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Coherence Physiology

The Embodied Substrate of Life-Coherent Medicine

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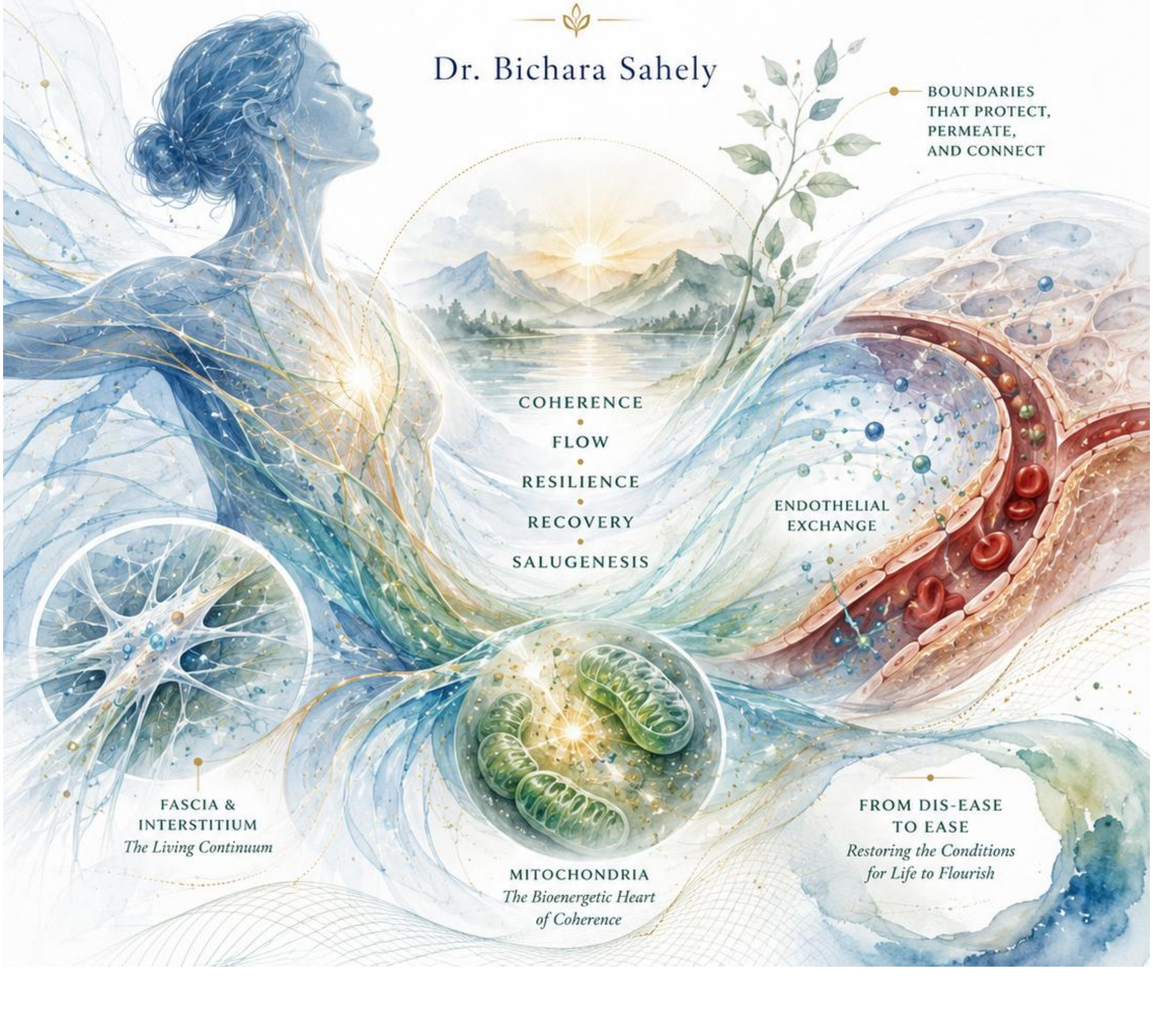

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The Embodied Substrate of Life-Coherent Medicine

Integrating Interfacial Water, Mechanobiology, Microvascular Exchange, Immune Surveillance, Mitochondrial Regulation, and Salugenesis

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Preface: Why Coherence Physiology Now

This white paper emerges from a growing recognition that chronic, multisystem, stress-mediated, environmentally contingent, and recovery-resistant illness cannot be adequately understood through an organ-by-organ model alone. Modern medicine has achieved remarkable success in acute disease, emergency care, surgery, infection, pharmacology, and specialty-specific intervention. Yet many patients continue to suffer in patterns that cross the boundaries by which medical knowledge has been organized.

The present paper proposes coherence physiology as a response to that gap. Its aim is not to reject established physiology or replace conventional medicine. Rather, it seeks to reconstruct physiology around the living organism as a dynamically coupled whole. It brings together evidence from fascia and interstitium research, mechanobiology, endothelial and microvascular medicine, mast-cell and innate immune surveillance, mitochondrial stress biology, sleep and recovery science, and the frontier question of hydrated biological interfaces.

This paper is written as the physiological foundation of life-coherent medicine. Life-coherent medicine is clinical care ordered toward the preservation, restoration, and expansion of life-capacity. It asks not only what disease process should be treated, but what conditions would allow the organism to reduce defense, restore exchange, regain energetic flexibility, and resume adaptive self-repair.

The paper is deliberately integrative, but it is not intended to be totalizing. Some domains, such as mechanotransduction, endothelial biology, microvascular dysfunction, mitochondrial stress signaling, sleep-immune regulation, and mast-cell surveillance, are strongly supported. Other claims, such as defensive lock-in, salugenesis, and field restoration, are integrative constructs. Broader claims concerning interfacial water remain exploratory and should be treated as frontier questions.

The purpose of this white paper is therefore not to close inquiry, but to open a more coherent one. Its central question is simple: what kind of physiology becomes possible when medicine remembers the living whole?

Abstract

Contemporary biomedicine has achieved remarkable success in acute disease, trauma, infection, organ-specific pathology, and targeted therapeutic intervention. Yet it remains less adequate for chronic, multisystem, stress-mediated, environmentally contingent, and recovery-resistant illness, where symptoms and dysfunctions often traverse conventional specialty boundaries. This white paper argues that this limitation is not simply a shortage of data, but a problem of explanatory architecture. The living organism is too often treated as an assemblage of discrete organs, pathways, and molecular targets rather than as a nested continuum of dynamically coupled processes.

This paper proposes coherence physiology as the embodied substrate of life-coherent medicine. It reconstructs physiology around seven interdependent domains: material substrate, hydrated interface, force and flow, exchange intelligence, boundary surveillance, energetic governance, and recovery trajectory. Drawing on fascia and interstitium research, interfacial-water theory, mechanobiology and biotensegrity, endothelial and microvascular medicine, mast-cell and innate immune surveillance, mitochondrial stress biology, sleep-immune regulation, and the biology of recovery, the paper develops an integrative model in which health is understood as coordinated adaptability across scales.

In this framework, chronic illness is interpreted not only as local lesion, pathway defect, inflammation, deficiency, or persistent exposure to insult, but also as defensive lock-in: a self-stabilizing state in which altered substrate conditions, disturbed force-flow relations, degraded exchange, heightened boundary surveillance, defensive mitochondrial allocation, autonomic instability, and incomplete recovery mutually

reinforce one another. Healing is correspondingly reconceived as salugenesis: the active restoration of the conditions under which the organism can resume adaptive self-repair.

The paper distinguishes carefully among established findings, integrative inferences, and exploratory frontier claims. Fascial continuity, mechanotransduction, endothelial glycocalyx function, microvascular dysfunction, mitochondrial adaptive-state regulation, mast-cell boundary surveillance, and sleep-immune recovery form the empirical backbone. Coherence physiology, defensive lock-in, salugenesis, and field restoration are integrative claims. Broader systemic implications of interfacial water remain promising but exploratory. This evidence-gradient discipline allows the model to remain both ambitious and scientifically transparent.

The paper concludes that life-coherent medicine requires a shift from coercive correction of downstream fragments toward restoration of the organism's conditions of coherence. Such a shift does not reject acute intervention, pharmaceutical treatment, or organ-specific knowledge. Rather, it resituates them within a larger physiological architecture concerned with preserving and restoring the living whole.

Keywords

Coherence physiology; life-coherent medicine; salugenesis; defensive lock-in; fascia; interstitium; interfacial water; mechanobiology; biotensegrity; endothelial glycocalyx; microvascular dysfunction; mast cells; innate immune surveillance; mitochondria; Cell Danger Response; energy resistance; chronic illness; prevention; healing; epistemic commons.

Executive Summary

This white paper begins from a simple but far-reaching proposition: the living organism is not best understood as an assemblage of discrete organs, pathways, and molecular targets, but as a nested coherence system whose health depends on the coordinated regulation of substrate, interface, force, flow, exchange, boundary surveillance, energetic governance, and recovery. Contemporary biomedicine has achieved extraordinary power in acute disease, trauma, infection, surgery, organ-specific pathology, and targeted intervention. Yet its prevailing explanatory architecture remains less adequate for chronic multisystem illness, where symptoms and dysfunctions frequently traverse conventional specialty boundaries.

The central aim of this paper is reconstructive. It proposes coherence physiology as the embodied substrate of life-coherent medicine. Coherence physiology does not reject established physiology, specialty knowledge, pharmacology, acute intervention, or organ-specific diagnosis. Rather, it resituates them within a broader understanding of the organism as a dynamically coupled continuum. In this view, the body is not first a set of separate parts later connected by transport and signaling. It is a living field of interdependent relations within which organs, tissues, cells, vessels, nerves, immune sentinels, connective matrices, and metabolic regulators arise as differentiated expressions of a larger organized whole.

The paper develops this architecture across seven interdependent domains. Fascia, extracellular matrix, interstitium, and connective continuity provide the material substrate. Hydrated interfaces raise the frontier question of whether water at biological surfaces participates in charge, transport, matrix behavior, and energetic organization. Mechanobiology and force-flow dynamics show that cells and tissues interpret strain, pressure, movement, shear, and fluid motion. Endothelium and microcirculation provide exchange intelligence, determining whether tissues receive oxygen, nutrients, immune access, and clearance. Mast cells and innate sentinels provide boundary intelligence. Mitochondria govern adaptive energy allocation. Recovery trajectory determines whether the organism exits defense or stabilizes in lock-in.

On this basis, chronic illness is reframed. Many chronic multisystem illnesses become more intelligible when understood as defensive lock-in across multiple layers of organismal regulation. Under such conditions, the organism may continue to behave as though threat remains present even when no single dominant lesion explains the clinical picture. Mechanical strain, impaired interstitial movement, altered microvascular exchange, mast-cell vigilance, autonomic dysregulation, mitochondrial defensive reprogramming, redox imbalance, poor sleep, and incomplete tissue repair may reinforce one another.

The positive counterpart of defensive lock-in is salugenesis. Salugenesis is the active biological process through which defense resolves, exchange normalizes, tissue relationships reorganize, mitochondrial flexibility returns, immune alarm de-escalates, autonomic regulation recalibrates, and adaptive participation becomes possible again. It is not a vague wellness concept. It is the physiology of healing understood as the restoration of the conditions under which the organism can resume self-repair.

This model changes the clinical question. Conventional medicine often asks: What lesion is present? What pathway is overactive? What marker is abnormal? What drug blocks the target? These questions remain important. Coherence physiology adds a deeper question: What conditions must be restored for this organism to relinquish defense and resume adaptive self-repair? The answer may include targeted pharmacological intervention, infection control, immune modulation, vascular treatment, nutritional correction, rehabilitation, sleep restoration, movement, trauma-informed care, environmental repair, autonomic recalibration, metabolic support, or reduction of inflammatory and mechanical burden.

The paper also addresses the political economy of knowledge. The fragmentation of physiology is not only a scientific accident. It is partly reinforced by institutional and commercial incentives that favor modular, targetable, patentable, and specialty-compatible explanations. Substrate-level, preventive, restorative, and systems-integrative questions often receive less support. A renewed physiology commons is needed so that micro-coherent research streams can be assembled transparently without premature dismissal or overclaiming.

Ultimately, this paper proposes that physiology becomes more transparent when medicine remembers the organism as a living whole. The body is not a machine that fails only when parts break. It is a relational field that suffers when the conditions of coherent adaptation are degraded and heals when those conditions are restored.

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Methodological Note: Evidence Gradient and Integrative Discipline

This white paper integrates literatures that differ in evidentiary maturity. For that reason, it uses an explicit evidence-gradient approach.

Some claims are treated as established or strongly supported. These include fascial and extracellular-matrix continuity, mechanotransduction, endothelial glycocalyx function, nitric oxide signaling, microvascular dysfunction, mast-cell tissue surveillance, mitochondrial stress signaling, and the role of sleep in immune-metabolic recovery.

Other claims are integrative. These include coherence physiology as a unifying architecture, defensive lock-in as a cross-domain model of chronic illness, salugenesis as a recovery logic, and field restoration as a clinical orientation. These claims are proposed as synthesis concepts that organize convergent findings across multiple domains.

A third group of claims remains exploratory. These include broader systemic implications of interfacial water and interface-dependent hydration. Such claims are included because living systems are saturated with hydrated biological interfaces, but they are not used as the empirical backbone of the model.

This evidence-gradient discipline is central to the paper. The aim is to be integrative without being totalizing, bold without overclaiming, clinically meaningful without becoming prescriptive beyond evidence, and open to frontier questions without abandoning scientific caution.

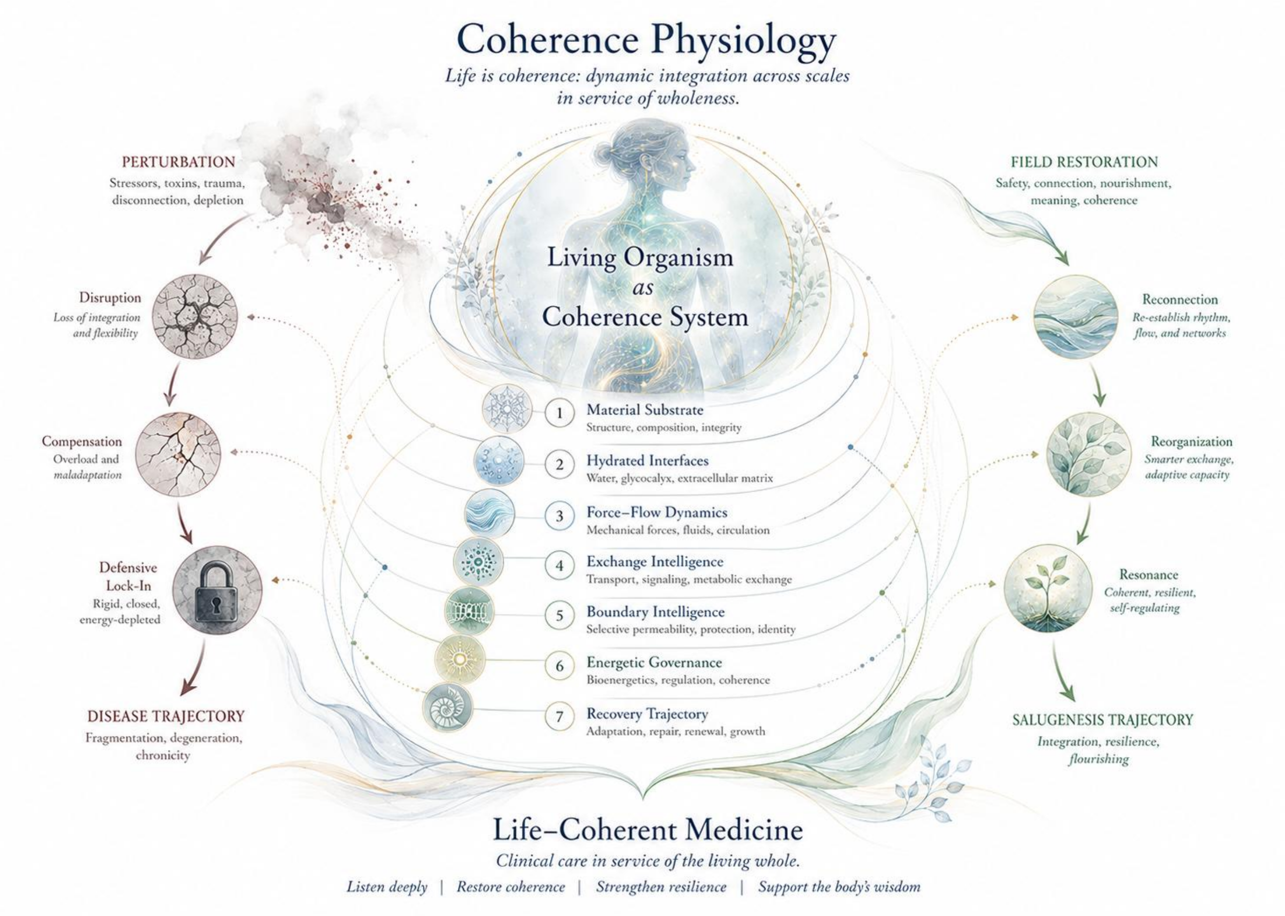

Figure 1. Coherence Physiology as the Embodied Substrate of Life-Coherent Medicine

The organism is represented as a nested coherence system rather than an assemblage of isolated organs. Health depends on the coordinated regulation of material substrate, hydrated interfaces, force-flow dynamics, exchange intelligence, boundary intelligence, energetic governance, and recovery trajectory. Chronic illness is interpreted as defensive lock-in across these layers, while healing is understood as salugenesis.

1. Introduction: Why Physiology Needs a Coherence Architecture

Modern biomedicine stands in a paradoxical position. Its achievements in acute infection, trauma, surgery, emergency care, organ-specific pathology, and targeted intervention are extraordinary. When disease presents as a discrete lesion, localized pathogen, correctable deficiency, obstructed vessel, surgical emergency, or targetable pathway, the modern biomedical model is often powerful, precise, and indispensable.

Yet the same model becomes less adequate when illness does not respect the boundaries by which medicine has organized itself. Chronic fatigue, persistent pain, dysautonomia, post-infectious syndromes, environmentally triggered illness, metabolic-vascular overlap disorders, fibrotic trajectories, inflammatory recurrence, chemical sensitivity, poor recovery after stress, and complex multisystem presentations often do not fit neatly into one organ, one pathway, one lesion, or one specialty (Institute of Medicine, 2015; Raj et al., 2022). The patient's experience may be whole, but the explanatory system divides it.

The deeper problem is architectural. Medicine has accumulated immense knowledge of parts, but it has not yet developed an equally mature account of the organism as a dynamically coupled whole. The result is that clinical reality may be fragmented faster than it can be integrated. The body becomes divided into systems, mechanisms are isolated from one another, and continuity is mistaken for coincidence.

This white paper begins from the proposition that physiology requires a coherence architecture: a framework capable of explaining how the living organism preserves adaptive wholeness across substrate, interface, force, flow, exchange, surveillance, energy allocation, and recovery. Coherence physiology is proposed here as that grammar. It names the study of how the living organism maintains adaptive coordination across scales.

Coherence, as used in this paper, does not mean uniformity, perfection, equilibrium, symmetry, or vague holism. It refers to the successful coupling of differentiated processes such that the organism can sense, respond, adapt, repair, and participate without becoming trapped in defense. A coherent organism is not static. It fluctuates, reorganizes, resists when resistance is necessary, and yields when yielding permits recovery.

The need for such a framework becomes most visible in chronic illness. Many chronic conditions cannot be adequately interpreted as simple extensions of acute disease. They often involve persistence without obvious ongoing insult, symptoms without proportional structural lesion, multisystem dysfunction without a single explanatory locus, and recovery failure long after the initiating event has faded. In such cases, the organism may not be merely damaged. It may be defensively organized (Naviaux, 2014, 2020).

Defensive lock-in does not imply that illness is imaginary, voluntary, psychogenic, or reducible to stress. Quite the opposite. It proposes that chronic illness can be profoundly biological precisely because biology is relational, embodied, and state-dependent. Mechanical strain, impaired interstitial movement, altered matrix compliance, disturbed microvascular exchange, endothelial dysfunction, persistent innate immune activation, mast-cell vigilance, autonomic dysregulation, mitochondrial defensive reprogramming, poor sleep, and incomplete repair may reinforce one another (Humphrey et al., 2014; Naviaux, 2014; Reitsma et al., 2007).

Life-coherent medicine is clinical care ordered toward the preservation, restoration, and expansion of life-capacity. It does not deny the necessity of drugs, procedures, diagnostics, emergency care, or targeted intervention. Rather, it asks that these be situated within a wider responsibility to the living whole.

2. From Organ Assemblage to Living Continuum

The first task of coherence physiology is to reconsider what kind of reality the organism is. Modern medicine has inherited an immensely useful but incomplete image of the body as an assemblage of organs, systems, tissues, cells, pathways, and molecular targets. This image has practical value, but its usefulness can become misleading when distinctions are mistaken for the organism's deepest reality.

The body is not first a collection of separate organs later joined together by vessels, nerves, hormones, and connective tissue. It is a living continuum that differentiates into organs while remaining materially, mechanically, fluidically, vascularly, immunologically, metabolically, and perceptually coupled (Adstrum et al., 2017; Benias et al., 2018; Humphrey et al., 2014; Naviaux, 2014; Reitsma et al., 2007). Organ boundaries are real, but they are not absolute. They are local differentiations within a shared field of life.

This distinction matters because the organ-assemblage model tends to make continuity appear secondary. Fascia becomes wrapping. Interstitium becomes empty space. Endothelium becomes lining. Microcirculation becomes plumbing. Mitochondria become power plants. Mast cells become allergy cells. Water becomes solvent. Each description contains partial truth, but each narrows the field of attention (Ball, 2017; Galli et al., 2005; Naviaux, 2014).

A living-continuum model reverses the order of interpretation. It begins not with isolated organs, but with the body's prior unity as a dynamic relational field. This field is composed of connective tissues, extracellular matrix, interstitial spaces, blood, lymph, endothelial surfaces, neural networks, immune sentinels, metabolic regulators, gradients, flows, pressures, tensions, hydration states, and recovery processes.

The heart, kidney, brain, gut, immune system, and musculoskeletal system are each both themselves and more than themselves. Each is a node in a continuum of exchange, metabolism, immunity, vascularity, sensation, mechanical constraint, and recovery. This is especially evident in chronic multisystem illness, where symptoms involve circulation, cognition, sleep, immune tone, digestion, pain, temperature regulation, exercise tolerance, mood, and recovery at the same time (Davis et al., 2023; Institute of Medicine, 2015).

In an organ-assemblage model, causality is often imagined as local, linear, and discrete. In a continuum model, causality may be distributed, circular, and state-dependent. Disturbed flow may amplify immune alarm; immune alarm may degrade endothelial exchange; degraded exchange may impair mitochondrial flexibility; mitochondrial defense may reduce repair capacity; reduced repair may increase matrix stiffness; matrix stiffness may alter sensory tone and autonomic regulation (Humphrey et al., 2014; Jaalouk & Lammerding, 2009; Naviaux, 2014).

The transition from organ assemblage to living continuum allows the rest of this paper to unfold. It allows fascia and interstitium to be seen as material substrate, interfacial water as a frontier substrate question, mechanobiology as a language of regulation, microcirculation as exchange intelligence, mast cells as boundary intelligence, mitochondria as energetic governance, chronic illness as defensive lock-in, and healing as salugenesis.

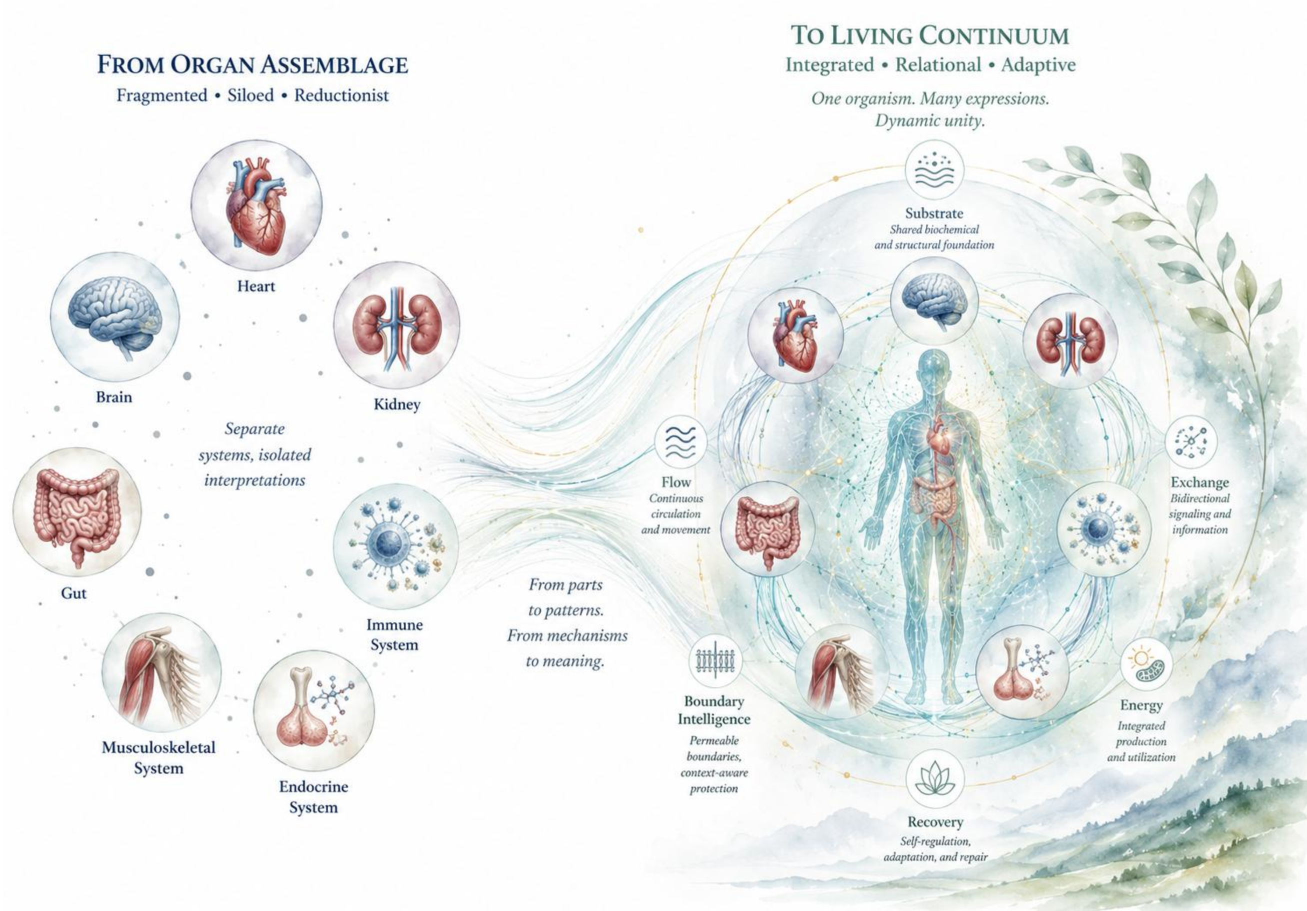

Figure 2. From Organ Assemblage to Living Continuum

Conventional biomedical models often begin with discrete organs, systems, and pathways. Coherence physiology reverses this order by understanding organs as differentiated participants within a shared living continuum of substrate, flow, exchange, boundary surveillance, energetic governance, and recovery.

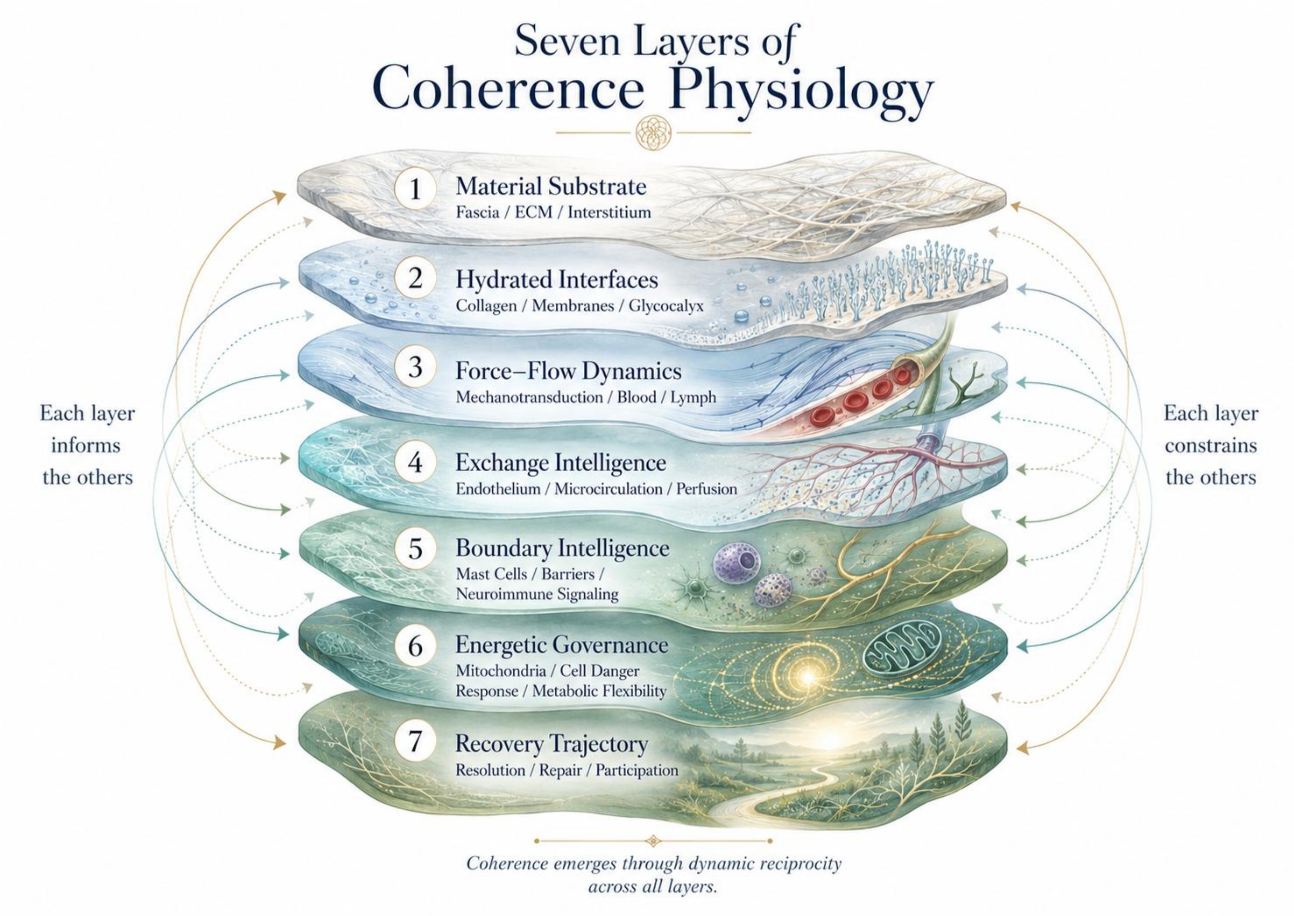

Figure 3. The Seven Layers of Coherence Physiology

Coherence physiology organizes the organism across seven interdependent layers: material substrate, hydrated interfaces, force-flow dynamics, exchange intelligence, boundary intelligence, energetic governance, and recovery trajectory.

3. The Material Substrate: Fascia, Interstitium, Matrix, and Continuity

If coherence physiology begins by recovering the organism as a living continuum, its first concrete task is to identify the material substrate through which that continuum is sustained. The body does not hold together by abstraction. It holds together through tissues, fluids, interfaces, tensions, pressures, gradients, membranes, matrices, and living boundaries.

Fascia is central to this reconstruction. It is increasingly understood as a three-dimensional continuum of collagen-containing connective tissues that extends across muscles, bones, viscera, vessels, nerves, adipose compartments, meninges, and body cavities (Adstrum et al., 2017). It participates in force transmission, tissue sliding, structural support, proprioception, nociception, interoception, vascular and neural passage, immune traffic, and local tissue regulation (Langevin, 2006).

In coherence physiology, fascia is one of the organism's primary substrates of relation. It allows local tissues to remain mechanically connected to the whole. It distributes force, permits or restricts sliding, changes its properties in response to strain and inflammation, and can become a medium through which disturbance persists. When fascia is mobile, hydrated, and integrated, it supports adaptive movement and recovery; when it is stiff, fibrotic, inflamed, or guarded, it may stabilize defensive lock-in.

The extracellular matrix extends this insight to the cellular scale. Cells live embedded in matrices whose stiffness, composition, hydration, architecture, and signaling properties shape cell behavior, differentiation, immune activation, vascular behavior, tissue repair, fibrosis, and gene expression (Humphrey et al., 2014; Jaalouk & Lammerding, 2009). The matrix is therefore not merely structural support. It is part of the cell's world.

The interstitium adds the fluidic dimension. It is a distributed, fluid-containing, collagen- and elastin-supported compartment through which signals, immune cells, metabolites, mechanical pressures, and inflammatory mediators move. It participates in shock absorption, hydration, transport, lymphatic drainage, mechanical buffering, and exchange (Benias et al., 2018).

The substrate is therefore both solid and fluid. Mechanical strain alters fluid movement. Fluid congestion alters tissue stiffness. Fibrosis alters exchange. Impaired lymphatic drainage sustains inflammation. Inflammation remodels matrix. Matrix remodeling changes mechanotransduction. Mechanotransduction alters cellular behavior (Humphrey et al., 2014; Schwager & Detmar, 2019).

The material substrate also carries memory. Injury, infection, inflammation, surgery, immobility, metabolic stress, vascular insufficiency, and chronic load can leave traces in matrix composition, collagen orientation, tissue stiffness, scar formation, sensory tone, and local immune readiness. These traces may outlast the initiating event, so that tissue continues to signal incompletion even after acute healing seems complete.

The substrate is also sensory. Fascia and connective tissues are richly innervated and participate in proprioception, nociception, interoception, and autonomic coupling (Adstrum et al., 2017; Langevin, 2006). The organism does not merely move through its connective tissues; it senses itself through them.

4. Hydrated Interfaces and the Frontier Question of Interfacial Water

If fascia, extracellular matrix, and interstitium provide the material substrate of organismal coherence, the next question concerns the medium within which that substrate becomes biologically active. Living tissues are hydrated, electrically active, interface-rich, and densely organized across surfaces. Proteins, membranes, collagen fibrils, cytoskeleton, endothelial linings, basement membranes, extracellular matrices, organelles, and connective tissues all present hydrophilic surfaces to water.

In much conventional physiology, water appears primarily as solvent, volume, medium of diffusion, osmotic participant, and carrier of dissolved substances. These roles are real and indispensable, but they may not exhaust the biological significance of water. In densely structured tissues, water is not only bulk fluid; it is water near surfaces, within matrices, around proteins, along membranes, inside gels, at vascular interfaces, and between collagen-rich structures (Ball, 2017; Israelachvili & Wennerström, 1996).

The frontier question of interfacial water begins here. Does water adjacent to biological surfaces acquire properties that differ from bulk water in ways that matter for physiology? Can interface-dependent hydration influence local charge organization, viscosity, transport, exclusion behavior, proton dynamics, mechanical properties, or energetic asymmetry? Pollack's work is important because it forces this question into view, especially through claims concerning exclusion zones, charge separation, structured hydration, and light-sensitive interfacial phenomena (Pollack, 2013; Zheng et al., 2006).

Coherence physiology does not require that every strong claim associated with interfacial water be accepted. It does require that the question be taken seriously. The body is full of biological surfaces whose function depends on hydration, charge, flow, and interface behavior. Collagen-rich fascia, extracellular matrix, endothelial glycocalyx, cell membranes, mitochondrial membranes, cytoskeletal structures, mucosal barriers, and protein assemblies all operate in hydrated microenvironments.

A disciplined framework must distinguish levels of claim. Direct observations of altered water behavior near hydrophilic surfaces should be separated from biologically plausible implications and from broad systemic extrapolations. The first two categories deserve serious investigation; the third remains exploratory and should not be treated as settled physiology (Elton et al., 2020).

The endothelial glycocalyx is a useful example of a hydrated interface already strongly established within mainstream vascular physiology. The glycocalyx is a hydrated, gel-like layer on the luminal surface of endothelial cells and participates in mechanosensation, permeability regulation, nitric oxide signaling, and vascular protection (Reitsma et al., 2007; Tarbell & Pahakis, 2006).

In this paper, interfacial water is given neither too little nor too much. It is not dismissed as irrelevant because some claims remain controversial. Nor is it elevated into an all-purpose theory. It is treated as a high-leverage frontier: a candidate substrate-level layer that invites renewed attention to biological water as structured, interface-dependent, and potentially physiologically consequential.

5. Force and Flow: Mechanobiology, Biotensegrity, Blood, Lymph, and Interstitial Movement

Once the organism is understood as a living substrate of fascia, matrix, interstitium, and hydrated interfaces, the next question is how that substrate becomes dynamically informative. A body is not merely a structure containing biochemical reactions. It is a moving, breathing, deforming, flowing, sensing, adapting field of relations.

Mechanobiology names this language. Cells and tissues do not merely endure force; they interpret it. Matrix stiffness, membrane tension, cytoskeletal deformation, shear stress, compressive load, tissue stretch, pressure gradients, and fluid movement can alter biochemical signaling, gene expression, immune behavior, vascular tone, mitochondrial function, and tissue remodeling (Humphrey et al., 2014; Jaalouk & Lammerding, 2009). Force therefore becomes information.

This corrects a purely molecular imagination of life. Molecules matter, but molecules do not act in empty space. They act in tissues whose mechanical state determines what is possible, probable, or dangerous. A cell embedded in a compliant, well-perfused, resolving matrix receives a different world than a cell embedded in a stiff, hypoxic, inflamed, compressed, or fibrotic matrix.

Biotensegrity provides one way of understanding distributed mechanical intelligence. In this model, living bodies maintain integrity through balanced relationships of tension and compression. Stability is not achieved by immobilizing parts, but by distributing stress across a continuous network (Ingber, 2008).

Blood flow is one of the most important forms of force-information. Circulation is not only bulk transport. Flow creates shear stress, and shear stress is read by endothelial surfaces. Endothelial surfaces respond through nitric oxide signaling, vasomotor regulation, barrier control, inflammatory modulation, and vascular remodeling (Reitsma et al., 2007; Tarbell & Pahakis, 2006). Thus, blood flow is both delivery and message.

Lymphatic flow is equally important. The lymphatic system clears interstitial fluid, transports immune cells, returns proteins to the circulation, participates in lipid absorption, and helps regulate inflammatory resolution. When lymphatic movement is impaired, tissues may become congested, inflammatory mediators may persist, edema may develop, immune trafficking may be altered, and local repair may be delayed (Schwager & Detmar, 2019; Ortega-Gómez et al., 2013).

Breathing and movement are everyday expressions of this coupling. Respiration changes thoracic pressure, venous return, lymphatic flow, fascial mobility, autonomic tone, diaphragm function, and emotional state. Movement distributes force, varies load, promotes lymphatic and venous return, maintains matrix pliability, supports mitochondrial function, informs proprioception, and recalibrates autonomic state. The organism's substrate becomes biologically meaningful through dynamic force and flow.

6. Exchange Intelligence: Endothelium, Glycocalyx, and Microvascular Regulation

If force and flow are primary languages of the organism, the endothelium and microcirculation are among the principal surfaces through which those languages are interpreted. The circulation is often described as a transport system, and this description is not wrong. Yet transport is only the most visible part of vascular physiology. At the level of the endothelium and microcirculation, circulation becomes interpretation.

The endothelium is not an inert lining. It is a living interface between blood and tissue, continuously exposed to shear stress, pressure, stretch, redox conditions, inflammatory mediators, oxygen tension, metabolic demand, circulating cells, hormones, and mechanical strain. Its responses shape vascular tone, permeability, coagulation, leukocyte adhesion, platelet behavior, nitric oxide availability, inflammatory signaling, angiogenesis, and remodeling (Cyr et al., 2020; Reitsma et al., 2007; Tarbell & Pahakis, 2006).

The endothelial glycocalyx is central to exchange intelligence. This hydrated, gel-like layer participates in mechanosensation, barrier regulation, nitric oxide signaling, anticoagulant function, anti-inflammatory behavior, and vascular protection. When the glycocalyx is degraded, the vessel loses part of its capacity to read flow correctly (Reitsma et al., 2007; Tarbell & Pahakis, 2006).

Nitric oxide links shear stress to vasodilation, perfusion matching, anti-inflammatory signaling, platelet inhibition, and mitochondrial oxygen use. Reduced nitric oxide bioavailability can alter tissue access, increase inflammatory tendency, reduce microvascular reserve, promote stiffness, and contribute to fatigue, exercise intolerance, cold extremities, angina-like syndromes, cognitive dysfunction, and impaired recovery (Cyr et al., 2020).

The microcirculation is where exchange intelligence becomes decisive. Large vessels deliver blood to regions, but capillaries and precapillary networks determine whether tissues actually receive what they need. Capillary recruitment, local autoregulation, endothelial barrier function, red blood cell transit, oxygen diffusion, venular drainage, immune-cell trafficking, and lymphatic return are all central to tissue viability.

Microvascular dysfunction is not a minor downstream complication. It can be an early and pervasive expression of coherence failure. Retinopathy, nephropathy, coronary microvascular dysfunction, cerebral small-vessel disease, peripheral microvascular disease, and impaired wound healing may be local expressions of broader disturbance in exchange regulation (Cheung et al., 2008; Horton & Barrett, 2021; Mauricio et al., 2023; Paulus & Tschöpe, 2013; Poggesi et al., 2016; Quick et al., 2021).

Exchange failure also links vascular physiology to mitochondrial regulation. Mitochondria depend on oxygen delivery, nutrient access, redox balance, waste clearance, and inflammatory context. When microvascular exchange is impaired, mitochondria may interpret the tissue environment as constrained or dangerous. Conversely, mitochondrial dysfunction can worsen vascular health through redox imbalance, inflammatory signaling, energy deficit, and impaired endothelial repair (Cyr et al., 2020; Naviaux, 2014).

Autonomic regulation shapes exchange intelligence through vascular tone, heart rate, venous return, sweating, thermoregulation, gut perfusion, and orthostatic adaptation. Dysautonomia can therefore be understood partly as a disorder of distributed exchange control (Raj et al., 2022).

7. Boundary Intelligence: Mast Cells, Innate Sentinels, Barriers, and Neuroimmune Signaling

If the endothelium and microcirculation provide exchange intelligence, the organism also requires boundary intelligence. It must decide what may enter, what must be excluded, what should be tolerated, what requires repair, what deserves alarm, and what must be remembered as threat. Biological boundaries are active zones of discernment, not inert walls.

Mast cells are central to this physiology of proportion. Their significance has often been narrowed by association with allergy, anaphylaxis, urticaria, and immediate hypersensitivity. These roles are real, but they are not the whole story. Mast cells are ancient, tissue-resident sentinels distributed throughout vascularized tissues and concentrated at sites where the organism meets challenge: skin, airways, gastrointestinal mucosa, perivascular spaces, perineural regions, connective tissues, and epithelial surfaces (Galli et al., 2005; St John & Abraham, 2013).

Their location gives them unusual integrative power. Mast cells respond to pathogens, toxins, allergens, tissue injury, mechanical stress, neuropeptides, complement activation, temperature changes, matrix disturbance, vascular signals, and inflammatory mediators. Their mediators can alter vascular permeability, smooth muscle tone, nociception, leukocyte recruitment, fibroblast activity, extracellular matrix remodeling, angiogenesis, and neuroimmune communication (Galli et al., 2005; Overed-Sayer et al., 2014).

Acute boundary activation is often protective. Mast-cell degranulation, vascular permeability, immune recruitment, and local inflammatory signaling can help defend against pathogens, contain injury, initiate repair, and coordinate tissue remodeling. The problem arises when the boundary response does not resolve. A chronically alarmed boundary can keep the organism in a state of vigilance even when no single dominant threat remains.

Mast cells and microvascular exchange are closely linked. Mast-cell mediators can alter vessel tone, increase permeability, recruit leukocytes, and modify the local exchange environment. Boundary surveillance is therefore inseparable from exchange intelligence (Galli et al., 2005; Overed-Sayer et al., 2014).

Mast cells and nerves are also coupled. Mast cells often reside near sensory and autonomic nerve fibers. Their mediators can sensitize nociceptors, influence neurogenic inflammation, and participate in bidirectional neuroimmune signaling. Nerves can release neuropeptides and other signals that influence mast-cell activation (Forsythe, 2019). This creates a loop through which tissue disturbance, pain, autonomic arousal, inflammation, and vigilance reinforce one another.

The gut, airway, skin, vascular wall, and connective tissue boundaries provide everyday examples. They must permit nourishment and relation while defending against danger. When boundary intelligence becomes chronically primed, ordinary foods, odors, temperature changes, exertion, stress, touch, pressure, microbial signals, or environmental exposures may provoke disproportionate symptoms. This does not make mast cells a universal explanation. It makes boundary regulation a key layer of coherence physiology.

Mitochondria are also implicated. Persistent mast-cell and innate immune activation can create inflammatory, oxidative, and metabolic conditions that influence mitochondrial state. Conversely, mitochondrial danger signaling can activate immune pathways and shape the tissue environment (Banoth & Cassel, 2018; Naviaux, 2014).

8. Executive Energetic Governance: Mitochondria, Cell Danger Response, and Energy Resistance

If boundary intelligence determines whether the organism interprets contact as safe, threatening, repairable, or intolerable, mitochondrial regulation helps determine what the organism can afford to do in response. Life is not only a matter of information. It is also a matter of energy allocation.

The older description of mitochondria as ATP-producing organelles remains true but incomplete. Mitochondria participate in redox signaling, calcium regulation, apoptosis, innate immunity, steroid synthesis, metabolic sensing, heat production, reactive oxygen signaling, mitokine release, and adaptive state regulation (Banoth & Cassel, 2018; Naviaux, 2014; Picard et al., 2019). They are not merely power plants; they are executive regulators of biological possibility.

The Cell Danger Response gives this principle a powerful biological form. It describes an evolutionarily conserved metabolic program through which cells respond to perceived threat by shifting from ordinary function toward protection. Oxidative phosphorylation may be downregulated, extracellular ATP and purinergic signaling may increase, redox state may change, and inflammatory, antiviral, and repair programs may be reorganized (Naviaux, 2014, 2020).

This is adaptive when danger is real and time-limited. The problem arises when the danger response does not resolve. A state that should have been temporary becomes stabilized. The organism remains organized around protection, containment, and energetic conservation even after the original trigger has diminished or passed (Naviaux, 2014, 2020).

Mitochondrial governance connects all previous layers. Substrate conditions affect mitochondrial state because cells embedded in stiff, inflamed, hypoxic, congested, or poorly drained tissues receive danger signals. Exchange intelligence affects mitochondria because perfusion and capillary function determine oxygen and nutrient access. Boundary intelligence affects mitochondria because inflammatory mediators, mast-cell activation, cytokines, and neuroimmune alarm shift cells toward defense (Banoth & Cassel, 2018; Naviaux, 2014).

Energy resistance shifts attention from energy amount to energy transformation. Chronic illness is often described as low energy, but the deeper question is whether the organism can convert available energetic potential into coordinated work, repair, and adaptive participation. When resistance rises, energy may be dissipated into oxidative stress, inflammatory signaling, inefficiency, pain, heat intolerance, autonomic instability, or metabolic noise rather than useful function.

In a coherent energetic system, demand produces adaptation within tolerable limits. In an energy-resistant system, demand may produce collapse, stress may produce prolonged flare, infection may produce long aftermath, and exercise may produce post-exertional malaise (Institute of Medicine, 2015; Vøllestad & Mengshoel, 2023).

Mitochondrial regulation also dissolves the false division between physical and psychosocial stress. Mitochondria respond not only to toxins, infections, nutrients, and oxygen, but also to stress biology, affective state, social threat, trauma, and lived experience (Picard & McEwen, 2018; Picard et al., 2019). This does not mean illness is all in the mind. It means subjective experience and cellular metabolism are connected through endocrine, autonomic, inflammatory, redox, and behavioral pathways.

Sleep is one of the most important mitochondrial therapies in the broad physiological sense. During sleep, the organism recalibrates endocrine rhythms, immune activity, autonomic tone, brain clearance, redox balance, and repair processes (Besedovsky et al., 2012, 2019). Chronic sleep disruption keeps mitochondria in a more stressed regulatory environment.

9. Defensive Lock-In: A Coherence Model of Chronic Illness

The preceding sections have reconstructed the organism as a living continuum composed of material substrate, hydrated interfaces, force-flow dynamics, exchange intelligence, boundary intelligence, and executive energetic governance. Chronic illness becomes more intelligible when these adaptive domains fail to return to proportion. The problem is often not that the organism lacks defenses. It is that defense persists.

Defensive lock-in is a self-stabilizing physiological state in which multiple layers of regulation become mutually entrained around protection, containment, and reduced adaptive openness. It is not a single disease, marker, pathway, or lesion. It is a pattern of organization. It may be entered through infection, trauma, toxin exposure, metabolic disease, chronic stress, inflammatory burden, injury, surgery, environmental exposure, sleep disruption, grief, overexertion, autoimmunity, or vascular injury. The initiating pathway may differ, but the resulting pattern may converge: the organism cannot complete the transition from defense to recovery (Davis et al., 2023; Naviaux, 2014, 2020).

In acute illness, the organism temporarily reorganizes around survival. Blood flow redistributes, inflammation rises, boundaries become more defended or more permeable, mitochondria alter energy allocation, appetite and sleep change, movement decreases, and pain discourages further injury. These responses are not mistakes. They are life trying to preserve itself under constraint.

Defensive lock-in occurs when this sequence stalls. The tissue substrate may remain inflamed, stiff, congested, or hypoxic. Microvascular exchange may be impaired. Boundaries may remain hypervigilant. Mitochondria may remain in danger signaling. Sleep may be disrupted. The autonomic nervous system may remain in unstable oscillation. Environmental exposures may continue. The system may no longer know how to stand down (Besedovsky et al., 2019; Naviaux, 2014; Raj et al., 2022).

This is why chronic illness often feels circular. Fatigue reduces movement; reduced movement impairs flow; impaired flow worsens tissue stiffness and microvascular function; microvascular dysfunction constrains mitochondria; mitochondrial defense worsens fatigue; fatigue narrows social life; stress and poor sleep amplify inflammation; inflammation activates boundaries; boundary activation worsens pain, permeability, and vascular instability; pain further reduces movement.

The material substrate participates early. Injury, inflammation, immobility, edema, scar formation, metabolic stress, or chronic mechanical load can alter fascia, extracellular matrix, and interstitium. Tissues may become less compliant, less mobile, less well drained, and more sensitive. Fibrosis, adhesions, altered sliding, local congestion, and matrix stiffness can change force transmission and sensory input (Humphrey et al., 2014; Jaalouk & Lammerding, 2009).

Exchange intelligence may degrade through endothelial dysfunction, glycocalyx injury, impaired nitric oxide signaling, capillary rarefaction, abnormal permeability, oxidative stress, venous pooling, and microvascular instability (Cyr et al., 2020; Reitsma et al., 2007). Boundary intelligence may become heightened through mast-cell reactivity and neuroimmune sensitization (Forsythe, 2019; Galli et al., 2005). Mitochondria may continue allocating energy toward defense, containment, inflammation, and conservation rather than growth, repair, movement, cognition, and participation (Naviaux, 2014, 2020).

Fatigue may represent protective energy rationing under conditions of impaired exchange, immune activation, mitochondrial defense, autonomic instability, poor sleep, and tissue alarm (Institute of Medicine, 2015; Naviaux, 2014; Raj et al., 2022). Post-exertional malaise, dysautonomia, chemical sensitivity, inflammatory flares, cognitive dysfunction, and variable tolerance are signs that adaptive thresholds have narrowed (National Institute for Health and Care Excellence, 2021; Vøllestad & Mengshoel, 2023).

Defensive lock-in is therefore the central pathological concept of coherence physiology. It honors the intelligence of defense while recognizing the suffering caused by its persistence. It avoids reducing chronic illness to damage alone, psychology alone, inflammation alone, mitochondria alone, or deconditioning alone. It shows how many partial mechanisms can become one lived state.

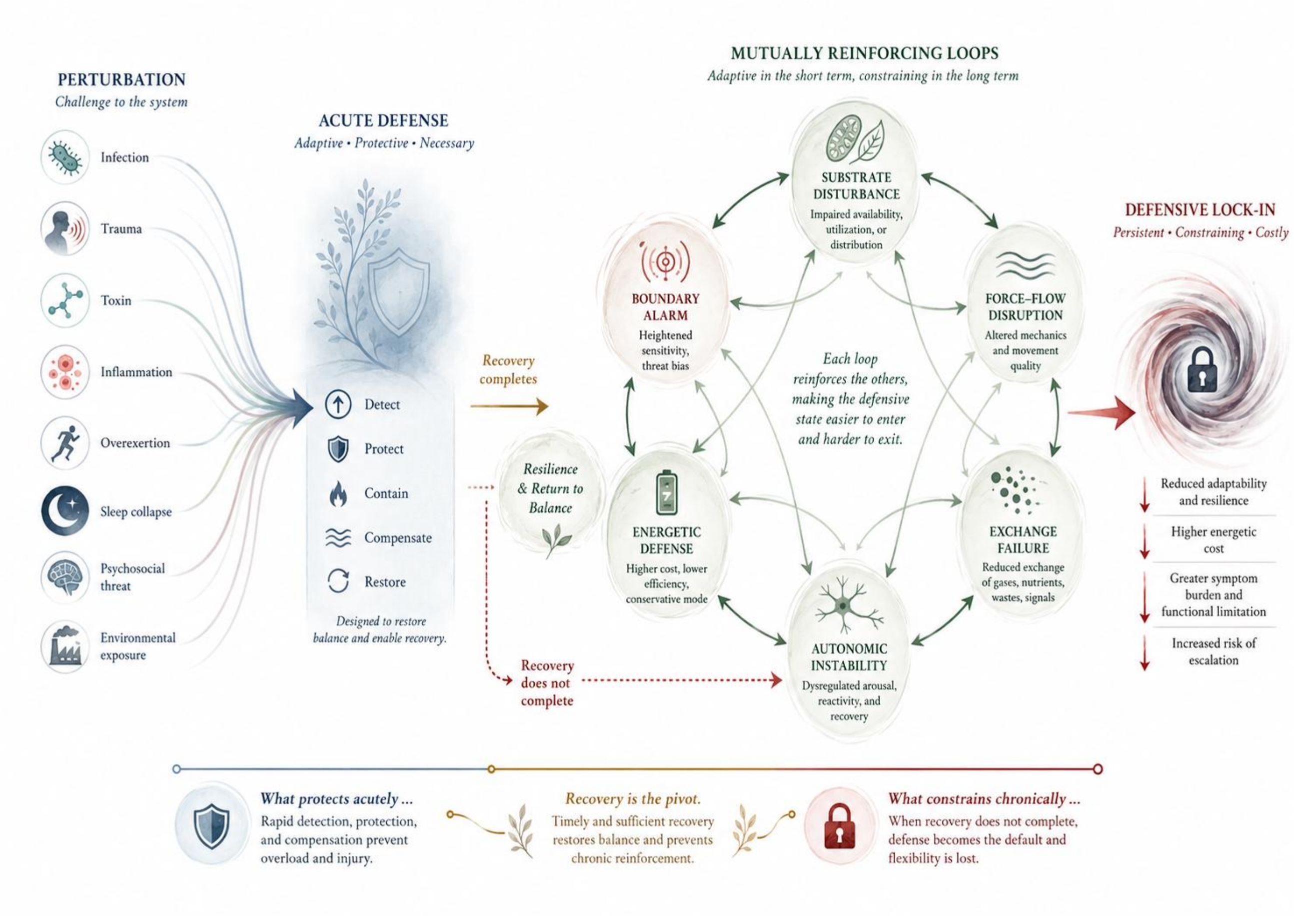

Figure 4. From Perturbation to Defensive Lock-In

Defensive lock-in occurs when protective responses fail to resolve and become mutually reinforcing across substrate disturbance, force-flow disruption, exchange failure, boundary alarm, energetic defense, autonomic instability, and incomplete recovery.

10. Salugenesis: The Biology of Recovery

If defensive lock-in names the pathophysiological state in which the organism remains organized around protection, salugenesis names the biological movement by which that state is resolved. It is the positive center of coherence physiology. Salugenesis is not the absence of disease, normalization of a biomarker, suppression of a symptom, or completion of a treatment protocol. It is the active restoration of the conditions under which the organism can resume adaptive self-repair.

The broader salutogenic tradition asked how health is generated and maintained; salugenesis, as used here, narrows that concern to the physiological restoration of adaptive self-repair after defensive lock-in (Antonovsky, 1979, 1987; Mittelmark et al., 2017).

In salugenesis, substrate conditions improve, fluid movement returns, vascular exchange becomes more reliable, boundary alarm de-escalates, mitochondrial energy allocation becomes more flexible, autonomic regulation stabilizes, sleep becomes restorative, inflammation resolves, tissues remodel proportionately, and adaptive participation gradually expands. This is an integrative synthesis of multiple recovery literatures rather than a single established pathway (Besedovsky et al., 2019; Humphrey et al., 2014; Naviaux, 2014; Reitsma et al., 2007).

The first layer of salugenesis is substrate restoration: fascia, extracellular matrix, interstitium, and connective tissues must regain enough pliability, hydration, mobility, drainage, and repair capacity to support coherent function. The second layer is restoration of force and flow: breath becomes fuller, movement becomes less threatening, venous return and lymphatic flow improve, and interstitial movement becomes less stagnant.

The third layer is restoration of exchange intelligence. Endothelium and microcirculation must regain responsiveness to match supply with need. Glycocalyx integrity, nitric oxide signaling, vasomotor flexibility, capillary recruitment, permeability regulation, and tissue clearance all participate in this process (Cyr et al., 2020; Reitsma et al., 2007; Tarbell & Pahakis, 2006).

The fourth layer is restoration of boundary intelligence. Mast cells, innate sentinels, epithelial barriers, vascular interfaces, gut mucosa, airway surfaces, skin, connective tissues, and neuroimmune loops must return toward proportionate discernment (Galli et al., 2005; St John & Abraham, 2013). The fifth layer is mitochondrial flexibility: energy allocation shifts from defense and conservation toward repair, differentiation, movement, cognition, digestion, and ordinary function (Naviaux, 2014; Picard et al., 2019).

Sleep restoration is central to salugenesis. Sleep supports autonomic recalibration, immune resolution, endocrine rhythm, brain clearance, mitochondrial repair, tissue healing, and emotional integration (Besedovsky et al., 2012, 2019). Inflammation resolution and lymphatic-interstitial clearance also matter: repair cannot proceed if inflammatory mediators persist and clearance remains impaired (Headland & Norling, 2015; Ortega-Gómez et al., 2013; Schwager & Detmar, 2019).

Pacing is another example of salugenic care. It is not resignation. It is the clinical discipline of respecting the organism's current energy envelope while gradually expanding adaptive range. For patients with post-exertional worsening, pacing prevents repeated energetic overdraft and may help avoid cycles of exertion-induced relapse (Gloeckl et al., 2024; National Institute for Health and Care Excellence, 2021).

The purpose of healing is not merely internal normalization. It is renewed life: the capacity to move, think, relate, work, create, care, rest, play, and inhabit the world with less fear of collapse. Salugenesis does not promise cure where cure is uncertain. It seeks the maximum truthful restoration of coherence possible under the conditions present.

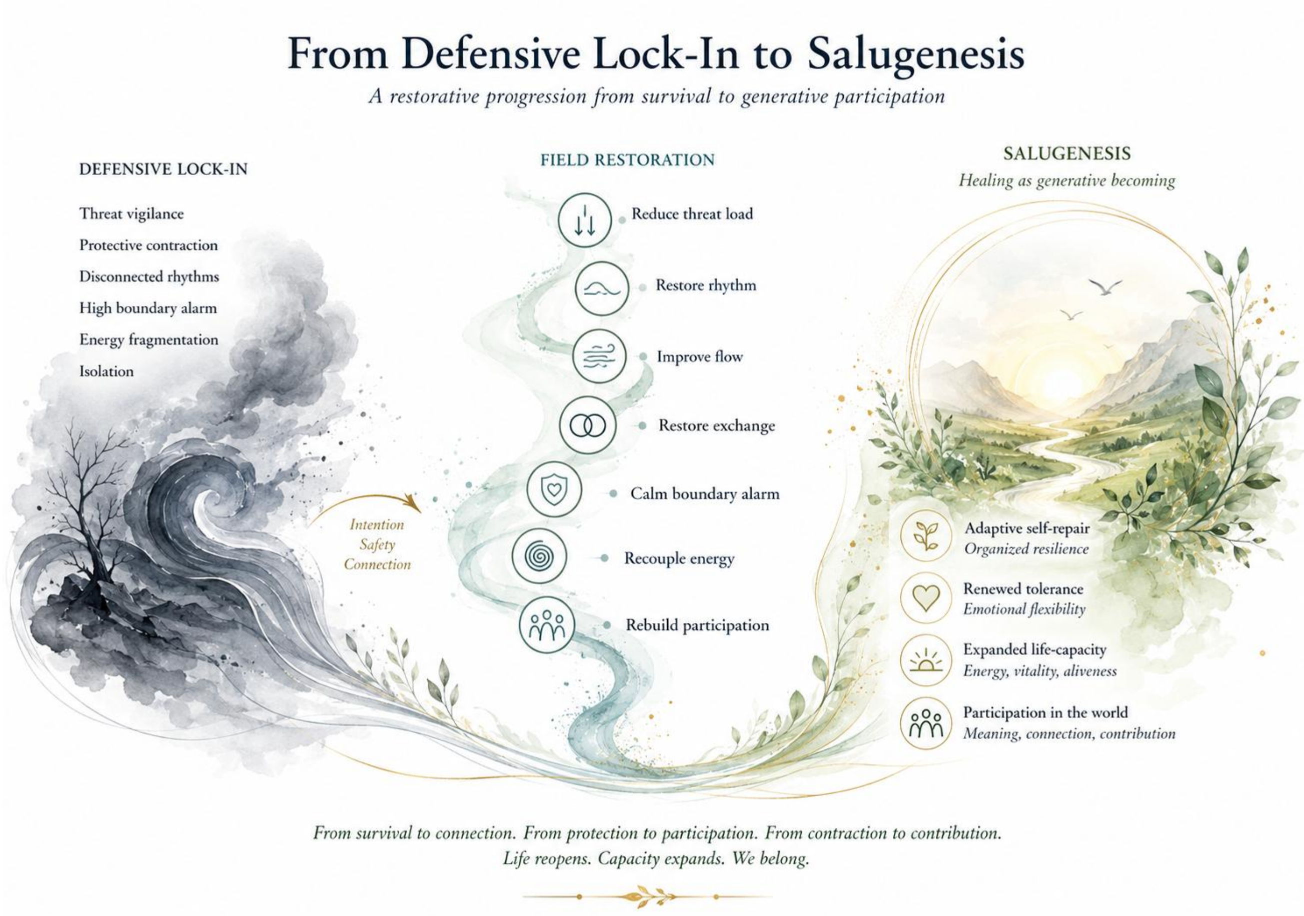

Figure 5. From Defensive Lock-In to Salugenesis

Salugenesis is the active biological movement from defensive lock-in toward restored adaptive coherence through reduced threat load, restored rhythm, improved force-flow dynamics, renewed exchange, calmer boundary intelligence, mitochondrial recoupling, and rebuilding of life participation.

11. Clinical Translation: From Pathway Suppression to Field Restoration

The clinical value of coherence physiology depends on whether it changes interpretation, assessment, and care without abandoning medical rigor. The central clinical shift is from pathway suppression alone to field restoration. Conventional medicine asks which lesion, pathogen, receptor, marker, pathway, risk factor, or organ system is responsible and how it can be corrected, blocked, replaced, suppressed, removed, or controlled. These questions remain indispensable.

Chronic multisystem illness often requires an additional question: what field conditions are preventing this organism from recovering? The answer may not lie in one abnormal marker or one blocked pathway. It may lie in the interaction among sleep disruption, microvascular dysfunction, autonomic instability, mitochondrial defense, inflammatory persistence, mast-cell reactivity, connective-tissue strain, gut-barrier disturbance, environmental exposures, trauma physiology, nutritional insufficiency, and cumulative life burden (Davis et al., 2023; Institute of Medicine, 2015; Naviaux, 2014; Raj et al., 2022).

Field restoration means restoring the conditions under which salugenesis can proceed. It includes substrate conditions, force-flow dynamics, exchange intelligence, boundary intelligence, energetic governance, autonomic regulation, recovery rhythms, and lived participation. It is not vague holism; it is a physiological strategy.

Assessment must remain both conventional and coherence-informed. Conventional assessment asks necessary safety questions: infection, malignancy, autoimmune disease, endocrine disease, anemia, kidney or liver disease, cardiovascular disease, neurological disease, sleep apnea, medication toxicity, nutritional deficiency, psychiatric emergency, or other treatable pathology must not be missed. Coherence physiology is not a shortcut around differential diagnosis.

Once danger and specific disease are addressed, coherence-informed assessment asks about restorative sleep, orthostatic intolerance, post-exertional worsening, triggers, inflammatory persistence, mast-cell reactivity, endothelial dysfunction, microvascular compromise, impaired lymphatic or venous return, tissue stiffness, pain sensitization, mitochondrial intolerance, environmental load, and the patient's functional envelope.

Sequencing matters. A patient with fragmented sleep may not tolerate rehabilitation. A patient with severe orthostatic intolerance may not benefit from upright exercise until perfusion support improves. A patient with mast-cell reactivity may flare from otherwise helpful foods, supplements, medications, or exposures. A patient with post-exertional malaise may need pacing before conditioning (Institute of Medicine, 2015; National Institute for Health and Care Excellence, 2021; Raj et al., 2022).

Recovery markers must include dynamic and lived measures, not only static tests. Clinicians should track sleep quality, recovery time after exertion, orthostatic tolerance, flare frequency and duration, food tolerance, pain stability, cognitive endurance, temperature tolerance, bowel regularity, activity envelope, emotional steadiness, and participation in meaningful life.

Targeted treatment and field restoration should not be opposed. A patient may need both pharmacology and environmental change, both volume support and recumbent conditioning, both anti-inflammatory treatment and sleep restoration, both antimicrobial therapy and mitochondrial recovery, both pain medication and gentle movement, both psychotherapy and vascular assessment. The question is whether care restores life-capacity truthfully.

The clinical encounter itself belongs to the field. Patients with chronic multisystem illness often arrive after years of dismissal or fragmentation. Listening, careful reasoning, validation, explanation, and shared planning are not substitutes for treatment, but they may reduce threat and restore orientation (Ardito & Rabellino, 2011; Flückiger et al., 2020).

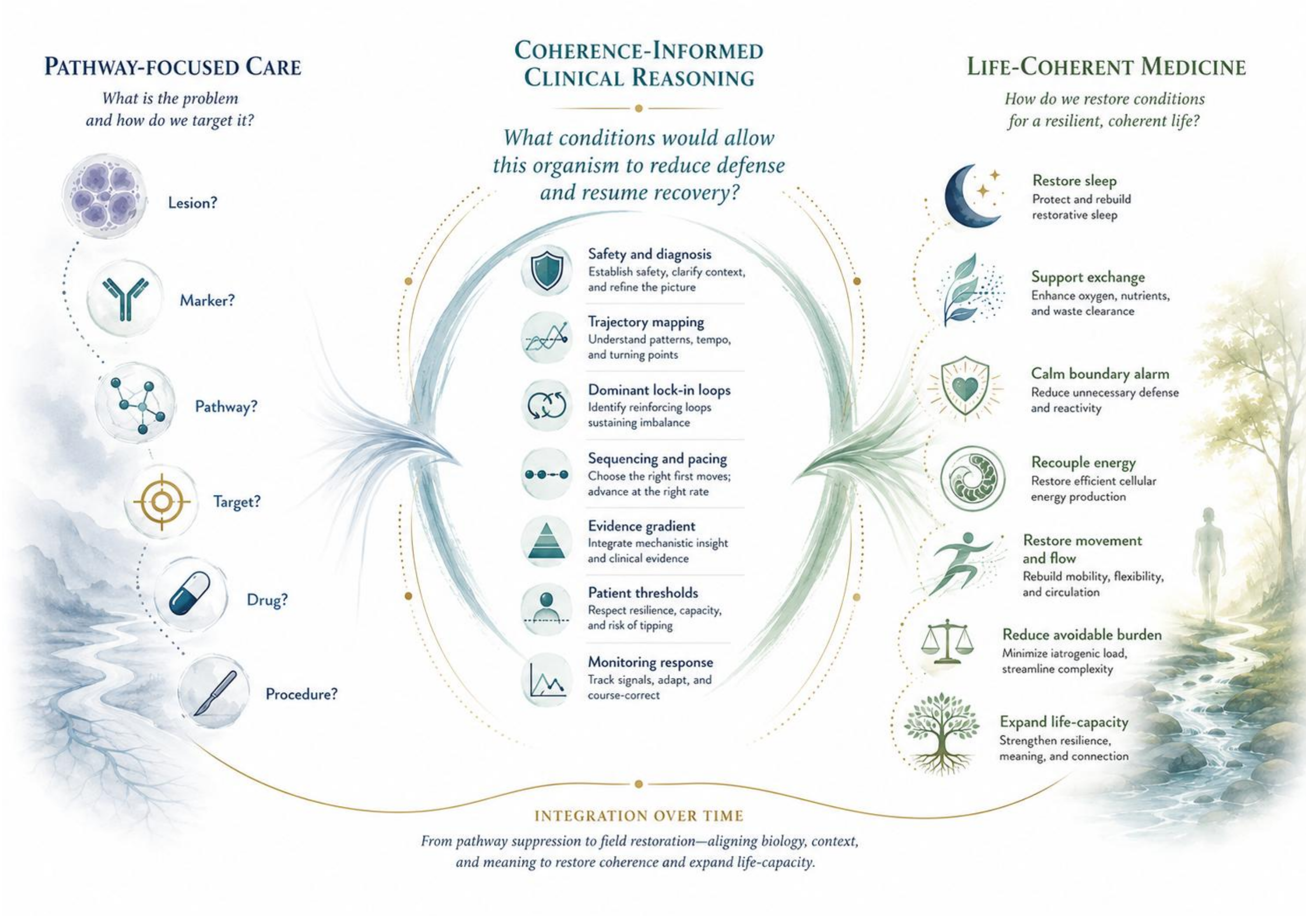

Figure 6. Clinical Translation: From Pathway Suppression to Field Restoration

Coherence physiology does not reject diagnosis, pharmacology, procedures, or pathway-focused care. It resituates them within a wider clinical question: what conditions would allow this organism to reduce defense and resume recovery?

12. Prevention: Protecting the Conditions of Coherence Before Lock-In Occurs

If salugenesis is the restoration of coherence after defensive lock-in has occurred, prevention is the protection of coherence before lock-in becomes established. Preventive medicine is often organized around risk-factor reduction. These risk factors matter, but prevention remains incomplete if it does not ask what conditions allow the organism to remain adaptive, recoverable, and resilient across time.

Coherence physiology expands prevention from risk control to field protection. It asks how the organism preserves its capacity to absorb perturbation, resolve inflammation, restore exchange, recalibrate energy, maintain boundary discernment, and return to participation after stress. This aligns with the salutogenic tradition while specifying physiological conditions of recovery capacity (Antonovsky, 1979, 1987; Mittelmark et al., 2017).

Prevention begins with the substrate. Fascia, extracellular matrix, interstitium, and connective tissues require movement, hydration, perfusion, nutrition, repair time, and protection from chronic inflammatory or mechanical burden. A body that is immobilized, overstrained, poorly nourished, sleep-deprived, inflamed, congested, or repeatedly injured will gradually lose tissue ease.

Microvascular and endothelial protection are central. Much chronic disease begins not with dramatic organ failure but with impaired exchange: endothelial dysfunction, glycocalyx injury, reduced nitric oxide bioavailability, capillary rarefaction, oxidative stress, abnormal permeability, and loss of perfusion reserve (Cyr et al., 2020; Reitsma et al., 2007; Tarbell & Pahakis, 2006).

Mitochondrial prevention preserves adaptive range. Mitochondria require oxygen, nutrients, hormonal balance, redox stability, circadian rhythm, movement, sleep, and reduced toxic burden. They also respond to psychosocial conditions: safety, isolation, stress, trauma, dignity, care, and meaning (Picard & McEwen, 2018; Picard et al., 2019).

Sleep deserves special emphasis. A society that treats sleep as expendable is degrading one of the central conditions of coherence. Sleep is not a private luxury; it is a physiological commons within the organism: a recurring window for autonomic recalibration, immune resolution, endocrine rhythm, memory processing, brain clearance, mitochondrial repair, tissue recovery, and emotional integration (Besedovsky et al., 2012, 2019).

Environmental prevention is unavoidable. Air pollution, heat stress, contaminated water, pesticides, heavy metals, endocrine-disrupting chemicals, occupational exposures, poor housing, mold, noise, and chronic urban stress are not external to physiology. They act through endothelium, mitochondria, immune boundaries, respiratory surfaces, nervous system regulation, and inflammatory pathways (Fuller et al., 2022; Gore et al., 2015; Kahn et al., 2020; Landrigan et al., 2018).

Stress prevention also requires precision. Stress is a whole-body demand state involving autonomic activation, endocrine signaling, immune modulation, vascular tone, mitochondrial allocation, sleep disruption, and behavior. Acute stress can be adaptive; chronic unresolvable stress narrows coherence (Juster et al., 2010; McEwen, 1998; McEwen & Stellar, 1993).

Prevention should also be humble. Not all illness is preventable. Genetics, aging, infections, accidents, environmental events, social conditions, and biological uncertainty exceed control. A coherence approach must not imply that illness reflects failure to live correctly. Prevention is not a guarantee. It is a commitment to reduce avoidable burden and preserve adaptive capacity where possible.

13. Epistemic Closure and the Need for a Physiology Commons

A coherence physiology cannot be built from biological evidence alone. It must also examine the conditions under which biological evidence becomes visible, credible, funded, organized, taught, and clinically translated. Physiology is produced through institutions, instruments, journals, funding streams, disciplinary boundaries, commercial incentives, professional hierarchies, regulatory pathways, and inherited metaphors of the body.

The fragmentation of physiology is not merely an intellectual oversight. It is partly structural. Specialization has produced enormous gains, but specialized knowledge can lack a commons in which partial truths are reassembled into an account of the living whole. Without such a commons, the patient may be the only person trying to integrate cardiology, neurology, immunology, gastroenterology, psychiatry, rehabilitation, environmental medicine, and primary care.

Epistemic closure occurs when a knowledge system becomes unable or unwilling to recognize phenomena that do not fit its preferred categories. It can arise from training, incentives, time pressure, diagnostic coding, reimbursement structures, publication norms, commercial interests, methodological habits, and fear of uncertain terrain. A clinician may dismiss a patient not from lack of compassion, but because the available map has no legitimate place for the pattern.

The political economy of knowledge matters. Research systems often favor modular, targetable, patentable, and intervention-ready mechanisms. A receptor can become a drug target; a pathway can become a trial; a biomarker can become a product; a device can become a procedure. Such developments can be valuable, but they may bias attention toward downstream, discrete, commercially enclosed interventions while underfunding substrate-level, preventive, ecological, behavioral, environmental, relational, and systems-restorative questions.

Coherence physiology must avoid both premature dismissal and premature inflation. Established findings should be named as established. Integrative inferences should be named as integrative. Exploratory hypotheses should be named as exploratory. Clinical use should be proportionate to evidence, safety, plausibility, and patient state.

Interfacial-water research provides a clear example. The idea that water near hydrophilic surfaces may have properties different from bulk water is a legitimate biophysical question; its relevance to collagen, matrix, glycocalyx, mitochondrial membranes, and cellular interfaces deserves study (Ball, 2017; Israelachvili & Wennerström, 1996; Pollack, 2013). But broad claims that interfacial water explains all physiology, chronic illness, membrane potentials, capillary propulsion, or healing interventions exceed the present evidence (Elton et al., 2020).

The commons must also protect against epistemic injustice. Patients with chronic multisystem illness often suffer not only symptoms but disbelief. Their reports are discounted because they are complex, fluctuating, hard to measure, or inconvenient to specialty boundaries. This disbelief can delay care, increase fear, erode trust, and deepen physiological threat (Buchman et al., 2017; Fricker, 2007; Kidd & Carel, 2017).

A physiology commons would allow fascia research, interstitial biology, mechanotransduction, endothelial medicine, glycocalyx research, lymphatic science, mast-cell biology, mitochondrial stress biology, autonomic medicine, sleep science, environmental health, rehabilitation, nutrition, trauma physiology, and recovery science to inform one another. It would be evidence-graded, patient-attentive, interdisciplinary, and life-serving.

14. Life-Coherent Medicine: Clinical Care in Service of the Living Whole

Coherence physiology becomes most important when placed within the wider life-coherence framework. The preceding sections have described the organism as a living continuum of substrate, interface, force, flow, exchange, boundary surveillance, energetic governance, and recovery. This section asks what such a physiology means for medicine as a practice of care.

Life-coherent medicine is clinical care in service of the living whole. It does not reject diagnosis, pharmacology, surgery, emergency intervention, specialty expertise, molecular medicine, or evidence-based treatment. Rather, it asks that all such interventions be situated within a larger responsibility: preservation, restoration, and expansion of life-capacity.

This framework is aligned with Maturana's biology of living. The organism is not a passive object acted upon by external causes. It is a self-producing system structurally coupled with its medium, bringing forth and conserving a world through its organization (Maturana & Varela, 1980, 1987). Health and illness cannot be understood apart from the worlds the organism is conserving.

This is why the clinical task cannot be merely coercive. The organism cannot simply be commanded to recover. It must be supported into a new structural coupling. The body must encounter conditions that make it safe enough, supplied enough, rested enough, and coherent enough to relinquish defense. In this sense, salugenesis is not only internal repair; it is world-restoration at the scale of the body.

Life-coherent medicine is also aligned with McMurtry's life-value onto-axiology. Value must be grounded in what enables life-capacity. At the clinical level, the ultimate test of care is whether it preserves or expands the patient's capacity to live: breathe, move, sleep, think, digest, relate, work, care, create, rest, and participate (McMurtry, 1998, 2013).

Galtung adds a further layer. Violence is not only direct harm; it includes avoidable impairment of life. At the scale of the body, chronic illness is often experienced as impairment of possible life: inability to stand, walk, work, think clearly, sleep deeply, eat freely, relate confidently, or plan a future. When such impairment is avoidable or worsened by social neglect, environmental exposure, fragmented care, medical dismissal, or economic conditions that deny recovery, it becomes part of structural violence (Galtung, 1969, 1990).

The clinical ethic that follows is non-forcing but not passive. Wu-wei medicine means action aligned with the organism's own conditions of viability. In acute danger, alignment may require decisive treatment. In fragile chronic illness, alignment may require gentleness, sequencing, pacing, and restraint. In all cases, the question is the same: does this action serve the organism's movement toward coherence?

Life-coherent medicine refuses the separation of body and world. Food systems, work rhythms, housing, air quality, water quality, family life, social trust, economic insecurity, trauma, care, movement environments, sleep culture, and exposure burdens shape physiology. A patient's mitochondria, endothelium, immune system, nervous system, and connective tissues do not live in abstraction. They live in a world (Maturana & Varela, 1980, 1987; Picard & McEwen, 2018).

15. Conclusion: Physiology as the Science of Embodied Life-Coherence

This white paper has argued that physiology becomes more transparent when medicine remembers the organism as a living whole. The body is not merely an assemblage of organs, pathways, receptors, biomarkers, and molecular targets. It is a dynamically coupled coherence system whose viability depends on coordinated regulation of substrate, interface, force, flow, exchange, boundary surveillance, energetic governance, and recovery.

The need for such a reconstruction arises most clearly in chronic multisystem illness. Many patients suffer in ways that do not conform to one organ, one lesion, one pathway, or one specialty. Their symptoms are distributed, fluctuating, state-dependent, environmentally sensitive, stress-responsive, exertion-limited, and recovery-resistant (Davis et al., 2023; Institute of Medicine, 2015; Raj et al., 2022).

Defensive lock-in is not a replacement diagnosis and should not be used to bypass careful clinical evaluation. It is a physiological pattern: a self-stabilizing state in which protective responses fail to resolve and begin to constrain life. Mechanical guarding, matrix stiffness, impaired flow, microvascular dysfunction, boundary vigilance, mitochondrial energy conservation, autonomic instability, inflammatory persistence, poor sleep, pain amplification, and reduced participation can reinforce one another.

The positive counterpart of defensive lock-in is salugenesis: the active restoration of the conditions under which the organism can resume adaptive self-repair. It involves substrate restoration, improved force-flow dynamics, renewed exchange intelligence, recalibrated boundary surveillance, mitochondrial flexibility, autonomic stability, restorative sleep, inflammatory resolution, and expanding participation in life.

The epistemic implication is that physiology requires a commons. Knowledge of the living whole cannot mature if each discipline guards its own fragment without shared integration. Fascia research, interstitial biology, mechanobiology, glycocalyx science, microvascular medicine, mitochondrial stress biology, mast-cell biology, autonomic medicine, sleep science, environmental health, rehabilitation, nutrition, trauma physiology, and recovery science must be allowed to speak to one another.

The broader life-coherence framework gives this physiology its ethical horizon. Maturana helps us see the organism as a living being structurally coupled with its world (Maturana & Varela, 1980, 1987). McMurtry helps us ground value in life-capacity (McMurtry, 1998, 2013). Galtung helps us recognize avoidable impairment of life as a form of violence (Galtung, 1969, 1990).

The paper's central claim can therefore be restated simply: the organism is a coherence system. Health is the capacity of this system to remain adaptively organized through disturbance. Chronic illness often reflects defensive lock-in across multiple layers of regulation. Healing is salugenesis: the restoration of conditions under which adaptive self-repair can resume. Medicine becomes life-coherent when it serves this movement.

The final image is not the body as machine, battlefield, or marketplace. It is the body as a living commons of relations: substrate, water, force, flow, exchange, boundary, energy, rhythm, memory, and repair. When this commons is protected, life has room to adapt. When it is degraded, life narrows into defense. When it is restored, life begins to move again. That movement is healing. That restoration is salugenesis. That science is coherence physiology. And that care, when practiced in service of the living whole, is life-coherent medicine.

Tables

Table 1. Core Components of the Coherence Physiology Model

Domain	**Primary processes**	**Role in coherence physiology**
Material substrate	Tissue continuity; structural support; force distribution; interstitial movement; sensory integration	Provides the body-wide substrate through which organs, tissues, vessels, nerves, immune cells, and fluids remain part of one living continuum
Hydrated interfaces	Interface-dependent hydration; charge distribution; local transport conditions; matrix behavior; glycocalyx hydration	Offers candidate substrate-level explanatory leverage for understanding how biological surfaces participate in coherence
Force-flow dynamics	Mechanotransduction; tissue strain; shear stress; pressure gradients; breathing mechanics; blood, lymph, and interstitial motion	Converts force, movement, pressure, and flow into biological information and adaptive response
Exchange intelligence	Perfusion matching; oxygen delivery; nutrient access; waste clearance; permeability regulation; immune-cell trafficking	Regulates provision and clearance between systemic circulation and local tissue need
Boundary intelligence	Barrier discernment; tissue surveillance; permeability modulation; neuroimmune signaling; repair initiation	Determines whether contact, exposure, injury, or perturbation is interpreted as tolerable, threatening, repairable, or escalatory
Energetic governance	Energy allocation; Cell Danger Response; redox signaling; hypometabolism; adaptive state regulation	Determines whether the organism allocates energy toward openness, repair, differentiation, defense, containment, or withdrawal
Recovery trajectory	Resolution; repair; autonomic recalibration; restored tolerance; renewed participation	Describes whether the organism exits defense and restores adaptive life-capacity or remains trapped in defensive lock-in

Note. This table presents an integrative interpretive model and should not be read as a diagnostic or treatment guideline.

Table 2. Evidence Gradient Across Coherence Physiology

Support level	Representative claims	Required caution
Established / strongly supported	Fascial and ECM continuity; mechanotransduction; endothelial glycocalyx function; nitric oxide signaling; microvascular dysfunction; mast-cell tissue surveillance; mitochondrial stress signaling; sleep-immune recovery	Cite from mainstream peer-reviewed literature and avoid overstatement beyond demonstrated scope
Integrative / partly inferential	Coherence physiology; defensive lock-in; salugenesis; field restoration; life-coherent medicine	Present as synthesis claims, not single-mechanism proofs
Exploratory / frontier-level	Broader physiological implications of interfacial water and interface-dependent hydration	Frame as promising but unsettled; avoid making interfacial water the master explanation
Speculative / not established	Claims that interfacial water explains all chronic illness, membrane potential in full, capillary propulsion in full, or broad therapeutic classes without direct evidence	Exclude from central claims unless clearly identified as speculative

Note. The evidence-gradient discipline is central to the manuscript. It permits integration without totalization.

Table 3. Chronic Illness as Multilayer Defensive Lock-In

Layer	Lock-in pattern	Clinical expression
Material substrate	Stiffness, fibrosis, edema, adhesions, impaired drainage	Pain, restricted movement, poor healing, tissue sensitivity
Force-flow dynamics	Guarding, shallow breathing, reduced movement, venous pooling, lymphatic stagnation	Fatigue, orthostatic symptoms, stiffness, post-exertional worsening
Exchange intelligence	Endothelial dysfunction, impaired capillary recruitment, abnormal permeability	Brain fog, cold extremities, poor healing, vascular headaches
Boundary intelligence	Mast-cell reactivity, barrier hypervigilance, neuroimmune sensitization	Food/chemical sensitivity, flushing, itching, pain flares
Energetic governance	Persistent Cell Danger Response, hypometabolism, energy resistance	Fatigue, PEM, cognitive slowing, prolonged recovery
Recovery trajectory	Incomplete healing, recurrent relapse, narrowed activity envelope	Reduced participation, unpredictable flares, loss of confidence

Note. This table is an interpretive aid, not a clinical guideline.

Table 4. Salugenesis Across Physiological Layers

Layer	Salugenic aim	Signs of early restoration
Material substrate	Restore tissue ease, drainage, mobility, and repair capacity	Less stiffness, reduced swelling, improved movement
Force-flow dynamics	Restore rhythmic movement, breathing, venous and lymphatic return	Better breathing depth, less heaviness, improved tolerance
Exchange intelligence	Restore perfusion, permeability regulation, nitric oxide signaling, and clearance	Warmer extremities, clearer cognition, better exertional tolerance

Layer	Salugenic aim	Signs of early restoration
Boundary intelligence	Restore proportionate discernment and reduce false alarm	Improved food tolerance, fewer flares, reduced reactivity
Energetic governance	Restore mitochondrial flexibility and reduce energy resistance	Rest becomes restorative; exertion causes less delayed worsening
Recovery trajectory	Expand life-capacity and participation without triggering collapse	Shorter flares, greater confidence, expanded activity envelope

Note. This table is an interpretive aid, not a clinical guideline.

Table 5. Clinical Translation Matrix: From Pathway Suppression to Field Restoration

Clinical concern	Pathway-focused question	Coherence physiology question
Fatigue	What deficiency, endocrine disorder, anemia, depression, or medication effect explains it?	Is the organism rationing energy because exchange, sleep, inflammation, mitochondria, autonomic regulation, or recovery capacity are impaired?
Pain	What tissue, nerve, joint, or central pain pathway is responsible?	What tissue, matrix, vascular, immune, nervous, and mechanical loops sustain threat signaling?
Dysautonomia	Is this cardiovascular, neurological, anxiety-related, or deconditioning?	Why is dynamic vascular and autonomic regulation failing under posture, heat, meals, stress, or exertion?
Post-exertional malaise	Is the patient simply deconditioned?	Does exertion exceed current mitochondrial, vascular, immune, and autonomic recovery capacity?
Good care	Was the correct diagnosis made and treated?	Did care preserve or expand life-capacity while respecting evidence and state?

Note. This table is an interpretive aid, not a clinical guideline.

Appendices

Appendix A. Glossary of Core Terms

Adaptive coherence. The organism's capacity to remain dynamically organized through disturbance, maintaining enough coordination among substrate, flow, exchange, boundaries, energy, and recovery to continue living, adapting, and participating.

Boundary intelligence. The capacity of biological interfaces to distinguish nourishment from threat, tolerance from alarm, and repair from escalation.

Cell Danger Response. A conserved cellular response to perceived threat in which metabolism, membrane behavior, purinergic signaling, redox state, immune signaling, and repair priorities shift toward protection and containment.

Coherence physiology. The study of how the living organism preserves adaptive wholeness through coordinated regulation of substrate, interface, force, flow, exchange, boundary surveillance, energetic governance, and recovery.

Defensive lock-in. A self-stabilizing physiological state in which protective responses fail to resolve and become mutually reinforcing across multiple layers of regulation.

Energetic governance. Distributed regulation of how energy is allocated among growth, defense, repair, movement, cognition, immunity, digestion, withdrawal, and participation.

Energy resistance. Difficulty transforming available energetic potential into coherent biological work, repair, and participation.

Exchange intelligence. The organism's capacity to regulate provision, clearance, perfusion, permeability, oxygenation, immune traffic, vascular tone, and tissue access.

Field restoration. The clinical orientation of restoring conditions that allow salugenesis to proceed, rather than only suppressing isolated symptoms or blocking downstream pathways.

Interfacial water. Water adjacent to hydrophilic surfaces that may behave differently from bulk water in ways relevant to charge distribution, exclusion behavior, viscosity, transport, and interface-dependent function. In this paper it is treated as a frontier domain.

Life-capacity. The capacity of a living being to breathe, move, think, relate, repair, create, care, rest, participate, and flourish.

Life-coherent medicine. Clinical care ordered toward preservation, restoration, and expansion of life-capacity.

Salugenesis. The active biological process through which the organism exits defensive lock-in and restores the conditions for adaptive self-repair.

Wu-wei medicine. A non-forcing clinical orientation that acts in alignment with the organism's present conditions of viability, reducing resistance and supporting recovery.

Appendix B. Foundational Propositions

1. The organism is not best understood as an assemblage of isolated organs, but as a nested living continuum.

2. Health is adaptive coherence across substrate, interface, force, flow, exchange, boundary surveillance, energetic governance, and recovery.

3. Chronic illness often reflects more than local lesion, pathway dysfunction, or persistent exposure; it may represent defensive lock-in across multiple physiological layers.

4. Fascia, extracellular matrix, and interstitium form part of the organism's material substrate of continuity, sensation, force transmission, fluid movement, immune traffic, and repair.

5. Hydrated biological interfaces may provide substrate-level conditions for charge, transport, matrix behavior, membrane function, and energetic organization, though broad claims remain exploratory.

6. Force and flow are primary languages through which the organism senses, adapts, and reorganizes.

7. Endothelium, glycocalyx, and microcirculation form distributed exchange intelligence.

8. Mast cells and innate sentinels are boundary interpreters linking immunity, vasculature, nerves, connective tissue, permeability, repair, and alarm.

9. Mitochondria are executive regulators of adaptive energetic state.

10. Salugenesis is the positive recovery logic of coherence physiology.

Appendix C. Limitations of the Present White Paper

Limitation 1. This white paper is an integrative theoretical synthesis, not a clinical guideline, diagnostic manual, or completed systematic review.

Limitation 2. The literatures integrated here are uneven in evidentiary maturity. Mechanotransduction, endothelial biology, microvascular dysfunction, mitochondrial stress signaling, sleep physiology, and mast-cell biology are stronger than some broader interfacial-water claims.

Limitation 3. Defensive lock-in should not become a catch-all diagnosis. It is a pattern of physiological organization, not a substitute for careful differential diagnosis.

Limitation 4. The framework does not provide disease-specific treatment protocols. Clinical application requires individualized assessment, evidence-based care, and professional judgment.

Limitation 5. The model is not meant to imply that all chronic illness is reversible. Salugenesis means restoration of life-capacity to the fullest truthful extent possible, not guaranteed cure.

Appendix D. Research Agenda

Dynamic physiology. Study chronic illness as a dynamic state using exertional response, recovery time, orthostatic testing, heart-rate variability, sleep architecture, inflammatory trajectories, vascular reactivity, and flare patterns.

Microvascular exchange. Investigate glycocalyx integrity, nitric oxide bioavailability, capillary recruitment, perfusion reserve, microvascular inflammation, and tissue oxygenation in chronic multisystem illness.

Mitochondrial state. Examine mitochondrial stress signaling, redox regulation, Cell Danger Response patterns, energy resistance, and their relation to fatigue and recovery.

Boundary regulation. Clarify how mast cells, epithelial barriers, vascular permeability, sensory nerves, autonomic regulation, and inflammatory thresholds interact.

Matrix and lymphatics. Study how matrix stiffness, fascial restriction, interstitial flow, lymphatic clearance, edema, fibrosis, and mechanical strain contribute to pain, inflammation, and recovery failure.

Interfacial water. Focus on concrete biological interfaces such as glycocalyx, collagen-rich matrix, mitochondrial membranes, mucosal barriers, basement membranes, and intracellular gels.

Salugenesis. Develop a science of recovery that explains why some patients recover after perturbation while others enter defensive lock-in.

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Back Cover Synopsis

Modern medicine is powerful when disease can be localized, targeted, or acutely corrected. Yet many chronic, multisystem, stress-mediated, and recovery-resistant illnesses remain difficult to understand within an organ-by-organ model. Coherence Physiology proposes a new explanatory architecture.

This academic white paper presents the organism as a nested coherence system whose health depends on coordinated regulation of substrate, hydrated interfaces, force, flow, exchange, boundary surveillance, energetic governance, and recovery. It integrates fascia and interstitium research, mechanobiology, endothelial and microvascular medicine, mast-cell and innate immune surveillance, mitochondrial stress biology, interfacial-water theory, and salugenesis into a disciplined model of chronic illness and healing.

Chronic illness is reframed as defensive lock-in: a state in which protective responses fail to resolve and become mutually reinforcing across multiple physiological layers. Healing is reframed as salugenesis: restoration of the conditions under which adaptive self-repair can resume. Bold but evidence-graded, this paper offers a physiological foundation for life-coherent medicine: clinical care in service of the living whole.

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Dr. Bichara Sahely, BSc (Biology), MBBS, DM (Internal Medicine), is a physician, systems thinker, and author whose work integrates internal medicine, physiology, life-value ethics, peace theory, autopoiesis, and ecological civilization. His writings develop the Life-Coherence Framework, a transdisciplinary approach to health, healing, governance, and civilization grounded in the preservation, restoration, and expansion of life-capacity.

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ChatGPT served as research and writing assistant for this white paper, helping to synthesize, structure, draft, and refine the manuscript in collaboration with Dr. Bichara Sahely. Responsibility for final curation, interpretation, and publication rests with the author.