care for patients with chronic back pain. JAMA Psychiatry 79, 13–23.
Why read it: An outside reader opens a wrong closure.

Krebs, E. E. et al. (2018). Effect of opioid vs nonopioid medications on pain-related function in patients with chronic back pain or hip or knee osteoarthritis pain (SPACE). JAMA 319, 872–882.
Why read it: A chain cure that does not fit form W.

Miller, T. M. et al. (2022). Trial of antisense oligonucleotide tofersen for SOD1 ALS. New England Journal of Medicine 387, 1099–1110.
Why read it: Silencing a faulty word.

World Health Organization (2019). World report on vision. / (2021). World report on hearing.
Why read it: 2.2 billion with impaired vision; 1.5 billion with hearing loss.

He, M. et al. (2015). Effect of time spent outdoors at school on the development of myopia among children in China. JAMA 314, 1142–1148.
Why read it: Daylight as a phase cure for the eye.

Heijl, A. et al. (2002). Reduction of intraocular pressure and glaucoma progression (EMGT). Archives of Ophthalmology 120, 1268–1279.
Why read it: Lowering pressure slows nerve loss.

Skin, bone, muscle and joints

Palmer, C. N. A. et al. (2006). Common loss-of-function variants of the epidermal barrier protein filaggrin are a major predisposing factor for atopic dermatitis. Nature Genetics 38, 441–446.
Why read it: The open seam of the skin.

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Disorders of the mind

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