Coherence Medicine: A Four-Part Theoretical Foundation

J. Konstapel, Leiden, 20-7-2026

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The Coherence Principle

A Theoretical Foundation for Living Systems

J. Konstapel, Leiden, 20-7-2026.

Paper 1 of 3. Followed by *The Coherence Taxonomy of Disease* and *Coherence Medicine*.

The Axiom

Every living organism is fundamentally a self-organizing information-processing network.

Everything below follows from this. Network Physiology, the Free Energy Principle, cybernetics, homeostasis, allostasis, immunology, and evolution are not separate theories that happen to resemble each other. They are special cases of one principle, discovered independently, in different centuries, by different disciplines, using different vocabulary for the same underlying structure.

The Cybernetic Lineage

Norbert Wiener named this structure first. *Cybernetics: Or Control and Communication in the Animal and the Machine* (1948) established that living systems and control systems share a common formal structure: a regulator senses a variable, compares it to a target, and acts to reduce the difference. W. Ross Ashby's *An Introduction to Cybernetics* (1956) extended this into the Law of Requisite Variety — a regulator can only control a system if the regulator's own variety of possible states matches or exceeds the variety of disturbances it faces.

This is the structure every later framework rediscovers. A living organism is not one regulator but a hierarchical network of regulators — cell, tissue, organ, organ system, organism — each a control loop, each nested inside a larger one. Disease is a fault in one or more of these nested loops. Different diseases are different regulatory faults, at different points in the hierarchy.

Network Physiology, the Free Energy Principle, and homeostasis/allostasis theory are what this cybernetic structure looks like when applied specifically to biology, seventy years after Wiener and Ashby wrote it down in general form.

Coherence, Defined

Health is the capacity of a living system to maintain coherent information exchange across multiple spatial and temporal scales while adapting to perturbation.

This definition makes coherence measurable rather than metaphorical. It decomposes into four components, each already operationalized in existing literature:

Synchronization — the degree to which coupled oscillatory subsystems move in phase. Formally captured by the Kuramoto order parameter:

$$r(t) \cdot e^{(i\psi(t))} = (1/N) \cdot \Sigma_i \, e^{(i\theta_i(t))}$$

where $\theta_i(t)$ is the instantaneous phase of subsystem i's dominant oscillatory mode. This is the one component of coherence with a fully specified, closed mathematical form, and it is the term this author's own clinical work (the PCLC taxonomy) has built on directly.

Connectivity — the topology of coupling between subsystems: which nodes influence which others, and how strongly. Bashan, Bartsch, Kantelhardt, Havlin, and Ivanov (2012) established the measurement methodology — time-delay stability analysis revealing physiological network topology directly from multi-system recordings.

Information flow — the directional transfer of information between subsystems, distinct from mere correlation. Measurable through transfer entropy and directed connectivity methods already standard in Network Physiology.

Adaptability — the system's capacity to reorganize its coherence pattern under perturbation, rather than merely holding one fixed configuration. This is where the Free Energy Principle enters directly: adaptability is, in Friston's terms, the system's capacity to minimize surprise across changing conditions rather than at a single set point.

Coherence at time t, C(t), is the joint state of these four components — not yet a single fitted scalar equation, because the four components live in different mathematical spaces (a phase-synchronization measure, a graph-topology measure, an information-theoretic measure, a dynamical-systems measure) and unifying them into one closed-form dC/dt is an open problem, not a solved one. What is solved, and what this paper commits to as its formal core, is r(t) — fully specified, already validated across eleven disease case studies in the companion taxonomy paper. The other three components are defined here with equal precision to what the existing literature already measures; integrating all four into a single equation is the next technical step, not a gap papered over with metaphor.

Special Cases of One Principle

Network Physiology (Ivanov, 2021; Bashan et al., 2012) is the connectivity and information-flow components of coherence, studied directly, at the physiological scale.

The Free Energy Principle (Friston, 2010; Friston, 2012; Hesp et al., 2019) is the adaptability component, generalized across every biological scale from cell to society — the mathematics of how a self-organizing system minimizes uncertainty to remain within viable states.

Homeostasis and allostasis (Bettinger & Friston, 2023) are what adaptability and connectivity look like at the level of a single regulated variable and its surrounding network, respectively — homeostasis as the classical, single-variable case; allostasis as its generalization to anticipatory, whole-network adjustment.

Immunology is a connectivity and information-flow problem at cellular scale: the immune network's capacity to distinguish self from non-self and coordinate response is a coherence property of an enormous, highly connected cellular network.

Evolution operates on coherence itself, not only on individual traits: a lineage's regulatory architecture — its Requisite Variety, in Ashby's terms — determines its capacity to remain viable under environmental perturbation across generations, exactly as an organism's regulatory

architecture determines its capacity to remain viable under perturbation across a lifetime. The same principle, one level up in scale and one order of magnitude slower in time.

What Follows

This principle is the foundation, not the application. Paper 2, *A General Theory of Regulation*, defines the formal vocabulary — feedback, feedforward, references, attractors, resilience distinguished from coherence — that the axiom above needs before it can be applied clinically. Paper 3, *The Coherence Taxonomy of Disease*, replaces organ-based and pathogen-based disease classification with a classification built directly on that vocabulary: which component of coherence has failed, and how. Paper 4, *Coherence Medicine*, works out the consequences for diagnosis, treatment, and — because a coherence-based system requires the same self-organizing structure it describes — the organization of a health system that does not require central control to function.

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A General Theory of Regulation

The Formal Vocabulary Between Principle and Practice

J. Konstapel, Leiden, 20-7-2026.

Paper 2 of 4. Builds on *The Coherence Principle*. Precedes *The Coherence Taxonomy of Disease* and *Coherence Medicine*.

Why This Layer Is Necessary

The Coherence Principle states the axiom: every living organism is a self-organizing information-processing network. That axiom does not by itself tell a clinician what to measure or a theorist what a "regulatory failure" formally is. Between an axiom and a disease taxonomy sits a layer of precisely defined terms — the equivalent, for this framework, of what Ashby's *Introduction to Cybernetics* was for control theory in general. This paper is that layer.

Feedback

A regulator senses a variable, compares it to a reference, and acts to reduce the difference between them. This is the elementary control loop — sensor, controller, effector, reference — and it is the structure every one of the five coherence-failure types in the taxonomy paper describes a specific way of breaking.

Feedforward

Feedback corrects after a disturbance has already displaced the system. Feedforward anticipates the disturbance and adjusts before displacement occurs, using a predictive model of the environment rather than only the current error signal. Allostasis (Bettinger & Friston, 2023) is feedforward applied to physiological regulation: the organism predicts environmental demand

and adjusts before disturbance becomes dangerous, rather than waiting to correct deviation after the fact. The Free Energy Principle formalizes feedforward as the general case: minimizing expected future surprise, not only current error.

References

The target state a control loop defends. A reference is not fixed by physical necessity — it is a set point the loop treats as correct, whether or not it currently serves the organism. This is the formal object that fails in the taxonomy's Type III (reference drift): the loop continues to function correctly, but defends a target that has itself shifted to an abnormal state.

Attractors

A system's stable configurations — states or trajectories the system tends toward and returns to after small perturbations. Health is not a fixed point but a resilient attractor: a configuration robust enough to absorb disturbance without being displaced into another stable configuration. Disease, formally, is the system occupying a different attractor — one that is itself stable (which is why many chronic diseases persist after their original trigger is removed) but biologically undesirable.

Coherence

Defined in Paper 1: the joint state of synchronization, connectivity, information flow, and adaptability across a coupled network. Coherence is an instantaneous property — the state of the system's regulatory loops at a given moment, not a claim about how that state will hold up over time or under repeated stress. That temporal, longitudinal property is resilience, defined separately below, precisely because the two are not the same thing and collapsing them loses information the taxonomy needs.

Synchronization

The degree to which coupled oscillatory subsystems move in phase, formalized by the Kuramoto order parameter r(t). The single fully specified, closed-form component of coherence, and the mathematical object the taxonomy paper's eleven case studies are built on directly.

Information Flow

The directional transfer of information between subsystems, distinct from correlation or mere co-occurrence. Where synchronization measures whether subsystems move together, information flow measures which subsystem is driving which — a directionality synchronization alone

cannot capture, measurable through transfer-entropy and directed-connectivity methods already standard in Network Physiology.

Adaptation

The system's capacity to change its coherence configuration — its synchronization pattern, its connectivity, its information-flow routing — in response to a specific perturbation. Adaptation is a first-order, reactive property: it describes what the system does in response to one disturbance, not its capacity to withstand many, or different kinds, over time.

Resilience, Distinguished from Coherence and Adaptability

Resilience is not coherence and is not adaptability, though it depends on both. C.S. Holling's foundational distinction (1973) separated **stability** — a system's tendency to return to equilibrium after a disturbance — from **resilience** — a system's capacity to absorb disturbance and persist, including by moving to a different but still viable configuration, without losing its essential function. Coherence, as defined in this framework, is closer to Holling's stability: a measure of the system's current organized state. Resilience is the longitudinal, repeated-perturbation property: not "is the system coherent right now" but "does the system's capacity to reorganize toward viable coherence hold up across repeated, varied, and unanticipated disturbance over time."

This gives the framework its full hierarchy:

coherence → adaptability → resilience → health

Coherence is the instantaneous joint state. Adaptability is the capacity to change that state in response to one perturbation. Resilience is the sustained capacity to do this repeatedly, across varied and unanticipated perturbation, without losing essential function. Health is the emergent, clinically observable property when resilience remains high enough to keep the organism within viable attractor space across its lifespan — not a fixed target state, but the standing capacity to keep finding one.

What This Layer Makes Possible

With feedback, feedforward, references, and attractors defined formally, and with coherence and resilience distinguished rather than conflated, the taxonomy paper's five failure types are no longer five clinical categories asserted by analogy to physics. They are five specific, formally distinct ways the regulatory structure defined here can fail: desynchronization (Type I), attractor lock-in (Type II), reference corruption (Type III), substrate loss (Type IV), and single-link failure

within an otherwise intact loop (Type V). Each is now traceable to a specific term defined in this paper, not only to a clinical pattern observed across eleven diseases.

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The Coherence Taxonomy of Disease

Toward a Regulatory Classification of Illness

J. Konstapel, Leiden, 20-7-2026.

Paper 3 of 4. Builds on *The Coherence Principle* and *A General Theory of Regulation*. Followed by *Coherence Medicine*.

From Organs and Pathogens to Regulatory Patterns

The International Classification of Diseases organizes illness by organ system, by pathogen, by anatomical site. This classification has organized clinical practice for over a century, and it will not be discarded — most acute, localized, single-cause conditions are well served by it. But it was never built to answer the question this paper asks: what has actually gone wrong with the organism's coherence, independent of which organ happens to show the symptom.

The Coherence Principle defines health as coherent information exchange across scales — synchronization, connectivity, information flow, and adaptability, jointly. Disease, on this framework, is not "diabetes" or "Parkinson's" or "atrial fibrillation" as primary categories. It is a specific kind of failure in that joint coherence state. Diabetes, Parkinson's, and atrial fibrillation are downstream expressions — often several different coherence failures wearing one clinical name, at different stages of one disease's progression.

Paper 2, *A General Theory of Regulation*, formally defines the terms this taxonomy uses: feedback, references, attractors, coherence, and resilience. Five regulatory categories, each traceable to a specific failure of that formal structure, exhaust the ways coherence can fail:

The Five Types

Coherence loss (Type I). Synchronization (r(t)) falls below the range that supports coordinated function; subsystems that should be coupled desynchronize. Atrial fibrillation's chaotic reentrant rotors. Sepsis's uncoupling of biological oscillators — identified independently by Godin and Buchman (1996) three decades before this vocabulary existed, using heart rate variability as the empirical proxy. Early type 2 diabetes: reduced intra-islet calcium/membrane-potential synchrony, reduced insulin pulsatility.

Pathological coherence (Type II). Synchronization rises above the adaptive range, or locks onto the wrong attractor. Parkinsonian beta-band (13–30 Hz) hypersynchrony between basal ganglia and motor cortex. Epileptic hypersynchronization. This category does not exist in organ-based classification as a category — Parkinson's and epilepsy sit in entirely separate ICD chapters despite sharing the identical regulatory pattern.

Reference drift (Type III). The loop — sensing, computation, execution — functions correctly, but the target itself has shifted, and the loop faithfully defends the wrong state. Baroreflex resetting in essential hypertension: acute resetting begins within minutes of sustained pressure elevation, complete resetting within roughly 48 hours. Beta-cell dedifferentiation in progressive type 2 diabetes: the cell reverts toward a progenitor-like identity rather than dying.

Node destruction (Type IV). The loop's physical substrate is eliminated outright — not a functional failure of a working loop, but removal of the loop itself. Autoimmune beta-cell destruction in type 1 diabetes.

Structural failure (Type V). One link in an otherwise intact loop malfunctions while reference and substrate remain correct. Sensor failure: diabetic peripheral neuropathy, degrading the position/pressure/injury feedback signal. Controller failure: central diabetes insipidus, where sensing and effector function normally but hypothalamic/pituitary computation fails. Effector failure: myasthenia gravis, where central command is correct but neuromuscular execution is blocked.

The Same Disease, Different Types, Over Time

A single ICD-coded disease routinely moves through several coherence types as it progresses — evidence that the organ-based label was never tracking the actual regulatory event. Type 2 diabetes begins as Type I (reduced intra-islet synchrony), progresses to Type III in the same tissue (beta-cell dedifferentiation), and in advanced disease progresses toward Type IV as beta-cell mass declines through outright loss. An intervention strategy calibrated to the Type I stage — restoring synchrony — has no default warrant once the same patient's disease has progressed to Type III or IV. The ICD code "type 2 diabetes" stays constant throughout. The regulatory classification does not, and that is the diagnostic information organ-based coding cannot supply.

Mapping Against ICD: A Working Table

Coherence Type	ICD-classified conditions expressing this pattern	Empirical proxy used
I — Coherence loss	Atrial fibrillation; sepsis/MODS; early type 2 diabetes	Phase-singularity mapping; HRV; islet Ca^{2+} synchrony
II — Pathological coherence	Parkinson's disease; epilepsy	Basal ganglia–cortex beta-band power; EEG hypersynchronization
III — Reference drift	Essential hypertension; progressive type 2 diabetes; cancer (per Levin's bioelectric reference-error framing)	Baroreceptor pressure-threshold shift; beta-cell identity markers
IV — Node destruction	Type 1 diabetes	Beta-cell mass / autoantibody status
V — Structural failure	Diabetic peripheral neuropathy; central diabetes insipidus; myasthenia gravis	Nerve conduction; ADH/osmolality mismatch; AChR antibody titer

This table is a working cross-reference, not a replacement of ICD codes — it sits alongside organ-based diagnosis as a second, orthogonal axis: not *where* the pathology shows up, but *what kind of regulatory failure* produced it. Full replacement of ICD-style classification is the long-term direction this taxonomy points toward; this paper's contribution is the classification structure and its demonstrated fit to eleven independently documented diseases, not a claim that the transition is complete.

Falsifiable Structure

Type-matched intervention outperforms type-blind intervention within a single disease where both have been tried — rhythm-control versus rate-control strategies in atrial fibrillation is the clearest existing test case. Joint monitoring across multiple coherence measures detects transitions between failure types earlier than single-marker monitoring calibrated to only one

type — critically ill patients moving between septic decoupling (Type I) and treatment-induced hypercoherence (Type II-like autonomic hyperactivation) is the clearest existing test case.

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Coherence Medicine

Diagnosis, Treatment, and the Organization of a Coherence-Based Health System

J. Konstapel, Leiden, 20-7-2026.

Paper 4 of 4. Builds on *The Coherence Principle*, *A General Theory of Regulation*, and *The Coherence Taxonomy of Disease*.

The Coherence Principle implies that medicine is fundamentally a science of restoring regulatory coherence. Disease classification, diagnosis, and treatment follow from this single premise. Everything below is a consequence of it, not a separate set of proposals bolted alongside it.

What Changes in Practice

Organ-based medicine and coherence medicine ask different questions at every stage of clinical practice, not only in theory:

Stage	Organ-based medicine asks	Coherence medicine asks
Intake	Which disease do you have?	Which regulatory loops appear unstable?
Monitoring	Cholesterol, blood glucose, blood pressure as isolated values	Coherence trajectory — r(t), connectivity, information flow, adaptability, tracked jointly over time
Prognosis	Five-year survival, disease-specific staging	Recovery of network coherence — trajectory back toward a resilient attractor, or continued drift away from one
Treatment	Protocol for diabetes, protocol for Parkinson's	Protocol for Type III reference drift, protocol for Type II pathological coherence — the same protocol applies across organ systems sharing a type

Stage	Organ-based medicine asks	Coherence medicine asks
Specialization	Cardiology, neurology, endocrinology	Synchronization specialists, reference specialists, regeneration centers, structural-repair specialists — organized by regulatory failure type, not by organ

This is not a relabeling exercise. A synchronization specialist trained in Type I coherence-loss patterns would, on this framework, treat atrial fibrillation, septic decoupling, and early type 2 diabetes as variations on one regulatory problem — using overlapping diagnostic tools and a shared evidence base, rather than three specialties that currently do not read each other's journals.

Diagnosis: Coherence State, Then Type

Diagnosis proceeds in two stages, using the vocabulary Paper 2 defines formally. First, establish coherence state: synchronization, connectivity, information flow, and adaptability, measured with whatever instrumentation the organ system allows. Second, classify against Paper 3's five types. Only then does treatment selection begin, because — as the taxonomy paper establishes — the five types call for interventions that are not interchangeable, and Type I versus Type II interventions are direct opposites.

Treatment: Type-Matched, Not Protocol-Matched

Type I calls for restoring lost coupling. Type II calls for suppressing excess or misdirected coupling — adaptive deep-brain stimulation's real-time detection and suppression of pathological beta-band synchrony is the existing clinical proof. Type III calls for correcting the reference itself, not the sensed variable — Levin's bioelectric tumor-normalization work is the model case. Type IV calls for replacing or regenerating the destroyed substrate. Type V calls for identifying and repairing the specific failed component. A therapy validated for one type carries no default warrant for another.

Restoring Coherence Without Correcting Cause

Geometric pacing — externally provided rhythmic, spatial, or proprioceptive reference signals, generalized in the 2026 Frontiers in Network Physiology perspective from the cardiac pacemaker case — restores functional stability by supplying a stable external reference that re-enables the system's own self-organization, without correcting the underlying etiology. This is the mechanism behind cueing interventions already used in neurological rehabilitation, and the justification for building coherence-restoring interventions that act without waiting for root-cause elimination.

Four Layers, Because Coherence Is Not One Channel

A single-sensor, single-output intervention reads one channel and answers with one output — real, and insufficient alone, because coherence is a property of the whole coupled system. The physiological layer: the sensor-controller-effector loops the taxonomy addresses directly. The behavioral layer: sleep, movement, breath, diet, as direct interventions on coupling strength, not lifestyle advice appended after treatment. The relational layer: coupling between one person's physiological state and another's — an open research direction. The experiential layer: subjective state, treated as co-equal with physiological state, where breath regulation, meditation, and movement practice (yoga, qigong, tai chi) already function as centuries-old geometric-pacing technologies, independent of whether their traditional mechanistic account is taken literally.

From Coherence to Resilience to Health

Paper 2 distinguishes coherence (instantaneous joint state) from resilience (the sustained capacity to reorganize toward viable coherence across repeated, varied perturbation). This distinction has a direct clinical consequence: a single favorable coherence reading is not evidence of health, and a single poor reading is not evidence of disease. What coherence medicine tracks is the trajectory — whether the organism's coherence-restoring capacity holds up across repeated challenge, which is a resilience measurement, not a snapshot. Treatment success is redefined accordingly: not "coherence is currently normal" but "the trajectory of repeated recovery is intact."

Organizing a System That Does Not Require Central Control

The Free Energy Principle describes self-organization without an external controller, at every biological scale it has been tested on. A health system built on the same principle inherits the same design requirement: it needs consensus and shared understanding among its parts to function, not centralized steering imposed on them. Shared diagnostic protocols — the coherence-type classification of Paper 3 — distributed across specialties that currently do not share vocabulary produce coordination the way the taxonomy paper shows cardiology,

neurology, and endocrinology already independently converging on Type I and Type II patterns in their own separate literatures, without a coordinating body having told them to. Coordination emerges from a shared framework practitioners use to communicate, not from hierarchical command over what each specialty does.

Falsifiability

A paradigm earns scientific interest by taking risk, not by accumulating supporting examples. The coherence paradigm makes predictions that differ from what organ-based medicine predicts, and that can fail:

1. Two clinically distinct diseases classified under the same coherence type respond to structurally similar interventions, better than either responds to a type-mismatched intervention validated for a different disease.
2. Recovery of coherence measures (r(t), connectivity, information flow) precedes clinically observable recovery, rather than following it — coherence as leading indicator, not trailing correlate.
3. Coherence indices predict disease progression and relapse earlier and more accurately than organ-specific biomarkers measured in isolation.
4. Type I interventions (coupling-restoring) measurably worsen outcomes in Type II patients (pathological hyper-coherence), demonstrating the types are not merely descriptive but functionally opposed.
5. Network-level coherence measurements predict relapse before symptom-level measurements do, across at least one condition currently monitored by symptom checklist alone.
6. Resilience trajectories (repeated-perturbation recovery capacity) predict long-term outcome better than single-timepoint coherence readings, confirming the coherence/resilience distinction has clinical, not only theoretical, weight.
7. Geometric pacing interventions, applied to a Type I condition without addressing root cause, produce measurable coherence restoration — replicating the cardiac pacemaker result outside cardiology.

Failure of any of these to replicate does not merely weaken a supporting example — it falsifies the specific mechanism claimed. That is the standard this paradigm sets for itself, and the standard by which it should be judged.

Toward a Disease-Free World

New diseases will appear. New pathogens will evolve. Genetic variation will always produce vulnerability. Organisms with highly coherent, highly resilient regulatory networks become increasingly robust to these perturbations regardless of which specific new perturbation arrives — resilience is a property of the network's standing capacity, not of having anticipated every possible threat individually.

The goal of medicine becomes optimization of coherence and resilience, not eradication of disease. This does not replace molecular biology, immunology, or genetics — Paper 1 places them explicitly as special cases of the same principle. It is a new organizing objective, built on a foundation (Paper 1), a formal vocabulary (Paper 2), a diagnostic structure (Paper 3), and now the treatment, practice, and organizational consequences, standing or falling on the predictions stated above.

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