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Modulating Hydrogen-Bond Networks and Vibrational Frequencies: A New Frontier in Therapeutic Intervention

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Abstract **Review Article**

This study explores how targeting hydrogen-bonding and vibrational dynamics clarifies the mechanisms through which biological information becomes meaningful in the contexts of health and disease. By focusing on chemically defined interactions, this framework emphasizes how physical constraints at the molecular level shape signaling behavior and cellular outcomes and may form the basis for new therapeutic modalities that serve as both treatments and prophylactic interventions.

Objective: *We investigate whether hydrogen-bond–mediated tuning of vibrational frequencies in effector–receptor interactions can modulate signal transduction efficiency. Amplification of signal transduction thereby reveals therapeutic opportunities to influence signaling through controlled perturbation of hydrogen-bond networks.*

Method: *We performed a comparative analysis of information transmission from genetic encoding to post-translational modification, to assess how cells integrate intrinsic and environmental cues while maintaining signaling fidelity. Emphasis was placed on chemical mechanisms underlying signal propagation, including ionic fluxes, second messengers, scaffolding and adaptor proteins, and molecular switches.*

Results: *Findings demonstrate that vibrational frequency contributes to molecular functional outcomes and that hydrogen-bond organization plays a central role in directing cellular information flow. Proton-coupled hydrogen-bond dynamics emerged as a regulator of cellular state. Local proton release associated with ATP hydrolysis can reduce pH, perturb hydrogen-bond networks, and alter enzyme conformation and activity, modulate ion channels and signaling pathways including Ca^{2+} signaling—and influence gene regulatory processes.*

Conclusions: *Disrupted signaling fidelity has profound consequences on cellular behavior, contributing to a wide spectrum of pathological conditions including inflammation, infection, neurodegeneration, and autoimmunity. High-fidelity signaling depends on chemically encoded mechanisms such as temporal gating, spatial compartmentalization, and feedback regulation to preserve specificity, amplification and to ensure signal clarity. Examples from calcium signaling, immunological synapse formation, and neurotransmission illustrate how cells maintain reliable information transfer under dynamic conditions. These observations suggest that therapeutic strategies targeting the chemical determinants of signaling accuracy—rather than isolated pathway components—may provide a complementary approach to disease modulation by restoring information flow at its molecular origin.*

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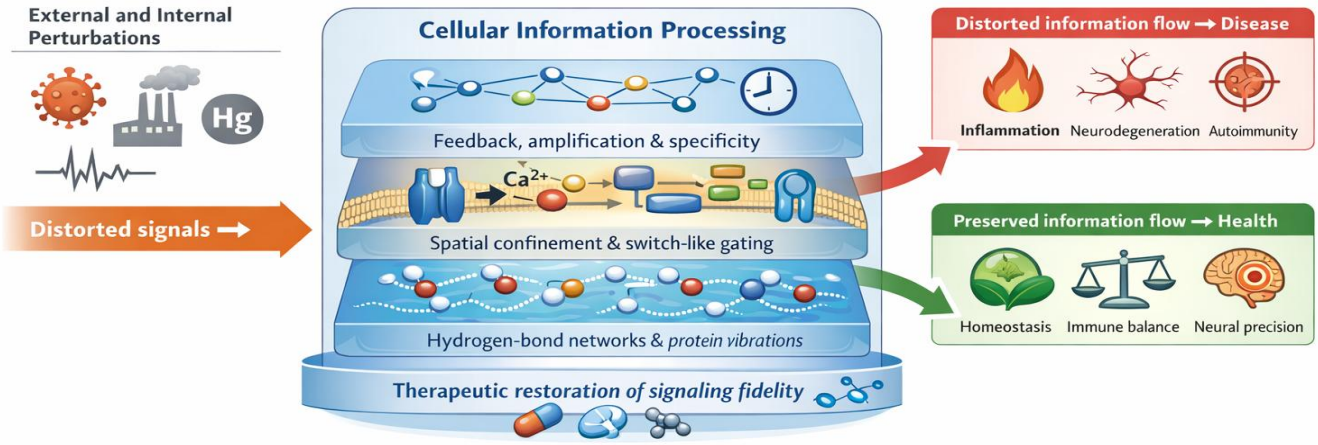

Figure 1. Graphic Abstract.

Introduction

Information as an Organizing Principle in Physical and Biological Systems

Information can be conceptualized not as a physical substance analogous to matter or energy, but as the organizational constraint that determines how energy acts on material substrates. Matter provides the structural medium, energy supplies dynamic capacity, and information specifies the permissible configurations and transitions within physical and biological systems [1]. Within this framework, both non-living and living systems can be understood as distinct regimes of information encoding, transmission, and transformation. This perspective has also informed contemporary models of cognition and consciousness, which treat these phenomena as emergent properties of structured information processing rather than as independent physical entities [2].

In biological contexts, information processing is most clearly instantiated by cell signaling networks, which encode environmental cues, propagate signals through defined molecular architectures, and decode these inputs into functional cellular responses [3,4]. Disruption of signaling fidelity has widespread consequences for cell fate decisions and organismal health, contributing to inflammatory disorders, infectious disease, neurodegeneration, and autoimmunity [5]. Many pathogens exploit this vulnerability by directly targeting host signaling components and RNA-processing complexes, thereby redirecting intracellular information flow to favor pathogen replication and persistence [6]. In parallel, environmental stressors including air pollutants, heavy metals, and contaminants associated with microplastics perturb redox balance and signaling network topology, promoting chronic inflammation and neurotoxic or immunomodulatory outcomes [7]. These perturbations converge on a common outcome: altered information flow across molecular networks, resulting in maladaptive cellular programs that underlie both acute and chronic disease.

Efficient communication between cells is essential for multicellular organisms to maintain homeostasis and adapt to fluctuating environments. Signal robustness and specificity are achieved through temporal modulation, spatial compartmentalization, and multilayered feedback regulation, which together limit noise while permitting amplification when required [8]. Calcium signaling provides a well-characterized example of dynamic intracellular information encoding. Localized Ca^{2+} microdomains and oscillatory signaling patterns selectively engage transcriptional regulators, including calcineurin–NFAT and CREB, enabling stimulus-specific gene expression programs. At specialized intercellular interfaces such as immunological and neuronal synapses, highly ordered spatial architectures and mechano-biochemical feedback mechanisms refine antigen discrimination and preserve synaptic fidelity through synchronized, Ca^{2+}-dependent vesicle fusion and receptor organization [9].

At the level of fundamental physics, several theoretical frameworks propose that information plays a central role in the emergence of macroscopic order. Miller has suggested that interactions between matter and energy inherently generate informational structure, rendering information a ubiquitous feature of physical reality rather than a derived abstraction [2]. In this view, the increasing complexity of the Universe reflects the continuous generation and propagation of elementary informational units. Early quantum interactions may have established a distributed network of quantum information that, through decoherence and environmental encoding, enabled the emergence of stable classical structures and, ultimately, biological systems.

Recent theoretical and experimental advances provide support for this information-centric view. Chiarelli and Touil and colleagues describe the Universe as a computation–information system in which quantum information, decoherence, and environmental encoding jointly give rise to macroscopic order and effective memory [10,11]. Complementing these models, Doucet and Deffner (2024) demonstrate mathematically that classical behavior can emerge generically from realistic physical conditions without invoking ad hoc collapse mechanisms. Experimental work by Zhu et al. (2025) extends these concepts by directly demonstrating redundant environmental records and the emergence of objective classical states in a controllable quantum platform, consistent with predictions of Quantum Darwinism. Related analyses by Strasberg et al. (2024) show that classical histories arise naturally from unitary quantum dynamics when attention is restricted to coarse-grained, physically relevant observables [12–14].

Collectively, these findings support a model in which classical reality emerges through continuous environmental encoding of information. Within this framework, complex systems arise from simple quantum informational units, with matter and radiation interpretable as physical carriers of information. In parallel, biological systems can be viewed as highly specialized information-processing entities that encode information in genetic sequences, protein conformations, signaling networks, and neural dynamics. Living systems maintain organization by expending energy to copy, transmit, and correct molecular information, thereby sustaining function in the face of constant environmental and thermodynamic perturbations [15]

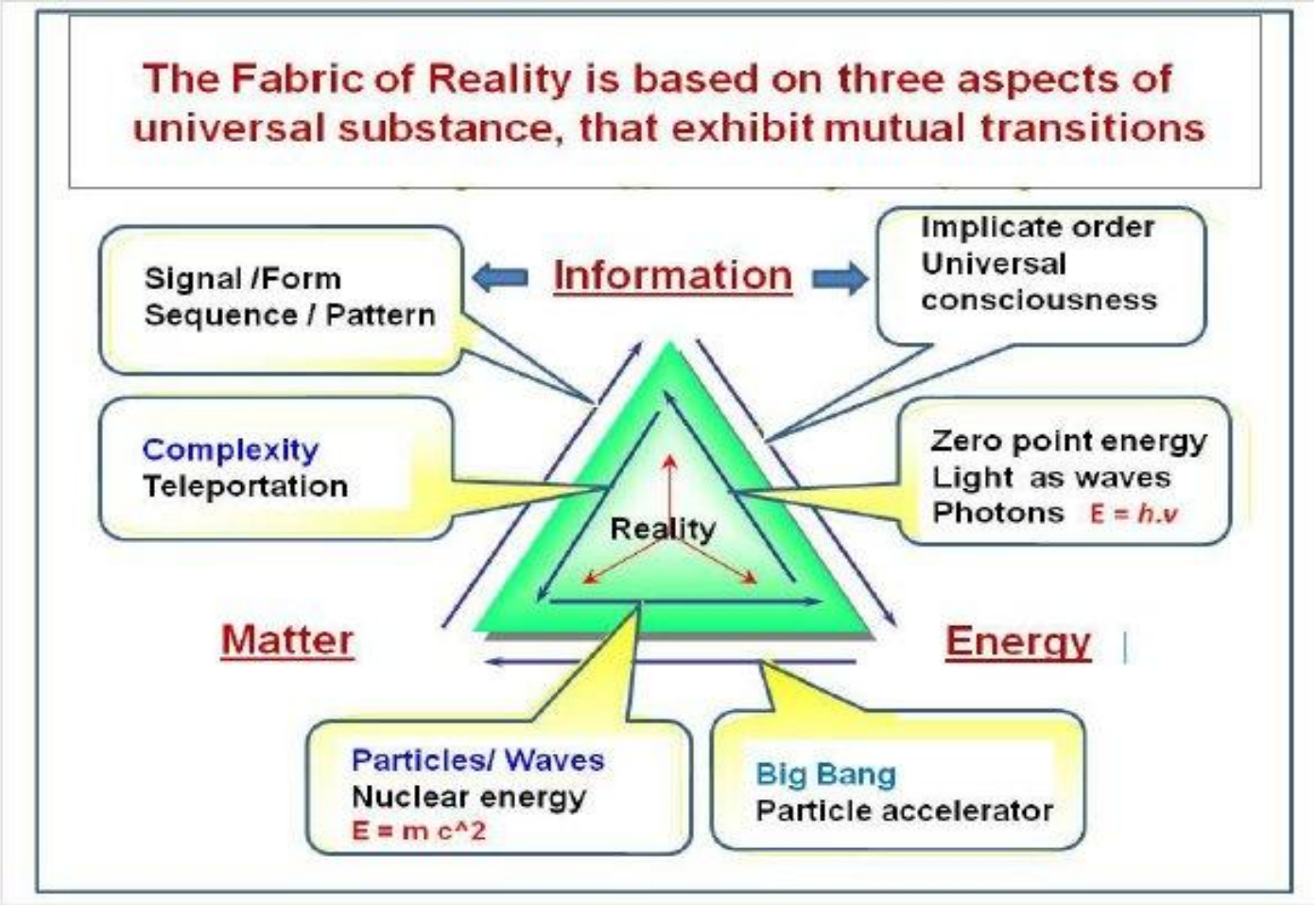

Fig. 2: The fundamental triad of energy/matter/information [Meijer, Dirk. (2013). Information: What Do You Mean? Syntropy Journal].

Information-Theoretic Principles in Molecular and Cellular Organization. Information-based frameworks are increasingly used to describe how ordered biological systems emerge from physical interactions. At small scales, quantum mechanical principles define the limits of information encoding and transmission, as quantum systems support superposition, interference, and phase-dependent dynamics. Experimental studies that demonstrate programmable logical operations in atoms and elementary particles establish that physical substrates can support information processing, providing general constraints relevant to biological organization, although they do not directly explain cellular complexity [15,16]. Although these findings do not directly explain biological

organization, they establish general constraints on how information can be stored and manipulated by matter. At the molecular and cellular levels, information is instantiated in the structure and dynamics of macromolecules, signaling networks, and gene regulatory circuits. Unified information-based models propose that matter and energy can be treated as carriers and drivers of information, respectively, rather than as independent explanatory categories [17,18]. In the nervous system, information processing is reflected in synaptic plasticity, where activity-dependent mechanisms modify connectivity. Despite extensive molecular characterization, it remains unclear how specific synapses are selected for modification during learning in vivo and whether plasticity rules are uniform across individual neurons [19]. Comparative analyses of biological and artificial learning systems are increasingly used to identify general principles of adaptive information processing [20].

Information-theoretic concepts also inform modern physics by linking entropy, uncertainty, and energetic cost to the emergence of structure. These approaches have been applied to gravitational systems and black hole thermodynamics to formalize information conservation under extreme conditions [21,22]. More broadly, information provides a useful organizational framework for describing how complex biological structures arise from simpler physical interactions, without implying ontological primacy [23].

Multiscale Information Processing in Cells and Tissues. Biological information transfer requires a carrier, an encoding scheme, and a decoding mechanism. In cells, ions, metabolites, and macromolecules act as carriers; temporal and spatial dynamics provide encoding; and receptors and downstream effectors decode signals [26]. Analogies with engineered communication systems, including optical and photonic networks, have been used to formalize biological signaling in terms of noise, bandwidth, and channel capacity [27,28]. Signaling pathways are often distinguished from metabolic processes by their regulatory function and relatively low energetic cost, although both are tightly coupled through shared energetic constraints [29,30].

Recent studies have identified active mechanisms that regulate the formation and dissolution of endoplasmic reticulum–plasma membrane contact sites, thereby shaping the amplitude and frequency of receptor-driven Ca^{2+} oscillations [31]. Calcium signaling encodes information through precisely controlled temporal patterns, including oscillation frequency and amplitude, which are selectively decoded by downstream sensors and transcriptional regulators to generate context-dependent cellular responses [32]. Beyond chemical signaling, endogenous bioelectric gradients influence cell behavior and tissue organization, particularly during development and regeneration. However, the mechanisms by which electrical signals are generated, sensed, and integrated with molecular pathways remain incompletely defined [33]. In neural systems, information transmission is described by formal coding schemes based on firing rate and spike timing, principles that also inform the design of spiking neural networks and other biologically inspired computational models [34].

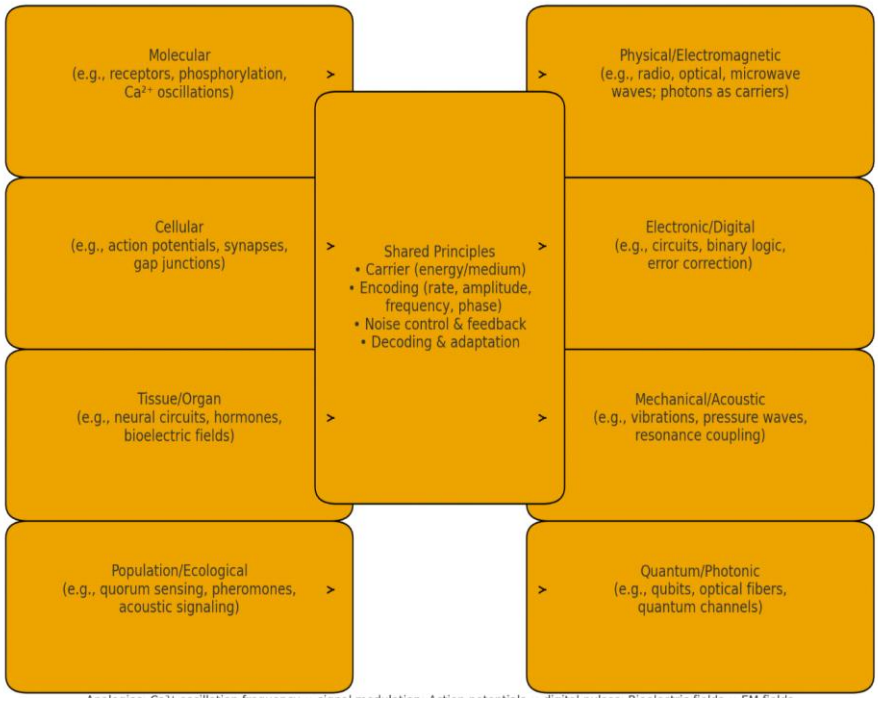

Fig. 3 shows information transmission pathways. Biological & non-biological

Method.

We conducted a comparative, multi-scale analysis of cellular information transmission with an emphasis on immune cell signaling. The analysis integrated genetic encoding, transcriptional regulation, post-translational modification, and downstream effector responses to examine how signaling fidelity is established and maintained across hierarchical biological layers. Cellular signaling was conceptualized as an information-processing system governed by spatial organization, temporal gating, and feedback regulation.

Information encoding at the genetic level was evaluated through established mechanisms of DNA–protein recognition, transcription factor binding specificity, and chromatin accessibility. Because DNA-binding proteins rely on organized hydrogen-bond networks for precise target recognition, the analysis considered how hydration structure, electrostatics, and hydrogen-bond geometry influence transcriptional accuracy and regulatory precision. Post-translational signaling mechanisms, including ion binding, phosphorylation, conformational switching, and protein–protein interactions, were analyzed as dynamic modulators of information transmission.

Calcium signaling was examined as a central integrator of intracellular information flow. Ca^{2+} dynamics, including oscillatory behavior, amplitude modulation, and spatial confinement, were analyzed for their role in encoding signaling information. Particular emphasis was placed on CO_2- and pH-sensitive hydrogen-bond networks that regulate protein vibrational modes and conformational landscapes. Vibrational coupling was evaluated as a mechanism linking physicochemical microenvironments to receptor activation, signal amplification, ligand residence time, and downstream signaling kinetics.

Integration of internal and environmental cues was assessed through coordinated actions of ions, second messengers, scaffolding and adaptor proteins, and molecular switches. Spatial compartmentalization and modular assembly of signaling complexes were examined as mechanisms that reduce noise and preserve specificity. Environmental stressors, inflammatory mediators, and pathogen-derived effectors were analyzed for their capacity to disrupt hydrogen-bond networks and vibrational coupling, leading to signal distortion and pathological rewiring.

This study employed an integrative, conceptual methodology grounded in established biophysical and signaling principles. Although no direct experimental manipulation was performed, the framework enables systematic evaluation of conserved mechanisms governing signaling fidelity and provides a transferable basis for hypothesis generation and therapeutic strategy development.

Results.

1. Vibrational frequency dictates molecule biological effect. This resonance-based amplification provides a physical basis for the remarkable sensitivity and efficiency observed in biological signal transduction.

2. Hydrogen-bond organization is driver of cellular information flow. Biological signaling fields often exhibit radial symmetry analogous to magnetic-field symmetry in physics. Hydrogen atoms and hydrogen-bond network symmetry play central role as a unifying regulator of cellular signaling specificity.

3. Proton-driven hydrogen-bond dynamics is a key regulator of cellular state

The free protons from ATP breakdown could lower pH, which then disrupts hydrogen-bond networks. These protons reorganize hydrogen-bond networks that control structural and functional states of enzymes, ion channels, and signaling pathways including Ca^{2+} signaling—and influence gene regulatory processes. This framework highlights hydrogen-bond symmetry as a measurable control parameter for cellular signaling.

Discussion.

We advance a framework grounded in matter–energy unity, wherein matter is understood as condensed energy and energy as an expanded state of matter. From this perspective, measurement does not generate physical events but instead reveals information already encoded within quantum systems. In the double-slit experiment, radiation emitted by an accelerated electron reflects particle-like behavior without necessitating a definitive wavefunction collapse; rather, it exposes epistemic and instrumental limits in resolving full quantum coherence. This view motivates a reexamination of the informational, energetic, and material boundaries underlying quantum theory and is supported by recent analyses by Laudisa and Ellerman [35,36].

The electron's dual manifestation—as a localized particle upon detection and as an extended wave under superposition and entanglement—suggests that both arise from a shared informational substrate. Analogously, biological signaling constitutes an information-processing task in which cells discriminate signal from noise, route information with precision, and amplify weak inputs into functional responses. These processes rely on three core principles of signal fidelity: clarity, specificity, and amplification, which are actively regulated by molecular components rather than passively transmitted.

Growing evidence indicates that both biological and physical systems exploit quantum phenomena to regulate function and sustain organized behavior [37,38]. Advances in quantum biology further demonstrate that living systems can maintain quantum coherence and spin-dependent chemical dynamics under physiological conditions, providing mechanistic pathways for electromagnetic influences on molecular and cellular processes [39–41]. On a broader scale, theoretical

frameworks in physics and information science increasingly converge on the view that matter and radiation inherently store, transform, and propagate information, implying that physical systems function as natural information processors [42–45].

Discrete coherent frequencies of non-ionizing electromagnetic fields have been shown to elicit stabilizing or destabilizing cellular responses, including frequency-specific modulation of kinase signaling and cellular proliferation [46–49]. In parallel, studies of vibrational strong coupling (VSC) demonstrate that polaritons can alter chemical reactivity, with maximal effects occurring when cavity and molecular vibrational frequencies resonate [50]. Collectively, these findings motivate the perspective that biological responses to electromagnetic fields, quantum coherence, and information-theoretic principles reflect a deeper informational structure embedded within physical law.

Non-targeted effects of low-dose ionizing radiation represent a system-level response in which unexposed cells exhibit coordinated changes following signaling from irradiated cells. Experimental evidence indicates early alterations in ion channel activity, calcium flux dynamics, and biophoton emission associated with these responses. These observations have prompted investigation into whether quantum-scale processes, including tunneling and correlated molecular interactions, could influence the initiation or modulation of intercellular signaling, although direct mechanistic links in biological systems have not yet been established [51,52].

Several integrative theoretical models have proposed that biological organization may arise from interactions across multiple physical scales, including thermodynamic and quantum-level effects, with coherence discussed as a potential emergent property under specific conditions rather than a universal determinant [53]. In parallel, information-based descriptions of physical systems have been increasingly applied in physics and biology to characterize how matter and radiation can encode, transmit, and transform signals relevant to system behavior [54].

The emergence of life requires not only the formation of complex organic molecules but also their assembly into ordered systems capable of storing and executing functional instructions. This principle is exemplified by the central dogma of molecular biology, in which nucleotide sequences in DNA or RNA specify the ordered synthesis of proteins with defined biological roles [55].

Together, these findings support the interpretation that certain biological responses to electromagnetic perturbations and coherence-related effects may be examined within an information-theoretic framework, in which complex behaviors emerge from constrained signal propagation governed by established physical principles.

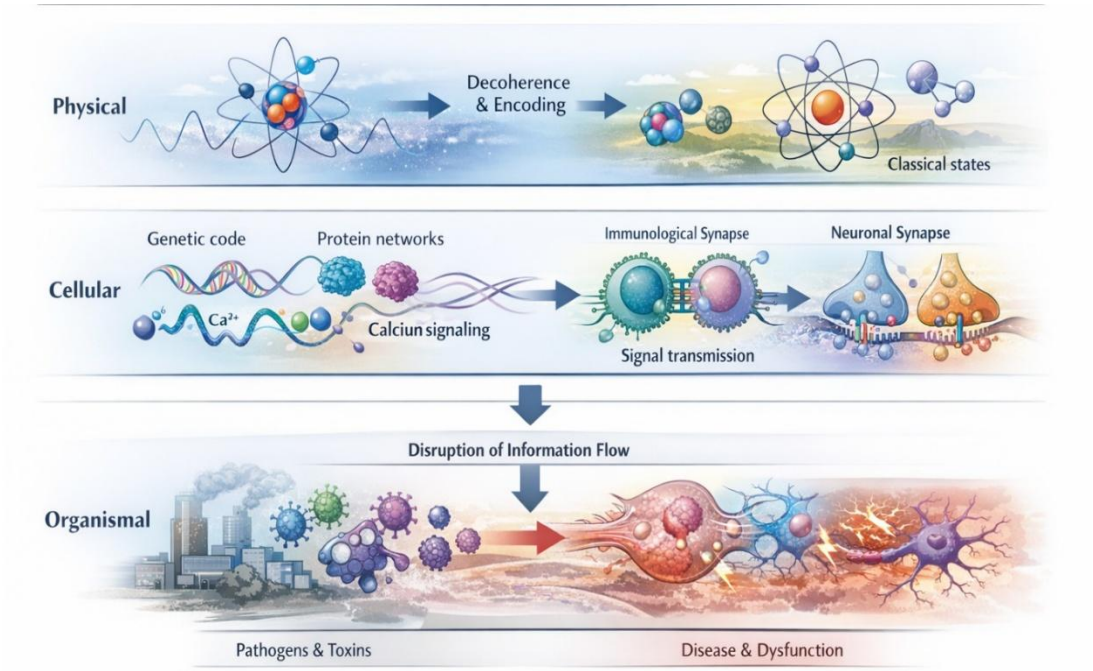

Fig. 4. Information flows across physical, cellular and organismal levels.

Summary. Quantum biology is an emerging frontier with the potential to reshape our understanding of cell signaling, disease mechanisms, and therapeutic strategies. Elucidating quantum-scale processes in biological systems requires highly sensitive, standardized measurement methods and a framework centered on information fidelity. Cells maintain signaling precision through evolved molecular strategies, including spatial confinement, scaffold-mediated routing, gating mechanisms, and signal amplification—that enable reliable information processing despite intrinsic intracellular noise. Operating across hierarchical levels from genetic encoding to post-translational regulation, these mechanisms integrate internal and external cues into coordinated cellular

responses. Evidence from calcium microdomains, immunological synapses, and neurotransmission demonstrates that signaling fidelity can be preserved in noisy environments. Disruption of this fidelity contributes to diverse pathologies, highlighting the therapeutic potential of restoring or re-engineering information flow through interdisciplinary approaches spanning molecular biology, medicine, telecommunications science, and structural biology.

First connotation, vibrational frequency dictates molecule biological effect. Vibrational frequency may dictate molecular biological effects, such that effector molecules recognize and sense target receptors not solely through static structural complementarity but also through dynamic frequency alignment. When the molecular oscillations of interacting partners achieve resonance, energy transfer becomes highly efficient, stabilizing the interaction and amplifying downstream signaling [56,57]. This supports the concept that oscillatory frequency constitutes a meaningful recognition parameter [58]. Resonance-based amplification thus provides a physical basis for the remarkable sensitivity and efficiency observed in biological signal transduction: structural complementarity initiates binding, whereas frequency coupling sustains and amplifies the signal. Such resonance may occur through vibrational matching (intramolecular phonon modes), electrodynamic coupling (dipole–dipole or charge oscillations), or collective synchronization within cellular networks of oscillating molecules [59,60].

For example, oscillatory cyclic adenosine monophosphate (cAMP) signaling drives collective cellular behavior and induces temporally coordinated developmental gene expression programs [61].

This framework aligns with the vibration theory of olfaction, which posits that a molecule's biological effect arises from its vibrational frequency. Moreover, biological structures possess intrinsic eigenfrequencies determined by their atomic configurations and bonding geometries, producing rotational, vibrational, and electronic fingerprints detectable across the electromagnetic spectrum [62,63]. These highly specific signatures enable the identification of proteins, metabolites, nucleic acids, and redox-active cofactors. Upon binding, receptor–effector pairs adjust their vibrational and electromagnetic oscillations toward resonance, enabling coherent energy exchange across the interaction interface. Cells may therefore exploit such resonant properties for mechanotransduction, frequency-encoded signaling, and long-range synchronization. In this sense, biological eigenfrequencies represent quantum signatures of cellular communication.

These ideas are further supported by the Resonant Recognition Model (RRM), which proposes that protein interactions can be electromagnetic in nature and involve specific spectral characteristics [64,65]. Within this framework, resonant protein–protein interactions require electromagnetic energy transfer between interacting partners.

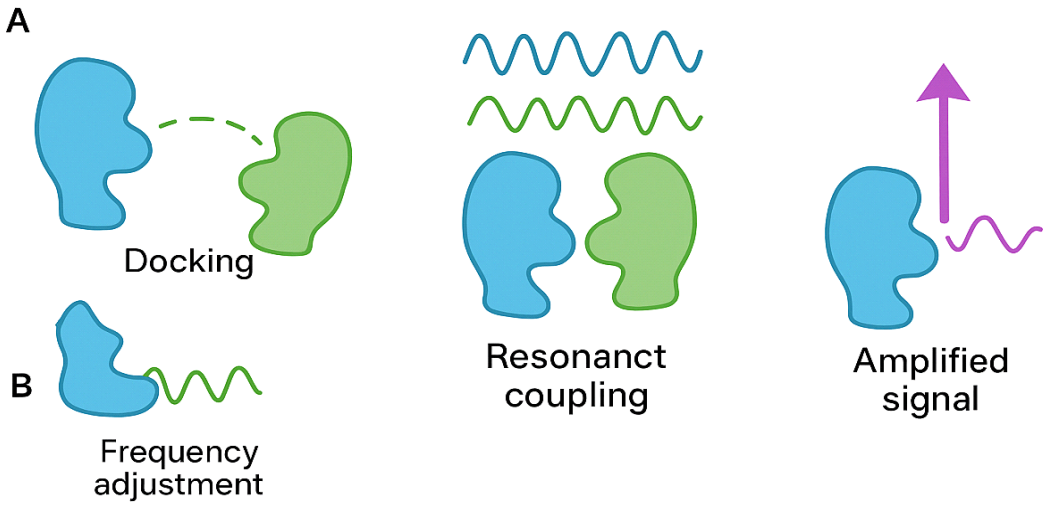

Fig. 5, Resonance- based recognition and signal amplification between receptor and effector molecules. Effector molecules recognize targeted receptors not only through structural and chemical complementarity but also by achieving dynamic frequency coupling. (A) Structural complementarity ensures specific docking between the effector's recognition domain and the receptor's active site, (B) Once bound, both molecules adjust their vibrational and electromagnetic oscillations toward state of resonance, enabling coherent energy exchange across the binding interface, (C) Resonant coupling stabilizes the active conformation, enhances signal transfer efficiency, and promotes amplification.

***Second connotation. Hydrogen-Bond Organization as a Driver of Cellular Information* Flow.** Biological signaling fields often exhibit radial symmetry analogous to magnetic-field symmetry in physics. Hydrogen atoms and the symmetry of hydrogen-bond networks play a central role as unifying regulators of cellular signaling specificity. Identifying hydrogen atom positions and visualizing the resulting hydrogen-bond networks are essential for understanding protein structure and function, including the resolution of precise drug–ligand interactions [66].

Analogous to magnetic-field symmetry, cellular systems employ polarized receptor distributions, membrane anisotropy, and tissue heterogeneity to encode directional information [67,68]. Hydrogen atoms and hydrogen-bond networks are critical in these processes because proton position, sharing, and tunneling shape local energy landscapes, vibrational modes, and proton-coupled electron transfer (PCET). Proton tunneling in PCET processes can be probed through photoluminescence experiments [69–71].

Emerging evidence indicates that hydrogen-bond symmetry connects Ca^{2+}-channel gating, enzyme transition-state stabilization, and immune-receptor fidelity [72]. DNA-binding proteins likewise depend on organized hydrogen-bond networks for precise target recognition [73]. Symmetric, low-barrier hydrogen bonds (LBHBs) can enhance proton tunneling and thereby influence local protonation dynamics that support efficient Ca^{2+} handling by transporters and channels such as SERCA, PMCA, and the STIM1–Orai1 complex [74]. Conversely, disruption of hydrogen-bond symmetry for example by changes in pH or CO_2, oxidative stress, or alterations in Ca^{2+} hydration can perturb proton-transfer equilibria and microenvironment electrostatics, leading to impaired Ca^{2+} signaling and reduced transcriptional fidelity as calcium signaling is fundamental to virtually all cellular life [75,76]. **Auwercx, J., et al.** (2025). Discusses channels that regulate Ca^{2+} homeostasis and responses to changes in cellular environments (pH, mediated proton dynamics), providing foundational context for how perturbations in electrostatics and local proton states influence signaling pathways including Ca^{2+}-dependent mechanisms [77]. **Kim et al.** (2025). provides high-resolution structural insight into human TRPC complexes that underlie Ca^{2+} entry mechanisms central work to cellular signaling, relevant to immune cells and physiological Ca^{2+} signaling modulation [78]. Zhao et al demonstrates that hydrogen-induced modulation of protonation states can drive calcium entry through TRPC4 channels, highlighting how changes in local proton environments (linked to hydrogen-bond dynamics and pH/CO_2 perturbations) affect Ca^{2+} signaling pathways [79]. Results showing that elevated CO_2 lowers intracellular pH and alters immune cell transcriptional responses [80,81].

Figure 6. Symmetric, low-barrier hydrogen bonds (LBHB) can enhance proton tunneling and thereby influence local protonation dynamics that support efficient Ca^{2+} handling by transporters and channels. Disruption of hydrogen-bond symmetry by changes in pH or CO_2, oxidative stress, or alterations in Ca^{2+} hydration can perturb proton-transfer and microenvironment electrostatics, leading to impaired Ca^{2+} signaling and reduced transcriptional fidelity.

Third connotation. Proton-driven hydrogen-bond dynamics is a key regulator of cellular state. Acidification observed during fermentation does not primarily result from the accumulation of organic acids but instead arises from proton (H^+) release during ATP hydrolysis [82], alongside documented hydrogen-bond restructuring of water in the hydration shells of metal ions [83,84]. Most organic acids are deprotonated in the cytosol and thus contribute minimally to intracellular acidification. Rather, free protons generated by ATP break down lower intracellular pH and disrupt hydrogen-bond networks.

These protons reorganize hydrogen-bond networks that control the structural and functional states of enzymes, ion channels, and transcription factors. Such disruptions can alter enzyme conformation and activity, modulate ion channels and signal pathways (including Ca^{2+} signaling), and influence gene regulation. This framework highlights hydrogen-bond symmetry as a measurable and dynamic control parameter governing cellular signaling and state transitions.

As demonstrated by Singh (2025) and further clarified by Yu (2025), hydrogen-bond networks can substantially amplify light–matter coupling under vibrational strong-coupling conditions. Studies by Biswas et al (2025) and Gimferrer et al. (2025) show that these hydrogen-bond–dependent interactions also reorganize vibrational energy-transfer channels. Moreover, cavity-enhanced field effects acting on hydrogen-bond geometries modify vibrational transition energies and absorption profiles, as quantified by Amadeo and Carter (2025). Extending beyond molecular spectra, He et al. (2025) provide direct evidence that dynamic modulation of hydrogen bonding can reshape the optical band structure in organic and framework-based photonic materials. and thus, reshaping the band structure [86-91].

Recognizing hydrogen-bond symmetry as a measurable control parameter and elucidating its effects on polaritonic light–matter coupling, establishes a conceptual foundation for designing advanced experimental strategies and therapeutic interventions. This framework directly addresses the quantum-chemical determinants of cellular signaling and is particularly pertinent to pathological conditions in which receptor–ligand interactions govern disease initiation and progression, including autoimmune disorders.

Conclusive analysis of results from first, second and third connotation. Vibrational frequency has been implicated as a determinant of molecular function, while hydrogen-bond organization contributes to the regulation of intramolecular and intermolecular information transfer. Hydrogen bonds can modulate local vibrational modes at effector–receptor interfaces, potentially influencing the efficiency and integration of downstream signal transduction. Such modulation may affect how biological signals are propagated or maintained at the molecular level, with possible implications for therapeutic modulation.

Methodological advances further support this framework. Chua *et al.* demonstrated that direct electron detectors operated in electron-counting mode substantially improve data quality, readout speed, and counting accuracy in cryo-electron microscopy [92]. Fang showed that ultrafast vibrational spectroscopy, including femtosecond stimulated Raman spectroscopy, can resolve dynamic protein motions on timescales directly relevant to biochemical function [93]. Kolossváry *et al.* introduced an approach using normal-mode analysis to characterize protein conformational transitions in a pharmacologically relevant context, exemplified by the JAK2 V617F mutation [94]. Verma provided experimental evidence that hydrogen bonds exhibit quantifiable variability in strength, underscoring their structural and dynamical significance [95]. Bondar highlighted how dynamic hydrogen-bond networks—including transient, water-mediated interactions—contribute to long-range conformational coupling, allostery, proton transfer, and functional regulation in proteins [96]. Tsujimura demonstrated that hydrogen-bond geometry and local environment directly shape vibrational behavior and proton dynamics [97].

Collectively, these studies support the plausibility that perturbations of hydrogen-bond networks can alter vibrational and conformational dynamics, thereby modulating signal transduction and allosteric regulation. This framework suggests that hydrogen-bond organization may represent a mechanistically grounded, albeit complex, target for therapeutic or synthetic biology strategies.

Conclusion. Information in biological systems is not a material entity comparable to matter or energy but instead reflects the organizational principles that constrain and coordinate molecular interactions. Both living and nonliving systems can therefore be viewed as distinct implementations of information processing governed by physical law. In cells, signaling pathways encode, transmit, and decode environmental cues within defined biophysical limits to generate specific functional outcomes. Disruption of signaling fidelity alters cellular behavior and organismal homeostasis and is implicated in diverse pathological states, including inflammation, infection, neurodegeneration, and autoimmunity. Pathogens exploit host information-processing architectures by targeting intracellular signaling and RNA-processing machinery to reprogram cellular networks. Environmental stressors and toxicants—including air pollutants, heavy metals, and microplastic-associated

contaminants—similarly perturb signaling organization, promoting inflammatory, neurotoxic, and immunomodulatory responses. Together, these insults distort information flow across molecular networks, driving maladaptive cellular programs that contribute to both acute and chronic disease. High-fidelity cell-to-cell communication requires mechanisms that preserve signal specificity, timing, and robustness, including spatial compartmentalization, temporal gating, and multilayered feedback control. Experimental and theoretical work indicates that molecular strategies such as scaffolding, confinement, and switch-like activation are central to maintaining signaling precision. Calcium signaling, immunological synapse formation, and neurotransmission exemplify how these mechanisms are integrated to ensure reliable information transfer in fluctuating biological environments. Cellular signaling operates hierarchically, integrating genetic, biochemical, and spatial regulation into coordinated information-processing systems. Perturbations at any level of this hierarchy can propagate across scales, ultimately manifesting as disease. These observations suggest that therapeutic approaches aimed at restoring signaling fidelity—rather than solely inhibiting individual pathway components—may yield broader and more durable effects by correcting distorted information flow at its origin. At the molecular scale, protein vibrational dynamics are increasingly recognized as functionally relevant contributors to biological activity rather than incidental thermal fluctuations. Hydrogen-bond networks shape these vibrational modes and influence conformational landscapes, receptor activation, signal amplification, ligand residence times, and signaling kinetics. Water structure and hydrogen-bond reorganization are therefore emerging as important regulators of biomolecular communication. Modulating hydrogen-bonding and vibrational dynamics may offer new avenues for therapeutic intervention, underscoring that signaling fidelity depends not only on molecular composition but also on the dynamic physical properties of biological matter.

Future directives and outlook.

By integrating concepts from molecular signaling, information theory, and emerging insights from quantum biology, this work addresses a gap in how biological information is structured and propagated across scales. The framework supports interdisciplinary inquiry spanning cell biology, structural biology, and medicine, with implications for diagnostic and therapeutic innovation. While no single model fully accounts for the origin of biological information, the present study clarifies how information acquires functional relevance in health and disease. Future studies should further examine interactions across physical and biological levels of organization.

Advances in understanding hydrogen-bond networks and protein vibrational dynamics suggest new avenues for modulating molecular function. Approaches that target these properties—including allosteric drug design (altering H-bond donors/acceptors to tune binding kinetics). Protein engineering (modulating conformational coupling networks stabilizers of protein misfolding diseases), and synthetic signaling systems for restoring or rewriting signaling at its molecular source are a well-grounded therapeutic concept which may enable more precise control of signaling behavior. Emerging modalities such as terahertz and infrared-based perturbations warrant cautious investigation within established biophysical constraints. Collectively, strategies aimed at restoring signaling fidelity at its molecular origins may complement existing pathway-focused therapies and contribute to more durable intervention strategies.

Abbreviations.

- The cell's cortical region is specialized layer of cytoplasmic proteins on the inner face of the cell membrane.
- ER–PM = endoplasmic reticulum–plasma membrane.
- SERCA= Sarco/Endoplasmic Reticulum Ca2+-ATPase
- PMCA = Plasma Membrane Calcium ATPase.
- STIM1–Orai1 complex. The STIM1-Orai1 complex forms the core of Store-Operated Calcium Entry (SOCE), a crucial cellular process where STIM1 (a calcium sensor in the endoplasmic reticulum) detects low ER calcium, then moves to the plasma membrane to activate Orai1 (a calcium channel pore-forming protein
- TRPC= TypeScript Remote Procedure Call.

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Abdelrazak Ali; Conceptualization, Data curation, Formal Analysis, and Supervision

Mohamed Ibrahim; Resources, Validation, and Writing original draft

Radwa Ali; Reviewing, Editing, Validation

Mohga Barbar; Methodology.

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