Hierarchical Oscillatory Dynamics in Biological Systems

A Multiscale Theory of Cellular Coherence, Emergent Function and Biological Regulation

J. Konstapel, Leiden, The Netherlands, 23 September 2026

Abstract

Biological systems show organised dynamics over a wide range of temporal and spatial scales. Calcium signalling, mitochondrial metabolism, membrane excitability, cytoskeletal remodelling, transcriptional feedback and circadian timing are all dynamic processes. They are usually studied as partly independent regulatory systems. This article states a unified framework in which biological organisation is a hierarchy of coupled oscillatory networks.

The framework extends phase-oscillator theory with intrinsic frequency, phase, amplitude, stochastic fluctuation and biophysically interpretable coupling. Five oscillator classes form the cellular basis: mitochondrial, calcium, circadian, membrane and cytoskeletal dynamics. They interact through metabolic, ionic and mechanical coupling. A generalised order parameter,

$$R(t) = \left| \frac{1}{N} \sum_{j=1}^{N} A_j(t)\, e^{i\phi_j(t)} \right|,$$

measures collective coherence. A separate persistence measure distinguishes transient synchronisation from stable dynamical organisation.

The central hypothesis is that biological function is an emergent property of multiscale oscillator coherence, not only of the state of individual molecular components. Cells become oscillatory units within tissues, tissues within organs, and organs within the organism.

The article adds nine propositions with complete proofs. They show that the amplitude-weighted order parameter is the natural collective variable; that a pair of oscillators locks under an exact condition; that coupling fixes the amplitudes at computable values; that the persistence measure separates transient from stable coherence; that an external rhythm entrains an oscillator within an exact window and

at a fixed phase offset; that coherence responds steeply near critical coupling; and that the level-to-level recursion takes an explicit form under locking. A numerical check confirms the critical-coupling result within finite-size error.

Keywords: biological oscillators; synchronisation; coherence; systems biology; multiscale dynamics; entrainment; circadian rhythms; calcium signalling; nonlinear dynamics

1. Introduction

Life is dynamic. ATP production fluctuates. Intracellular calcium rises and falls. Membrane potentials oscillate. Transcriptional networks produce rhythmic expression. Cytoskeletal structures assemble and disassemble. Circadian clocks coordinate physiology over roughly 24-hour cycles. These processes interact through chemical, electrical, mechanical and informational pathways.

Biological rhythms are well established. So is the mathematics of oscillators and synchronisation. Kuramoto-type models give a canonical description of collective phase synchronisation (Kuramoto, 1984; Strogatz, 2000). Physiology has documented coupled rhythmic processes at cellular, tissue and organism level (Glass, 2001).

Less developed is a framework that connects these observations across scales. This article starts from one proposition:

> A biological system can be represented as a hierarchy of coupled oscillatory systems, in which collective dynamics at one level become dynamical variables at the next.

This does not claim that every biological process is strictly periodic. Nor does it reduce function to one coherence variable. It claims that oscillatory organisation is one fundamental layer of biological architecture.

A useful image is a fishnet. Each knot is an oscillator. Each thread is a coupling. A pull on one knot travels through the threads. The net holds its shape through the pattern of its connections, not through any single knot.

The article proceeds as follows. Section 2 states the model. Section 3 gives the coupling channels. Section 4 lists the oscillator repertoire. Sections 5 to 12 develop coherence, locking, hierarchy, specialisation, entrainment and state transitions, each with proofs where the model permits them. Section 13 gives the experimental programme. Section 17 states the status of each claim.

2. Biological systems as coupled oscillator networks

A biological unit C consists of N interacting oscillatory processes:

$$C = \{O_1, \dots, O_N\}, \qquad O_i = (\omega_i, \phi_i, A_i),$$

with intrinsic frequency ω_i, phase ϕ_i and amplitude $A_i \geq 0$.

The phase equation is

$$\frac{d\phi_i}{dt} = \omega_i + \sum_{j \neq i} A_j K_{ij} \sin(\phi_j - \phi_i + \alpha_{ij}) + \eta_i(t). \qquad (1)$$

The amplitude equation is

$$\frac{dA_i}{dt} = \gamma_i(A_i^* - A_i) + \beta_i \sum_j K_{ij} A_j \cos(\phi_j - \phi_i). \qquad (2)$$

Throughout, $K_{ii} = 0$, so the sum in (2) runs effectively over $j \neq i$. Here $\gamma_i > 0$ is the relaxation rate towards the intrinsic amplitude A_i^*, β_i is the amplitude-coupling gain, α_{ij} is a phase lag and η_i is noise.

This extends the phase-only model by letting amplitude take part in coupling. Interaction strength and frequency mismatch then determine whether oscillators stay independent, synchronise partly or lock (Pikovsky, Rosenblum & Kurths, 2001). The biological extension lies in giving K_{ij} a physical meaning.

3. Three biological coupling channels

3.1 Metabolic coupling. Metabolic processes influence each other through shared energetic resources and redox states:

$$K_{ij}^{met} = k_{met} \frac{[ATP]_{shared}}{[ATP]_{total}}.$$

This is a conceptual representation, not a full kinetic model. It encodes that metabolic oscillators couple through shared energetic states.

3.2 Ionic coupling. Calcium is the best-established intracellular oscillator that propagates in space. Its oscillations arise from nonlinear interaction of stores, IP_3 receptors, membrane transport and calcium-dependent feedback. Calcium signals propagate within and between cells (Dupont, Combettes & Leybaert, 2007; Leybaert & Sanderson, 2012):

$$K_{ij}^{ion} = D_{eff} \nabla^2[\mathrm{Ca}^{2+}] f_{ij}.$$

This embeds calcium-mediated coupling in the oscillator architecture. It does not replace mechanistic calcium models.

3.3 Mechanical coupling. The cytoskeleton transmits force and deformation:

$$K_{ij}^{mech} = \frac{E_{cyto} C_{ij}}{d_{ij}^2}.$$

3.4 Total coupling.

$$K_{ij} = w_1 K_{ij}^{met} + w_2 K_{ij}^{ion} + w_3 K_{ij}^{mech}. \qquad (3)$$

Synchronisation is therefore not attributed to one mechanism. It results from several physical channels acting at once. Because (3) is linear in the channels, a perturbation $\delta K^{(m)}$ in one channel changes the total coupling by exactly $w_m\, \delta K^{(m)}$. Section 12 uses this to locate channel-specific thresholds.

4. The cellular oscillator repertoire

Oscillator	Approximate frequency domain	Principal substrate
Mitochondrial	0.1–1 Hz	respiration, ATP production
Calcium	0.01–0.5 Hz	Ca^{2+} stores and transport
Circadian	~1 cycle / 24 h	transcriptional feedback
Membrane	1–100 Hz	ion channels, membrane transport
Cytoskeletal	µHz–mHz	actin, motors, mechanical dynamics

These ranges are model parameters, not universal constants. They vary strongly between cell types and conditions.

The evidence is strongest for calcium and circadian systems. Calcium dynamics are documented from subcellular to organ scale (Dupont et al., 2007). Mammalian circadian physiology is a hierarchy of cellular, tissue and systemic oscillators (Reppert & Weaver, 2002; Dibner, Schibler & Albrecht, 2010). Mitochondria are tightly integrated with calcium signalling and metabolism (Giorgi, Marchi & Pinton, 2018; Cartes-Saavedra, Ghosh & Hajnóczky, 2025).

5. Coherence as a state variable

5.1 The order parameter

The complex order parameter is

$$Z(t) = \frac{1}{N} \sum_{j=1}^{N} A_j(t)\, e^{i\phi_j(t)} = R(t)\, e^{i\psi(t)}. \qquad (4)$$

$R = |Z|$ is the coherence and ψ the collective phase.

Proposition 1 (the order parameter is the mean field). For every i,

$$\sum_{j \neq i} A_j \sin(\phi_j - \phi_i) = NR \sin(\psi - \phi_i).$$

Hence, with uniform coupling $K_{ij} = K/N$, $\alpha_{ij} = 0$ and $\eta_i = 0$, equation (1) becomes exactly

$$\frac{d\phi_i}{dt} = \omega_i + KR\,\sin(\psi - \phi_i).$$

Proof. The term $j = i$ contributes $A_i \sin 0 = 0$, so the sum may include it. Then

$$\sum_j A_j \sin(\phi_j - \phi_i) = \mathrm{Im}\left(e^{-i\phi_i} \sum_j A_j e^{i\phi_j}\right) = \mathrm{Im}\left(e^{-i\phi_i}\, NRe^{i\psi}\right) = NR\sin(\psi - \phi_i).$$

Substituting $K_{ij} = K/N$ into (1) gives the stated form. ■

This proposition answers why Z weights each oscillator by its amplitude. Each oscillator feels the others only through R and ψ. The amplitude-weighted order parameter is therefore not a descriptive choice. It is the quantity that drives each phase.

5.2 Bounds and normalisation

Proposition 2 (bounds). Let $\bar{A} = \frac{1}{N}\sum_j A_j > 0$. Then $0 \le R \le \bar{A}$. Equality $R = \bar{A}$ holds if and only if all oscillators with $A_j > 0$ share one phase.

Proof. By the triangle inequality, $|Z| \le \frac{1}{N}\sum_j |A_j e^{i\phi_j}| = \bar{A}$. Equality in the triangle inequality holds if and only if all non-zero terms point in the same direction, that is, share one phase. $R \ge 0$ holds because it is a modulus. ■

The normalised coherence $\tilde{R} = R/\bar{A} \in [0, 1]$ therefore separates phase alignment from amplitude.

5.3 Frequency similarity is not coherence

Proposition 3. Two systems with identical frequency sets and identical amplitudes can have $R = \bar{A}$ and $R = 0$ respectively.

Proof. Let every $A_j = A$. In system 1 set $\phi_j = 0$ for all j; then $R = A$. In system 2 set $\phi_j = 2\pi j/N$, the splay state. Then

$$Z = \frac{A}{N}\sum_{j=0}^{N-1} e^{2\pi i j/N} = 0,$$

because the N-th roots of unity sum to zero for $N \ge 2$. The frequencies play no role in either value. ■

Frequency similarity is therefore not network coherence.

5.4 Persistence

Temporal persistence is measured by

$$S_\tau = \frac{1}{T-\tau} \int_0^{T-\tau} R(t)\, R(t+\tau)\, dt. \qquad (5)$$

Proposition 4 (persistence separates transient from stable coherence). (a) If $R(t) \equiv R_0$, then $S_\tau = R_0^2$ for every lag $\tau < T$. (b) If $R(t) = R_0$ on an interval of length L inside $[0, T]$ and 0 elsewhere, then

$$S_\tau = R_0^2 \, \frac{\max(0,\, L-\tau)}{T-\tau}.$$

(c) In general, $0 \le S_\tau \le \sup_t R(t)^2$.

Proof. (a) The integrand equals R_0^2 everywhere. (b) The integrand is R_0^2 exactly when both t and $t+\tau$ lie in the interval, and 0 otherwise. The set of such t has length $\max(0, L-\tau)$. (c) Both factors are non-negative and bounded by $\sup R$. ■

Proposition 4 makes the distinction precise. Take a transient burst of coherence $R_0 = 0.8$ lasting $L = 10$ minutes in a record of $T = 60$ minutes. At lag $\tau = 20$ minutes, $S_\tau = 0$. A stable state with the same peak gives $S_\tau = 0.64$. The pair (R, S_τ) therefore separates instantaneous coordination from persistent coordination.

6. From cellular coherence to biological function

The central hypothesis is

$$F(t) = \mathcal{F}\big[R(t), S(t), K(t), A(t), \omega(t)\big], \qquad (6)$$

where $F(t)$ is the functional state. Function is taken to depend on the configuration and temporal coordination of interacting processes. It does not depend only on the concentrations of individual molecules.

High coherence is not always beneficial. Epileptic activity and pathological cardiac synchronisation show that synchronisation cannot be equated with health. The claim is therefore:

> **Biological function depends on appropriately structured and regulated coherence, not on maximal coherence.**

The relevant variable is not $\max R$ but $R_{appropriate}(t, \omega, \text{context})$. The system keeps coherence where coordination is functional. It keeps independence where independence is required.

7. Two-oscillator locking and amplitude under coupling

The claims about locking and amplitude can be stated exactly for small cases.

Proposition 5 (locking condition). Let $N = 2$, $A_1 = A_2 = 1$, $K_{12} = K_{21} = K > 0$, $\alpha = 0$, $\eta = 0$, and $\Delta\omega = \omega_2 - \omega_1$. The phase difference $\theta = \phi_2 - \phi_1$ satisfies

$$\frac{d\theta}{dt} = \Delta\omega - 2K \sin\theta.$$

(a) The pair locks if and only if $|\Delta\omega| \leq 2K$. The stable locked difference is $\theta^* = \arcsin(\Delta\omega/2K)$ with $\cos\theta^* > 0$. (b) If $|\Delta\omega| > 2K$, θ drifts with period $T_{beat} = 2\pi/\sqrt{\Delta\omega^2 - 4K^2}$.

Proof. From (1), $\dot{\phi}_1 = \omega_1 + K\sin\theta$ and $\dot{\phi}_2 = \omega_2 - K\sin\theta$. Subtracting gives the equation for θ. (a) Fixed points require $\sin\theta^* = \Delta\omega/2K$, which has solutions if and only if $|\Delta\omega| \leq 2K$. The linearisation is $\frac{d}{dt}\delta\theta = -2K\cos\theta^*\,\delta\theta$, stable when $\cos\theta^* > 0$. (b) Without fixed points, θ increases monotonically. The time for one cycle is

$$\int_0^{2\pi} \frac{d\theta}{\Delta\omega - 2K\sin\theta} = \frac{2\pi}{\sqrt{\Delta\omega^2 - 4K^2}},$$

a standard integral for $|\Delta\omega| > 2K$. ■

This is the locking law of Adler (1946). It turns the verbal statement "coupling and mismatch decide between independence and locking" into one inequality.

Proposition 6 (amplitude fixed points). Let all oscillators share γ, β, A^*, let each row of K sum to $k = \sum_j K_{ij}$, and let all amplitudes be equal, $A_j = A$.

(a) In the in-phase state, (2) becomes $\dot{A} = \gamma A^* - (\gamma - \beta k)A$. If $\beta k < \gamma$, A converges exponentially to

$$A_{sync} = \frac{\gamma A^*}{\gamma - \beta k} > A^*.$$

If $\beta k \geq \gamma$, A grows without bound.

(b) For $N = 2$ in antiphase ($\theta = \pi$), A converges to $A_{anti} = \gamma A^*/(\gamma + \beta k) < A^*$.

(c) For uniform coupling $K_{ij} = k/(N-1)$ in the splay state, A converges to $A_{splay} = \gamma A^*/\big(\gamma + \beta k/(N-1)\big)$.

Proof. (a) With equal phases, $\cos 0 = 1$ and the coupling sum is $\beta A \sum_j K_{ij} = \beta k A$. The equation is linear with rate $\gamma - \beta k$. It is stable if and only if that rate is positive, with the fixed point stated. (b) With $\cos\pi = -1$ the coupling term is $-\beta k A$, which gives rate $\gamma + \beta k > 0$. (c) In the splay state $\sum_{j\neq i} \cos(\phi_j - \phi_i) = -1$, because the

full sum over all N roots of unity is 0 and the $j = i$ term is 1. The coupling term is therefore $-\beta Ak/(N-1)$. ■

Proposition 6 adds a consequence the phase model alone cannot show. Coherence and amplitude reinforce each other. In-phase coupling raises amplitude above its intrinsic value. Dispersion lowers it. It also yields a boundedness condition that the model requires: $\beta k < \gamma$.

A worked example: $\gamma = 1$, $\beta = 0.25$, $k = 2$, $A^* = 1$. In phase, $A_{sync} = 1/(1-0.5) = 2$. In antiphase, $A_{anti} = 1/(1+0.5) = 0.67$. The amplitude-weighted coherence of the in-phase pair is $R = 2$, three times the amplitude of the antiphase pair.

8. Emergence through hierarchical recursion

The framework is multiscale. Oscillators form a cell, cells form a tissue, tissues form an organ, and organs form the organism. The same principle recurs:

$$L_n = \mathcal{G}(L_{n-1}, K_n), \qquad (7)$$

where L_n is the dynamical state of level n. A higher-level oscillator is not a new entity. It emerges from collective dynamics of lower-level oscillators. Circadian organisation is an established example: cellular clocks throughout the body, and coupled clock populations in the suprachiasmatic nucleus that form a central pacemaker (Dibner et al., 2010; Maywood, 2020). Calcium waves show how local events become coordinated intracellular and intercellular dynamics (Leybaert & Sanderson, 2012).

Under locking, the recursion (7) can be made explicit for the phase and amplitude variables.

Proposition 7 (a locked cluster is an oscillator). Assume $\alpha_{ij} = 0$, $\eta_i = 0$, and the balance condition $A_j K_{ij} = A_i K_{ji}$ for all i, j. This holds, for example, for equal amplitudes and symmetric coupling. Then

$$\frac{1}{N}\sum_i \frac{d\phi_i}{dt} = \bar{\omega} = \frac{1}{N}\sum_i \omega_i.$$

If the cluster is phase-locked, every oscillator rotates at the common frequency $\Omega = \bar{\omega}$.

Proof. Sum (1) over i. The coupling terms pair up. The (i, j) term is $A_j K_{ij} \sin(\phi_j - \phi_i)$. The (j, i) term is $A_i K_{ji} \sin(\phi_i - \phi_j) = -A_i K_{ji} \sin(\phi_j - \phi_i)$. Under the balance condition each pair sums to zero. Hence the mean phase velocity equals $\bar{\omega}$. In a locked state all $\dot{\phi}_i$ are equal, so each equals $\bar{\omega}$. ■

Corollary (explicit form of $\mathcal{G}$ under locking). A locked cluster at level $n-1$ enters level n as a single oscillator with

$$\omega^{(n)} = \bar{\omega}^{(n-1)}, \qquad \phi^{(n)} = \psi^{(n-1)}, \qquad A^{(n)} = R^{(n-1)}.$$

The collective frequency, phase and coherence of one level are the frequency, phase and amplitude of a unit at the next. This is the precise meaning of "collective dynamics at one level become dynamical variables at the next".

In a locked cluster the phase differences θ^*_{ij} and the coherence R are constant, while the collective phase advances as $\psi(t) = \psi_0 + \bar{\omega}t$. The invariant content of a locked cluster is therefore the pattern $\{\theta^*_{ij}\}$ together with the phase ψ_0 at the moment of locking.

With non-zero phase lags α_{ij}, the locked frequency shifts away from $\bar{\omega}$. This is known from the Kuramoto–Sakaguchi model. The corollary then holds with Ω in place of $\bar{\omega}$.

9. Bidirectional hierarchy

A purely bottom-up hierarchy is insufficient. Higher levels feed back on lower ones:

$$L_1 \leftrightarrow L_2 \leftrightarrow \cdots \leftrightarrow L_n.$$

Circadian systems regulate metabolic programmes. Metabolic state in turn acts on the circadian machinery (Reinke & Asher, 2019). The architecture is therefore a recursive control system: local dynamics, collective dynamics and systemic dynamics act on each other in both directions.

In the notation of Section 8, feedback enters as a dependence of lower-level couplings on higher-level variables, $K^{(n-1)}_{ij} = K^{(n-1)}_{ij}\big(R^{(n)}, \psi^{(n)}\big)$. Homeostasis is then the continual regulation of relationships among oscillatory subsystems, not the maintenance of fixed concentrations.

10. Cell specialisation as dynamical reweighting

Different cell types need not have different oscillator architectures. Specialisation can partly arise through different coupling weights:

$$K^{cell}_{ij} = w^{cell}_{ij} K^{base}_{ij}.$$

Cell identity is then approximately the oscillator repertoire plus the coupling topology plus the coupling weights. The original model proposes stronger membrane coupling in neurons, stronger metabolic weighting in hepatocytes and strong calcium–membrane coupling in cardiomyocytes.

Proposition 5 makes this quantitative for any pair.

Corollary (locking threshold per cell type). With unit amplitudes and symmetric coupling, a pair (i, j) locks in a given cell type if and only if

$$w^{cell}_{ij} \;\geq\; w^*_{ij} = \frac{|\omega_i - \omega_j|}{2K^{base}_{ij}}.$$

A worked example with illustrative values from Section 4: a calcium oscillator at 0.05 Hz and a mitochondrial oscillator at 0.20 Hz. Their angular mismatch is $2\pi \times 0.15 = 0.94$ rad/s. With $K^{base} = 1$ s^{-1} the threshold is $w^* = 0.47$. A cell type with $w = 0.6$ locks the pair; a cell type with $w = 0.3$ does not.

Differentiation therefore predicts a change in which pairs lock, with unchanged intrinsic frequencies. That is measurable as a change in coupling topology rather than in gene expression alone.

11. Entrainment and environmental regulation

Biological oscillators are continuously exposed to external periodic influences. External rhythms act on each oscillator through its phase:

$$\frac{d\phi_i}{dt} = \omega_i + \sum_j K_{ij} \sin(\phi_j - \phi_i) + \sum_k \epsilon_{ik} \sin(\Omega_k t + \psi_k - \phi_i). \qquad (8)$$

Circadian biology is the clearest example: light synchronises endogenous oscillators to the day–night cycle (Golombek & Rosenstein, 2010).

Proposition 8 (entrainment window). Consider one oscillator with one external rhythm and no internal coupling: $\dot{\phi} = \omega + \epsilon \sin(\Omega t + \psi - \phi)$ with $\epsilon > 0$. Let $\delta = \phi - \Omega t - \psi$. Then

$$\frac{d\delta}{dt} = (\omega - \Omega) - \epsilon \sin \delta.$$

(a) The oscillator locks to the external rhythm if and only if $|\omega - \Omega| \leq \epsilon$. (b) The stable locked offset is $\delta^* = \arcsin\big((\omega - \Omega)/\epsilon\big)$, with $\cos \delta^* > 0$. (c) If $|\omega - \Omega| > \epsilon$, the oscillator slips relative to the rhythm with period $2\pi/\sqrt{(\omega - \Omega)^2 - \epsilon^2}$.

Proof. Differentiating δ gives the stated equation. The rest follows exactly as in Proposition 5, with $2K$ replaced by ϵ. ■

Entrainment is therefore not binary. It holds inside a window set by the detuning $|\omega - \Omega|$ and the forcing strength ϵ. In a network, coupling, phase-response properties and topology modify this window. Outside it, the oscillator slips. Inside it, external stimulation reorganises the network.

Corollary (the entrained invariant). While an oscillator is locked, its phase distance to the external rhythm is constant and equal to δ^*. A locked configuration therefore carries a fixed offset δ^*_k to every rhythm k that entrains it.

Worked example. An endogenous clock has a period of 24.2 h and light a period of 24.0 h. Then $\omega - \Omega = 2\pi(1/24.2 - 1/24.0) = -0.00216$ rad/h. Locking requires $\epsilon \geq 0.00216$ rad/h. With $\epsilon = 0.01$ rad/h, $\delta^* = \arcsin(-0.216) = -0.218$ rad. That is a lag of about 50 minutes behind the light cycle, fixed for as long as the entrainment holds.

12. Biological state transitions

Transitions between functional and dysfunctional states may occur through changes in network stability, not through gradual deterioration of components. Below a critical coupling K_c the network is desynchronised; near K_c it is partly synchronised; above K_c it locks.

For the mean-field model of Proposition 1, the threshold and the steepness near it are exact.

Proposition 9 (critical coupling and steep response). Let $A_j = 1$, $K_{ij} = K/N$, $\alpha = 0$, $\eta = 0$, and let the intrinsic frequencies follow a Lorentzian distribution with half-width Δ in the limit $N \to \infty$. Then the stationary coherence is $R = 0$ for $K \le K_c$ and

$$R = \sqrt{1 - K_c/K} \quad \text{for } K > K_c, \qquad K_c = 2\Delta,$$

and

$$\frac{dR}{dK} = \frac{K_c}{2K^2\sqrt{1 - K_c/K}} \;\longrightarrow\; \infty \quad \text{as } K \downarrow K_c.$$

Proof. The stationary value and $K_c = 2\Delta$ are the exact results of the Ott–Antonsen reduction for the Lorentzian case (Ott & Antonsen, 2008). They agree with Kuramoto's self-consistency argument, which gives $K_c = 2/(\pi g(0))$ with $g(0) = 1/(\pi\Delta)$. Differentiating $\sqrt{1 - K_c/K}$ gives the derivative. Its denominator vanishes as $K \to K_c^+$. ■

Proposition 9 is the precise form of the claim that a small perturbation can produce network instability and a large functional transition. Near threshold, a small change in coupling gives a disproportionate change in coherence. By the linearity of (3), a perturbation in channel m reaches threshold when $w_m\,\delta K^{(m)} \ge K_c - K$. The channel with the largest weight carries the smallest critical perturbation.

Numerical check. For this article the mean-field model was integrated with $N = 4000$ oscillators, Lorentzian half-width $\Delta = 0.5$ (so $K_c = 1$), Euler step 0.05, 3000 steps, random initial phases and seed 1.

K	0.6	0.8	0.9	1.0	1.1	1.2	1.5	2.0
R simulated	0.033	0.034	0.015	0.105	0.287	0.391	0.557	0.697
R theory	0	0	0	0	0.302	0.408	0.577	0.707

Below threshold the simulated values lie at the finite-size level $1/\sqrt{N} \approx 0.016$ and its low multiples. Above threshold they lie within 0.02 of theory. The rise from $K = 1.0$ to $K = 1.1$, a change of 10 percent in coupling, raises R from finite-size noise to 0.29.

13. Experimental programme

A decisive experiment measures at least three oscillator classes in the same preparation: intracellular calcium; mitochondrial membrane potential or metabolic activity; and membrane electrical activity.

For each oscillator one estimates $\omega_i(t)$, $A_i(t)$ and $\phi_i(t)$, for example by Hilbert transform after band-pass filtering. The coupling matrix is then estimated as $\widehat{K}_{ij} = f\big(\Delta\phi_{ij}, \Delta A_{ij}, \text{perturbation response}\big)$.

The critical comparison is H_0, independent oscillators, against H_1, coupled hierarchical oscillators. The propositions above sharpen what H_1 predicts:

- **From Proposition 5:** pairs lock when $|\Delta\omega| \leq 2K$. A channel-selective perturbation that lowers K below $|\Delta\omega|/2$ must produce drift, with beat period $2\pi/\sqrt{\Delta\omega^2 - 4K^2}$.
- **From Proposition 6:** loss of phase alignment must be accompanied by loss of amplitude, towards A^* or below.
- **From Proposition 4:** a transient response must show $S_\tau \to 0$ at lags beyond its duration. A stable reorganisation must not.
- **From Proposition 8:** a periodic stimulus locks the preparation only inside the window $|\omega - \Omega| \leq \epsilon$, at the offset δ^*. Outside it, the preparation slips with the stated period.
- **From Proposition 9:** the dose–response curve of coherence against a channel perturbation must be steepest near the threshold.

Perturbations should target one channel at a time: metabolic (for example FCCP), calcium-mediated or mechanical. Restoring the channel should restore coherence along the same curve.

14. The central prediction

> **Loss of biological function is accompanied by measurable alteration of multiscale dynamical coherence.**

It need not be accompanied by the loss of any single oscillator. A dysfunctional cell may retain normal mean ATP, normal mean calcium, normal membrane potential and normal expression of individual proteins. It may nevertheless show altered phase relations and reduced stability between its subsystems.

Proposition 3 shows that this is possible in principle: identical frequencies and amplitudes admit both $R = \bar{A}$ and $R = 0$. Dynamical measurements can therefore detect state transitions that concentration-based measurements miss.

15. From correlation to causality

A major challenge is to distinguish coherence leading to function from function leading to coherence. Both may hold. The framework predicts reciprocal causality: coupling shapes coherence, coherence shapes function, and function adapts coupling.

Experimental intervention is required to resolve the direction. Selective disruption of one coupling pathway, followed by its restoration, is the strongest test. If restoring a specific pathway restores a lost functional state, the coherence hypothesis gains causal support.

16. Implications for systems biology

The framework shifts biology from a component-centred to a dynamical description. The traditional question is: *Which component is abnormal?* The oscillator framework adds: *Which dynamical relationships have changed?*

The biological state becomes

$$\text{State}(t) = \{A_i,\ \omega_i,\ \phi_i,\ K_{ij},\ R,\ S_\tau\}.$$

A disease state can then be represented as a change in network topology or dynamical stability, not only as a list of abnormal molecules. This agrees with the observation that biological rhythms interact across scales and can show several synchronisation regimes at once (Goldbeter & Yan, 2022).

17. Status of the claims

Claim	Status
Biological oscillators, calcium-wave coordination, mitochondrial–calcium coupling, hierarchical circadian organisation	Established in the literature (refs. 3–14)
Propositions 1–9 and their corollaries	Proved in this article, under the stated assumptions
Numerical check of Proposition 9	Computed for this article; reproducible from the stated parameters
Coherence (R, S_τ) as a general state variable of function, eq. (6)	Hypothesis, with the predictions of Sections 13–14
Experimental results reported in the 2025 source manuscript	Not used as evidence here; they require independent reproduction

18. Conclusions

Biological systems contain interacting oscillators, they synchronise, and coupling produces collective dynamics from intracellular processes to whole organisms. This article integrates these principles in one mathematical architecture and proves its core relations.

1. The amplitude-weighted order parameter is the exact mean field acting on each phase (Prop. 1).

2. Coherence is bounded by mean amplitude and is independent of frequency similarity (Props. 2–3).
3. Persistence separates transient from stable coherence (Prop. 4).
4. A pair locks exactly when $|\Delta\omega| \leq 2K$ (Prop. 5).
5. Coherence and amplitude reinforce each other; boundedness requires $\beta k < \gamma$ (Prop. 6).
6. A locked cluster is itself an oscillator with frequency $\bar{\omega}$ and amplitude R. Its invariant content is the pattern of phase differences and the phase at locking (Prop. 7).
7. Cell specialisation is a shift in locking thresholds (Section 10).
8. An external rhythm entrains within the window $|\omega - \Omega| \leq \epsilon$, at a fixed phase offset δ^* (Prop. 8).
9. Near critical coupling, coherence responds without bound to small changes in coupling (Prop. 9).

The resulting picture runs from oscillation through coupling, synchronisation and coherence to emergence and function. Function in turn regulates coupling and produces a new dynamical state.

The contribution is not the observation that biological systems oscillate. It is the proposal that multiscale coherence and its persistence are quantitative variables linking molecular dynamics to cellular, tissue, organ and organism function. The propositions above state exactly what that proposal predicts.

Annotated references

1. Kuramoto, Y. (1984). *Chemical Oscillations, Waves, and Turbulence*. Springer. *Why read?* The source of phase-coupled oscillator theory and of the order parameter. Proposition 1 generalises its mean-field identity to amplitude-weighted oscillators. *Reading advice:* Chapter 5 contains the self-consistency argument behind Proposition 9.

2. Pikovsky, A., Rosenblum, M. & Kurths, J. (2001). *Synchronization: A Universal Concept in Nonlinear Sciences*. Cambridge University Press. *Why read?* The standard treatment of phase locking, entrainment and synchronisation transitions. *Reading advice:* Chapter 3 on forced oscillators matches Proposition 8. Chapter 8 matches Proposition 5. Chapter 12 matches Section 12.

3. Glass, L. (2001). Synchronization and rhythmic processes in physiology. *Nature* 410, 277–284. *Why read?* The bridge between nonlinear dynamics and medicine. It shows that physiological rhythms arise from nonlinear mechanisms interacting with each other and with the environment.

4. Reppert, S. M. & Weaver, D. R. (2002). Coordination of circadian timing in mammals. *Nature* 418, 935–941. *Why read?* Direct evidence for a hierarchy of circadian oscillators, central and peripheral.

5. Dibner, C., Schibler, U. & Albrecht, U. (2010). The mammalian circadian timing system. *Annual Review of Physiology* 72, 517–549. *Why read?* Describes

cellular, tissue and systemic levels of circadian organisation, the empirical counterpart of Section 8.

6. Maywood, E. S. (2020). Synchronization and maintenance of circadian timing in the mammalian clockwork. *European Journal of Neuroscience* 51, 229–240. *Why read?* Shows that intercellular coupling contributes to robustness and amplitude of the collective rhythm, the empirical counterpart of Proposition 6.

7. Reinke, H. & Asher, G. (2019). Crosstalk between metabolism and circadian clocks. *Nature Reviews Molecular Cell Biology* 20, 227–241. *Why read?* Documents the two-way coupling between metabolism and clocks that Section 9 requires.

8. Goldbeter, A. & Yan, J. (2022). Multi-synchronization and other patterns of multi-rhythmicity in oscillatory biological systems. *Interface Focus* 12, 20210089. *Why read?* Shows that biological systems can hold several oscillatory regimes and synchronisation states at once.

9. Leybaert, L. & Sanderson, M. J. (2012). Intercellular Ca^{2+} waves: mechanisms and function. *Physiological Reviews* 92, 1359–1392. *Why read?* The empirical basis for local calcium dynamics becoming coordinated multicellular signalling.

10. Dupont, G., Combettes, L. & Leybaert, L. (2007). Calcium dynamics: spatio-temporal organization from the subcellular to the organ level. *International Review of Cytology* 261, 193–245. *Why read?* An early explicit connection of calcium dynamics across organisational scales.

11. Cartes-Saavedra, B., Ghosh, A. & Hajnóczky, G. (2025). The roles of mitochondria in global and local intracellular calcium signalling. *Nature Reviews Molecular Cell Biology* 26, 456–475. *Why read?* Current evidence for mitochondrial–calcium interaction, which supports treating metabolic and calcium oscillators as coupled.

12. Giorgi, C., Marchi, S. & Pinton, P. (2018). The machineries, regulation and cellular functions of mitochondrial calcium. *Nature Reviews Molecular Cell Biology* 19, 713–730. *Why read?* The mechanisms coupling calcium handling, mitochondrial metabolism and ATP production.

13. Saini, C. et al. (2011). The mammalian circadian timing system: synchronization of peripheral clocks. *Cold Spring Harbor Symposia on Quantitative Biology* 76, 39–47. *Why read?* Shows that systemic timing requires synchronisation of distributed cellular oscillators.

14. Golombek, D. A. & Rosenstein, R. E. (2010). Physiology of circadian entrainment. *Physiological Reviews* 90, 1063–1102. *Why read?* The physiological basis of Section 11: how endogenous oscillators are set by environmental time cues. *Reading advice:* Read the sections on phase-response curves beside Proposition 8.

15. Adler, R. (1946). A study of locking phenomena in oscillators. *Proceedings of the IRE* 34, 351–357. *Why read?* The origin of the locking law in Propositions 5 and 8. *Reading advice:* The derivation is short and the equation is the same.

16. Ott, E. & Antonsen, T. M. (2008). Low dimensional behavior of large systems of globally coupled oscillators. *Chaos* 18, 037113. *Why read?* The exact reduction behind Proposition 9 for Lorentzian frequency distributions.

17. Strogatz, S. H. (2000). From Kuramoto to Crawford. *Physica D* 143, 1–20. *Why read?* The clearest account of the Kuramoto transition and its history. *Reading advice:* Sections 2–4 are sufficient for this article.

18. Matthews, P. C., Mirollo, R. E. & Strogatz, S. H. (1991). Dynamics of a large system of coupled nonlinear oscillators. *Physica D* 52, 293–331. *Why read?* Coupled phase–amplitude oscillators, including amplitude death. The background to Proposition 6 and its boundedness condition.

19. Konstapel, J. (2025). *Hierarchical Oscillatory Dynamics in Biological Systems: A Mathematical Framework for Cellular Coherence, Health, and Therapeutic Intervention*. Unpublished manuscript. *Why read?* The source of the five-oscillator architecture, the amplitude–phase equations, the coherence metrics and the hierarchical extension. Its reported experiments await independent reproduction.