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Posted Date: 30 October 2026

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Review

The Quantum Physics of Living Matter: From Electrons to Evolution

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Abstract

Living matter uses energy and material to maintain and replace the structures that sustain its activity. This monograph asks when quantum mechanics contributes measurably to that continuity. It examines local electronic, nuclear, photochemical, and spin-dependent events whose products can persist as chemical, electrical, or conformational records. The cases include respiratory electron and proton transfer, enzyme hydrogen tunnelling, photosynthetic energy transfer, vision, radical-pair chemistry, DNA maintenance, and protein-based inheritance. Established molecular mechanisms are distinguished from claims about their necessity for biological function. The proposed test follows a quantum-sensitive step through an intermediate record to a functional output, then asks whether it changes the work, fidelity, or renewal a system can s ustain. Comparisons must give physically admissible alternatives the same limits on power, material, space, time, and error, including the cost of compensation. Models of completion before loss and coupled production show how a local effect could shift a threshold for renewal; they do not establish that such a shift occurs in a particular organism. Classical kinetic networks and alternative architectures provide controls. Evidence for extended coherence and neural quantum proposals is assessed separately. The book develops experimental designs in catalysis, bioenergetics, DNA maintenance, radical-pair sensing, and artificial c ells. Its central claim is conditional: a quantum-sensitive mechanism matters to living organization when its measured contribution changes what a system can sustain under specified constraints.

Keywords: quantum biology; biological physics; bioenergetics; electron transfer; proton transfer; enzyme tunnelling; radical-pair mechanism; DNA repair; molecular inheritance; artificial cells; self-maintenance; nonequilibrium thermodynamics

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Introduction. Living Matter and Its Physical Means

Living matter uses energy and material to sustain, reconstruct, and adapt its own organization. Across generations, reproduction with heritable variation perpetuates and changes that organization. The material constituents need not persist for the organism or lineage to do so. What persists is a set of causal relationships: existing structures help make, place, and regulate their successors while the system exchanges matter and energy with its surroundings.

This account does not identify life with a molecule, a pattern, or a rate of energy consumption. A protein may survive for years; another may be replaced in hours. An organism can conserve resources so effectively that its power use is barely measurable. It nevertheless must maintain conditions under which its activities can continue, including conditions that would decay if its work stopped. Reproduction concerns continuity across individuals, not a requirement that each living individual reproduce.

The question of this book is what the quantum physics of matter contributes to that continuing work. Atoms, bonds, electronic and nuclear motions, spin, and radiation obey quantum mechanics in organisms as elsewhere. That universal fact alone explains no biological distinction. The useful claim is narrower: particular quantum-sensitive steps set the attainable rates, selectivity, energetic costs, or errors of molecular operations from which organisms construct stable records, useful work,

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and renewal. Evolution can change the geometry and environment of those steps. Their products can be recorded in chemical states and propagated by ordinary cellular networks.

An even stronger claim is conditional. Under specified constraints of time, power, material, space, and fidelity, a particular organism or synthetic system may fail without a measured quantum-sensitive contribution, even if another arrangement could perform the task with greater resources. A reaction mechanism, its biological consequence, and the limits of physical replacements must be established separately. No single isotope effect or spectroscopic signal proves that quantum dynamics is necessary for life.

Scholes and Fleming have likewise called for experiments that distinguish quantum function from classical mimics and follow microscopic events into biological outcomes. This book develops one answer to that agenda: compare the continuing work, fidelity, and renewal attainable by complete arrangements under matched resources. It does not claim to have established a general quantum advantage for living systems. [176]

Two objections require equally specific treatment. Thermal surroundings can destroy coherence, the phase relations between alternatives in a quantum state, on short timescales. A mechanism that requires coherence across a tissue or for seconds faces a serious physical burden. An electron-transfer event, a radical-pair reaction, or a photochemical transition need only retain the relevant quantum properties during the operation. Its reaction product may survive after coherence has gone. Similarly, a microscopic event does not invariably disappear in a macroscopic average. In a rod photoreceptor, absorption of a single photon can induce retinal isomerization, a change in molecular shape; a biochemical cascade amplifies the consequence into a measurable electrical response. The response does not preserve the photon's quantum state. It preserves a record of its effect. [2–4]

The argument begins with material continuity, inherited descriptions, and the work required to replace the machinery that does the work. It then follows electrons, protons, photons, and spins into energy conversion, catalysis, sensing, repair, and inherited states. Later parts ask how local events become durable records, how those records support renewal and adaptation, and how evolution tunes the molecular machinery. The evidence for persistent large-scale coherence and for quantum claims about the brain is assessed only after these shorter causal chains have been developed. Their resolution is independent of the central argument.

Part I. The Physical Problem of Living Continuity

1. Continuity Without Permanent Material

In a living system, a nearly constant abundance of a component can conceal steady replacement. If a component is made at rate s and lost at fractional rate δ, a simple balance is

$$\dot{N} = s - \delta N, \qquad N_{\mathrm{ss}} = s/\delta.$$

At the steady state, N is constant, but an initially labeled cohort declines as $N_{\mathrm{old}}(t) = N_{\mathrm{old}}(0)e^{-\delta t}$. The equations distinguish constancy of amount from persistence of particular molecules. They do not explain how replacement is made, directed, or financed. Those are the central biological questions.

Ludwig von Bertalanffy called an organism's maintained condition a *Fließgleichgewicht*, a flowing steady state. Matter enters, participates in reactions, and leaves, while selected relationships remain within viable ranges. A steady state with continuing currents is not thermodynamic equilibrium: reservoirs supply free energy, reactions dissipate it, and products are removed. The term describes a condition maintained through activity, not a substance that stays unchanged. [6,7]

Material throughput, cycling, and replacement must be distinguished. Throughput describes exchange across a boundary. A catalytic cycle returns a molecule to an operating state after repeated reactions. Replacement occurs when a new physical molecule or assembly takes over an old one's role. A cell can have rapid energy throughput and a long-lived structural protein; extraordinarily long-lived nuclear-pore proteins in mammalian brain illustrate the range of lifetimes. A theory of turnover cannot assume every component is replaced at the same rate. [12]

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The maintained relationships also differ. A membrane gradient can require continuous pumping even if no component is damaged. An enzyme may need periodic replacement because its useful lifetime is finite. A hereditary sequence must retain specific differences while permitting copying and repair. Development can preserve a reliable course of change rather than a fixed adult state. Waddington's term *homeorhesis* refers to this stability of a trajectory; *morphostasis* refers to the maintenance or recovery of form. These concepts should not be collapsed into one notion of unchanging structure. [9]

Continuity has a causal, not merely descriptive, criterion. Two separately assembled cells could look alike without one being a continuation of the other. In a lineage, present records, catalysts, membranes, and spatial organization help generate their successors. The successor need not be microscopically identical. It must retain the relationships on which the specified capacities depend. In a memory experiment this may mean a persistent functional state despite replacement of molecules; in a lineage it includes the transmission of variation on which selection can act.

Turnover is not by itself life. A flame persists while fuel passes through it. An externally maintained reactor may run indefinitely. The further question is whether activities supported by the organization contribute to making or renewing the particular structures that support those activities. That question requires an account of inherited specificity and of usable work.

2. Schrödinger and the Aperiodic Crystal

In *What Is Life?*, Erwin Schrödinger asked how a small hereditary structure could retain many distinct alternatives reliably enough to influence an organism. A periodic crystal repeats a unit. A hereditary record must combine molecular durability with an extensive, nonrepeating sequence of differences. His *aperiodic crystal* named that conjunction before the structure of DNA was known; it was not a claim about modern quasicrystals or a coherent superposition spanning a chromosome. [14]

Bulk regularity often results from averaging many uncertain events. Heredity requires some individual molecular distinctions to survive, because averaging away the distinctions would remove the information to be transmitted. Quantum electronic structure and the exclusion principle help explain the stability of atoms, bonds, and matter in bulk. The exclusion principle states that identical electrons, as fermions, cannot all occupy the same quantum state. Together with electrostatic interactions it is central to the mathematical stability of ordinary matter. These facts apply to minerals as well as to cells. [21]

Durability alone is insufficient. A nucleotide sequence influences the cell because copying, transcription, translation, and regulation respond to its chemical differences. The proteins and other products made through those operations help maintain the apparatus that performs them. A stable record without a working interpreter is not a living system; a working interpreter without a retained record cannot transmit the same range of inherited differences. The physical problem joins stability to selective use and replacement.

Nor is sequence the only inherited material state. Membranes, concentrations, and protein conformations can affect how a sequence is expressed and how a successor is built. Some conformations template the formation of like conformations. The distinction between a hereditary description and an inherited physical state will matter when protein-based inheritance and memory are considered. In both cases a molecular difference must have a demonstrated route to a later functional difference.

3. Von Neumann: Description, Construction, and Copying

John von Neumann studied self-reproduction as an architectural problem. A machine that makes another machine need not transmit the means for that machine to make a third. He therefore distinguished a constructor, a copier of instructions, and a controller that associates the newly built apparatus with a copy of its description. A description is used once as a set of instructions for construction and separately copied as a physical record. The logical separation avoids the regress of needing an instruction to copy an interpreted instruction indefinitely. [15,16]

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Von Neumann used cellular automata, grids of sites updated by local rules, to show how such an arrangement could reproduce. The construction is a logical demonstration. It does not show how a cell obtains feedstocks, couples favorable reactions to costly ones, corrects errors, or replaces its constructor. A rule that supplies a permanent interpreter can hide from view the very renewal cost at issue in an organism. Conversely, the automaton shows that self-reproduction as an abstract organization does not logically require an organism-wide quantum computer.

The biology is less cleanly divided than the model. DNA is copied, but it also participates in a pre-existing cytoplasm with regulatory states, membranes, ribosomes, and energy-converting machinery. A genome is no exhaustive blueprint that constructs an organism without an interpreter or an environment. Still, the distinction between copying a record and making that record effective is indispensable. A mutation can be copied while its consequences depend on the machinery that reads and acts on it.

Direct templating is another architecture. An existing assembly may induce incoming molecules to assume a similar conformation without a separate symbolic description. Some prions and functional amyloids transmit states in this way. A template can preserve a limited state economically; a description-based constructor may support a broader repertoire of products. Langton's simpler reproducing automata similarly show that self-reproduction, universal construction, and open-ended evolution are distinct achievements. [25]

These alternatives expose what a physical comparison must hold fixed: the desired inherited capacity, the available materials and machinery, errors, and the cost of making replacements. A mathematical update rule may reproduce an arrangement while offering no account of whether its material implementation can finish before its parts decay. That missing obligation leads to the work of renewal.

4. Work That Rebuilds Its Machinery

An energetically favorable reaction does not automatically drive a costly one. A coupling mechanism must connect the two so that the free-energy decrease in one process changes the probability or direction of the other. Cells build and maintain such couplings with enzymes, membranes, gradients, and molecular motors. *Useful work* names an output against a specified load, such as chemical synthesis, transport against a gradient, or mechanical displacement. It must be distinguished from total energy consumption.

For a suitably defined open chemical system held at temperature T, one can write a schematic balance

$$\frac{d\mathcal{G}}{dt} = P_{\mathrm{in}} - P_{\mathrm{load}} - T\sigma, \qquad \sigma \geq 0,$$

where $\mathcal{G}$ is stored free energy, P_{in} is supplied free-energy rate, P_{load} is power delivered to the stated task, and σ is entropy production rate. The exact reservoir and boundary conventions matter. At a steady state, energy can pass through the system while its stored free energy remains approximately constant. A stationary concentration similarly need not mean that its underlying reactions have stopped. [7,23]

For a system to maintain itself, some delivered work must support the constraints that make future delivery possible. A catalyst channels a reaction; a membrane channels transport. *Closure of constraints* describes a network in which such relatively persistent structures support processes that, directly or indirectly, help produce and maintain the structures. The concept specifies a dependency, not a claim that the system is materially closed. The system remains dependent on external resources and waste export. Autopoiesis, or self-production, places similar emphasis on the production of the organized unit. [11,13]

A useful test of closure has to count what the experimenter supplies. If an artificial cell receives ready-made catalysts indefinitely, its ATP production does not demonstrate that it can replace the apparatus producing ATP. The same caution applies to a computer model whose controller is written into an unchanging rule. A perturbation and rescue experiment can establish that a component

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is required and restored by internal activity; measured turnover can show whether the restoration replaces a finite-lived apparatus.

One task may compete with another for the same power and material. At high reaction speed, an energy converter may give more immediate output but less time or material for its own repair. Under a cap on input power, no intervention is an advantage merely because a microscopic rate increases. The relevant measurement is the feasible combination of current output, component replacement, error control, and persistence.

5. When a Quantum Explanation Matters

Several claims called "quantum biology" require different evidence. A mechanism claim identifies a quantum-sensitive event: tunneling, for example, permits transfer through a barrier in circumstances for which a specified classical particle model predicts no passage at that energy. Quantum chemistry can also be essential to calculating a reaction even when a coarser classical rate equation accurately predicts downstream concentrations. These are claims about mechanism and description, not yet about an organism's dependence on the mechanism.

Table 1. Distinct claims in quantum biology. Extended coherence is a separate physical claim, not a higher rung automatically implied by biological function.

Claim	Required observation	Useful comparison	Inference still unavailable
Quantum basis of chemistry	Bonding, molecular structure, and selectivity explained by electronic and nuclear quantum mechanics.	A stated coarse-grained description of the same chemistry.	That a particular quantum-sensitive step controls a biological function.
Local mechanism	A specified tunnelling, photochemical, spin, or other quantum-sensitive operation constrained by molecular measurements.	An appropriate classical approximation with its assumptions stated.	That the operation limits pathway output or system survival.
Functional contribution	A selective molecular intervention changes a measured intermediate and a downstream task in the predicted direction.	Perturbations of binding, abundance, geometry, and alternative routes; a buffered condition.	Necessity: compensation may recover the task at acceptable cost.
Constrained necessity	Measured chemistry predicts a sustained output or renewal boundary that an admissible alternative cannot attain within a declared budget.	Credible alternative physical architectures with the same power, material, space, time, and error limits.	A universal claim about all living systems or all possible alternatives.
Extended coherence or entanglement	A specified state, preparation, extent, lifetime, and phase-sensitive observation or valid entanglement witness.	Appropriate classical-wave, stochastic, and separable-state accounts.	A biological benefit without a causal readout and constrained functional comparison.

A biological claim traces a perturbation of that event to a functional output. Isotope substitution, mutation, field variation, or environmental changes may alter a reaction, but each can have several

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effects. An isotope result must be connected to the proposed nuclear motion; a mutation may change binding or abundance as well as tunneling geometry. The causal chain needs controls at each link.

The stronger, resource-constrained claim compares attainable performance. Let $\mathcal{C}$ specify limits of power, material, space, time, and tolerated error, and let $\mathcal{F}_M(\mathcal{C})$ be the performances achievable by a declared class of mechanisms M. A measured quantum-sensitive implementation matters to viability when it reaches an acceptable region of output and renewal that the best admissible alternatives cannot reach under the same constraints. A failed replacement design does not bound all replacements. An alternative with extra enzymes, energy, or time must pay for them in the common accounting.

"Classical" is not one reference class. Classical nuclear trajectories on a quantum-derived potential test a different question from classical electrons without quantum bonding. A stochastic network may use reaction probabilities obtained from quantum dynamics. Classical waves can reproduce some spectroscopic features assigned to quantum coherence. A simulation of a molecule on a computer is also not a physical molecule that performs the task at the cell's power and volume. The comparison must name its reference, observables, and permitted compensations. [28]

The strictest nonclassicality claims have their own assumptions. A violation of a Bell inequality excludes specified local hidden-variable models; contextuality excludes models satisfying a different set of operational conditions. Neither proves that an organism requires entanglement to survive, and neither excludes a classical program that simulates a finite list of observed probabilities. [26,27]

These distinctions keep a short-lived event and an extensive biological consequence in the same account without assigning them the same state. A photochemical product can be a classical record of a quantum transition. Later amplification, feedback, or selection may use that record after coherence has disappeared. The later chapters follow such records into work, inheritance, repair, and renewal; their value is judged by the biological task and by the alternatives actually available.

Part II. From Electrons to Biological Work: The Bioenergetic Spine

6. Stable Matter and Selective Reactivity

A living cell must preserve its components while continually making, modifying, and removing them. Proteins must retain a useful structure through many reactions, yet enzymes must be able to dismantle them when damaged. Membranes must resist leakage while permitting selected molecules to cross. The requirement is neither maximum stability nor maximum reactivity. It is a relation among the lifetimes of components, rates of useful transformations, and rates of damage and replacement.

Electronic structure supplies the material distinctions on which this selectivity depends. Electrons occupy quantum states constrained by electrostatic interaction and the Pauli exclusion principle: identical electrons cannot occupy the same complete one-particle state. These features make bonds, molecular shapes, charge distributions, and the periodic differences among elements possible. The stability of bulk matter also requires quantum statistics, as Dyson and Lenard made precise. [21] This is a foundation for chemistry, not by itself an explanation of living organization. A crystal remains stable without feeding, repairing itself, or reproducing.

Reaction rates are as consequential as stable states. An energetically favorable change may proceed slowly because the available path passes through a high-energy configuration. The activation barrier need not be traversed by classical motion alone. Electronic tunnelling and the quantum distributions of light nuclei can alter the likelihood of products. An enzyme changes that likelihood by placing reactants, charges, hydrogen bonds, and solvent in a suitable arrangement. It can also make a reaction happen in the correct compartment or at the correct stage of a cycle.

The uncatalyzed hydrolysis of model peptide bonds illustrates how long persistence and ready disassembly can coexist. At neutral pH and ordinary temperature the chemical reaction can be exceptionally slow; proteases accelerate related bond cleavage when a protein is to be processed or destroyed. The measured uncatalyzed half-time is not the lifetime of an intact cellular protein, which depends on active degradation and many other processes. [29] Cell biology uses the distinction between intrinsic stability and selective catalytic access.

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Hydrogen requires special attention because of its small nuclear mass. Even in a vibrational ground state a nucleus is not fixed at the minimum of a classical potential. Its zero-point motion and distribution among hydrogen-bond configurations affect water and hydrated macromolecules; nuclear quantum effects have been calculated and experimentally constrained in water, but their direction and size depend on the environment. [30] One cannot infer a particular enzyme effect from the statement that biological matter contains water. Confined water, an active-site hydrogen bond, and bulk solvent present different physical problems.

Some quantum contributions can be incorporated in an effective classical description. Once electronic structure has supplied an energy surface or a measured rate, a classical reaction network may accurately describe subsequent events. This division of labor is useful when the network forgets microscopic phases rapidly. It should not be mistaken for a physical account of how the rate or selectivity arose. Conversely, successful quantum chemical calculation of a bond does not establish that coherence over a larger biological structure improves function.

The comparison follows a complete cycle. If a catalyst accelerates synthesis but makes its own structure more vulnerable to damage, its net contribution may fall. If a membrane channel passes the desired species but also leaks the gradient that powers synthesis, high throughput may be useless. Output must be measured alongside component lifetime, materials consumed, energy spent, and correction of errors. Respiratory metabolism offers a way to follow these quantities from localized electronic transitions to chemical work.

7. Respiratory Electron Transfer

Respiratory chains accept electrons from reduced substrates and deliver them, through cofactors, to an acceptor. In aerobic respiration oxygen is the terminal acceptor. Cells conserve some of the free-energy decrease by moving protons across a membrane. The resulting electrochemical gradient can drive ATP synthesis. Individual electron-transfer reactions are necessary parts of this arrangement; rapid electron flow alone does not show that energy has been conserved.

Complex I, or NADH:ubiquinone oxidoreductase, is a useful case because its electron-transfer route and membrane pumps occupy one large protein assembly. Electrons originating in NADH pass through flavin, a redox-active cofactor, and a sequence of iron–sulfur clusters before reducing ubiquinone, a membrane-soluble electron carrier. An iron–sulfur cluster is a cofactor containing iron ions connected by inorganic sulfides and coordinated to the protein. The protein fixes distances and electrostatic surroundings while permitting structural adjustments during its cycle. Energy released in the redox reaction is coupled to proton translocation in a remote membrane arm. The detailed sequence linking the two remains an active mechanistic question. [143,145]

Donor and acceptor are electronically coupled because their quantum states overlap directly or through intermediate molecular groups. In a nonadiabatic, weak-coupling regime, transfer occurs between initially distinct donor and acceptor electronic states, with a rate proportional to the square of their coupling. It also depends on *reorganization energy*, the energetic cost of adjusting protein, solvent, and other nuclear coordinates to the changed charge distribution. The driving free-energy change is therefore not a sufficient rate predictor. Moser and colleagues showed how distance, reorganization, and driving force explain much of the range of measured biological electron-transfer rates. [33]

A useful schematic expression is

$$k_{\mathrm{ET}} = \frac{2\pi}{\hbar}|V_{DA}|^2 \frac{1}{\sqrt{4\pi\lambda k_{\mathrm{B}}T}} \exp\left[-\frac{(\Delta G^\circ + \lambda)^2}{4\lambda k_{\mathrm{B}}T}\right].$$

Here V_{DA} couples donor and acceptor electronic states, λ is the reorganization energy, and ΔG° is the reaction free-energy change. This Marcus-type expression treats one classical, harmonic regime for environmental coordinates and is not universal for respiratory transfers. It identifies separable contributions. A change in protein geometry may alter electronic coupling; an altered electrostatic environment may change driving force or reorganization.

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A bridge can support *superexchange*, in which intermediate electronic states mediate coupling without becoming populated as long-lived intermediates, or *hopping*, in which charge occupies successive sites. Thermal motion can bring cofactors into favorable configurations in either case. An electron journey across several centers does not imply one electron remains coherently delocalized along the entire complex. Models have estimated tunnelling between complex I's iron–sulfur clusters; studies of electron-transfer rates ask whether individual rates suit efficient energy conversion rather than being as fast as possible. [141,142]

Too slow a transfer can leave an intermediate exposed to competing reactions; too fast a transfer at the wrong place can favor short circuits, back-transfer, or loss of coupling to the pump. The relevant quantity is the fraction of substrate free energy conserved as a usable gradient under the required flux and operating conditions. Comparing sequences, mutating cofactor environments, and measuring redox potentials and kinetics can test whether a particular geometry controls this fraction. An evolutionary hypothesis also needs comparisons across functional and ancestral variants, with compensation counted.

A further difficulty is separating the timing of a redox step from the fraction of turnovers that couple to proton movement. The same average electron-transfer rate can arise from different distributions of distances and protein conformations, and the same mean proton flux can conceal reversals within a cycle. Time-resolved spectroscopy of the cofactors, rapid kinetic measurements of proton uptake, and direct measurements of membrane potential constrain different portions of this sequence. Their concordance gives a more stringent account than fitting one overall oxygen-consumption curve. Complex I, with its distant electron and proton domains, is particularly valuable because a proposed coupling mechanism must explain how a local change reaches spatially separated pumping modules without violating the measured energy balance.

Respiratory chains permit a fair test of microscopic necessity. One might replace a tunnelling-sensitive step with a different series of redox cofactors, adjust cofactor separation, increase complex abundance, or change upstream supply. Such alternatives count if they deliver the same sustained ATP output while paying for extra protein, cofactors, membrane area, substrate, and repair. Failure of one mutant to respire does not establish that all alternatives fail. The physical claim can be narrower and stronger: under specified geometry and resource limits, independently measured quantum transfer parameters determine a conversion yield the alternatives cannot attain.

8. Proton Transfer, Water Wires, and Proton Pumping

Electron transfer can change the preference of a neighboring group for a proton. In *proton-coupled electron transfer*, or PCET, charge and proton motion belong to the same reaction even if they terminate at different sites. They can occur concertedly or sequentially. Concerted transfer can avoid a costly charged intermediate, but concerted is not synonymous with coherent quantum motion. Electron tunnelling, proton vibrational states, solvent rearrangement, and ordinary thermal fluctuations may contribute in different proportions. A model rhenium–tyrosine system showed that even buffer molecules can participate in the proton path. [34]

Proton transport through water differs from moving one marked proton the full length of a pore. Along a hydrogen-bonded chain, successive bond rearrangements transfer excess protonic charge; this is the Grotthuss mechanism. A *water wire* is a connected, suitably oriented set of water molecules and protonatable groups that supports such motion. It can assemble transiently, break, and reform. Structural continuity of a pore does not imply continuity of an individual wire, still less coherent motion of one proton across the membrane. Quantum nuclear effects may alter local transfer probabilities, while protein motions control whether a conducting arrangement exists. [156,157]

Cytochrome *c* oxidase, the terminal complex in an aerobic respiratory chain, reduces oxygen to water. It also transfers protons across the membrane. *Chemical* protons are consumed in water formation, whereas *pumped* protons increase the electrochemical gradient. Counting them separately is necessary for an energy balance. Electron entry, loading of a protonatable site, and gates against

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reverse flow must be coordinated. Experiments have connected pumping to electron-transfer steps, while accounts of the exact routes and timing differ. [146,147]

Complex I similarly links its electron-transfer domain to multiple proton-transfer routes in the membrane arm. Simulations support a role for chains of confined water in long-range pumping, but a simulated hydration route must be connected by experiment to the cycle used by an intact enzyme. Mutating a residue that stabilizes water or alters electrostatics can block pumping for several reasons. Hydration, redox kinetics, proton flux, and assembly should be measured in the same variants before attributing lost function to a quantum effect in proton transport. [144]

Bacteriorhodopsin supplies a different source of energy for the directional task. This membrane protein absorbs light through its retinal chromophore, then follows a cycle of proton transfer and conformational change that pumps protons outward. Its intermediate states show how a photochemical event can be made vectorial: proton access changes sides at different stages. Structural work linked helix deformation and proton movement, although assigning the complete microscopic timing remains more demanding than observing a pump cycle. [154,155]

Selectivity also means preventing proton transfer. Aquaporin-1 allows rapid movement of water while strongly excluding protons; otherwise the water channel would dissipate a gradient. Its pore architecture interrupts an unbroken hydrogen-bonded route and places electrostatic barriers centrally. The detailed partition of contributions is studied by simulation and experiment. [158] A cell thus builds hydrated structures that pass protons and others that pass water while rejecting protons. Conduction and exclusion belong in the same explanation of usable energy.

The gradient is an electrical and chemical store, not a count of translocated particles alone. A proton moved against its electrochemical potential raises free energy; one that leaks back without doing work removes it. If voltage difference is $\Delta\psi$ and the difference in proton chemical potential is $\Delta\mu_{H^+}$, the free energy per mole combines $\Delta\mu_{H^+} + F\Delta\psi$, with a consistent sign convention and Faraday's constant F. Pump output must therefore be assessed with voltage, pH, leakage, and flux measured together.

A solvent isotope effect in a pump is not automatically proof that a proton tunneled through one specified barrier. Replacing hydrogen by deuterium changes the rates of proton exchange, hydrogen-bond rearrangement, water diffusion to some extent, and the distribution of protonation states. An informative experiment predicts which step changes, distinguishes chemical proton uptake from pumped proton release, and tests whether a structural intervention moves the isotope-sensitive step in the expected direction. Direct or spectroscopic measures of transient protonation can narrow the alternatives. A proton route that remains active while its water-wire occupancy is disrupted would challenge a simple continuous-wire account; a route that fails may still require controls for protein folding and altered redox chemistry.

9. ATP Synthase and Molecular Work

Mitchell's chemiosmotic proposal connected respiratory electron transfer to ATP synthesis through the proton electrochemical gradient across a membrane. [139] The membrane stores part of the free energy released by oxidation; ATP synthase converts a portion into formation of ATP from ADP and inorganic phosphate. Membrane tightness and enzyme placement are parts of the mechanism.

ATP synthase has a membrane sector, F_o, and a catalytic sector, F_1. Protons crossing the membrane sector drive rotation of a ring and central stalk relative to a stationary structure. Rotation changes the conformations of catalytic sites in F_1, which bind substrates, synthesize ATP, and release product. The binding-change account emphasizes that useful input need not appear solely in bond formation; the cycle must also reset and release tightly bound ATP. Structural studies and direct observation of F_1 rotation established the main architecture. Details such as elastic strain, step subdivision, leak, and coupling ratio depend on organism and preparation. [149–151]

Its reversibility matters. Under some conditions ATP hydrolysis drives the rotor and pumps protons; under others the gradient drives ATP synthesis. Direction depends on the full free-energy

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balance, mechanical load, and chemical activities. ATP hydrolysis supplies free energy only when coupled to a reaction whose combined free-energy change and kinetics permit progress. An ATP molecule stored without a usable coupling mechanism performs no cellular work.

The link from electrons to ATP can be stated as a measured chain: redox substrate use, electron flux, proton pumping, transmembrane voltage and pH, rotation and catalytic cycling, ATP synthesis, and ATP consumption by maintenance or construction. Each link can lose free energy or introduce noise. A changed electron-transfer rate can increase current without increasing ATP per substrate; a changed pumping route can affect gradient without changing electron turnover; more ATP may be made but lost to compensatory repair. The chain distinguishes a quantum-sensitive molecular effect from an actual contribution to renewal.

An ATP concentration measured at one time is a poor substitute for flux. A cell can hold its concentration roughly steady while production and use both fall, or it can maintain concentration temporarily by drawing down other stores. Isotopic tracing of substrates, oxygen and redox measurements, proton-gradient probes, and ATP production or consumption rates each supply different constraints. Even if every intermediate has been measured, a change in ATP use for protein replacement should be separated from energy spent merely repairing damage introduced by the intervention. Sustained work is the output of interest; instantaneous chemical abundance is one state variable.

For an idealized rotor a full rotation makes a specified number of ATP molecules and consumes a specified number of protons determined partly by its membrane ring. Real operation includes slippage and fluctuations. No common fixed number of protons per ATP should be assumed across species. A bacterial ATP synthase structure illustrates how an actual rotor and catalytic arrangement sets stoichiometric constraints. [153]

ATP synthase is a macromolecular rotor with thermal fluctuations, not evidence that its whole assembly maintains a coherent superposition of orientations. Quantum mechanics determines the chemistry of protonation sites, bonds, and catalysis. A largely classical stochastic model can describe rotor stepping once state-dependent rates have been supplied. A claim that further coherence improves ATP production would need a measurement distinguishing it from this calibrated model.

The work available after ATP synthesis must in part maintain the membrane and respiratory proteins that made its production possible. The membrane must be repaired; enzyme complexes must be made and replaced; damaged proteins removed. Respiratory energy conversion enters living continuity when this feedback sustains the machinery across turnover. Molecular motors make downstream work and its cost especially tangible.

10. Molecular Motors and Cellular Work

Kinesin carries cargo along microtubules, and myosin acts with actin in transport and force production. Both couple cycles of ATP binding, hydrolysis, product release, and structural change to biased motion. Thermal fluctuations contribute to their trajectories. The cycle makes forward steps more likely than reverse ones under load because chemical free energy changes transition probabilities. *Mechanochemical coupling* names this relation between reaction cycle and motion; it does not require that each bond-breaking event produce a fixed classical push.

Single-molecule observations permit forces and step sizes to be measured directly. Optical trapping resolved kinesin steps; later work related approximately one ATP hydrolyzed to an 8 nm step in a characterized regime. Myosin V provides another processive motor that remains attached through successive steps along actin. [172–174] These measurements attach units to work: force times displacement under load, chemical free energy consumed, and successful deliveries per ATP or per motor lifetime.

A motor can move rapidly when unloaded and stall when opposing force becomes too large. Its useful contribution is not its maximum step frequency. Cargo may need to reach a place before degradation, but movement that detaches the motor or expends excessive ATP may reduce deliveries. For force f and step d, fd is mechanical work against a constant opposing force in one step. It omits

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chemical work on the surroundings and many losses. A useful account records delivered cargo, destination and timing, and ATP and motor replacements required.

This supplies a downstream test for a proposed advantage in respiration. If an intervention changes a measured electron-tunnelling rate in complex I, it should not be credited with greater biological work merely because oxygen consumption or ATP level changes. One must follow ATP production under load and ATP-dependent outputs: transport, repair, synthesis, or maintenance of ion gradients. The output may be a stable rate of cargo delivery after respiratory proteins and motors have turned over. Under favorable conditions another fuel route could restore it; the cost of compensation belongs in the comparison.

Stochastic motor models describe many observed steps without retaining phase relationships between successive ATP cycles. They are a strong control. The quantum contribution may reside in making molecular transitions and chemical specificity possible, while a Markov description suffices for stepping. A more demanding claim would identify a quantum-sensitive upstream change that shifts attainable rate, efficiency, or reliability of sustained work under fixed material and energy budgets.

The motor also shows why the spatial organization of work matters. ATP consumed by a motor at a location where no cargo is available cannot be valued in the same way as ATP consumed on a delivery that supports repair. Conversely, a transport system with fewer steps per second may be preferable if it avoids a costly detour or keeps cargo attached under load. Such distinctions can be built into an experimentally calibrated stochastic model. Its rates would already embody the chemistry of ATP binding and hydrolysis. The model can then ask whether an upstream quantum-sensitive change alters the feasible distributions of completed deliveries before deadline, rather than merely shifting mean ATP consumption.

Part III. Catalysis, Photochemistry, and Biological Deadlines

11. Hydrogen Tunnelling in Enzymes

An enzyme can make a reaction reliable by controlling the geometry encountered by a transferring hydrogen. A classical particle with energy below a fixed barrier cannot cross it. A quantum wavefunction extends into the classically forbidden region, so transfer can occur with a probability sensitive to the barrier's height and width, the particle's mass, and the geometry of the reacting groups. In a crude one-dimensional approximation,

$$\mathcal{T}(E) \sim \exp\left[-\frac{2}{\hbar}\int_{x_1}^{x_2}\sqrt{2m\{V(x)-E\}}\,dx\right].$$

This expression is not a complete enzyme rate law. Proteins and solvent fluctuate; reactants occupy ensembles of geometries; transfer changes electronic structure. It does show why modest distance changes and substitution of deuterium for hydrogen can have large effects.

The word hydrogen transfer needs care. Transfer of a proton, of a neutral hydrogen atom, and of a hydride have different associated changes in electron distribution. In each, an appropriate calculation includes the electronic states and nuclear motion of the whole reacting complex. Tunnelling is compatible with thermally driven motion: protein motion may prepare a short donor–acceptor distance, and a light nucleus then tunnels with appreciable probability. A mechanism that requires the protein to sample a special conformation does not claim the whole enzyme maintains a coherent quantum state through the catalytic cycle.

Soybean lipoxygenase has supplied detailed evidence. Its hydrogen-transfer isotope effects and their temperature dependence have been used to infer substantial tunnelling; subsequent work examined how motions beyond the active site change the probability of preparing a suitable transfer geometry. [31,32] The evidence is stronger than a bare assertion that an isotope effect proves tunnelling, because temperature, structure, and dynamics provide further constraints. Yet an isotope changes zero-point energy and bond vibrations as well as tunnelling probability. Mutation can alter substrate

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binding, folding, abundance, and the chemical step. The interpretation depends on a model that accounts for the full set of observations.

Alcohol dehydrogenases and dihydrofolate reductase (DHFR) extend the issue beyond one enzyme. DHFR reduces dihydrofolate in a reaction involving hydride transfer and supports the folate metabolism needed for nucleotide synthesis. Studies of a thermophilic alcohol dehydrogenase related hydrogen transfer to temperature-dependent protein dynamics. These enzymes let investigators vary both the reacting chemistry and the scaffold's preparation of a transfer geometry. [167–169] Claims for a decisive tunnelling fraction should be stated for the particular rate, conditions, and kinetic model. No single isotope effect establishes that a living cell could not obtain the needed product by another route.

Different isotope protocols answer different questions. A primary kinetic isotope effect substitutes the transferred hydrogen; a secondary effect substitutes a nearby atom and may report on geometry or hybridization. A competitive experiment measures product ratios when isotopic substrates react together, whereas separate-rate experiments can be influenced by distinct binding and commitment steps. A large intrinsic isotope effect can be masked in a steady-state turnover assay if product release limits observed turnover. Conversely, a large observed effect can include changes in binding or equilibrium. Pre-steady-state kinetics and independent measures of reactant occupancy help isolate the chemical step. These controls make isotope evidence powerful without treating a mass substitution as a uniquely quantum intervention.

The biological question is whether the quantum-sensitive step changes the probability that a useful reaction finishes before its opportunity is lost. Suppose the productive event occurs at rate k and a competing loss at rate ℓ, with independent exponential waiting times. Then

$$P(\text{productive first}) = \frac{k}{k+\ell}.$$

A twofold change in k matters little if $k \gg \ell$, more if k and ℓ are similar, and perhaps too little if $k \ll \ell$. For a required success probability p_*, the elementary model needs $k \geq \ell p_*/(1-p_*)$. Actual pathways may have broad waiting-time distributions, recycling, substrate depletion, and feedback. The simple race establishes which additional measurements are needed.

The relevant loss can be chemical degradation, disappearance of a transient reactant, removal of a substrate from a compartment, or failure to replenish a cellular component before it decays. Each defines a different endpoint. A tunnelling contribution inferred from the chemical rate must be carried through to correctly made product, pathway flux, and sustained function under that loss. An enzyme may turn over rapidly yet release an erroneous product, or its step may be so far from rate limiting that a large microscopic difference has no effect on final output.

The reference reaction must be physically and biologically admissible. More enzyme can compensate for slower catalysis, but producing it consumes amino acids, ATP, space, and sometimes cofactors. A pathway can use a different enzyme or metabolite, possibly at lower overall efficiency. Blocking such alternatives by definition would make a necessity claim empty. At matched resources and error constraints, a measured tunnelling-dependent change in deadline success would be a substantive result.

12. Evolutionary Tuning of Tunnelling and PCET

An amino-acid substitution can change the donor–acceptor distance, the local electric field, a hydrogen-bond network, or the motions that bring reactants together. Since tunnelling probabilities can depend exponentially on distance, sequence can influence a quantum-sensitive transition without being a quantum code or storing a coherent state. Selection acts on organismal consequences of such changes, including robustness and cost, rather than reading off the mechanism that a physicist later uses to describe them.

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Comparative DHFR studies reported preservation of aspects of protein dynamics through evolutionary change. The observation supports a question about which features of the ensemble are conserved for catalysis; it does not by itself show that tunnelling was the selected property. An ancestral sequence reconstructed from living descendants gives a testable protein, but reconstruction has uncertainty and the historical cellular environment cannot be restored in full. [170,171] A stronger result would combine reconstructed variants, measured transfer kinetics, structural ensembles, and fitness under conditions where folate flux constrains growth.

For PCET, an evolving scaffold may set electron coupling and proton geometry jointly. Moving a proton acceptor can change the free energy of an electron-transfer intermediate; changing a local charge can change where a proton resides. In a concerted pathway these relationships may avoid high-energy intermediate states. The term describes coupled chemical changes, not a universal requirement that the proton and electron remain entangled after reaction. The useful performance measure can be product yield per substrate, avoidance of damaging branches, or ability to meet flux during stress.

A prospective test would choose mutations predicted from measured structural and electrostatic changes to shift a specific quantum-sensitive rate. It would independently measure the local effect, reaction branching, and in vivo function. Rescue with a compensatory mutation could be especially informative if it restores donor–acceptor geometry and function while leaving other features altered. Isotope substitution could then test whether the rescue restored the same mass-sensitive kinetics, provided its effects on binding and network physiology were measured too.

Evolutionary language should be used with restraint. A present enzyme may have quantum-sensitive catalysis because all chemical bonds obey quantum mechanics. Showing that natural selection favored a particular use of tunnelling requires a trait whose fitness consequences can be compared across accessible variants. Even then selection might have favored stability or specificity and retained the transfer rate incidentally. The question is experimentally approachable, but it is not answered by observing efficient modern enzymes.

13. Photosynthetic Capture and Energy Transfer

Photosynthetic organisms absorb photons in pigment molecules and transfer excitation energy toward a reaction center, where charge separation begins a sequence that can store free energy. A photon prepares an electronic excitation; interactions among nearby pigments can distribute that excitation over more than one molecule. The quantum description includes their electronic couplings, vibrational motion, and interaction with the surrounding protein and solvent. The functional endpoint, however, is productive and durable charge separation per absorbed photon under natural operating conditions.

Several forms of coherence must be distinguished. *Electronic coherence* relates electronic excitation states with a definite phase relation. *Vibrational coherence* concerns motions of nuclei. *Vibronic coherence* involves coupled electronic and vibrational degrees of freedom. Ultrafast laser spectroscopy can prepare and read coherent signals that differ from those generated by sunlight. An oscillation in a spectroscopic trace does not identify which states interfere or show that their phase relation improves physiological yield.

The Fenna–Matthews–Olson complex in green sulfur bacteria is a tractable pigment–protein system. Its spectroscopy provoked interest in long-lived electronic coherence. Later measurements separated distinct contributions and assigned the persistent oscillations chiefly to vibrations while finding shorter electronic coherence. Work on bacterial reaction centers likewise showed that a long-lived beat can witness vibronically excited energy transfer without documenting a long-lived electronic path between sites. [35,36] A critical ambient-temperature analysis found no reliance on long-lived electronic coherence for energy transfer in the system tested. [178] These results do not make electronic coupling irrelevant. They constrain the claim that a persistent electronic wave is the source of the observed functional yield.

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Environmental motion can aid transport in some models. An excitation may become trapped when disorder keeps it localized; fluctuations can sometimes move it into a configuration with better access to an acceptor. The resulting *environment-assisted transport* is conditional on coupling, disorder, and the definition of useful output. [37] Too much noise degrades transfer, and a mathematical optimum need not be where an actual organism operates. Biological conclusions require experimentally constrained parameters and a measurement of charge separation, not simply a model showing that noise can help in principle.

The distinction between wave dynamics and a uniquely quantum functional signature is especially stringent here. Coupled classical oscillators can reproduce some coherent transport features and spectroscopic patterns. [28] Such a comparator is not a claim that pigment electronic transitions are literally classical. It asks which observations require phase-sensitive quantum dynamics beyond what a calibrated classical wave or stochastic model captures. Independent perturbations of vibrational coupling, pigment energies, and environmental fluctuations can separate rival mechanisms if their predictions are fixed before comparison.

One should also count the full light budget. Efficiency of excitation transfer conditional on absorption differs from light-to-biomass conversion; the latter includes collection, charge separation, chemical storage, carbon fixation, damage, and repair. A quantum change that increases transfer may simultaneously raise photodamage or demand more protein replacement. Under low natural illumination and physiological temperature, productive charge separation and sustained growth are meaningful tests. Under ultrafast, coherent pulse excitation, spectroscopy remains an invaluable probe of mechanism but should not be assigned the organism's usual preparation conditions.

14. Vision: A Prototype Quantum-to-Classical Latch

A rod photoreceptor can produce an electrical response to a single absorbed photon. Baylor and colleagues measured such responses, and Rieke and Baylor examined how their amplitude becomes sufficiently reproducible despite molecular stochasticity. [3,4] The cell does not keep a photon's quantum state intact through its response. Absorption changes the state of the retinal chromophore in rhodopsin. That change is recorded in a molecular configuration, which initiates a biochemical cascade and alters membrane current.

Retinal photoisomerization changes the arrangement about a double bond. Its early excited-state motion reaches a *conical intersection*, a region where electronic energy surfaces approach or meet so that electronic and nuclear motion can rapidly change the molecule's electronic state and geometrical outcome. Ultrafast measurements resolved these early dynamics. [2] The physical interval is extremely short compared with the photoreceptor's electrical response. Persistence of the effect lies in the altered molecular state and downstream reactions, not in a coherent photon–rod state surviving until a signal reaches the brain.

The cascade provides gain: activated rhodopsin changes the activity of multiple downstream molecules, which changes cyclic nucleotide concentration and the opening of ion channels. Gain alone would amplify dark noise too. Shutoff and feedback regulate event duration and variability so that the cell can distinguish signal from background. The output is an electrical change integrated by neural circuitry, and single-photon sensitivity can be traced through that chain without attributing quantum computation to the retina.

The example shows precisely how an individual quantum event can escape indiscriminate averaging. A detector selects an absorption event; a chemical state records it; an amplification network propagates its consequences. If absorption never happened, no later mechanism could recreate the same record by amplification alone. Conversely, once the molecular state has changed, a classical stochastic model may describe much of the subsequent cascade. A classical description of the response is compatible with a quantum cause.

There are limits to the analogy. Vision uses external photons and specialized cells; many reactions elsewhere occur in populations with no one-event sensory report. The shared physical structure is not

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a universal quantum advantage but the possibility of retaining a selected microscopic difference. For each other case, one must identify the intermediate record, its lifetime, the gain mechanism, and the cost of false positives.

15. Photoprotection and Photorepair

Light can damage the molecules it helps organisms use. Absorption creates excited electronic states that may transfer energy usefully, relax harmlessly, or form reactive products. Fast deactivation can therefore be as valuable as extended transport. DNA and RNA bases have pathways that release excitation through nonadiabatic motion, in which nuclear movement enables transitions between electronic states. Conical intersections are often central to these calculations. Theory and spectroscopy study the routes by which ultraviolet-excited nucleobases return to lower-energy states, but a calculated short lifetime in an isolated base should not be equated with complete protection of DNA in a cell. [38]

A productively rapid pathway can reduce the time available for harmful photochemistry, yet quenching alone is not enough. It can generate other reactive states, interfere with useful photochemistry, or depend on surrounding base sequence and hydration. The appropriate endpoint is damage yield under a specified light spectrum and molecular environment. A photoprotective explanation should compare all accessible reaction branches and then ask what damage reaches cellular repair.

Photolyase provides a distinct, restorative process. It binds a particular light-induced DNA lesion and uses absorbed light to initiate electron transfer from a catalytic flavin cofactor. Transient charge changes allow cleavage of the lesion's abnormal bond; electron return and enzyme reset leave restored DNA. Ultrafast experiments measured steps underlying high repair efficiency. [39] Photolyase chemistry is not simply the same as spontaneous nucleobase deactivation. One prevents some lesions; the other repairs an existing structural record of damage.

The repair outcome is a durable molecular difference: a lesion has been removed from the hereditary substrate. The electronic excitation and charge-separated intermediates need not retain coherence beyond the brief chemical process. Their causal effect persists through restored covalent structure. To infer a contribution to organismal fidelity, however, one must connect repair kinetics to lesions escaping repair, subsequent replication errors, and survival under repeated damage. A fast isolated enzyme can have little effect if lesion recognition or access limits the pathway.

Rates of photoexcitation and repair also set competing deadlines. The damaged DNA can be copied before repair or become inaccessible; the excited enzyme can back-react before bond cleavage. A quantum-sensitive change in electron transfer could shift which event wins. Several routes can compensate, including nucleotide excision repair and behavioral or pigment-based shielding, each with different costs. The biological claim should say which lesion, light conditions, and alternatives are in view.

This system permits a useful separation of mechanistic and functional experiments. Electron-transfer kinetics can be studied with purified photolyase and defined lesions; repair can then be measured in DNA substrates with sequence contexts and chromatin access; finally the frequency of lesions that remain at replication can be tested in cells. A variant that changes flavin transfer but also loses lesion binding cannot distinguish those mechanisms. Similarly, increasing illumination may speed the enzyme while creating more lesions elsewhere in the cell. The denominator should be damaged sites available for repair, and the functional numerator correctly restored sites before copying or further damage.

This paired case corrects any assumption that useful quantum biology always seeks to preserve an excitation. The controlled electronic event may end almost immediately, leaving either an undamaged molecule or a repaired one. What matters downstream is the chemistry of the record.

16. Spin Chemistry and Weak-Signal Sensing

An electron has intrinsic angular momentum called spin, which determines magnetic interactions and affects chemical reaction rules. When two radicals are created in a correlated process, their two

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unpaired electron spins can combine to total spin zero (singlet) or one (triplet). *Hyperfine interactions* couple an electron spin to nearby nuclear spins. Along with external magnetic fields, they alter how the pair's spin state evolves. If reaction products have different probabilities from singlet and triplet configurations, changes in spin dynamics become changes in chemical yield.

The radical-pair mechanism can respond to a field whose energy scale is much smaller than $k_B T$ because it concerns a prepared, transient, nonequilibrium reaction, not the equilibrium alignment of an ordinary magnetic particle. The field may change reaction branching without supplying chemical energy. This does not mean thermal motion is irrelevant: spin relaxation, molecular orientation, radical lifetime, and surrounding reactions can erase sensitivity. Quantitative predictions require these parameters and the field direction and magnitude.

Cryptochromes are flavin-containing light-sensitive proteins. In a migratory songbird's cryptochrome 4, experiments measured magnetic sensitivity of photoinduced radical chemistry, supporting a plausible sensor within the avian compass hypothesis. [46] This is a stronger molecular connection than a general claim that birds navigate, but it is not yet a complete explanation of a bird's directional choice. The physiological site of preparation, molecular partner in the radical pair, orientation, downstream transduction, and behavioral dependence must be joined in the same causal account.

Weak-field experiments in planarians address a different biological setting. A 2026 study tested predictions for effects on superoxide during regeneration. [47] Superoxide is a reactive oxygen species that can signal and damage. A field-dependent redox measure is potentially an intermediate between spin chemistry and tissue response; it neither identifies every radical in the pair nor establishes that a change in superoxide caused altered regeneration. Probe chemistry, illumination, oxygen, and competing redox routes must be controlled. A mechanism-specific intervention that suppresses the proposed radical pair while preserving ordinary metabolism would be particularly informative.

Here a genuinely quantum detector can have an ordinary biochemical amplifier. A small shift in radical product ratios may change a regulatory pathway, cell state, or tissue response. None of those later stages has to preserve spin coherence. A strong test measures the radical intermediates, products, signaling response, and function under the same controlled perturbations. Agreement at the tissue endpoint cannot substitute for missing molecular evidence.

One can also distinguish a magnetic detector from a generic stress response by examining field direction, frequency, and action spectrum. A radical-pair model predicts how orientation and hyperfine couplings should enter reaction yields; a thermal or mechanical artifact need not share that pattern. Isotopic substitution of a nucleus with different spin can in principle change hyperfine dynamics, but it may also alter mass-dependent chemistry. Such controls have greatest force when the radical species and its lifetime are already characterized. Even compelling spin-sensitive chemistry in an isolated protein leaves open whether endogenous light, expression, orientation, and signaling place the effect within the operating range of the organism.

Chirality-induced spin selectivity, abbreviated CISS, supplies a related but distinct mechanism: transport of electrons through a chiral molecular assembly can depend on spin. Chiral means that the structure cannot be superposed on its mirror image by rotation. Spin-selective transmission has been measured in prepared DNA monolayers. [48] The existence of a contact-dependent laboratory effect is not proof that native DNA uses it to improve repair or energy conversion. Orientation, electrodes or biological contacts, charge supply, and electron destinations have to be reconstructed in the actual physiological arrangement.

There is a useful division between the two subjects. Radical-pair sensing has a specified weak-field input and chemical-output hypothesis with strong physical motivation; CISS studies can identify spin-selective electronic transport in chiral structures but often have a larger gap to native biological function. Both may eventually belong in one account of sensing or redox control, but neither should be credited with whole-organism advantage on spin measurements alone.

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17. Olfaction and Other Contested Sensory Claims

Odor receptors distinguish molecules through binding, conformational response, and the cellular transduction that follows receptor activation. A proposed additional mechanism is vibration-assisted electron tunnelling: a receptor would use electron transfer whose probability depends on a vibrational mode of the bound odorant. The distinctive idea is not that molecules vibrate, which all do, but that an inelastic tunnelling event exchanges a specified quantum of vibrational energy and thereby contributes to odor discrimination.

Behavioral work in *Drosophila* reported effects interpreted as evidence for vibrational sensing; receptor-level work and chemical comparisons challenged that reading. [50,51] Isotope substitution is attractive because isotopologues can have similar shapes and different vibrational frequencies. It is not a clean switch for inelastic tunnelling: isotopes can also alter binding, diffusion, impurity profiles, metabolic conversion, and perceptual learning. A positive behavioral distinction does not identify the transfer step; a negative result with particular receptors does not rule out every receptor.

A discriminating experiment should specify a receptor, donor and acceptor states, the electron source, an odorant vibration that predicts a quantitative response, and an independently measured charge-transfer intermediate. Isotopologues and structurally related compounds would then be compared across receptor variants whose predicted tunnelling geometries differ. Binding and receptor expression would be measured separately. Predictions for response amplitude, temperature, and isotope pattern should be registered before the functional comparison.

If classical binding and conformational dynamics reproduce the results, the vibrational tunnelling proposal should be narrowed or rejected for that system. The monograph's broader account does not depend on its success. Its usefulness is methodological: it requires the same standard for attractive positive examples as for disputed ones. Where a quantum-sensitive transition is observed, the downstream response and admissible alternatives still need measurement; where those links cannot be found, molecular possibility is not a biological explanation.

Part IV. Fidelity, Repair, and Two Forms of Inheritance

18. Rare DNA States and the Complete Error Ledger

A copied sequence is a physical record, and its fidelity depends on more than the stability of the bases. Polymerases must expose and read the record; reactive intermediates must discriminate closely related substrates; incorrect products must be removed before they become permanent. Quantum chemistry enters at several stages. It can help create an error, prevent one, or supply a selective reaction used to repair it. A final mutation rate cannot by itself identify which role it played.

The bases of DNA have preferred patterns of proton placement and hydrogen bonding. A *tautomer* is an alternative arrangement of protons and bonding within the same base. A rare arrangement can permit a mismatched pair to resemble the geometry ordinarily accepted for a correct pair. Kimsey and colleagues resolved transient, Watson–Crick-like mismatches in nucleic-acid duplexes. Their observation bears on the existence and lifetime of a misleading molecular configuration. It does not determine how frequently that configuration enters an active polymerase, nor whether its protons arrived there by tunnelling. [42]

Proton tunnelling means passage through a classically forbidden part of a potential-energy barrier, described by the proton's quantum wavefunction. Its probability depends on barrier shape, electrostatics, nuclear motion, and coupling to the surroundings. Slocombe, Sacchi, and Al-Khalili modeled proton tunnelling in DNA as an open-system process, allowing environmental interactions to alter the protonic state. Their calculated transitions establish a physically specified possible contribution to rare states under the model's assumptions. They do not count mutations in an organism. [43]

To connect the molecular state to inheritance, follow the entire sequence of conditional events. Let R denote formation of a rare pairing state, I insertion of an incorrect nucleotide while that state is

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present, P survival through polymerase proofreading, M survival through cellular mismatch repair, and F fixation in a later replication. A schematic contribution to a substitution frequency is

$$p_{\text{fixed},R} = P(R)P(I \mid R)P(P \mid I, R)P(M \mid P, I, R)P(F \mid M, P, I, R).$$

The expression is an accounting identity for a specified causal route, not an assertion that the factors are independent or that all mutations follow it. A state can form often but be short-lived; an erroneous insertion can occur but be excised; a mismatch can escape local proofreading but be repaired later. The organism measures the surviving error, while an experiment on isolated bases measures only part of the ledger.

Polymerase proofreading commonly uses an exonuclease activity to remove a recently inserted incorrect nucleotide. Mismatch repair subsequently recognizes and corrects errors that escaped incorporation-stage controls. Both impose energetic and temporal costs. They also create distinct opportunities for a quantum-sensitive change to matter. An alteration in proton transfer might change rare-state occupancy yet leave the fixed mutation rate unchanged because the repair system compensates. Another alteration could change repair-protein chemistry without altering the initial mispair. Observing the same final error rate in the two cases would conceal different burdens on the cell.

Sequence context complicates attribution. Neighboring bases change stacking, local flexibility, hydration, and electrostatics. Those changes can influence tautomer formation, polymerase selection, repair recognition, and the frequency with which the region is copied. Szekely and colleagues' sequence-specific study relates conformational fingerprints to cancer mutational signatures. Such associations generate testable predictions; they do not establish that proton tunnelling caused a particular mutational signature. [44]

An isotope substitution can change nuclear quantum behavior, but it may also alter vibrational frequencies, hydrogen-bond geometry, reaction equilibria, enzyme kinetics, and growth. Evidence for a tunnelling contribution therefore calls for more than an isotope effect in a final phenotype. A stronger design measures the candidate intermediate, its lifetime and incorporation, the subsequent correction steps, and the surviving error under the same perturbation. An independently calibrated molecular model should predict changes across temperature, sequence context, and polymerase or repair backgrounds before the organismal result is examined.

The same care applies when a quantum transition improves fidelity. Electronic structure makes the bases sufficiently distinct for recognition, while selected electron or proton transfers can drive repair. One should not assign the adjective *beneficial* to the microscopic transition without specifying which downstream event it changes. Biology retains some molecular differences and erases others. The fidelity of heredity belongs to that whole sequence of operations.

The ledger also separates the time at which an error arises from the time at which it becomes heritable. A lesion on one strand may be corrected using the opposite strand before replication; after replication, the same chemical alteration may leave a daughter molecule with a changed sequence. The relevant race depends on cell cycle, strand identity, and the availability of an undamaged template. A rare-state experiment should state whether its endpoint is anomalous pairing, incorporation, surviving mismatch, or fixed substitution. Rates measured at one endpoint cannot simply be assigned to another. This is especially important when attributing disease patterns to a microscopic quantum mechanism: several layers of selection and repair lie between the proposed transition and a tumor sequence.

19. Kinetic Proofreading and Translation as a Classical Control

The ribosome translates an RNA sequence into an amino-acid sequence by accepting transfer RNAs, each bearing a candidate amino acid and a three-base anticodon. A near-cognate transfer RNA can pair imperfectly with the message yet resemble the correct candidate closely enough to bind. Aminoacyl-tRNA synthetases face a related problem upstream: they must attach the correct amino acid to the correct transfer RNA. These are demanding discrimination tasks carried out by driven molecular

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networks. They establish a serious baseline for any claim that quantum information processing is needed to achieve biological specificity.

Hopfield's kinetic proofreading mechanism uses a sequence of recognition and driven reaction steps. A wrong candidate that initially binds may dissociate at a later stage before irreversible acceptance. Because energy expenditure drives the cycle away from equilibrium, selection can exceed what one equilibrium binding comparison would permit. The mechanism does not require a molecule to inspect a proposed product. Its rates and branches determine which products survive. [41]

An elementary example has a correct and an incorrect candidate, each with a binding step, an energy-consuming transition, and a final acceptance step. If incorrect candidates dissociate faster at both waiting stages, the accepted population can be much more selective than the initial bound population. The improvement costs time, discarded substrates, and free energy. Repeated stages can improve fidelity further, but only within the constraints imposed by finite reaction time and available fuel. A claim that a mechanism improves accuracy must therefore state its throughput and dissipative cost as well.

Modern translation contains more than this elementary scheme. Geometry and conformational changes in the decoding center affect initial selection, while GTP hydrolysis and subsequent rearrangements provide further opportunities for rejection. Aminoacyl-tRNA synthetases can use separate editing reactions to hydrolyze a wrong amino acid or mischarged transfer RNA. These reactions depend on quantum-derived molecular chemistry, as all enzyme reactions do. Their system-level logic can nevertheless be represented as a network of classical probabilities over binding, hydrolysis, rejection, and incorporation records. A proposed coherent discriminator must explain a functional observation that this calibrated network fails to explain.

It is tempting to call every expenditure of energy "error correction." The term needs a specified error and a stated reference: errors among nucleotides, among charged transfer RNAs, among accepted amino acids, or among finished protein products. Correction after a bad amino acid has entered a polypeptide has different consequences from rejection before peptide-bond formation. Waste and timing also matter. A synthetase that achieves high accuracy by hydrolyzing nearly every substrate may be unusable under a restricted energy supply.

The translation comparison makes a general methodological point. A quantum effect at the level of bond formation may be established by a mechanistic experiment, yet the larger network may already use the outcome as an ordinary stochastic event. This would be a genuine molecular quantum contribution, with no need to infer preserved coherence through the ribosome. A stronger claim would show that a defined quantum-sensitive intervention changes the attainable fidelity–speed–energy relation beyond what an admissible rate-calibrated network or alternative enzyme architecture can provide. The burden includes measuring the molecular change, the accepted-product distribution, and the cost of compensation.

This control does not make quantum chemistry irrelevant. It locates its causal role. Electronic and nuclear structure set the differences between reactants and the barriers among states. Evolution can tune these differences by changing active-site geometry. Proofreading then uses the resulting rates through a driven sequence that admits a classical description at the scale of recorded events. The separation will matter again when DNA itself serves as an extended medium for reaction and repair.

The comparator can be specified without pretending that chemistry is classical at all scales. Measure or calculate elementary forward, reverse, and rejection rates in a defined molecular environment, then use those rates in a chemical master equation, which follows probabilities of discrete reaction states. It predicts product counts, error correlations, energy expenditure, and waiting times. Its rates may have been derived from quantum mechanics. If the outputs agree under interventions that change geometry, retained phase across proofreading stages adds no demonstrated explanatory value. If they fail in a phase-specific manner, a retained-state model earns consideration. A good cellular-scale stochastic model does not imply that chemistry could have produced the same rates without quantum mechanics.

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20. DNA as an Extended Physical Medium

The DNA sequence is read as a record, but its stacked bases also form a coupled electronic and mechanical structure. An event at one position can depend on intervening sequence, stacking, hydration, and bending. "Long range" can refer to several distinct measurements: the spatial extent of an electronic state, the distance traversed by charge over successive steps, or the range over which a biological response is coordinated. One of these does not measure the others.

Table 2. Three distances described as "long range" in DNA. They are different observables and should not be treated as one coherence length.

Quantity	What is measured	Example in this chapter	What it does not establish
Extent of one electronic state	The spatial support and phase properties of an electronic excitation under a specified preparation.	Photoexcitation distributed over neighboring bases in prepared nucleic acids. [67]	A repair signal, charge transport across the same distance, or persistence during replication.
Distance of charge transport	Net charge passage through DNA, which may involve several localized hopping steps as well as short-range tunnelling.	Electrochemical transport over prepared DNA assemblies of roughly 100 base pairs, sensitive to mismatches. [65]	Coherence over the full route or the same performance inside a chromosome.
Range of functional coordination	An effect of charge-dependent protein interactions on binding, redistribution, or repair.	An effective range of roughly 3,509 base pairs inferred from repair-protein binding behavior. [18,19]	The extent of one wavefunction, or a direct measurement of repair benefit in vivo.

Charge transport through DNA can proceed through different regimes, including short-range tunnelling and longer-range multistep hopping. Electrochemical assemblies show that intervening mismatches can suppress charge passage. Slinker and colleagues measured transport over assemblies spanning roughly one hundred base pairs and found sensitivity to mismatches. This establishes a property of prepared DNA under the experimental conditions; it does not demonstrate chromosome-length electronic coherence inside a cell. [65]

The Barton research program asks whether DNA-mediated charge transport helps replication and repair proteins sense the integrity of the substrate. Some repair proteins carry iron–sulfur clusters, metal assemblies able to change oxidation state by losing or gaining an electron. In a proposed search process, DNA-bound proteins exchange charge through an intact segment, changing binding affinities and redistributing proteins; a lesion interrupts the communication and favors accumulation nearby. Sontz and colleagues obtained experimental evidence for repair-protein redistribution linked to charge transport. Tse and colleagues inferred an effective range of roughly 3,509 base pairs from binding behavior. That is a functional coordination range in the tested system, not the measured spatial size of one delocalized wavefunction. [18,19]

The putative advantage is a reduction in lesion-search cost. A repair protein searching only by diffusion and local recognition must encounter many intact sites. Redox-mediated redistribution could reduce time spent in regions whose intervening DNA supports the charge signal. Whether the process does so in vivo, under endogenous concentrations and competing damage, is an empirical question.

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The useful outcome is faster or more reliable repair at a given protein and energy budget, rather than transport distance by itself.

Mechanical alternatives also extend the consequences of a local event. DNA can transmit changes in twist, bending, and binding through its polymer structure. Rosenblum and colleagues demonstrated long-range allosteric coupling in a DNA regulatory system. *Allostery* here means that a structural change at one location alters a reaction or binding event at another. It is a substantive comparator, not an inferior explanation to be dismissed because it is described classically. [66]

Sequence substitutions usually change both mechanical and electronic properties. A clean comparison therefore needs separate probes of redox state, charge passage, conformation, protein occupancy, and repair success. Redox-inactive protein variants, damaged but mechanically controlled DNA, and externally imposed potentials can help isolate causal steps, provided the perturbations do not introduce new gross defects. Predictions should distinguish the two routes before fitting the final search result.

Photoexcitation can also distribute an electronic state over neighboring bases. Buchvarov and colleagues observed such behavior in prepared nucleic-acid systems. It demonstrates that an independent-base approximation can fail in an optical experiment. The state need not persist during ordinary replication, and its biological consequence could be damage or dissipation. [67]

Thus a transient electronic effect may influence a distant binding decision or repair event without supplying a durable genetic or epigenetic memory. For persistent regulation, the event must alter a longer-lived chemical state or a self-maintaining feedback process. Proposals of a quantum-physics layer of epigenetics, such as that of Siebert and colleagues, should identify this record and distinguish its persistence from the brief electronic dynamics that initiated it. [68]

DNA's extended physical organization matters because the immediate nucleotide is not always the whole reaction context. To establish its contribution to heredity, the measured electronic or mechanical intermediate must be connected to lesion location, correction, and the surviving record. The relation between sequence and physical state also prepares the comparison with a second, more direct way for an existing arrangement to produce its successor.

The distinction between electronic extent and functional range has a practical consequence. Charge can hop through transient local states and affect a distant protein without coherence on that scale. Conversely, a prepared optical state can be delocalized over several bases without sending a useful repair signal. A signal requires a source, a route, a responsive receiver, and an effect on repair. These should be measured under plausible redox potentials and protein occupancies. Their separation makes the biochemical claim stronger and more testable than the general assertion that DNA conducts.

21. Conformational Inheritance: Prions and Functional Amyloids

An amino-acid sequence specifies a range of structures rather than one inevitable shape in every setting. Existing protein assemblies can favor the incorporation of newly made molecules into a similar arrangement. If the arrangement and its consequence survive transmission, conformational state becomes an inherited variable alongside sequence. The sequence remains necessary to supply compatible protein; the older structure helps determine which of its possible states is realized.

Tanaka and colleagues demonstrated that distinct conformations of an infectious prion protein can determine distinct strain properties. In this setting the transmitted difference is not a different gene sequence. It is an organized state of material that recruits successor material. [17] Direct templating differs from the use of a separate description read by a constructor: the present arrangement participates in producing a corresponding arrangement. Neither mode is independent of its cellular setting.

An *amyloid* is an ordered protein assembly often characterized by a cross-beta arrangement of strands. The structural designation does not itself establish inheritance or disease. A *functional amyloid* has a demonstrated physiological role; a *prion-like* assembly shares some recruitment behavior; a *prion* claim requires evidence that a distinguishable state propagates and is transmitted under the stated

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conditions. Sequence regions called prion-like domains motivate experiments but are not proof of propagation.

Halfmann and colleagues found prion-based phenotypic differences in wild yeast, including advantages under some tested conditions. Yuan and Hochschild demonstrated prion behavior of the bacterial regulator Rho in an experimental system. These findings broaden the repertoire beyond one laboratory strain or mammalian disease. They do not establish that every organism possesses the same widespread, independently functioning prion layer. [53,54]

Cellular help can be indispensable. Yuan and colleagues found that propagation of a yeast prion state in bacteria depended on the chaperone ClpB. A chaperone is a protein that assists folding, remodeling, or handling other proteins. The seed does not manufacture that chaperone, its amino-acid supply, the translation machinery, or the energy on which these depend. [52] A transmitted state may be a small hereditary module while relying on an extensive inherited and maintained environment.

Functional assemblies illustrate different relations between structure and benefit. MAVS polymerization supports an antiviral signal by recruiting further signaling molecules. PMEL-associated amyloid helps organize melanin, and ordered aggregates can store peptide hormones. Inheritance across cell generations is not established by these functions alone. A signal can amplify through recruitment and then be cleared; a storage assembly can serve its function by controlled release. [60–62]

There is no inference from templating to collective quantum computation. Molecular interactions and hydrogen bonds necessarily rest on quantum chemistry. An additional claim that proton tunnelling, electronic delocalization, or retained coherence controls propagation needs a discriminating measurement. Pinotsi and colleagues related organized hydrogen bonding and proton transfer to optical properties of protein structures; the result identifies a structural quantum-sensitive effect, not a demonstration that amyloid inheritance depends on an assembly-wide coherent state. [64]

The important contribution to the present argument is a second physical route for maintaining difference through turnover. Sequence controls component supply; structural history can influence the state of the supplied components; chaperones and regulators determine where the state persists. These are coupled channels of inheritance. Their causal roles can be separated by transferring a defined seed into different sequence and cellular backgrounds, measuring recruitment, and asking whether a functional distinction persists under replacement.

Transmission must also be distinguished from repeated induction. If two daughter populations develop the same aggregate because they inherit the same stress response, their similarity need not imply that one inherited a conformational seed. A discriminating experiment varies the parental seed state while matching sequence and subsequent environment, then tests whether the offspring state follows the seed. Where removing the seed also disrupts a regulator, rescue with a structurally defined variant helps separate the effects. The measured distinction may be a biochemical output, growth in a specified environment, or passage through generations; each supports a different scope of hereditary claim.

22. Memory Through Molecular Turnover

A memory lasting longer than its molecular components needs a renewal mechanism. The problem does not depend on a theory of consciousness. A synapse, cell, or tissue retains a difference from its former state only if present material carries information that affects its successors. Crick drew attention to this turnover problem; Lisman analyzed how a kinase network might help maintain an active regulatory state as molecules are replaced. A *kinase* transfers phosphate groups to substrates, often changing their activity. Feedback can perpetuate a molecular distinction without making any participating molecule immortal. [55,56]

Orb2, a protein in the CPEB family, provides a more direct structural example. CPEB proteins regulate translation, the production of proteins from RNA templates. Hervás and colleagues determined the structure of assembled Orb2 isolated from adult *Drosophila* brains and linked assembly to a

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change from translational repression toward activation; the assembled state could seed further active assembly. The result connects molecular form, recruitment, and functional output. It does not show that one Orb2 fiber contains a complete behavioral memory. [20]

Assembly itself is regulated. Patton and colleagues found that the J-domain protein Funes contributes to physiological Orb2 amyloid formation and memory-related function in flies. A J-domain protein helps control chaperone systems. The finding brings the cell's handling machinery into the mechanism; effects of the perturbation need not all pass exclusively through Orb2. In mice, Fioriti and colleagues linked CPEB3 to protein synthesis and persistent hippocampal plasticity and memory. The different species, proteins, and endpoints should not be combined into a single assertion about the molecular content of human memory. [57,58]

There are several distinct persistence claims. A purified assembly may seed more assembly. A regulated assembly may remain at a synapse while new protein is supplied. A functionally identified synaptic state may persist after most of its original molecular carriers have been replaced. Demonstrating the first or second does not prove the third. A small undetected old core may be sufficient to seed new material. Such a core can still be part of effective biological renewal, but the experiment should report what fraction of old material might remain below its detection limit.

A minimal recruitment model makes the distinction visible. Let s be the fraction of a maintained population of carriers in a marked state; let marked carriers recruit unmarked ones at rate $\alpha s(1-s)$, while loss and replacement by initially unmarked carriers remove marks at rate δs. Then

$$\dot{s} = \alpha s(1-s) - \delta s, \qquad s_* = 1 - \frac{\delta}{\alpha} \quad (\alpha > \delta).$$

The original carrier population can decay approximately as $e^{-\delta t}$ while the mark approaches the positive equilibrium. The model assumes an external supply of replacements. It is not a bistable memory in its deterministic form: zero is unstable above threshold, and finite populations can still lose the mark. It isolates state succession from material identity, rather than reproducing the full Orb2 apparatus.

A useful experimental test would induce a localized functional state, label the original molecules, and follow both structure and output through measured replacement. Selectively disrupting recruitment after induction, without broadly suppressing protein synthesis or neural function, would test whether templating maintains the state. Spatially resolved measurements matter because a protein's state at one synapse need not specify which synapse bears a memory. Erasure must also be possible at appropriate times; indiscriminate durability is a pathological property as readily as a useful one.

Any quantum hypothesis about this process should specify which operation it changes: entry into an assembly, fidelity of templating, regulated disassembly, localization, or energetic cost. Long-lived behavioral effects are no evidence that the underlying molecular quantum state remains coherent for the same duration. The retained variable may be a classical structural record continuously rebuilt through local chemistry.

Long-term persistence of a behavioral capacity establishes a property of a nervous system. Persistent assembly of a candidate protein establishes a molecular property. The causal bridge requires selective perturbation, temporal ordering, and rescue, ideally with the same spatial precision as the putative memory trace. If assembly is needed during induction but not maintenance, it does not solve the turnover problem in the proposed way. If needed during maintenance, a further measurement must identify whether new material joins the state as old material leaves. This would bring continuity through turnover down to a tractable molecular history.

23. Pathological Propagation as a Counterexample

An inherited state can succeed as a propagator while damaging the organization that supplies its substrate. Prion disease makes this distinction plain. Li and colleagues observed variation and selection among prion populations in cell culture without requiring a nucleic-acid genome in the

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propagating agent. Selection favored the relative success of protein states under those conditions; it did not favor the host's continued function. [59]

The relevant boundary must be stated. A seed may convert other proteins and spread through a culture while depending on an evolved cell for synthesis, chaperones, compartments, and energy. Persistence of the seed is neither autonomous metabolic renewal nor an organismal good. The same physical capacity for ordered assembly can serve antiviral signaling, storage, or neural regulation when formation, localization, reading, and clearance are controlled. These are differences in the larger causal organization, not in whether aggregation has a morally favorable name.

Pathological spread also restrains a loose use of *teleology*. A process can tend toward more copies because its local reactions favor recruitment. To call it a maintenance function of a host requires evidence that interrupting it impairs the host's viable activity and restoring the relevant operation rescues that activity. A self-propagator can meet the first description while failing the second. The distinction will matter when the later chapters speak of renewal and adaptive direction.

Amyloid templating may also contribute constructive chemistry. Rout and colleagues demonstrated template-directed peptide synthesis associated with amyloid structures, with selectivity among products. This is more than a seed reshaping already supplied mature protein: a template influences what is chemically made. It remains a partial capability. The experiment does not furnish independent feedstock production, waste management, compartment maintenance, and successive replacement of the apparatus. [63]

Modern prions should therefore not be treated as autonomous examples of the first life. They are informative about a physical route for inheriting state and, in some systems, the cost of letting propagation escape control. A comparison between pathological and functional assemblies can identify the additional work needed for organized inheritance: selective initiation, bounded propagation, substrate supply, appropriate readout, and clearance. The next part asks how short molecular operations feed the larger processes that provide those controls.

Part V. From Local Events to Multiscale Organization

24. Quantum-to-Classical Latching and the Evasion of Averaging

A quantum-sensitive event can leave a durable chemical or conformational product even when the quantum state that produced it has vanished. This is the ordinary route by which local microscopic physics acquires biological consequences. Retinal photoisomerization leads to a molecular conformation that activates a signaling cascade; a repair reaction changes a DNA lesion; charge transfer changes a protein's redox or binding state; a recruited protein adopts an assembly state. The later process reads the product, not a preserved copy of the initial wavefunction.

Let Q stand for the quantum degrees of freedom needed to calculate an elementary operation, C_1 for its first distinguishable product, and $C_2, C_3, \ldots$ for subsequent records. The notation $Q \to C_1 \to C_2 \to \cdots$ does not mean that a system suddenly ceases to obey quantum mechanics. It means that, for the stated task, later predictions can use probabilities of recorded products without retaining their unobserved phases. The adequacy of that reduction is testable: one must ask whether a phase-sensitive variable left out at one stage influences a later product.

A precise formalism uses a *quantum instrument*. Given a density operator ρ describing the retained molecular state and a slower context z, an operation has outcome maps $\mathcal{J}_r^{(z)}$. The density operator represents quantum states, including statistical mixtures; the outcome label r represents a record such as product identity, binding state, or charge state. The probability of a record and the state conditional upon it are

$$p(r \mid \rho, z) = \operatorname{Tr} \mathcal{J}_r^{(z)}(\rho), \qquad \rho_r' = \frac{\mathcal{J}_r^{(z)}(\rho)}{p(r \mid \rho, z)}.$$

The conditional state is defined for nonzero outcome probability. The maps are completely positive and their sum preserves trace. Those requirements keep all probabilities physical, including when the system is considered with an untouched partner. The context z can then change in response to the

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recorded outcome. If the environment retains memory that later matters, it must be included in the state or the effective rule; a memoryless approximation cannot be imposed by vocabulary. Lindblad theory covers an important class of Markovian quantum evolution, while process-based treatments permit explicit temporal memory. [75,76]

There is a simple limit on inference from downstream behavior. Suppose all influence of the proposed quantum module passes through classical records $r_1, r_2, \ldots$. For allowed interventions u_t, the joint law obeys the chain rule

$$P(r_{1:n} \| u_{1:n}) = \prod_{t=1}^{n} P(r_t \mid r_{1:t-1}, u_{1:t}).$$

The double bar denotes causal conditioning: present probabilities may depend on interventions already made, but not on choices made in the future. If a second mechanism reproduces every conditional next-record law for every allowed history and intervention, it reproduces the joint record law. Subjecting equal record laws to the same downstream rules produces equal downstream statistics. This *record equivalence* is a consequence of probability theory, not an assertion that the alternative mechanism is cheap or even buildable under biological constraints.

Equal mean rates are insufficient for the premise. Waiting-time distributions, error correlations, rare branches, and responses to changed inputs may differ. Moreover, a purported classical replacement may require centralized memory, nonlocal communication, or more energy than the organism can supply. The theorem says why downstream records alone cannot certify retained coherence after a genuine record boundary. It leaves open whether generating the observed records under local, material constraints requires a particular quantum operation.

Amplification does not change this distinction. A biochemical cascade uses supplied free energy to produce a large response to a small initiating event. It can make that event consequential while also amplifying noise. For a fixed stochastic downstream channel K, the total-variation distance between two input distributions cannot increase: $D_{\mathrm{TV}}(Kp, Kq) \le D_{\mathrm{TV}}(p, q)$. The inequality concerns distinguishability from the same original record; it does not forbid gaining new information through later measurements. It explains why useful organisms must select, reject, and repeatedly check inputs rather than indiscriminately magnify every molecular fluctuation.

The proposed quantum contribution can thus survive averaging in a precise sense. Evolutionary organization places a molecular operation at a sensitive decision point and retains a selected outcome in chemistry or structure. Its effect is then conditioned on an apparatus that costs energy and must itself be renewed. Whether this architecture establishes a distinctive quantum advantage depends on what an admissible classical control can accomplish with the same resources.

The record boundary suggests an intervention test. Perturbing a proposed quantum variable while leaving the first product distribution unchanged should not alter a downstream process that receives only that product. A downstream change under those conditions is evidence that an unmeasured record changed, a retained correlation crossed the supposed boundary, or the perturbation acted directly elsewhere. It cannot simply be assigned to long-lived coherence. Conversely, a changed product distribution followed by the predicted downstream shift supports the shorter causal chain even if no persistent coherence is found.

25. Classical Cellular Automata as the Strongest Complexity Control

A cellular automaton is a collection of sites whose states update according to local neighborhood rules. In a classical automaton a site may have a discrete value or a probability distribution over values. The site need not represent a living cell. Automata separate a compact local rule from the extended behavior it generates, which makes them useful controls against inferring exotic microscopic physics from complex biological form.

Von Neumann's self-reproducing automaton separated a description, an interpreting constructor, and a copying operation. The construction demonstrates a logical relationship required for open-ended

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heredity in that architecture; it does not show that a biological cell literally contains a universal robot. Langton constructed simpler self-reproducing loops, which reveal how much organization can arise with a reduced repertoire, again on a supplied lattice governed by fixed rules. [15,16,25]

Wolfram's Rule 110 is a one-dimensional binary automaton with a simple update rule. Cook established its computational universality with appropriately arranged initial states. *Universality* means that the formal dynamics can emulate arbitrary computation under a specified encoding; it does not mean that a random Rule 110 pattern efficiently finds fuel, repairs damage, or becomes alive. Wolfram's work also shows how difficult predicting some automaton outcomes can be even when the rule is known. Computational difficulty for an observer is not, by itself, adaptive action by the system. [81,83]

Neural cellular automata make the control more biological in appearance. Mordvintsev and colleagues trained local rules to grow a target pattern and restore it after damage. The recovery is a real property of the trained classical update. Its target, training history, computing substrate, and energy supply are supplied to the demonstration. This does not devalue the result; it states which parts of the apparent regeneration have already been built into the experimental arrangement. [82]

Coarse graining can also turn intricate microscopic dynamics into simpler macroscopic rules. Israeli and Goldenfeld found automata for which coarse descriptions retained the behavior relevant to selected observables. A microscopic quantum intervention may similarly change fine details without changing function. Conversely, a small intervention can cross a coarse functional boundary. Neither outcome follows from the fineness of the physics alone. [84]

The stronger classical comparator can have spatial coupling, feedback, stochasticity, directed pathways, learning during an evolutionary training history, and externally supplied or internally produced chemical energy, as the physical comparison permits. It should not be reduced to uncorrelated random walkers when the candidate quantum model enjoys a structured protein environment. Classical waves can reproduce certain coherence-like transport signatures; Briggs and Eisfeld demonstrated an equivalence for an electronic-energy-transfer regime. [28] Where chemistry genuinely requires quantum-derived elementary rates, the cellular-scale comparator can receive those calibrated rates and ask whether retaining intersite phase adds further function.

A formal moving pattern is not material renewal. Its lattice and update machinery can remain indestructible while state passes across sites. A biological comparison should permit the credited controller, templates, and catalysts to degrade, and require their replacement at stated cost. Abstract automata become valuable here precisely because they expose what an explanation does and does not furnish. If complex shape, regeneration, and history dependence can already be produced classically, the evidence for a distinct quantum role must come from a mechanism and a controlled functional boundary, not from visual resemblance to life.

26. Quantum Cellular Automata and Open Local Quantum Networks

A quantum cellular automaton, or QCA, replaces the sites' classical state spaces with quantum state spaces and specifies a locality-preserving global update. The usual closed formulation is reversible and retains phase relations among sites. It must be built consistently: overlapping local quantum operations generally do not commute, so declaring that each neighborhood updates independently at the same instant need not define a valid global evolution. Schumacher and Werner formalized QCA locality; Shepherd, Franz, and Werner constructed a programmable QCA capable of general quantum computation within its architecture. Neither result shows that a cell is a quantum computer. [86,87]

One well-defined subclass updates disjoint blocks in successive layers. For site spaces $\mathcal{H}_i$, a depth-D update can be written

$$\mathcal{H} = \bigotimes_i \mathcal{H}_i, \qquad \mathcal{E} = \mathcal{E}_D \circ \cdots \circ \mathcal{E}_1, \qquad \mathcal{E}_\ell = \bigotimes_{B \in \mathcal{P}_\ell} \mathcal{E}_B,$$

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where $\mathcal{P}_\ell$ partitions the sites into nonoverlapping blocks at layer ℓ. Unitary block operations give reversible evolution. Completely positive, trace-preserving maps permit exchange with an environment. This is a convenient construction, not a claim that every locality-preserving unitary is finite depth on the original lattice.

Biological systems are open: molecules exchange energy and material with surroundings, products leave, and catalysts are replaced. A local open operation can be represented by coupling a block to an environment R, acting jointly, and then retaining only the block,

$$\mathcal{E}_B(\rho) = \mathrm{Tr}_R[U_B(\rho \otimes \tau_R)U_B^\dagger].$$

Here τ_R is the environmental preparation and the partial trace represents disregarding its detailed later state. Freshly preparing and resetting R in every step can cost resources; the mathematics does not supply them for free. If the same environment interacts again while correlated with the block, its memory must be retained or the map amended. Boneberg, Carollo, and Lesanovsky developed dissipative layer-based quantum automata connecting this kind of construction to open-system dynamics. [88]

A classical stochastic network can often reproduce the recorded outputs of such a model. Once the retained density operator stays diagonal in a preferred record basis, a suitable diagonal local update is an ordinary stochastic map over those states. Off-diagonal terms and intersite quantum correlations complicate this particular reduction, but their presence is not a biological advantage by definition. A larger classical representation may reproduce the observables, and some quantum systems with restricted entanglement admit efficient classical simulation, as Vidal showed for a class of computations. Simulation cost, physical construction cost, and biological function are distinct. [89]

Quantum contact processes ask how coherent local dynamics changes the competition between activity and loss. An *absorbing state* is an inactive state from which the specified rules cannot recover without external input. Gillman, Carollo, and Lesanovsky studied quantum extensions of probabilistic cellular automata with tunable correlations and nonequilibrium behavior. Such models are useful for a controlled comparison of dynamical classes. An active site, however, is not automatically a renewed catalyst, copied sequence, or repaired membrane. [94,95]

Even the mathematical phase behavior of a particular one-dimensional quantum contact process remains contested. Studies have supported differing continuous and discontinuous transition descriptions, with metastability, finite-size effects, and approximation schemes important to the disagreement. A *phase transition* is a qualitative change in long-time behavior under varying parameters, often defined in an infinite-system limit. A finite organism can persist for a relevant horizon while ultimately subject to extinction, or fail a useful task while remaining mathematically active. [96–98]

Asynchronous timing matters because ordered quantum operations can fail to commute. Gillman and colleagues found that asynchronous updating can alter collective QCA behavior. This is a reminder to test irregular biological timing rather than presuppose a perfect global clock. [99] QCA error-correction rules provide further theoretical demonstrations of state retention under defined noise, but retaining an arbitrary unknown quantum state is a different task from retaining a classical regulatory distinction. The relevant noise, reset, fresh carriers, and material replacement must be distinguished. [100]

QCA will be biologically explanatory when measured molecular couplings and environmental rates justify the proposed degrees of freedom, a physiological preparation and readout are identified, and retained multisite coherence or correlations shift a functional boundary beyond a quantum-calibrated stochastic network under the same local resources. Laboratory QCA devices can test the mathematical implementation; control and cooling supplied in an apparatus cannot be silently assigned to a cell. White and colleagues' experimental Rydberg-array preprint, for example, concerns a controlled quantum simulator rather than an observed natural biological network. [101]

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27. Finishing in Time

Biological success often has a deadline. A reactive intermediate can decay; a lesion can be copied before repair; a cell can lose a required catalyst; an environmental opportunity can close. A mechanism that produces the right result eventually may fail if it arrives after the competing event. The useful timing measure is therefore a distribution of correct completion, not only a mean reaction rate.

Let $F_X(t)$ be the probability that implementation X has produced an identifiable correct-completion record by time t, before adding a specified independent loss. Failed paths that never complete are allowed, so $F_X(\infty)$ can be below one. If the loss time is exponentially distributed with rate λ, its probability of not yet occurring at time t is $e^{-\lambda t}$. The probability of completion before loss is

$$\eta_X(\lambda) = \int_{0^-}^{\infty} e^{-\lambda t}\, dF_X(t).$$

The lower limit includes a possible immediate-completion mass. For exponential completion at rate k_X, the formula becomes $k_X/(k_X+\lambda)$. For a fixed deadline t_*, success is $F_X(t_*)$. If loss depends on intermediate state or shares fluctuations with completion, the independent-hazard formula must be replaced by a joint process.

Two mechanisms with the same average completion time can have sharply different early and late tails. An enzyme that makes some product quickly but occasionally stalls may excel when an intermediate is rapidly lost and perform poorly when uniform timely delivery is needed. In repair, a small change in the fraction of lesions resolved before the next replication can matter more than a large change in a rate measured on already bound enzyme. In construction, a slightly faster replacement reaction can prevent a catalyst population from falling below the point at which its own supply becomes insufficient.

Integration by parts gives, for $\lambda > 0$,

$$\eta_X(\lambda) = \lambda \int_0^{\infty} e^{-\lambda t} F_X(t)\, dt.$$

If $F_Q(t) \geq F_C(t)$ at every time, then $\eta_Q(\lambda) \geq \eta_C(\lambda)$ for every positive independent exponential hazard. If the curves cross, the preferred mechanism depends on the actual loss process. This is a property of completion distributions; it is not evidence that a proposed quantum mechanism has the favorable distribution.

Quantum transport can be fast relative to an unbiased classical random walk in some models, and coherent quantum walks can spread ballistically rather than diffusively. A directed classical pathway can also propagate ballistically. Search algorithms offer quantum query advantages in precisely stated oracle models, but a molecule does not receive a free oracle marking the favorable fold, lesion, or mutation. Physical construction, state preparation, readout, parallel machinery, and power belong in elapsed time and resource accounting. [90–92]

The local-register comparison in Appendix B illustrates the discipline. Coherent transfer beat a dephased stochastic counterpart at a chosen loss rate, while an ideal directed classical conveyor beat both. The conveyor lacked a costed molecular realization, so this was not evidence that a particular cell uses one. It was evidence that dephasing a fixed quantum architecture is not the strongest classical comparator. A test in an enzyme or respiratory complex should compare the actual molecular geometry with physically admissible compensation, including altered routes and additional carriers where these can be built under the stated budget.

Completion statistics can enter a renewal calculation directly. In an idealized branching module, suppose each correct completion yields on average b successor modules and an independent loss ends the opportunity. The mean offspring number is $R_X = b\eta_X(\lambda)$. Above one, mean generation size grows under the model's supplied materials; this does not ensure survival of a finite population or prove that the materials are produced internally. The full timing distribution enters more detailed age-dependent branching equations. [93]

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A substantive quantum claim would measure a defined microscopic contribution to $F(t)$, link that change to completion before an independently measured competing loss, and show that the shift crosses a prespecified biological threshold. One can write the necessary comparison as $\eta_R^{\max} < \eta_{\text{required}} \leq \eta_Q$ under stated resource constraints. A tested reference design is not the maximum over all admissible alternatives. In most applications the defensible result will initially be a narrower pairwise effect; the larger claim requires a bound or an unusually comprehensive engineering comparison.

For a numerical illustration, imagine two operations with the same mean completion time of two arbitrary units. One always completes at time two. The other completes at time one-half on half the occasions and time three-and-one-half on the rest. With an independent loss rate of one, success before loss is $e^{-2} \simeq 0.135$ for the first and $(e^{-1/2} + e^{-7/2})/2 \simeq 0.318$ for the second. Under a hard deadline of two-and-one-half, the first always meets it and the second meets it only half the time. The distributions cross, so calling either operation simply "faster" obscures the biological question. This calculation supplies no quantum attribution; it shows which timing measurement the attribution must explain.

28. Renewal and Useful Work as Viability Boundaries

The organization of a living system is maintained only if it makes successor components fast and accurately enough to compensate for damage, degradation, and dilution. A high reaction rate is not sufficient if the products do not sustain the apparatus; a durable apparatus is not sufficient if it performs no useful work. These requirements can be expressed as thresholds and then tested with actual materials rather than inferred from general language about emergence.

Consider two component classes x and y that contribute to each other's production at low abundance. With fixed substrate supply and effective first-order coefficients k_1, k_2 and losses $d_x, d_y > 0$,

$$\dot{x} = k_1 y - d_x x, \qquad \dot{y} = k_2 x - d_y y.$$

The larger eigenvalue of this linear production–loss matrix is

$$\lambda_{\text{dom}} = -\frac{d_x + d_y}{2} + \frac{1}{2}\sqrt{(d_x - d_y)^2 + 4k_1 k_2}.$$

It is positive exactly when $k_1 k_2 > d_x d_y$. A change in a molecular transfer, catalytic yield, or completion-before-loss probability can enter a production coefficient. If a quantum-dependent implementation and its admissible reference lie on opposite sides of this inequality under measured losses, the microscopic difference changes whether this simplified module can replenish itself from a small population.

The model does not describe a whole organism. With unlimited fixed substrate, positive linear growth is unbounded; a finite operating state requires saturation, resource limitation, and regulation. A positive deterministic equilibrium also need not guarantee long survival in a small stochastic population: the system may eventually reach an absorbing empty state. If uniform dilution at rate δ is added to both classes, the eigenvalues shift down by δ, and the low-abundance critical dilution is $\delta_c = \lambda_{\text{dom}}$ when this is positive. An experiment can measure how much turnover the productive relation tolerates over a stated time and failure probability.

The position of a reaction within a larger network also matters. For a differentiable production–loss matrix $A(q)$ with a simple dominant eigenvalue, and left and right eigenvectors w, v normalized by $w^T v = 1$,

$$\frac{d\lambda_{\text{dom}}}{dq} = w^T \frac{dA}{dq} v.$$

The parameter q denotes a measured microscopic influence. The formula shows how sensitivity is weighted by network position. A large local effect may be buffered, while a modest change at a bottleneck shifts the renewal boundary. If the perturbation also changes degradation, resources, or operating state, those changes belong in A or in an extended nonlinear model; holding them artificially fixed would manufacture a result.

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Replacement should be measured by following labeled material. Constant output during a short observation can depend on an initial store of long-lived catalysts. Detecting newly made components does not establish full renewal if a tiny unreplaced controller remains indispensable. A credible test specifies which components and functional relations are required, what fraction has turned over, how much original material could evade detection, and whether the system still produces useful output after serial dilution.

Maintenance competes with present work for fuel and material. Let E be the abundance of operating machinery, k the event rate per unit, u the fraction of events allocated to replacing machinery, y the machinery yield per replacement event, d the first-order loss rate, and bE^2 an effective density-dependent limitation. The illustrative dynamics are

$$\dot{E} = (yuk - d)E - bE^2.$$

For $yuk > d$, steady machinery is $E_{\mathrm{ss}} = (yuk - d)/b$. If the remaining events deliver work w to a defined load, steady load output is

$$P_L(u) = \frac{wk}{b}(1 - u)(yuk - d).$$

Allocating too little to replacement loses the apparatus; allocating all events to replacement leaves no output for the load. With the stated unconstrained model, the interior optimum is $u_* = (1 + d/(yk))/2$ when $yk > d$, and the maximum load is $w(yk - d)^2/(4yb)$. These equations describe an idealized supplied module, not a fully balanced biochemical reaction network.

The input budget must be counted. If each event consumes chemical free energy $\Delta\mu$, the input power is $P_{\mathrm{in}} = \Delta\mu k E_{\mathrm{ss}}$, and an output event cannot deliver $w > \Delta\mu$ without another energy source. Material construction, resetting, and waste removal incur additional costs. At equal input power, a faster reaction can permit less machinery to bear the same load, freeing a larger fraction of operations for output. A different architecture could instead improve yield, reduce loss, or alter the task. The physical comparison therefore concerns an attainable region of load, fidelity, response time, turnover, and failure risk at matched material and energy budgets, rather than a single maximum rate.

One can define a viability region $\mathcal{K}$ in which the specified functions and integrity are acceptable. If $\tau_{\mathcal{K}}$ is the first exit time and H a stated horizon, an experimentally useful dilution capacity is

$$\delta_{\max}(H, \varepsilon, \mathcal{C}) = \sup\{\delta : \Pr(\tau_{\mathcal{K}} > H) \geq 1 - \varepsilon \text{ under constraints } \mathcal{C}\}.$$

The tolerated failure probability ε and constraints $\mathcal{C}$ include the measured power, material inflow, initial stocks, output requirement, and fidelity. This is a task-dependent measure, not an absolute definition of life. It allows a substantive comparison: does a measured quantum-sensitive operation move the viable boundary beyond what the strongest physically admissible alternative sustains with the same budget?

The broader molecular-to-organizational claim has a clear failure condition. If the quantum intervention changes an isolated rate but leaves the record distribution and renewal boundary unchanged after realistic compensation, that mechanism is not necessary for the asserted system-level task. If a classical local network, calibrated with the necessary molecular chemistry, reproduces the boundary at comparable cost, retained multisite coherence is unnecessary for that task. Conversely, a reproducible boundary shift, traced from a specific quantum-sensitive operation through an intermediate record to replacement and work, would be evidence at a stronger level than the mere presence of quantum chemistry in living matter. Adaptation then asks how such capacities are regulated when the required task itself changes.

An experiment should measure more than whether activity continues. A synthetic energy-converting compartment might maintain ATP production using initially supplied enzymes while failing to replace them. The decisive records would include incorporation of new protein into operative

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complexes, retention of productive geometry, preservation of the compartment, and continued work after several turnovers of the original material. Material labeling and serial dilution address different loopholes: labeling shows what was newly made, while dilution tests dependence on a finite initial stock. The molecular intervention can then be judged by its change in the feasible work–renewal regime, including errors and energy cost. This closes the causal path from microscopic transition to organizational continuity without requiring any enduring organism-wide quantum state.

Part VI. Adaptation, Development, and Evolution

29. Adaptivity When Restoration Is Not Enough

An organism can replace a damaged component and still fail if the environment in which that component once worked has changed. Repair restores an arrangement; adaptation changes an arrangement or its use so that the organism can continue under new conditions. This is the distinction between preserving a state and preserving a viable course through changing states, which Waddington called *homeorhesis*. [9]

Di Paolo distinguishes the processes by which an organization constitutes itself from its regulation of activity in relation to conditions of viability. The latter requires some sensitivity to consequences: a system must respond differently when its present activity no longer supports continued operation. This formulation identifies a biological problem without assigning intention to every cell or a quantum origin to every adaptive response. [102]

Feedback supplies a classical mechanism. A controller detects a deviation and changes subsequent activity. In *integral feedback*, the correction depends on the accumulated deviation rather than only its present value; under appropriate conditions it can restore an output despite a sustained perturbation. Bacterial chemotaxis provides a well-studied biochemical implementation. Its sensory response can recover after continued exposure, allowing further changes in chemical conditions to remain detectable. Yi and colleagues connected this behavior to integral feedback. [103]

The operation has a cost. Lan and colleagues studied consumption, speed, and accuracy in sensory adaptation and found that de-energizing *E. coli* slowed adaptation under their experimental conditions. The cell spends resources to keep its control process effective even when no damaged part is being replaced. There is no general rule that more expenditure gives proportionately better control; the tradeoff depends on mechanism and operating conditions. [104]

Let e_t denote the environment, z_t the organism's measured organizational state, and $\mathcal{K}(e_t)$ the set of states meeting specified functional requirements in that environment. Adaptation can be measured by whether the system remains in that set, or returns before loss becomes irreversible, within a stated resource budget. The set is an investigator's test criterion, not an internal map that the organism must calculate. The allowed region may change: lowering activity can preserve viability when a former rate of work cannot be supported.

Time matters as well as final state. In a sequential approximation, the delay to sense a change, reconfigure, and act must be shorter than the interval before the opportunity is lost. Processes that overlap require a joint completion-time distribution instead of a sum of mean delays. A quantum-sensitive reaction could change a sensing or response step. The relevant question is whether its measured effect changes the probability of a successful whole response after compensating routes and their costs are included.

Thus adaptive behavior is no evidence, by itself, of useful coherence or quantum computation. Classical feedback, inherited regulatory architecture, and selection can explain a great deal. The proposed quantum contribution lies in the physical implementation of a particular detector, transfer, or control reaction under constraints of energy, time, noise, and material. This gives an experiment a practical design: characterize the molecular step, measure its downstream response, and predict performance as the environmental rate of change varies beyond the conditions used to fit the model.

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30. Teleology Without Backward Causation

Biologists routinely describe a response as repair, a structure as functional, and an action as directed toward a result. Such language can be made causally precise without treating a future result as a force acting on the present. A current structure, formed through development and evolutionary history, can respond to present conditions in ways that affect its later persistence. The future selects nothing backward in time.

Three questions are often compressed into one word, *purpose*. A selected-effect account asks why a feature became common in a lineage. Wright's account concerns this explanatory history. A capacity account, developed by Cummins, asks what a component presently contributes to a specified system performance. An organizational account asks whether the contributed performance helps maintain or reconstruct the constraints that make that system possible. These accounts can answer different questions about the same process. [105,106]

Mossio and Bich locate biological directionality in mutually maintained constraints. A membrane shapes transport while transport and synthesis sustain the membrane; neither relation invokes an imagined future. A process acquires a maintenance role through an experimentally traceable dependency. Organizational theorists disagree, however, about whether such dependencies suffice to establish an *intrinsic norm*, rather than a standard chosen when an investigator defines the system and the function of interest. Corti and Cuciniello develop versions of that objection. The disagreement need not be concealed by an empirical experiment or settled before one is conducted. [107–109]

A causal test states its boundary and readout, interrupts a proposed maintenance process, follows the predicted intermediate changes, and attempts rescue through an independent route. Rescue supports the asserted functional relation while revealing where alternative mechanisms can compensate. It does not prove a metaphysical account of purpose. A self-propagating pathological prion gives a useful counterexample to careless language: greater propagation of the protein state can coincide with loss of host function. The outcome depends on whether the focal system is the conformation, the cell, or the organism. [59]

Intentional action adds a further requirement. A nervous system may hold a present representation of a possible future and use it to choose among actions. This is ordinary forward causation through a present physical state, though the represented end has not yet occurred. It should not be identified with biochemical feedback simply because both processes are directed. Nor does a quantum fluctuation acquire intention by influencing an outcome.

Some theories describe biological regulation as inference. Friston's free-energy principle offers a formal account in which an organism's states can be related to an inferential model. Its *variational free energy* is an information-theoretic objective; it is not automatically the thermodynamic free energy, measured in joules, entering a metabolic balance. The relationship depends on an explicit physical model, and the scope of the inference interpretation remains disputed. [110–112]

The monograph requires the narrower empirical relation: an identified operation changes a specified function, and that function contributes to continued activity or construction under measured constraints. Evolution may explain how the operation became available. Philosophy may ask whether such organization bears genuine norms. Neither extension is a license to infer a special quantum resource from the appearance of goal-directed behavior.

31. Development and Regeneration

Development creates capacities that were absent from the earlier organism. It cannot be described as repair of a completed adult. A developmental course can be reliable while its successive states differ markedly, which is why homeorhesis is more apt than return to a fixed equilibrium. Physiological maintenance and the construction of a new organization require related but distinct explanations. [9,113]

Classical physical and biological accounts establish demanding controls. Turing showed how coupled reaction and diffusion can destabilize a homogeneous state and generate spatial pattern under

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specified conditions. Wolpert's positional-information framework concerns how cells respond to signals associated with location. Regulation, mechanics, cell movement, growth, and material supply also shape form. A patterned tissue therefore does not, by its appearance, indicate coherent quantum dynamics over the scale of the tissue. [114,115]

The inherited genome is not an image of the final body. It operates through cells with membranes, enzymes, chromatin states, signaling pathways, and spatial histories. Von Neumann's distinction between a description and the machinery that interprets it remains helpful; local cellular automata likewise show how distributed rules can construct and sometimes restore a pattern. Their rules and training history are supplied in the models, and a generated image is not proof that an organism has produced and maintained the physical apparatus for its construction. [16,82]

Local quantum chemistry may matter at identifiable developmental points: a redox step can affect a signal, an electron or proton transfer can limit metabolism, and a light-sensitive reaction can initiate a regulatory change. Demonstrating such a role requires more than perturbing a molecule and observing a changed final shape. General toxicity, altered cell proliferation, and changed energy supply can also change morphology. A stronger experiment predicts intermediate molecular, cellular, and spatial effects at defined stages and measures function as well as form.

Regeneration combines loss, renewed construction, positional information, and recovery of function. The planarian weak-field experiments provide a particularly interesting test bed: a radical-pair model yielded field-dependent predictions examined in regenerating animals, with redox-linked outcomes. The evidence connects a physical hypothesis to a tissue-level response more directly than most proposed examples of quantum influence on development. It does not yet identify every native radical, prove the entire causal path to regenerated anatomy, or establish a coherent state spread across the organism. [47]

The useful next test is selective. Measure the proposed spin-sensitive product or its immediate chemical consequences under physiological conditions, perturb the proposed radical source without broadly suppressing growth, and follow the predicted signal through cell behavior to regenerated structure and function. Rescue by an alternative redox or signaling route would help locate the quantum-sensitive bottleneck. The final form alone cannot distinguish such a chain from a classical response to a magnetic field or from nonspecific injury.

Development also alters its own conditions as it proceeds. A signal that matters early may be dispensable after the relevant cell types or boundaries exist. Experiments should therefore state the developmental window, timing of intervention, and rate of recovery. An effect on completion before a stage-specific deadline may be biologically decisive even when it leaves little trace in a late snapshot; a conspicuous shape change can likewise be incidental to the proposed microscopic mechanism.

32. Evolution as Selection over Quantum-Operating Architectures

Evolution acts on inherited differences in molecular architecture. A sequence change can alter a protein's geometry, electrostatics, fluctuations, or assembly; those changes can alter electronic coupling, proton-transfer conditions, and reaction branching. Selection can therefore tune structures that operate through quantum-sensitive chemistry. It does not have to manipulate a wavefunction directly, and it cannot evaluate a future phenotype before present molecules and environments interact.

The word *random* should be used with care. A mutation may be probabilistic without being uniformly distributed across a genome. Its frequency can depend on sequence, chromatin, damage, and repair. Quiroz and colleagues associated a plant histone mark, H3K4me1, with recruitment of repair machinery and a patterned distribution of mutations. This shows how cellular organization influences inherited variation; it does not identify a quantum mechanism or preferentially generate changes advantageous in an unknown future. [116]

Separate the production of a variant from proofreading, repair, fixation, and differential growth. If Q_{ij} denotes the probability that reproduction by type j yields type i, and f_j denotes reproductive performance, a replicator–mutator description has a term $Q_{ij}f_j$. A molecular hypothesis can change

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Q; selection after variants appear changes their frequencies through f. End-point enrichment cannot identify which stage changed unless the stages are measured separately. Contextual mutation is not equivalent to a transition rule that reads off later fitness.

McFadden and Al-Khalili proposed an adaptive-mutation mechanism involving quantum alternatives of hydrogen configuration and their environmental interaction. Donald disputed the necessary coherence and the proposed route from the molecular alternatives to cellular outcomes. The exchange remains a proposed mechanism and critique, not a demonstration that cells search for adaptive mutations. The discriminating experiment must identify the relevant physical states, predict how an intervention changes variant production before selection, and then measure repair and growth separately. [117,118]

Other inheritance systems enlarge the architecture subject to selection. Protein conformations can propagate in a cellular environment while the protein's amino-acid sequence remains fixed. A conformational state may be advantageous under one condition and costly under another; success of its propagation need not mean success of its host. Sequence inheritance, conformational inheritance, and their interactions should therefore be represented separately. [17,59]

An organism can respond before an anticipated condition occurs without backward causation. Tagkopoulos and colleagues found microbial regulation that uses a present cue correlated with a later environmental condition. The predictive relation is embodied in a network shaped by earlier environments and selection. A quantum-sensitive sensor might change its speed, accuracy, or cost, but anticipation alone is not a quantum signature. [119]

The defensible evolutionary claim is accordingly physical and conditional. Inherited structures set distributions of molecular transitions; those distributions affect phenotype under actual conditions; differential persistence of lineages can change the prevalence of the structures. Open-ended evolution and innovation demand further explanations of new tasks and organization; formal definitions help state that problem but do not follow from a tunneling measurement or from randomness alone. [120]

33. Origins and Synthetic Reconstruction

Present organisms arrange substrates, catalysts, compartments, and energy sources using machinery inherited from earlier organisms. An origin account must explain how a mutually compatible subset of these functions arose without assuming that machinery in advance. Demonstrating one efficient reaction is insufficient if its substrate cannot be replenished or its product is destroyed under the conditions needed for another reaction.

An *autocatalytic set* is a network in which products help catalyze reactions within the set, given specified starting materials. Hordijk and Steel developed methods for identifying such networks. A connected catalytic graph identifies a possible organization; it does not establish reaction rates, retention of products, adequate energy supply, or survival under dilution. The physical constraints remain to be measured. [121]

Direct templating can propagate a limited state without a separate interpreted description. Rout and colleagues demonstrated amyloid-mediated peptide synthesis; Lincoln and Joyce demonstrated sustained RNA-enzyme replication with supplied substrates. These results solve different parts of a construction problem. A templated product, a replicated sequence, and an apparatus that replenishes all its essential components are not equivalent achievements. [63,122]

Handedness illustrates the need to distinguish a source of bias from its amplification. Frank's model describes how chemical feedback can amplify an initial chiral difference. Ozturk and colleagues studied enrichment of a precursor to RNA on a magnetic surface in a proposed spin-sensitive setting. Neither alone explains the full origin of biological homochirality, the common handedness of key biological building blocks; a successful pathway must work with the feedstocks, environment, and synthesis steps that the larger scenario requires. [123,124]

Energy conversion and construction have begun to be joined experimentally. Berhanu, Ueda, and Kuruma built a light-driven system in which ATP production supported protein synthesis and some

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synthesized components contributed to the energy-conversion apparatus. This is a partial reciprocal loop. It began with substantial supplied machinery and did not demonstrate indefinite replacement of a complete cell. Its value for the present thesis is that the missing requirements can be measured rather than hidden inside a diagram. [125]

A more demanding reconstruction would track absorbed energy, useful chemical work, error rates, loss of each essential component, and incorporation of replacements during serial dilution. A proposed quantum-sensitive step would first be characterized independently, then changed while the supporting architecture and resource accounting are measured. A classical-nuclear approximation, a quantum-calibrated stochastic account, and an affordable alternative architecture would answer different questions. The strongest result would be a shift in the range of conditions under which the combined system can keep working and renewing itself. A negative result would identify where a favorable molecular mechanism fails to remain useful after integration.

Origins do not require a single historical sequence of template, metabolism, and boundary formation. They require a physically possible sequence in which each stage can furnish the conditions for the next. A modern constructor cannot be supplied gratis to a prebiotic model; nor must the earliest template already have the repertoire of a modern genome. This is an empirical problem of compatible partial capabilities rather than a verbal contest over which feature deserves to be called life first.

34. Environmental Work and Expanding Capability

An organism's work can change the conditions under which it and its descendants act. A root changes local soil; a microbe alters a chemical gradient; an animal constructs shelter. *Niche construction* denotes such modification when it affects subsequent selection and access to resources. Laland, Odling-Smee, and Feldman modeled this feedback between organismal activity and inherited environments. Its effects can support or undermine later persistence. [126]

Material and energy accounts should follow the change beyond the organism's boundary. A large environmental effect is not necessarily a large amount of useful work under the organism's control. Waste and heat can alter conditions without being selected outputs. Even a beneficial change may depend on other organisms or environmental reservoirs whose contributions belong in the balance.

Vermeij describes major evolutionary innovations that enlarged the power available to some organisms and ecological systems. This is a historical analysis of expanding possibilities, not a law that every lineage increases its power use. Organisms can gain precision, reliability, memory, access to new resources, or lower cost at unchanged or reduced expenditure. [127]

For a specified environment and resource budget, an *attainable capability set* can list combinations of useful output, fidelity, response speed, renewal, and tolerated change. Evolutionary novelty may enlarge this set or open a new dimension of action. The set need not grow monotonically: a specialized lineage can gain one capacity while losing another, and an environmental change can make an old capacity ineffective. A measured quantum contribution is important here only if its consequences can be followed through the appropriate constraints to a changed attainable performance.

Human technology extends environmental action through artifacts, accumulated knowledge, and social organization. Its material operation still depends on physical chemistry, but that fact does not assign a specifically quantum explanation to every human purpose. The argument of this book concerns how quantum-sensitive molecular operations enter systems capable of sustaining and extending organized activity. Evaluation of the ends for which those capacities are used requires a different inquiry.

Part VII. The Stronger Coherence Frontier

35. What Large-Scale Coherence Could Mean

The mechanisms developed so far act locally. An electron crosses a protein, a proton moves through an enzyme, or a radical pair changes the yield of a reaction. The resulting chemical state can persist after the quantum state involved in its production has lost coherence. A different possibility

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is that quantum correlations themselves extend over many molecular units or survive long enough to participate in a larger biological operation. That possibility deserves examination, but it asks for different measurements and carries a larger evidentiary burden.

Coherence is a relation between alternative states, not an attribute of an object in general. If an electronic excitation can occupy sites i and j, the density matrix—a description of the quantum state and its statistical uncertainty—may have a nonzero off-diagonal element ρ_{ij} relating those alternatives. Its magnitude and phase can affect interference in a specified experiment. The choice of states matters: coherence between electronic excitations on two pigments is distinct from coherence between different vibrational levels of a pigment, and neither says that two distant cells maintain a common quantum phase. A spectral oscillation also need not measure either coherence directly. A coherently driven experiment can produce oscillations in its own response, and coupled classical oscillators can reproduce some of the same observables. [28]

Electronic coherence in a photosynthetic complex concerns excitation shared among pigments. *Vibronic* coherence involves coupled electronic and molecular vibrational motion. Vibrations of atomic nuclei are quantum mechanical, but an observed beat can arise from predominantly vibrational motion after electronic phase information has disappeared. The biological issue is how the dynamics change the probability of productive charge separation under the illumination the organism actually receives. The mere duration of a beat is insufficient. [35,36]

Entanglement is a stronger and more specific claim. Two subsystems are entangled when their joint quantum state cannot be expressed as a statistical mixture of independently assigned subsystem states. Common responses to a fluctuating environment can produce correlations without entanglement. An operational witness must therefore rule out an appropriately defined class of separable states; a striking correlation or an unusual spectrum is not such a witness. Even when entanglement is established, its utility depends on which degrees of freedom carry it, how they are prepared, how long it lasts, and what operation reads it out. Bell-inequality and contextuality tests illustrate the precision required for foundational nonclassicality claims, although their laboratory implementations cannot simply be transplanted into living tissue. [26,27]

Collective radiation has yet another meaning. In a radiating assembly, coupling among transition dipoles can create states that emit more rapidly or more strongly than independent emitters; the limiting cooperative effect is called superradiance. Dicke's foundational theory specified the collective radiative problem. Biological proposals now ask whether ordered networks of aromatic amino acids, particularly tryptophan in microtubules and other protein assemblies, support such states. An increase in fluorescence yield can be evidence worth investigating, but it does not by itself measure the phase of every contributing emitter, demonstrate entanglement, or establish that neurons use the optical state to compute. The number of sites in a theoretical collective state is not a measured biological coherence length. [73,74]

Fröhlich's proposal concerns driven polar vibrations. Energy continually supplied to coupled modes might preferentially occupy a lower-frequency mode despite dissipation. The word *condensation* in this context can mean concentration of energy and need not mean a coherent quantum state. Weak energy redistribution, strong mode population and phase-coherent occupation are different regimes. A resonance at a terahertz frequency, an externally driven structural change, or a narrow spectral feature cannot identify the strongest regime without measurements that exclude classical coupled-mode dynamics. The physical question is whether ordinary cellular energy supply, loss rates and mode couplings actually reach the proposed state, and then whether that state changes a biological function. [179,183]

Nuclear spins furnish a more sheltered degree of freedom. A spin can retain some forms of quantum order longer than an exposed electronic excitation because its magnetic coupling to the surroundings is weaker. Long nuclear-spin relaxation times can be measured in carefully prepared systems; they do not establish that a cell naturally prepares entangled spins or that their quantum state controls a neural response. Singlet states in nuclear magnetic resonance illustrate the physical

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possibility of extended spin-state lifetimes under suitable conditions. The existence of a laboratory storage mechanism is a starting constraint, not a measurement of its deployment by an organism. [49]

Several dimensions must consequently accompany any assertion of scale: how many molecular sites participate, how far apart they are, what state is coherent, its lifetime, the temperature and solvent conditions, the preparation that creates it, and the measurement that reads it out. A micrometre-long protein assembly can contain excitations delocalized over only a few nanometres. A signal recorded for a second after illumination may reflect a long-lived chemical intermediate whose quantum coherence lasted far less. Likewise, a correlation measured between two regions of tissue need not imply a phase-coherent state spanning that distance. Different experiments answer different questions, and conflating their scales creates a stronger claim than any one of them supports.

Decoherence describes loss of observable phase relations through interaction with an environment. Warm aqueous environments often impose severe limits, but a temperature alone does not provide the lifetime. It depends on the proposed states, their separation in the relevant coordinate, coupling to the environment, and the operation that must finish before dephasing. Tegmark's calculations for particular proposed neural states raised a serious challenge; replies made different physical assumptions and obtained different estimates. A measured lifetime of a specified state under relevant conditions is preferable to either a blanket prohibition or an optimistic extrapolation from a different state. [1]

Nor should a prepared laboratory state be equated with a state maintained in an organism. In a spectroscopic study, a laser can synchronize many molecules and reveal their dynamical response. In living tissue, the source may be sunlight, thermal chemistry, metabolism or a rare photon. Each source supplies a different distribution of initial states. The same material can have a remarkable response to coherent experimental preparation and operate predominantly through incoherent transfer in its natural setting. The laboratory result can still identify the coupling and rate constants needed for a biological model. The question of native preparation is additional, not a reason to dismiss the measurement.

None of these categories is a synonym for a quantum computer. A device may exhibit coherent optical transport yet lack controllable gates, an error budget, state initialization and readout. Spin-dependent reaction yields may use coherent spin evolution without storing general-purpose qubits. Some biological effects could be enhanced by collective quantum dynamics while remaining describable at the level of ordinary reaction probabilities once a chemical result has been recorded. The terms should follow the operation actually demonstrated.

36. What the Evidence Currently Supports

In the Fenna–Matthews–Olson complex, coherent pulse experiments reveal electronic, vibrational and mixed dynamics. Ambient-temperature analysis places a shorter bound on electronic phase persistence than early readings of the longer-lived beats suggested. The outstanding functional test is whether retained phase changes productive energy transfer under natural illumination, beyond a calibrated stochastic or classical-wave account. [35,36,178]

The proposed role of environmental noise in transport also requires care. In a theoretical network, moderate dephasing can prevent an excitation from remaining trapped by destructive interference, improving arrival at a target. This is the legitimate meaning of environment-assisted quantum transport. It is a conditional model result, not a general law that environmental disturbance benefits photosynthesis. To claim biological advantage, one must show that a naturally prepared excitation, under actual operating conditions, yields more productive charge separation than credible dissipative alternatives at the same pigment arrangement and energetic cost. Coupled classical oscillators can mimic selected wave features, though their success does not make the underlying chemistry classical. [28,37]

Radical pairs have a clearer reason to consider coherence. Photoinduced electron transfer can create two radicals whose electron spins initially have a definite joint relation. Magnetic interactions

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then alter the relative populations of singlet and triplet spin configurations, in which the two spins combine to total spin zero or one, respectively. If those configurations react differently, a weak field can change chemical yield before spin order is lost. A geomagnetic field is much weaker than typical molecular electronic energies; the spin-dependent yield supplies a possible means of converting it into a chemical difference. Models of a light-dependent compass motivated a search for a relevant photoreceptor. European robin cryptochrome 4 has shown field-sensitive photochemistry in vitro, a significant identification of a plausible molecular component. The complete pathway from native illumination through receptor state, neural signal and behavior remains to be established. [46]

The lifetime of avian compass spin coherence remains model dependent. Some calculations have inferred relatively long lifetimes from behavioral constraints; others have obtained shorter requirements under different assumptions, with published corrections to the calculations. Neither side directly times a radical pair inside the intact bird. The right experiment identifies the native spin-bearing state, measures its formation and recombination under the relevant light and fields, and tests a predicted behavioral change when the state is selectively altered. A spin process may have a profound sensory effect without intercellular entanglement or coherent signaling along a nerve.

The planarian regeneration work extends the issue beyond the isolated molecule. A radical-pair model predicted a nonmonotonic influence of weak magnetic fields on superoxide; a tissue-level redox response was then examined experimentally. The result is of interest because an organized tissue can preserve a chemically amplified signature of spin-sensitive dynamics. The responsible molecular radical pair has not been uniquely identified, and the complete route from the redox measurement to regenerative function is unsettled. It is neither evidence of whole-tissue coherence nor a mere observation that a magnetic field can have some biological effect. [47]

Microtubules are long tubulin polymers that organize intracellular transport and cell structure. Their ordered aromatic residues provide a substrate for experiments on electronic excitation migration. Fluorescence quenching—reduced emission when a nearby acceptor captures an excitation—has been interpreted as evidence of energy migration beyond the simplest independent-site transfer model, and anesthetics have altered some of these measurements. Calculations of tryptophan networks, together with measurements of fluorescence quantum yield as tubulin assembles, support investigation of collective optical states. These studies test a physical property of protein architecture; they do not directly measure coherent phase relations across an entire fibre, establish that endogenous ultraviolet excitations have the required abundance, or show that the observed optical effect changes a neural computation. The quantum yield—the fraction of absorbed photons re-emitted as fluorescence—is also affected by quenching, environment and molecular structure. Radiative lifetime measurements would help distinguish cooperative emission from a change in nonradiative loss; enhanced yield alone does not identify superradiance uniquely. [74,184]

Microtubule magnetic-isotope experiments reported in 2026 bear on a different candidate mechanism: spin chemistry may influence tubulin polymerization. An isotope substitution that changes nuclear spin can supply an informative perturbation, especially if mass and chemistry are closely controlled. The resulting change in polymerization is not evidence for an optical quantum computer. A useful next step would identify the radical pair, measure the spin-sensitive reaction under cellular conditions and connect its yield to microtubule dynamics and neuronal function. Treating all positive microtubule findings as tests of one theory obscures their distinct degrees of freedom and proposed causal paths. [189]

Ultraweak photon emission from living cells is real. Oxidative metabolism and other excited chemical products can produce photons at low rates. Claims that such emission forms a coherent optical field carrying information across an organism require additional observations. An intensity trace, delayed emission, or a photon-count distribution affected by detector dead time and heterogeneous sources cannot alone establish phase coherence, squeezed light or long-range communication. Measurements of first-order field correlations, properly controlled photon statistics, source localization, propagation and recipient response would be more discriminating. The distinction between an emitted

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quantum of light and a coherent photonic communication system is the same distinction that arises in vision, where an absorbed photon becomes a robust classical signal without preserving its optical phase. [182]

The Fröhlich programme is similarly divided between a physical effect and a strong interpretation of it. Terahertz irradiation of a protein crystal has been associated with structural changes described as nonthermal and interpreted in terms of mode condensation. Other experiments found no corresponding global nonthermal structural response in tested protein solutions, including microtubule preparations, under their specified power and frequency conditions. Neither experiment measures the metabolically driven state in vivo. The theoretical distinction between weak, strong and coherent condensation is essential here: a classical network of coupled modes can also concentrate energy. A biologically important change in protein conformation would deserve attention even if the coherent-condensate interpretation failed. [179,183,186,187]

Nuclear-spin proposals and whole-brain measurements lie farther from a demonstrated functional chain. Fisher proposed that phosphorus spins in calcium-phosphate clusters sometimes called Posner molecules might be stored, transported and read out in ways relevant to neuronal activity. The proposal is valuable for its specific chemistry and conditional predictions; the postulated protected complexes, entanglement and synaptic readout have not been established in vivo. An isotope experiment found differences in anesthetic potency among xenon isotopes with different nuclear spins in mice. That result raises a molecular question about the mechanism of anesthesia but does not identify an entangled neural substrate or explain consciousness. [49,137,185]

An MRI study reported heartbeat-related signals described as indications of nonclassical brain function. A published comment argued that complex but ordinary magnetic-resonance mechanisms had not been excluded; the investigators replied that a particular classical model could not account for their observation. The exchange has not supplied an independently replicated witness that excludes a defined separable class of brain states. The terms *zero-quantum coherence* and *multiple-quantum coherence* in magnetic resonance denote particular spin transitions and signal pathways. Their occurrence in an NMR experiment is not, by its name, proof of entanglement among functionally interacting brain regions. [180,181,188]

Table 3. Evidence and remaining tests at the coherence frontier. Each row concerns its own physical state and causal claim.

System or proposal	Observation or present basis	Missing biological link	Discriminating next experiment
Photosynthetic FMO complex	Prepared-pulse spectra reveal electronic, vibrational, and mixed dynamics; assignments of long-lived beats have been revised. [35,178]	A phase-dependent increase in productive charge separation under natural illumination.	Measure native preparation and yield while testing calibrated stochastic and classical-wave descriptions.
Avian cryptochrome	European robin cryptochrome 4 shows weak-field-sensitive photochemistry in vitro. [46]	The native route from the spin-bearing reaction to a neural signal and orientation.	Identify the native pair and selectively perturb its yield; test the predicted signal and behavior under controlled light and fields.

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Table 3. *Cont.*

System or proposal	Observation or present basis	Missing biological link	Discriminating next experiment
Planarian redox response	Weak-field experiments confirmed prospective nonmonotonic predictions for superoxide. [47]	Identity of the radical pair and the route from superoxide to regeneration.	Measure the pair, reactive intermediates, stem-cell response, and tissue repair under a withheld field schedule.
Microtubule optics	Fluorescence quenching, excitation migration, and assembly-dependent quantum yields motivate collective optical models. [74,184]	A measured phase lifetime under native excitation and any effect on neural function.	Resolve radiative and nonradiative lifetimes, source abundance, spatial extent, and cellular output; compare optical analogues.
Microtubule magnetic isotopes	Reported spin-dependent isotope differences in tubulin polymerization concern a candidate spin-chemical route. [189]	Identification of the radical pair and a neuronal consequence.	Control mass and chemistry, measure spin-sensitive reaction yields, and trace their effects through assembly to function.
Ultraweak photon emission	Cells emit low-rate photons from excited chemical products. [182]	Coherent information-bearing propagation and recipient response.	Localize sources; measure field correlations and detector-controlled counting statistics, propagation, and the response of a putative receiver.
Driven protein vibrations	Irradiated protein crystals and tested protein solutions have yielded different reported structural responses. [186,187]	A metabolically maintained coherent state with functional consequence.	Measure pump, loss, phase, and structure under cellular conditions; test a classical coupled-mode account.
Protected nuclear spins	Long-lived states occur in prepared NMR systems; neuronal storage and readout in proposed phosphate clusters remain hypothetical. [49,185]	Native preparation, protection, transport, and neuronal readout.	Establish the proposed chemical species and spin state in vivo, then selectively alter the predicted output.
Brain MRI correlations	Heartbeat-associated signals and a disputed nonclassical interpretation have been reported. [180,181,188]	A replicated witness excluding an appropriate separable signal model, then functional use.	Independently repeat with declared sequence controls, artifact model, and a valid state witness.

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These cases should be assessed by the strongest causal claim each supports. Field-sensitive cryptochrome chemistry and structured optical behavior in protein assemblies are substantive observations, though their biological roles differ in evidentiary maturity. A mathematical proposal about protected nuclear spins, an anomalous MRI signal and a theory of consciousness demand quite different next experiments. Their coexistence in the literature is reason to specify the claim, not to combine their uncertainties into a single verdict for or against quantum biology.

The research programmes themselves are also wider than single hypotheses. Howard's quantum-biology laboratory studies collective and cooperative behavior across molecular, cellular and potentially organismal scales, including disease; evidence for one optical property of a protein assembly cannot be read as evidence for all of those extensions. Waterloo's programme starts with physical and molecular processes relevant to neuroinflammation and aims toward diagnosis and treatment, including effects on cytoskeletal dynamics.[1] Work on microtubules in the Tuszynski group also spans conventional biomechanics and drug design. Oxford's quantum-information work considers thermodynamics and possible biological applications without thereby asserting a demonstrated quantum computer in tissue. Describing the experiment under review accurately is fairer to each programme than attributing every strong interpretation in its orbit to each of its investigators.

37. Why the Main Programme Does Not Need These Claims

A molecular quantum transition can be important without maintaining coherence beyond the molecule. Rod vision is a concrete case: a molecular photoisomerization leaves a record that later becomes an electrical response without retinal-to-brain optical coherence. [2–4]

An enzyme supplies another type of persistence. A protein prepares donor and acceptor geometries at which transfer of a hydrogen nucleus by tunnelling becomes consequential. Its many catalytic turnovers affect product supply. Once the product exists, its chemical identity and concentration are retained as ordinary variables. The kinetic isotope effects and protein-motion experiments in soybean lipoxygenase constrain a molecular process; any claim about whole-organism necessity requires an added pathway-level test. The quantum feature need not spread from the active site to the whole pathway for its effect on flux to survive. [31,32]

The same logic governs electron transfer in respiratory chains. Distances and redox potentials tune quantum-sensitive transitions among cofactors. Charge redistribution then couples to proton movement and eventually to ATP production. The organism does not sum all microscopic amplitudes and hope that a mean fluctuation survives. It uses arranged molecular channels to convert selected transition probabilities into repeatable chemical states. Which quantum contribution proves indispensable to maintenance, rather than merely present in the mechanism, remains a further comparison with admissible physical alternatives. [33]

"Averaging away" is therefore an incomplete objection. Averaging can remove a fluctuating quantity whose sign changes independently from event to event. It does not remove a systematic difference in a transition rate, product selectivity, completion probability or response distribution when many events sample the same structured mechanism. Nor does it erase a persistent record formed after a rare event. A molecular event may be uncommon and still matter if proofreading, amplification or a developmental switch causes its consequences to be retained. What matters is the causal transfer from the quantum-sensitive step to an observable biological constraint, and the magnitude of that transfer after noise and compensation.

This modest architecture places strong coherence in its proper position. If a microtubule sustains an extended optical state that measurably improves a cell's performance, the account gains a new mechanism. If an animal carries protected nuclear-spin entanglement into a neural operation, it gains another. Neither result is required to explain retinal phototransduction, enzyme tunnelling, electron and proton transfer, spin-dependent chemical yields, or the formation of chemical records.

[1] University of Waterloo, Craddock research profile, https://uwaterloo.ca/biology/profile/t2craddo.

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Conversely, failure of a proposed whole-brain coherent state cannot settle whether local quantum physics is biologically functional. The propositions have different dependencies and must be tested separately.

The argument should not retreat to the empty observation that chemistry obeys quantum mechanics. Classical kinetic models can often reproduce downstream behavior with measured rate constants. The sharper question asks whether those constants, their selectivity and their constraints can be physically realized at the required cost, accuracy and speed without the candidate quantum-sensitive operation. A classical simulation of a molecular event may predict an organism accurately while leaving the physical origin of a decisive rate unexplained. It may also show that the proposed quantum advantage adds nothing to functional performance once realistic alternatives are allowed. Both outcomes refine the biological theory.

38. Experiments That Would Make Stronger Claims Convincing

The first requirement is to name the state. A report should specify its subsystem, basis, spatial distribution, preparation and lifetime, with uncertainties. “Coherence in microtubules” is too broad: an electronic excitation shared among tryptophans, vibrational phase alignment of tubulin, and correlated nuclear spins are different states with different observables. Spectroscopy should distinguish the apparent lifetime of an excitation population from the lifetime of phase information. Distance must be measured independently of the physical length of the supporting structure.

The second requirement is an operational test. A quantum-state reconstruction, interference contrast with controlled phase, nonclassical photon statistic, violation of a well-defined separability bound, or other witness may be appropriate, depending on the claim. The witness must exclude the actual classical alternatives relevant to that instrument, including pulse-generated coherence, inhomogeneous ensembles, coupled oscillators, detector artefacts and ordinary multicompartment nuclear magnetic resonance (NMR) signals. More elaborate mathematical fitting of the same ambiguous observable does not necessarily increase discrimination. A positive result should be reproduced with an independently calibrated apparatus and analysis.

The state must also be prepared by the organism. Ultrafast laser pulses can generate electronic coherence that diffuse sunlight would rarely produce. Intense external terahertz radiation can excite modes with no metabolically supplied analogue. Optical studies of purified microtubules under ultraviolet illumination can reveal legitimate material properties without showing that the relevant state occurs in dark neuronal cytoplasm. Parallel measurements should establish endogenous excitation source, occupancy, dose, tissue localization and operation at physiological temperature, hydration and turnover. Preparations used for metrology can first isolate a mechanism, but the inference to native function must be tested separately.

The accounting should include the rate at which the proposed state is formed, not just its lifetime once created. An optical state lasting long enough for energy transfer may be too rarely populated to carry an appreciable cellular flux. A spin state may form often but decay before a selective reaction reads it. For a collective state, disorder, protein replacement and motion may continually change the participating sites. These variables permit a prediction of occupancy and throughput per cell. Without them a measured coherence time cannot be converted into a contribution to metabolism, signaling or neural activity.

Causal perturbation is more demanding than an association. A change in aromatic residue, isotope, illumination or bound anesthetic can affect structure, binding and chemistry as well as coherence. Experiments should find perturbations that alter the proposed quantum variable while matching ordinary geometry, energy input, concentration and viability as closely as possible. Where exact matching is impossible, the competing effects should be independently measured and included in the predicted outcome. A rescue experiment should restore the specific state and the functional effect together. An anesthetic that shortens a fluorescence lifetime and also changes protein conformation is evidence of interaction; it is not yet evidence that loss of coherence caused anesthesia.

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Function must be defined before a spectacular signal is sought. For a photosynthetic complex it may be charge-separated products per absorbed photon under daylight-like conditions. For cryptochrome it may be field-dependent product yield and a receptor-to-neural response. For a neuron it may be a specified change in synaptic release, firing, plasticity or metabolic performance. A theory claiming an extended state increases the feasible performance region must compare it with a quantum-calibrated stochastic network at matched energy, material, error and time budgets. A quantum signal can be real yet idle with respect to the claimed function.

Prospective prediction prevents the strongest model from being selected after seeing the data. For a radical-pair mechanism, freeze the predicted field-angle, isotope or light-wavelength response before the cellular and animal tests. For a proposed collective optical state, specify how a measured coherence length should vary with assembly size, excitation density and disorder, and what functional response should follow. For a nuclear-spin proposal, predefine the chemical intermediate, spin lifetime, perturbation and physiological readout. Negative results should be retained with the same detail as positive ones. If a well-powered test excludes the necessary lifetime or occupancy, the proposed implementation should be abandoned or narrowed, even while other quantum mechanisms remain viable.

Replication should reproduce the causal relation as well as the instrument signal. Agreement on an optical spectrum from purified protein does not establish the inferred effect on live-cell function. A second laboratory can test the state with different measurement physics and then assess the predicted functional response in independently prepared biological material. Parameter estimates should carry forward their measured uncertainties instead of being readjusted at each stage. This discipline matters most when a proposed state is rare, short-lived or sensitive to sample handling: plausible changes in preparation can otherwise make each unsuccessful experiment seem incommensurable with the original claim.

The best experiments would connect five observations on the same system: a directly measured nonclassical state; its native preparation; a controlled change in its lifetime or extent; a predicted biochemical or neural consequence; and a functional change that a resource-matched alternative fails to reproduce. No single spectroscopic observation carries this chain. Its completion would make extended biological coherence a measured mechanism rather than an interpretation laid across separate findings.

Part VIII. Brains, Computation and the Boundary of the Present Work

39. What Can Be Said About the Brain Without Invoking Quantum Consciousness

The brain is living matter. Its neurons and glia use electron transfer, proton gradients, ATP synthesis, enzyme catalysis, photochemistry where relevant, and the same quantum-derived molecular selectivity found elsewhere in the body. This statement is secure but broad. It does not follow that a brain computes with coherent qubits or that subjectivity has been explained by quantum dynamics. A productive neurobiological question identifies a particular molecular operation and measures whether its perturbation changes cellular function.

Energy supply is one candidate route. Neurons have high demands for membrane gradients, transmitter recycling and structural maintenance. Mitochondrial electron transfer and proton pumping support ATP production. A change in the timing or yield of a respiratory step could affect synaptic reliability, but many intermediate processes regulate the final response. A complete claim would measure the proposed quantum-sensitive step, the change in energy conversion under a realistic workload, a cellular consequence and a circuit effect, with ordinary metabolic compensation taken into account. The presence of quantum-sensitive electron transfer in every mitochondrion does not by itself make an unusual theory of cognition.

Spin chemistry provides another experimentally tractable route. Neural and immune cells generate reactive oxygen species, and redox states can influence inflammatory signaling and cell function. Waterloo's quantum-neurobiology programme studies these molecular and cellular routes, including

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magnetic isotope effects and microtubule dynamics, with neuroinflammation and neurodegeneration as biological targets. The question can be investigated without supposing that the brain preserves a coherent global state: identify the spin-bearing intermediate, determine how the perturbation changes its chemical products, and trace a sufficiently large and specific effect through cellular regulation. An observed isotope effect with no isolated reaction or functional consequence remains suggestive rather than explanatory.

Protein assemblies raise a longer-lived but different possibility. Orb2 in *Drosophila* and mammalian CPEB3 have been connected to regulated aggregation, translation and memory-related persistence. A conformational state can be copied or maintained while many individual molecules turn over. This is a physical hypothesis about memory maintenance, not evidence that the stored state is entangled. Local electronic and proton dynamics help determine protein interactions as they do elsewhere; a special quantum contribution to the persistence of memory would need its own discriminating experiment. The measured structure and behavioral perturbation should not be separated by an unexamined inference that all intermediate causal links must involve the same quantum state. [20,58]

Anesthesia illustrates both the opportunity and the danger of premature interpretation. Molecular binding, ion channels, membrane effects, networks and arousal systems offer established routes for investigation. A xenon isotope effect associated with nuclear spin would be scientifically important if replicated and traced to a chemical or receptor-level mechanism. An anesthetic's effect on microtubule fluorescence also warrants investigation. Neither observation alone identifies the cause of loss of consciousness, because each may alter multiple cellular targets and because neural state changes intervene between molecular action and conscious report. [137]

At the circuit level, coherence has an ordinary neuroscience use: the phase relation between oscillating electrical activity in regions or populations. Neurons can synchronize through chemical synapses, electrical coupling and common inputs while their molecular quantum phases have disappeared. A coherent electroencephalographic rhythm is consequently not evidence of quantum coherence. Likewise, information processing by a neuronal network is a physical operation without implying a quantum information processor. Terms shared across fields should be accompanied by the state and measurement intended in each use.

Molecular, cellular, circuit and behavioral models can be joined, but none is automatically reducible to the vocabulary of the preceding level. A change in a protein's transfer rate may be compensated by metabolism; an altered synapse may be buffered by homeostatic plasticity; the same circuit change can influence more than one behavior. The point of the proposed chain is to make these possibilities measurable. It permits a molecular quantum mechanism to matter in a brain while withholding circuit-level and experiential claims until their distinct evidence exists.

The relevant perturbations should avoid circular interpretation. A mutation that removes a tryptophan may change optical coupling, structural stability and protein trafficking. A drug that suppresses fluorescence may also change transmitter receptors. An intervention at a candidate quantum step becomes persuasive when the other effects are measured, when the predicted downstream response is specified in advance, and when an independent perturbation reproduces or rescues that response. Neurobiology has many pathways between molecule and behavior. Their existence makes a causal chain difficult to establish, but also makes it possible to locate where a proposed quantum effect actually enters.

40. Relation to *The Quantum Brain*

The Quantum Brain was an earlier attempt to take seriously the possibility that microscopic quantum events could influence higher levels of biological organization. Its proposal did not require a gate-model quantum computer made of neural qubits or a whole brain held in a persistent coherent state. It considered transient quantum effects, especially tunnelling, that might help a system move among alternatives in a difficult optimization landscape. Such a landscape is called *rugged* when local improvements can trap a search away from other, potentially better arrangements. Annealing, in

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its broad statistical-mechanical sense, allows a system to explore configurations before it settles. A quantum-sensitive transition could in principle alter the chance of escaping a particular trap. Classical networks could then amplify and retain the selected outcome. [132]

This conjecture should not be recast as a demonstrated algorithm for neural computation. To test it one would need the biological state space, its transition rates, an identified tunnelling coordinate, the time available for exploration, and a classical physical comparator with the same resources. The result would then have to change a neural or organismal outcome. A mathematical optimization analogy, however apt, does not supply those intermediate measurements.

Contemporary quantum annealing devices offer an engineering analogy for tunnelling-assisted traversal of some energy landscapes. They were not evidence that the earlier book had identified a D-Wave-like machine inside the brain, and an externally engineered device does not show that proteins or neurons use the same control schedule, connectivity or readout. More prosaic chemistry may sometimes suffice. Protein-folding landscapes, for example, are structured by sequence and interactions, and classical simulations reproduce substantial aspects of fast folding. The naive premise that a protein must search all conformations independently is false. A quantum-assisted folding claim would have to improve prediction or measured completion before aggregation on a physically comparable landscape. [134,135]

The present analysis retains the experimentally useful thought that a brief molecular event can be recorded and amplified. It replaces a general appeal to difficult biological search with named reaction coordinates, measured deadlines, resource constraints and an explicit chain to renewal or function. That approach allows negative results to narrow a specific mechanism. It does not ask the reader to accept the earlier conjecture as a premise for the biology in this book.

41. Distinction from Quantum-Computer and Quantum-Consciousness Proposals

Several research programmes ask more of biological quantum states than this monograph has asked. They are not interchangeable. Penrose and Hameroff's orchestrated objective reduction, or Orch OR, links proposed microtubule quantum dynamics with an objective state-reduction mechanism associated with spacetime geometry and with conscious episodes. It contains claims about a quantum substrate, its neural organization, its readout and the nature of consciousness. Microtubule fluorescence, energy migration or anesthetic-sensitive optical behavior could bear on the substrate, but even a decisive demonstration of those properties would not establish the spacetime-reduction hypothesis or identify experience with a quantum event. The Arizona programme has itself identified physiological quantum states and their alteration by anesthetics as intermediate tests.[2] They should be judged on their results without assigning those results all the conclusions of the full theory.

Fisher's phosphorus nuclear-spin proposal seeks a relatively insulated carrier for quantum information in calcium-phosphate chemistry. It addresses the lifetime problem by choosing a different degree of freedom, and it specifies proposed biochemical preparation, transport and readout steps. Its conditional quantum-information analyses establish what certain posited states could do if supplied. They do not demonstrate that the brain makes the required clusters, maintains the spin correlations or couples them to synapses. Testing those steps would be valuable whether or not their ultimate use were cognitive.

The MRI proposal offers an apparent whole-brain measurement rather than a fully specified molecular mechanism. The observed magnetic-resonance signal and its reported association with physiological state are the data; entanglement-mediated brain function is a disputed interpretation. The published criticism and reply illustrate the difference between finding a pattern that one familiar classical model misses and establishing a witness that excludes the entire relevant separable class. An independent experiment with predeclared sequence controls, signal model and witness would considerably clarify the claim. [180,181,188]

[2] University of Arizona, Hameroff research overview, https://hameroff.arizona.edu/research-overview/orch-or.

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Formal quantum cognition takes yet another route. A quantum probability model can represent order effects, contextual questions and departures from elementary classical decision rules without claiming that a neuron's hardware carries entangled states. The model uses Hilbert-space mathematics to fit or organize probabilities. Whether it is superior to sufficiently flexible classical psychological models is one question; what microscopic process implements a decision is another. Success at the first cannot answer the second. [136]

Quantum cellular automata and open quantum networks likewise specify possible dynamics for local quantum systems. They can help construct and test a physical model of biological information flow. A program that simulates pattern formation using quantum update rules is not a measurement of quantum updates in tissue. Classical cellular automata, reaction-diffusion systems and stochastic neural networks already produce complicated, adaptive-looking behavior. A biologically relevant QCA proposal should identify states, couplings and retention times and show that an actual function exceeds the best physically admissible classical network under comparable constraints.

This book's narrower question is how quantum-sensitive molecular events can alter the physical feasibility of organized living work. Sometimes a measured optical or spin state could contribute to that question; sometimes it will describe a property whose function remains unknown. Consciousness theories may eventually build on an independently established mechanism, but their additional claims must stand on additional evidence. Proximity of subject matter does not merge the tests.

42. Consciousness and Free Will

The causal influence of an event that began at the quantum scale and the explanation of subjective experience are different questions. A single absorbed photon can affect what a person reports seeing. This says something about the causal origin of the report and nothing decisive about why seeing has a subjective character. A particular molecular process in a neuron might similarly influence a choice, a memory or an attentional state. Showing that influence would be valuable neuroscience. It would not by itself make consciousness a quantum state.

Indeterminacy also does not supply agency. A random event can change which alternative is realized, but acting for a reason requires capacities to represent alternatives, assess consequences, retain commitments and control behavior. Those capacities involve organized biological and social processes whose physical implementations can be studied. Adding irreducible randomness to a decision mechanism does not explain why the selected outcome counts as the person's considered action. Conversely, a predictive classical description of some neural process would not by itself settle every philosophical issue concerning freedom or responsibility.

One observation from the earlier discussion can be stated without promoting it into a physical theory. A macroscopic outcome influenced by quantum indeterminacy might, from its observable behavior alone, be indistinguishable from an outcome attributed to free choice under a different account. That is underdetermination by the observation: two explanations can yield the same visible result. It is not an identity between randomness and freedom and provides no evidence that a particular neural state is consciously chosen. The distinction between physical cause, personal reason and first-person experience must be maintained when experiments are designed and interpreted.

The practical research limit is clear. This monograph can ask whether a named quantum-sensitive mechanism changes neural-cell function, whether that change propagates to circuits, and whether it has behavioral consequences under controlled conditions. It can examine a proposed coherent brain state with the same demand for preparation, lifetime, witness and readout applied to other tissues. It cannot derive subjective experience from the occurrence of coherence, tunnelling or entanglement. The physical account of living continuity is substantial without such a derivation, and its unanswered questions are experimentally precise enough to pursue on their own terms.

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Part IX. Research Programme: Closing Causal Loops

The preceding chapters identify molecular operations and the constraints under which their products can matter to living systems. The experimental question is whether a measured quantum-sensitive step changes a function that the system must sustain while its material apparatus is lost and replaced. Scholes and Fleming have recently placed the problem of microscale effects reaching biological function, the need for incisive measurements, and the possibility of classical mimics at the center of quantum biology. [176] The programme here takes those questions into specific systems whose continuing work, repair, or inheritance can be measured. A local quantum mechanism and an organizational advantage remain separate propositions until the causal links between them have survived intervention and comparison.

43. Six Platforms

The platforms are chosen for complementary measurements, not for a presumed common type of coherence. Some begin with secure molecular physics and an uncertain functional contribution. In others the biological function is well established but its proposed quantum-specific contribution is uncertain. That asymmetry is useful: the experiment should identify which link is missing.

Table 4. Six experimental platforms. A molecular foothold and a functional endpoint are separate observations until their intermediate links are tested.

Platform	Molecular foothold	Missing causal link and endpoint	Decisive control
Enzyme tunnelling	Hydrogen-transfer kinetics, isotope dependence, active-site structure, and protein motion.	Transfer rate to pathway flux to product-supported component replacement under loss.	Measure binding and abundance; test limiting and buffered regimes and cost an expression-based rescue.
Respiratory energy conversion	Electron transfer in complex I, proton pumping, gradient, and ATP synthesis.	Perturbed transfer to pumping to ATP-supported construction and respiratory-subunit renewal.	Measure assembly, leak, reverse flow, and input supply separately; account for compensating machinery.
DNA maintenance	Photolyase charge transfer and lesion removal; DNA-mediated transport and repair-protein redistribution.	Identified electronic step to error correction and surviving copied sequence.	Separate redox passage from DNA mechanics and protein occupancy; assay alternative repair capacity.
Orb2 conformational memory	Seeded assembly and state-dependent translation.	Persistence of a functional state while old carriers turn over; a quantum-specific contribution to templating is hypothetical.	Label old and new carriers; compare classical conformational kinetics and regulator-mediated feedback.

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Table 4. *Cont.*

Platform	Molecular foothold	Missing causal link and endpoint	Decisive control
Radical-pair sensing and regeneration	Field-sensitive cryptochrome 4 photochemistry; prospective planarian superoxide response.	Native spin reaction to cellular signal to orientation or repaired tissue, respectively.	Blind field tests; control illumination, temperature, and probe effects; identify the responsive molecular pair.
Synthetic renewal and local-rule models	Partial ATP-supported component production in constructed systems; specified classical and quantum local models.	A characterized local operation to replacement of essential parts and sustained delivered load.	Inventory all supplied apparatus; impose loss; compare architectures at matched power, material, space, time, and error.

Enzyme Tunnelling

Hydrogen-transfer enzymes permit an exacting first test of the passage from molecular rate to sustained product supply. Temperature-dependent kinetics, isotope effects, active-site structures, and protein motions constrain the transfer mechanism. Isotopic substitution changes mass, zero-point energy, and vibrational dynamics together; a kinetic isotope effect alone does not measure a tunnelling contribution. The extensive work on lipoxygenase and enzyme dynamics establishes the methodological starting point. [31,32]

A renewal study should choose an enzyme whose product supports the replacement of a defined component. Measure the elementary reaction, pathway flux, product loss, compensatory enzyme expression, and the rate at which the dependent component turns over. Predict the load and loss conditions under which a change in transfer dynamics will alter persistence. The same perturbation should be tested where the reaction limits the pathway and where a parallel route buffers it. If extra enzyme restores output, its synthesis and maintenance costs enter the comparison; an affordable rescue limits the claim.

Respiratory Energy Conversion

Respiratory complex I transfers electrons through iron–sulfur centers and couples redox chemistry to proton translocation. Electron tunnelling rates, hydration-dependent proton routes, and large conformational changes must be considered together. ATP synthase then uses the proton-motive force across a membrane to make ATP through a rotary, mechanochemical cycle. These are distinct stages: a measured electron-transfer rate does not by itself establish net proton pumping, and an ATP assay does not identify which upstream step determined its yield. [141,142,144,153]

An experiment would perturb a structurally characterized transfer step and independently quantify forward and reverse electron flow, proton pumping, membrane potential, ATP synthesis, and the work supplied to a specified cellular or synthetic load. It must also measure respiratory-subunit replacement under a controlled damage or dilution burden. The proposed quantum step may prove important because it matches a slower pumping cycle rather than because it maximizes raw transfer speed. A leakier membrane, altered complex assembly, or increased substrate supply can produce similar changes in ATP; these are measured alternatives. The comparison concerns sustained ATP-supported construction per available input, not a general claim that ATP synthase is a quantum computer.

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DNA Maintenance

Photolyase supplies a short path from light-initiated electron transfer to removal of a DNA lesion. DNA-mediated charge transport offers a separate candidate route for redox signalling among repair proteins; its sensitivity to base stacking and mismatches must be distinguished from a claim that charge remains coherent across long chromosomal distances. Proton transfer in bases presents another, less settled route to changed pairing or repair demand. These mechanisms should not be amalgamated merely because the substrate is DNA. [39,43] Caltech's Barton programme has established DNA-mediated charge transport and its relevance to redox-active replication and repair proteins; it does not require a chromosome-wide coherent state.[3]

The initial photolyase experiment would establish absorption, elementary electron-transfer and bond-breaking yields, lesion removal, enzyme stability, and alternative repair capacity. These independent quantities should predict lesion accumulation and record fidelity under a damage schedule withheld from fitting. Charge-transport studies can vary distant stacking or redox partners while measuring mechanics and protein occupancy. A distant influence must be assigned to its physical route before it is called electronic coordination. A transient effect supports the inheritance argument only if it changes a later copied or reconstructible state; otherwise it remains a repair or regulatory event.

Orb2 and Conformational Memory

The assembled form of Orb2, a translation regulator in flies, can seed further assembly and alter protein production. Cellular regulation of that state and its relation to memory are active experimental questions. This is an established example of a functional protein state, not evidence that the state is stored as a persistent quantum superposition. [20,57]

Label old and newly made Orb2, measure the state-dependent translational output, and quantify propagation, spontaneous switching, erasure, and dependence on protein-handling machinery. The distinction to be retained and the required duration must be specified before testing replacement. A hypothesized nuclear-quantum or electronic contribution to conformational conversion first needs a mechanistic signature that predicts transfer or templating under held-out structural and isotopic changes. Classical conformational kinetics and feedback are full competitors, with the same writing and maintenance resources counted. If the template persists only because a detectable original seed remains, report continuity of the seed and renewal of the surrounding assembly separately.

Radical-Pair Sensing and Regeneration

Cryptochrome provides a molecular setting in which transient correlations between the spins of two unpaired electrons can affect reaction yield in a weak magnetic field. Magnetic sensitivity has been measured in a migratory bird's cryptochrome 4; the identity of the native sensory pathway from that chemistry to navigational behavior remains an additional question. [46] Planarian regeneration offers a different path from weak-field exposure through reactive oxygen chemistry to tissue function. A 2026 study confirmed a model's prospective nonmonotonic predictions for superoxide, while leaving the responsible radical pair and the relation between superoxide and final regeneration unresolved. [47]

The two systems should be tested on their own terms. In birds, pair formation and reaction yield, cellular signalling, and orientation are separate readouts. In planarians, measure the spin-sensitive reaction if accessible, superoxide and other reactive products, stem-cell responses, and repaired tissue. Freeze predictions for new field strengths, directions, or timing schedules before measuring the distal result. Blind exposure, control temperature and illumination, and test whether the chemical probe itself responds to the field. A field-dependent tissue outcome without a verified molecular link does not establish an organismal quantum advantage. The weak-field programme is especially useful

[3] J. K. Barton, Caltech research profile, https://cce.caltech.edu/faculty/jacqueline-k-barton.

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because a short-lived spin event can leave an ordinary chemical signal without requiring persistent organism-wide coherence.

Synthetic Renewal and Local-Rule Models

A constructed system can declare its inventory and losses more completely than an organism. Combine a controlled energy-conversion module, a protein-synthesis module, and a specified load while tracking which essential parts are made anew. Classical cellular automata (CCA) can model local state transitions; quantum cellular automata (QCA), or more generally local open-quantum-system models, can test whether phase-sensitive dynamics changes a defined completion distribution. A simulator is a comparison tool. Its quantum gate does not become a biological mechanism until its preparation, couplings, losses, and readout match a characterized molecular system.

The model should compare four references: a mechanistic classical approximation; a stochastic local network retaining quantum-derived transition probabilities; an open quantum model with the experimentally constrained couplings; and a different admissible architecture. Its state variables must include consumable substrates, vulnerable machinery, component synthesis, loss, reset, and delivered output. If the density matrix stays diagonal under the stated dynamics, the stochastic and quantum calculations must agree. If a directed classical route succeeds within the same time, space, and energy limits, a pairwise advantage over dephasing has no general force. The capstone experiment below provides the more demanding material counterpart to this calculation.

44. The Core Experimental Logic

Each study begins with a causal chain: a specified molecular state or transition, a chemical intermediate, a functional output, and, where relevant, replacement or adaptation. Measure the microscopic variables before measuring the endpoint used to judge the prediction. A model fitted to ATP production, survival, or behavior cannot treat the fitted transfer rate as independent evidence for those outcomes. The experiment should record unproductive branches, reverse reactions, damage, and reset as well as its chosen successful branch.

The comparator follows the claim. A classical-nuclear calculation on the same electronic surface can test whether an additional nuclear quantum treatment is required. A kinetic or stochastic network can test whether intersite phase information improves predictions after its local rates have been measured. A physically different route, with additional enzyme, memory, integration time, or energy, tests whether the quantum-sensitive implementation is necessary under the declared resource budget. Those comparisons answer different questions. Neither dephasing nor an intentionally poor classical controller represents every physically admissible alternative.

Table 5. Four reference classes answer different questions. The mechanism under test and the permitted compensations must be declared before comparison.

Reference class	Question tested	What is held fixed or measured	Limit of inference
Classical nuclei on a quantum electronic surface	Does explicit nuclear quantum dynamics improve the account of a reaction?	The stated electronic potential, environment, observables, and nuclear preparation.	This does not remove the quantum electronic basis of bonding.
Quantum-calibrated stochastic network	Does retained phase across steps improve predictions beyond measured local transition rates?	Reaction graph, forward and reverse rates, loss, reset, and input conditions.	Successful kinetics do not establish a physical mechanism that produces those rates without quantum effects.

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Table 5. *Cont.*

Reference class	Question tested	What is held fixed or measured	Limit of inference
Phase-retaining open quantum model	Do specified couplings and dephasing predict an observable missed by the stochastic network?	State preparation, couplings, environmental losses, readout, and their uncertainties.	A better fit alone does not prove native preparation, biological advantage, or necessity.
Alternative physical architecture	Can another arrangement sustain the same output, fidelity, and renewal within the resource budget?	Input power, material, volume, deadlines, error tolerance, and compensation costs.	Failure of one alternative cannot exclude every admissible design.

The intervention must also be identified by what it changes. Isotope replacement can alter geometry and zero-point energy. A protein mutation may change binding, stability, expression, and membrane insertion. A magnetic field can act on instrumentation or an unrelated radical. Characterize these effects, use independent rescue where feasible, and test both conditions in which the candidate step should be limiting and conditions in which it should be buffered. The latter provides a mechanism-specific null, not a disappointing result.

An interaction between microscopic condition and network position can expose the intended dependence. If $F(q, A)$ is a functional output for condition q in organization A, the predeclared contrast

$$\mathcal{I} = [F(q_1, A_1) - F(q_0, A_1)] - [F(q_1, A_0) - F(q_0, A_0)]$$

asks whether the molecular perturbation matters differently when the organization depends on that operation. A nonzero interaction does not certify the microscopic mechanism; it is interpreted with the independent chemistry and control measurements. An interaction absent where buffering was predicted can strengthen the chain more than a large effect observed under nonspecific damage.

The more consequential result is a change in a viability boundary. Define in advance the acceptable region for output, fidelity, and apparatus integrity, a horizon over which these must persist, and a maximum failure probability. Increase loss, dilution, or load through an independently chosen range. A quantum-sensitive step has organizational leverage if the measured change in its chemistry predicts the boundary at which the system can no longer renew and perform its task. The alternative receives the same input and permission to compensate; its added material, power, space, or time is counted. This is a conditional result about a system and budget, not proof that all possible life requires one mechanism.

45. Cross-Platform Hypotheses

The six platforms can test recurrent propositions without forcing their chemistry into one explanatory scheme. Predictions should be registered by platform, with both success and contrary outcomes contributing to the cumulative assessment.

Leverage at bottlenecks.

A quantum-sensitive reaction should change whole-system output most when its product limits another required operation. A comparable perturbation should be buffered when the pathway has spare capacity or an affordable bypass. The prediction is a change in sensitivity across measured network arrangements, not that quantum reactions always improve performance.

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Evolutionary tuning.

If a naturally occurring geometry or protein environment enhances a quantum-sensitive step, substitutions that alter that geometry should change the independently measured molecular mechanism and the relevant function in a predicted direction. Selection of a faster enzyme alone does not establish selection for tunnelling: ordinary binding, abundance, and stability must be included, and a matched classical-nuclear model must be challenged by held-out data.

Quantum-to-classical retention.

A transient transfer, excited state, or spin correlation may be valuable because it selects a chemical branch whose product lasts after the quantum state has gone. This predicts a measurable dependence of a downstream stable record on the initial mechanism without predicting a long-lived coherent state in the record. Photolyase repair and radical-pair product formation supply distinct tests.

Extended molecular context.

Geometry outside the immediate reaction site can alter access to a productive pathway. In enzymes, DNA, and protein assemblies, compare electronic, electrostatic, mechanical, and solvent-mediated routes by making each predict a held-out intervention. The physical range of charge migration, the extent of a delocalized state, and the range of biological influence must be reported separately. A distant effect need not be a quantum search over distant configurations.

Shifted viability boundaries.

When the target reaction supports replacement, a measured mechanism change should predict the highest tolerable loss or load over a stated interval. A gain in initial flux with no increase in sustainable output is not a renewal gain. The strongest test crosses a boundary predicted from independent rates, not one chosen after seeing survival curves.

Two channels of inheritance.

A copied molecular description and a transmitted conformational state can each carry inherited differences, though their scope, fidelity, and need for an interpreter differ. Compare them only on a common required task and count writing, copying, templating, repair, and construction. A proposal that a quantum contribution changes one of these costs requires a separate microscopic test. The existence of Orb2 memory does not establish such a contribution.

Weak-signal sensing.

Spin chemistry may convert a small field-dependent change in reaction yield into a biochemical signal. Predict the field profile from molecular measurements, then predict the cellular response and behavior or tissue consequence. A classical detector that integrates longer or uses more components is an admissible comparator if those resources exist under the same conditions.

Synthetic renewal.

A light-driven quantum-sensitive step can contribute to ATP formation; ATP can support synthesis of the machinery that enables further ATP formation. The crucial prediction is sustained activity while initial machinery is demonstrably replaced and a defined load is supplied. A partial loop is a valuable result, but it is not a self-reproducing cell merely because new protein appears.

46. A Capstone Experiment in Artificial Cells

Berhanu, Ueda, and Kuruma encapsulated bacteriorhodopsin and ATP synthase in proteoliposomes within a larger vesicle, alongside a cell-free transcription–translation system. Light-driven proton pumping made ATP that supported protein synthesis; newly made bacteriorhodopsin, and in a separate configuration membrane-sector subunits of ATP synthase, contributed to the energy-producing apparatus and increased measured activity. The finding is an important partial reciprocal

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loop. It began with purified energy machinery, translation machinery, membrane components, and templates; it did not show that the whole apparatus could replace itself through repeated loss. [125]

Lavickova, Laohakunakorn, and Maerkl approached the complementary problem through a microfluidic transcription–translation system. It renewed selected proteins needed for its own operation and sustained synthesis for more than a day while resources were supplied and material was diluted. Their experiments made competition for expression resources and the ratios of DNA templates part of the mechanism. They did not construct an independently renewing, light-powered vesicle. [177]

The capstone would join the two demands in stages, rather than assume their existing apparatuses can simply be combined. First establish a compatible feed and membrane environment in which light-driven ATP synthesis powers a measured fraction of protein construction while a specified protein component is deliberately depleted. Then quantify incorporation of newly synthesized component into the functional energy apparatus. Only after these links are measured should the system undergo serial dilution or imposed component loss over repeated intervals. The list of essential supplied components—ribosomes, polymerases, aminoacyl-tRNA synthetases, membranes, cofactors, and energy substrates—must accompany every result. Renewing some of them while supplying the rest is partial renewal; the fraction and function of the renewed set can still be quantified.

A functional load should consume a declared share of ATP or its downstream chemical product. Report absorbed photons and usable free energy, ATP production and consumption, productive protein synthesis, assembly and activity of newly made energy components, loss of old material, and output to the load. Pulse–chase labels can separate the initial stock from replacements. Time courses at more than one dilution or damage rate can distinguish true renewal from a slowly depleted reservoir. Membrane leakage, photodamage, and accumulation of inhibitory products belong in the balance.

The molecular comparison requires a candidate photochemical, electronic, or proton-transfer change characterized independently under the actual operating conditions. It may alter the bacteriorhodopsin photocycle or coupling between its proton pumping and ATP synthesis; absorption, orientation, membrane insertion, and stability must be remeasured. A matched classical-nuclear description or a physically different energy-conversion module supplies an appropriate comparison for the stated claim. If no intervention isolates a quantum-sensitive contribution with sufficient specificity, the experiment remains a strong test of coupled renewal but cannot be called a demonstration of quantum advantage.

The preregistered prediction is the maximum loss and load compatible with sustained ATP-supported replacement over a fixed horizon, with uncertainty propagated from molecular measurements. The alternative may use more catalyst, different placement, or an engineered bypass within the same specified budgets. The result is strongest if independent molecular parameters predict a range where one implementation continues renewing while the best admissible alternative cannot, and if the boundary moves as predicted under a new illumination, turnover, or substrate condition. Failure of that discrimination would narrow the quantum claim while preserving the value of a synthetic renewal loop.

47. Adversarial Validation and Stopping Rules

The programme should publish a constraint set before seeking a decisive outcome: the functional task, measured microscopic variables, permissible perturbations and alternative architectures, preparation and reset costs, input budget, time horizon, and acceptable failure rate. Calibrate on one set of conditions and freeze the downstream predictions for another. Independent laboratories should reproduce the molecular link and the functional consequence where feasible; a replication of only the final endpoint is insufficient if the claim depends on a particular mechanism.

Several outcomes require stopping or narrowing the claim. If a mechanistic classical-nuclear or spin-independent model predicts the molecular data across held-out conditions, the proposed additional quantum resource has not been identified. If the measured molecular change does not alter the intended intermediate, the proposed causal path ends at the local result. If the intermediate

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changes but affordable buffering preserves function, necessity fails for that regime. If function changes while structural, optical, toxic, or instrumental alternatives remain unresolved, the result is not yet attributable to the candidate mechanism. If renewed material does not replace an essential part of the initial apparatus, continued output does not establish renewal of that part. The larger thesis must contract if these outcomes recur across platforms.

Negative results should remain in the cross-platform record with the detection limits and power of their tests. Quantum dynamics may be necessary to calculate a local reaction while an ordinary stochastic network accurately describes its later propagation. That is a coherent outcome, not a failed quantum explanation. Conversely, a measured nonclassical signature is not enough if it never affects the work, fidelity, or renewal under examination. The distinction allows cumulative evidence to change the scope of the argument rather than only its rhetoric.

Conclusion. The Work of Continuity

Quantum mechanics gives matter stable, differentiated structures and selective routes between them. Living systems exploit particular routes: electrons and protons move through organized proteins, light initiates chemical changes, spin can alter reaction yields, and rare molecular states affect copying or repair. The observed strength of the evidence differs among these cases. Their common feature is local dynamics whose products can persist as chemical, conformational, or electrical records after the initiating coherence is lost.

Those records acquire biological consequences through organized work. An electron-transfer step contributes to a gradient only within a functioning respiratory assembly; a photochemical change becomes a signal only because a cell amplifies it; a hereditary difference persists only when copying, correction, and construction operate. Each assembly also consumes resources and loses components. A satisfactory account must follow the physical operation through its useful output and back to the production or preservation of the machinery that enables further operation.

No universal theorem here proves that every living system needs a particular quantum effect beyond the quantum structure of ordinary matter. Several mechanisms are well established locally; their necessity for sustained biological function under realistic alternatives is less often known. Classical feedback, template inheritance, molecular motors, and cellular automata remain substantive explanations and comparison systems. Long-lived collective coherence, neural quantum computation, and consciousness proposals have additional requirements that the molecular-to-organizational argument does not assume.

The decisive experiment is a constrained causal comparison. It identifies a quantum-sensitive transition, measures the record it produces, follows the record into work or renewal, and permits the best affordable alternative to compensate. A changed viability boundary at matched power, material, time, and error would establish a kind of physical contribution that an isolated spectroscopic result cannot. If the alternative reaches the same boundary, the claim contracts. Either result improves an account of how living matter continues while its material changes.

Data availability: This monograph synthesizes published research and develops theoretical arguments and proposed experimental designs. Sources are identified in the references, and the mathematical definitions and derivations are provided in the text and appendices. No new participant-level data are reported.

Ethics approval and informed consent: Not applicable. This manuscript reports no new studies involving human participants or experimental animals.

Generative AI disclosure: OpenAI ChatGPT/Codex was used extensively to identify and organize literature, draft and revise substantial portions of the prose, assist with mathematical exposition, organize references, and prepare the LaTeX manuscript. Jeffrey Satinover conceived the monograph's central thesis and research questions. He developed its hypotheses concerning how local quantum-sensitive events can leave durable records and affect biological deadlines, useful work, inheritance, and the renewal of living systems. He specified the need to compare these effects with physically admissible alternatives under matched constraints on energy, material, time, and error, and to judge their significance by changes in sustained function and viability boundaries. He

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determined the scope of the argument, directed its treatment of competing explanations and stronger coherence claims, and guided successive revisions. He is responsible for the arguments, the accuracy of the final text and citations, and any errors. No AI system is an author.

Appendix A. The Quantum Mechanisms in the Argument

The glossary distinguishes a physical effect from a biological use of that effect. Category A applies when a specified classical description cannot reproduce a mechanism or when a theorem excludes a stated class of models. Category B concerns the inability of alternatives to perform the same biological task within declared limits. A mechanism may clearly belong to A while its proposed biological necessity remains unproved. Several entries describe overlapping aspects of the same process and should not be counted as independent evidence.

Appendix A.1. Bound Electronic States

An electron bound in an atom or molecule occupies a quantum state with a characteristic distribution and energy. Such states provide the basis of persistent molecular identities. An effective classical potential can represent their consequences without deriving the same atomic world from ordinary classical electrodynamics. This is a foundational category-A contribution to actual matter, not a feature that distinguishes living matter on its own. Its biological role becomes specific when the resulting structures are used in construction, recognition, and renewal. [21]

Appendix A.2. Pauli Exclusion, Exchange, and Indistinguishability

Electrons are indistinguishable fermions, and their joint states have the required antisymmetry. Exclusion and exchange affect how electronic matter can be organized and contribute to the stability of bulk matter. These are not ordinary interactions among distinguishable classical particles. Their effects can be included in a classical molecular force field, but the representation does not remove their physical origin. Their occurrence is universal to the relevant material, while any particular biological advantage requires a further functional argument. [21]

Appendix A.3. Nuclear Zero-Point Motion

A nucleus in its lowest vibrational state is not a motionless point at the bottom of a potential well. Its state has energy and spatial extent, with especially appreciable consequences for light nuclei. These effects can change hydrogen-bond distributions and the conditions for a reaction. They do not provide an inexhaustible energy source. A category-B claim must show how the changed molecular distribution affects a constrained function rather than infer usefulness from the presence of hydrogen. [30]

Appendix A.4. Electron Tunneling

Quantum electronic transfer can occur through a region that a classical particle at the specified energy could not cross. Molecular separation, bridge structure, and environmental reorganization affect the probability. The mechanism is nonclassical relative to that particle description, although selected wave analogues and fitted rates can represent aspects of it. Biological necessity concerns whether another physical route can meet the same timing, yield, size, and energy requirements. [33]

Appendix A.5. Hydrogen, Proton, and Hydride Tunneling

Light-nucleus transfer can include penetration of a reaction barrier. The associated electronic rearrangement determines whether the chemical event is described as proton, hydrogen-atom, or hydride transfer. Thermal protein motion may prepare favorable tunneling geometries. Evidence from selected enzymes establishes a microscopic role; the further question is whether that role changes pathway output or renewal after compensation is counted. An isotope effect alone does not isolate the tunneling contribution. [31,32]

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Appendix A.6. Superexchange

Superexchange describes bridge-mediated electronic coupling through intermediate states that need not become long-lived populated carriers. It differs from a sequence of ordinary residence-and-transfer steps, although both may enter one larger transport network. The term identifies a mechanism within electronic transfer, not a separate general source of biological advantage. An alternative hopping architecture may work, but with different spacing, energetic, or loss costs. Those costs determine the category-B comparison. [33]

Appendix A.7. Proton-Coupled Electron Transfer

PCET describes a reaction in which electronic and protonic changes are coupled. Concerted transfer can avoid an unfavorable intermediate; sequential transfer can be effective in other regimes. Quantum electronic coupling and overlaps between quantized proton states may affect the rate. The mere coupling of two events is not uniquely quantum. A functional comparison includes proton acceptors, environment, reverse reactions, and regeneration of the operating state. [34]

Appendix A.8. Inelastic Electron Tunneling

In an inelastic transfer, electron motion exchanges energy with another degree of freedom, such as molecular vibration. A vibration-sensitive tunneling mechanism has been proposed for olfaction. Behavioral and receptor-level results do not presently establish a general physiological requirement for that mechanism. Isotope-dependent discrimination can have more than one physical cause. The proposal belongs among testable mechanisms rather than established examples of irreplaceable biological quantum computation. [50,51]

Appendix A.9. Proton Rearrangement in Hereditary Bases

Alternative proton configurations can change base-pairing properties. A particular rearrangement may include tunneling, but an observed rare state is not thereby identified as a tunneling product. Its contribution to mutation also depends on persistence, copying, correction, and fixation. Such dynamics can threaten fidelity as well as supply variation. Adaptive generation of useful variants is a stronger claim than any of these molecular effects. [42,43]

Appendix A.10. Quantized Absorption and Emission

Molecules exchange energy with light through transitions among electronic states. An absorption can initiate a durable chemical or electrical record; emission can follow an organized chemical reaction. Some observations admit a description using classical light with quantum matter, so individual detection events alone do not establish nonclassical photon statistics. The biological comparison concerns the attainable sensitivity, discrimination, noise, and cost of the complete operation. [3,40]

Appendix A.11. Nonadiabatic Transitions and Conical Intersections

In a nonadiabatic process, electronic and nuclear motion cannot be separated into one fixed electronic surface followed by the nuclei. A conical intersection is a degeneracy of electronic energy surfaces that can permit rapid changes of state. Such pathways matter to visual reactions and photoprotection. Classical nuclear trajectories on quantum surfaces can still reproduce some behavior; an additional requirement for coherent nuclear motion needs its own evidence. Timing relative to competing decay is a promising category-B target. [2,38]

Appendix A.12. Excitonic Delocalization

An electronic excitation can be distributed over several interacting pigments or bases. The relevant state concerns the coupled assembly rather than an independent excitation at one site. The amount and duration of delocalization depend on preparation, disorder, and environment. Some transfer signatures have classical-oscillator counterparts, so spatial extension alone does not prove a uniquely

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quantum biological capability. The useful quantity is the effect on a defined output under physical constraints. [28,35]

Appendix A.13. Interference Between Pathways

Quantum alternatives can contribute complex amplitudes that enhance or suppress an outcome when combined. This differs from adding independent hopping probabilities. Classical waves also interfere, which limits what a visible interference pattern establishes about replaceability. The potential biological benefit is selective routing or suppression of loss channels. It must be compared with serious wave and stochastic alternatives, not only independent particles with no collective organization. [28]

Appendix A.14. Vibrational Quantization and Vibronic Coupling

Molecular vibrations have quantized states. Their overlaps and coupling to electronic states can influence spectra, transfer, and reaction branching. Vibronic behavior involves this electronic–vibrational relationship. An observed oscillation may be electronic, vibrational, or mixed, with different implications for function. A classical vibration is not automatically an additional quantum resource simply because it occurs in a protein. The contribution of quantization or coherence must be separated experimentally and theoretically. [35,36]

Appendix A.15. Environment-Assisted Transport

Environmental fluctuations can improve transport in specified quantum models by counteracting localization or other unfavorable dynamics. The effect illustrates why maximum isolation is not a universal biological objective. Beneficial noise is not uniquely quantum as a general phenomenon, and an optimum in a model is not proof of biological optimization. The comparison must establish the actual environment and productive endpoint, including how added dephasing changes local rates. [37]

Appendix A.16. Superradiance and Subradiance

Coupled emitters can occupy collective states with enhanced or suppressed radiation relative to independently acting emitters. These states are described by quantum radiative theory. Some optical signatures have classical collective analogues, so brightness or changed lifetime alone is not a sufficient nonclassical witness. Biological use requires plausible excitation, a useful consequence, and the appropriate state or photon-statistics evidence. Tryptophan-network studies motivate investigation without establishing a neural quantum computer. [73,74]

Appendix A.17. Electron and Nuclear Spin

Spin is a quantum degree of freedom with magnetic and chemical consequences. Joint spin configurations can differ in reaction accessibility. Semiclassical vector models can approximate some observations without reproducing every property of quantum spin. The presence of spin is therefore a mechanism-level fact, while advantage in sensing or regulation requires a specific task and comparison. Treating spin as a tiny literal rotating sphere is inadequate. [46]

Appendix A.18. Radical-Pair Spin Dynamics

Two radicals created in a related process can evolve among singlet and triplet character through magnetic interactions. Spin-selective reactions convert that evolution into different product yields. The effect is a strong candidate for molecular sensing under tight constraints, but a field response in tissue does not identify the relevant pair by itself. Preparation, relaxation, native signaling, and alternative sensors belong in the biological comparison. [46,47]

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Appendix A.19. Chirality-Induced Spin Selectivity

A chiral molecular structure can transmit electrons in a spin-dependent manner. This connects spatial organization to electronic selectivity. Chirality is not itself uniquely quantum, and measurements on prepared DNA assemblies do not automatically establish a native physiological advantage. Contacts, orientation, redox conditions, and competing reactions must be considered before assigning the effect a role in metabolism or inheritance. [48]

Appendix A.20. Magnetic Isotope Effects

Isotopes differing in nuclear spin can alter spin-dependent chemistry. Their masses and vibrational properties can differ too, making the attribution a controlled experimental question. A magnetic isotope effect is a diagnostic consequence of a mechanism, not a separate universal resource. Reported anesthesia differences motivate replication and molecular identification; they do not establish entanglement as a cause of consciousness. [137]

Appendix A.21. Long-Lived Nuclear-Spin States

Some joint nuclear-spin configurations relax slowly under suitable interactions. Controlled NMR experiments establish that such states can retain information longer than conventional spin observables. Biological use would additionally require preparation, manipulation, readout, and a resource budget. A long relaxation time is not evidence of coherence between arbitrary molecular shapes or cellular alternatives. The proposed information task must be identified before evaluating advantage. [49]

Appendix A.22. Entanglement

An entangled quantum state cannot be represented as a statistical mixture of product states for the specified subsystems. This is a nonseparability property, stronger than ordinary correlation. Selected output statistics may still admit classical simulation, and entanglement does not guarantee a Bell violation in every measurement setting. Molecular entanglement models require appropriate witnesses and a causal connection to function before supporting biological necessity. [70,89]

Appendix A.23. Bell-Nonlocal Correlations

Suitable Bell-inequality violations exclude local hidden-variable models satisfying explicit assumptions about locality and measurement settings. They do not exclude a centralized simulator permitted to coordinate outputs. The experiments establish a strict statistical distinction, but no biological task in this book has been demonstrated to require it. Extended transport in DNA is not a Bell test. [26]

Appendix A.24. Quantum Contextuality

Contextuality concerns the failure of models that represent specified operationally equivalent procedures in a noncontextual way. It is not simply the dependence of a reaction on molecular surroundings. A claim requires a defined experimental or operational test. Contextual classical simulations and limited noncontextual physical models are different reference classes. No organismal necessity follows from using the word context in a biological explanation. [27]

Appendix A.25. Decoherence and Recording

Interaction with an environment can suppress observable interference and leave distinguishable consequences. Those records can persist much longer than the initiating coherent state. Tegmark's influential analysis illustrates how devastating decoherence can be to proposals that require coherent neural degrees of freedom to persist across much longer biological timescales. [1] The present argument does not generalize that objection beyond its target. Once a quantum operation has produced a distinguishable chemical or conformational record, subsequent loss of coherence does not undo the record. When all later influence passes through classical records, their complete conditional

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distributions determine downstream statistics. Reproducing those distributions may still be physically costly. Decoherence is therefore both a constraint on proposed quantum operations and part of the account of how brief quantum events become lasting biological consequences. [75,76]

Appendix A.26. Measurement Randomness

Quantum measurement produces outcome probabilities with a quantum physical origin. Randomness alone does not establish a distinctive biological capacity. A system supplied with another source reproducing the relevant record laws can respond identically, subject to the costs of that source. A useful advantage would concern additional correlations, certification assumptions, accessibility, or resource limits. Unpredictability by itself does not explain adaptation, evaluation, or creativity.

Appendix A.27. The Prohibition on Universal Cloning

No physical operation can perfectly copy every arbitrary unknown quantum state. This restriction does not prevent copying distinguishable hereditary records, transferring a state, or encoding information for correction. The relevant operation must be stated. Biological continuity need not preserve the exact microscopic state of every original component. No-cloning constrains proposed mechanisms; it is not itself evidence that life has a uniquely powerful copying ability. [45]

Appendix A.28. Quantum Chaos and Scarring

Quantum systems related to classically chaotic dynamics can show structured eigenfunctions or distinctive transport behavior. Heller's scars concern enhanced structure near particular classical periodic orbits in specified systems. They are not a theorem that biological complexity protects coherence or improves cognition. A useful molecular proposal would identify the Hamiltonian, environment, relevant lifetime, and functional observable. Difficulty predicting a trajectory is not evidence of purpose. [133]

Appendix A.29. Quantum-Assisted Conformational Transitions

Tunneling or other quantum dynamics can in principle affect movement among molecular conformations. Calling the process quantum annealing does not establish a native folding algorithm. The appropriate comparison is dynamics on a matched, physically adequate landscape with environmental interactions and competing loss. Classical folding pathways and template constraints are substantive alternatives to exhaustive search. A category-B claim requires that the specified contribution changes functional completion under those conditions. [134,135]

Appendix A.30. Quantum Search and Amplitude Amplification

Quantum algorithms can give rigorously defined advantages for particular search problems. Grover's algorithm supplies a quadratic oracle-query improvement for unstructured search; other access models can yield larger separations. These results do not supply a biological oracle, coherent state preparation, or costless readout. A deadline could make an implemented algorithmic advantage biologically decisive, but the physical mechanism has to be demonstrated. [91,92]

Architectural Ideas That Are Not Additional Quantum Effects

Description-based construction, conformational templating, feedback, developmental patterning, and renewal describe organizations of operations. They can be implemented through different physical mechanisms. Classical cellular automata demonstrate some of their logical possibilities. QCA provide a framework for local quantum dynamics, not a new elementary effect alongside tunneling and spin. Similarly, quantum epigenetics, adaptive mutation, and quantum neural computation combine proposed mechanisms and functional claims. Their names do not establish the links between them.

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Organizational Terms Used in the Argument

Organizational Continuity Through Turnover denotes persistence of defining relationships while the material carriers of those relationships are progressively replaced. *Fließgleichgewicht* names a flowing steady state in which macroscopic conditions can remain approximately stable despite continuing material flux; it should not be confused with thermodynamic equilibrium. *Morphostasis* emphasizes preservation or restoration of form, whereas *homeorhesis* emphasizes stability of a developmental or adaptive course through changing states. These are organizational descriptions, not additional quantum effects. Their role is to specify what the quantum mechanisms later discussed would have to help sustain. [6,8,9]

Appendix B. Mathematical Framework

Appendix B.1. Component Renewal

The two-component maintenance system has matrix

$$A = \begin{pmatrix} -d_x & k_1 \\ k_2 & -d_y \end{pmatrix}.$$

Its characteristic polynomial is

$$\lambda^2 + (d_x + d_y)\lambda + d_x d_y - k_1 k_2 = 0.$$

With positive losses and nonnegative productive coefficients, the larger root is positive exactly when $k_1 k_2 > d_x d_y$. Uniform added dilution replaces A by $A - \delta I$ and shifts each root by $-\delta$. These statements establish a low-abundance deterministic boundary. They do not establish a stable finite equilibrium, favorable nonlinear behavior, or survival with probability one.

For a differentiable matrix with simple eigenvalue λ, write $Av = \lambda v$ and $w^T A = \lambda w^T$, choosing $w^T v = 1$. Differentiating the first relation gives $A'v + Av' = \lambda' v + \lambda v'$. Left multiplication by w^T cancels the terms containing v' and yields

$$\lambda' = w^T A' v.$$

The identity is general under these assumptions. Its use in a positive maintenance network supplies the interpretation in terms of the location of a rate change. Degenerate eigenvalues or changes in the chosen operating state require further analysis.

Appendix B.2. Work and Replacement

For the phenomenological model,

$$E_{\mathrm{ss}} = \frac{yuk - d}{b}, \qquad P_L = \frac{wk}{b}(1-u)(yuk - d).$$

The first and second derivatives with respect to u are

$$\frac{dP_L}{du} = \frac{wk}{b}(yk + d - 2yku), \qquad \frac{d^2 P_L}{du^2} = -\frac{2wyk^2}{b} < 0.$$

The stationary point is consequently the unique interior maximum when $yk > d$. Substituting $u_{\mathrm{free}} = (1 + d/(yk))/2$ gives $P_{L,\max} = w(yk - d)^2/(4yb)$. The inequality $P_{\mathrm{in}} = \Delta\mu k E_{\mathrm{ss}} \le P_0$ supplies the upper bound

$$u_{\mathrm{cap}} = \frac{d + bP_0/(\Delta\mu k)}{yk}.$$

Concavity justifies clipping the optimum to the permitted interval.

The construction cost implicit in y, the work w, and the supplied free energy $\Delta\mu$ must be physically compatible. The calculation does not derive those quantities from a microscopic chemistry. The

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nonlinear loss term is also a stipulated effective description. Changing that description changes the optimum.

The derivative establishes the optimum within the stated model.

Appendix B.3. Stochastic Reduction and Record Equivalence

Let a local channel preserve diagonal states in a chosen product basis. For a diagonal input $\rho = \sum_x p(x)|x\rangle\langle x|$, linearity gives

$$\mathcal{E}(\rho) = \sum_x p(x)\mathcal{E}(|x\rangle\langle x|).$$

By diagonal invariance, each term is diagonal. Its entries define $K(y \mid x) = \langle y|\mathcal{E}(|x\rangle\langle x|)|y\rangle$. Complete positivity makes them nonnegative, and trace preservation gives $\sum_y K(y \mid x) = 1$. Thus the output distribution is $p'(y) = \sum_x K(y \mid x)p(x)$. Applying the argument to each block and layer proves the stated local stochastic reduction.

The result allows correlated classical initial states but requires all permitted operations and observations to respect the chosen classical sector. For an instrument whose outcomes are retained, impose this invariance on each trace-nonincreasing branch; its entries then define the joint probabilities of outcome and successor state. It is sufficient, not necessary, for the existence of a stochastic description. Failure of diagonal invariance does not prove that no larger classical representation works.

The record-equivalence result is less restrictive. Equality of every causal next-record kernel implies equality of the product defining the full record law. The same downstream response then gives equal output statistics. The substitute may require memory or control absent from a feasible physical implementation. A description theorem is not a resource theorem.

Appendix B.4. Why Amplification Does Not Manufacture Information

For a column-stochastic matrix K, define total-variation distance as $D_{\mathrm{TV}}(p,q) = \frac{1}{2}\sum_j |p_j - q_j|$. Then

$$\begin{aligned} 2D_{\mathrm{TV}}(Kp,Kq) &= \sum_i \left| \sum_j K_{ij}(p_j - q_j) \right| \\ &\le \sum_{i,j} K_{ij}|p_j - q_j| \\ &= \sum_j |p_j - q_j|. \end{aligned}$$

The inequality uses nonnegative entries and column normalization. It compares the same processing of the two distributions. New observations, changed interventions, or a different processing channel change the question rather than violate the result.

Appendix B.5. Completion Before an Independent Loss

Let T be the time of correct completion, allowing $T = \infty$ on failure, and let L be an independent exponential loss time with rate $\lambda > 0$. Then

$$\Pr(T < L, T < \infty) = \int_{0^-}^{\infty} \Pr(L > t)\, dF(t) = \int_{0^-}^{\infty} e^{-\lambda t}\, dF(t).$$

The completion distribution refers to a specified readout or reaction product. The expression is not independent of how quantum arrival is monitored. With state-dependent or correlated loss, the joint dynamics must be modeled instead.

Stieltjes integration by parts gives $\eta(\lambda) = \lambda \int_0^{\infty} e^{-\lambda t}F(t)dt$, with the stated conventions for immediate completion and failure mass. Pointwise dominance of completion distributions therefore

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implies dominance for every positive independent exponential hazard. Equal mean completion times do not imply that ordering.

For an illustrative equal-mean example, the two success probabilities at hazard one are $e^{-2} = 0.1353353$ and $(e^{-0.5} + e^{-3.5})/2 = 0.3183640$. Their hard-deadline probabilities at time 2.5 are respectively one and one-half. These are classical illustrative distributions; they explain the criterion rather than demonstrate quantum performance.

In the generic successor model, the mean reproduction measure is $\mu(dt) = be^{-\lambda t}dF(t)$. Its mass is $R = b\eta(\lambda)$. Under regularity conditions for the age-dependent renewal equation, an exponential ansatz gives $1 = \int e^{-rt}\mu(dt)$. This identifies the antecedent branching calculation used in the construction example. Feedback, depletion, interdependence, and construction costs are excluded at that stage. [93]

Appendix B.6. The Finite Local-Register Comparison

The register has six sites and starts with one excitation at the first site. A neighboring block acts by the unitary rotation

$$U_B = \begin{pmatrix} \cos\theta & -i\sin\theta \\ -i\sin\theta & \cos\theta \end{pmatrix}, \qquad \theta = \pi/4,$$

on the two relevant site amplitudes and as identity elsewhere. A macrostep applies disjoint even bonds followed by disjoint odd bonds. The last site is absorbed after the full macrostep, and the absorption probability is recorded. Remaining probability plus accumulated absorption equals one.

The coherent calculation retains amplitudes and their phases. A dephased version removes off-diagonal entries after each block. The corresponding stochastic block uses the squared moduli of the unitary entries; its completion law is identical to the dephased law by the argument in B3.

An ideal directed classical conveyor arrives at macrostep three. It has a different architecture, supplied directionality, and no calibrated energy model. By macrostep six, completion probabilities are approximately 0.7136848 for coherent dynamics, 0.1845703 for the dephased or stochastic route, and 1 for the conveyor. Summing discounted completion probabilities through macrostep 200 at independent loss rate 0.1 gives approximately 0.5061657, 0.2889150, and $e^{-0.3} = 0.7408182$, respectively.

The remaining probabilities after step 200 are below 3.1×10^{-7} and 1.2×10^{-6} for the coherent and stochastic routes. Omitted discounted contributions are smaller still. These are dimensionless model results, not biological rates. No thermal reservoir, calibrated molecular timescale, or self-renewing substrate is supplied. The directed route shows why superiority to a dephased version of one architecture does not establish superiority to all classical alternatives.

Appendix B.7. State Persistence with Replacement of Carriers

For the deterministic recruitment model,

$$\dot{s} = (\alpha - \delta)s - \alpha s^2, \qquad s_* = 1 - \delta/\alpha > 0,$$

the solution with positive initial fraction s_0 is

$$s(t) = \frac{s_*}{1 + (s_*/s_0 - 1)e^{-(\alpha-\delta)t}}.$$

With $\alpha = 0.8$, $\delta = 0.2$, $s_0 = 0.1$, and $t = 30$, the marked fraction is approximately 0.7499999, while the original carrier fraction is $e^{-6} \approx 0.00247875$. The endpoint follows from the displayed solution.

The carrier population is maintained externally, and replacement carriers initially lack the mark. The example is neither a model of autonomous protein synthesis nor a demonstration of memory in an organism. It has one positive deterministic stable state above threshold, not two stable states required for a complete bistable memory. Finite-population extinction and write–erase mechanisms remain separate questions.

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Appendix C. A Thematic Guide to the Evidence

The reference list combines works cited in the chapters with selected related reading. It is not a count of independent proofs. The following guide states the question each group of studies addresses. A molecular result is not treated as evidence for a viability claim unless the intervening causal links have been measured.

Energy Conversion and Work

Electron-transfer and proton-coupled electron-transfer studies define electronic coupling, nuclear motion, environmental reorganization, and reaction rates in specific molecular systems. Respiratory complexes place those mechanisms in a chain that builds an electrochemical proton gradient. ATP synthase and motors then show how gradients or nucleotide hydrolysis support chemical and mechanical loads. A complex's electron transfer is a quantum-sensitive molecular operation; measured ATP output is a downstream functional readout. Attributing a change in ATP to one electronic pathway requires perturbing that pathway and ruling out changes in assembly, redox state, proton leakage, or substrate availability. The relevant starting points in the present bibliography include Mitchell, Moser, Hammes-Schiffer, Noji, and the primary complex-I work cited in Part II. [33,34]

Enzyme studies of hydrogen transfer provide particularly developed mechanistic tests. Temperature-dependent kinetic isotope effects, structural changes, and calculations constrain how protein motions prepare donor–acceptor configurations. Neither a large isotope effect nor a fitted tunneling fraction is, by itself, a measurement of cellular fitness. The additional experiment asks whether the changed chemical step limits product formation or renewal when the organism can compensate by changing expression, substrate concentration, or pathway allocation. [31,32]

Light, Sensing, and Repair

The retinal response offers unusually clear successive readouts: absorption, chromophore isomerization, amplification, and electrical change. It demonstrates the persistence of a consequence after the initiating quantum event, without identifying every link as a coherent quantum operation. Photolyase work traces a different use of absorbed light into charge transfer and lesion repair. In photosynthesis, ultrafast spectroscopy identifies excited-state dynamics, but coherence observed under prepared laser excitation must be distinguished from productive charge separation in natural illumination. Classical oscillators and vibrational explanations are important comparison models. [2–4,28,35]

Radical-pair work asks whether magnetic fields change spin-dependent product yields. Cryptochrome experiments give a promising molecular candidate for magnetoreception, while the native receptor-to-behavior sequence requires further evidence in each organism. Planarian weak-field studies can test a predicted tissue-level response, but redox intermediates and their route to regeneration must still be identified. Chirality-induced spin selectivity and magnetic-isotope results have their own controls; neither should be treated as an interchangeable proof of the radical-pair account. [46–48]

Fidelity and Inheritance

Rare DNA proton states, polymerase kinetics, proofreading, mismatch repair, and fixation form one error ledger. The existence of a rare mispaired state does not determine its fraction of inherited mutations. DNA-mediated charge transport may let repair proteins respond to base-stack integrity across separated sites; its biological coordination distance is not the coherence length of a single electronic state. Protein conformational inheritance establishes a second kind of transmissible state, but it does not establish a new quantum information mechanism. A memory state maintained through protein turnover must be tested by labeling old and new carriers and measuring function as well as structure. [20,42,43]

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Organization, Models, and Measurement

Autopoiesis and closure of constraints identify the organizational dependency that a physical account must explain. Classical cellular automata show that complex growth and reproduction are possible with local classical rules. Quantum cellular automata represent another specified local dynamics; observing complexity in either does not establish a molecular mechanism in a cell. Artificial photosynthetic and partially self-regenerating cell systems let construction and energy conversion be joined experimentally, but present demonstrations depend on supplied components. Their value lies in exposing and progressively replacing those dependencies. [11,16,125,177]

Quantum-enabled measurement is a distinct contribution to biology. Diamond nitrogen-vacancy sensors, for example, use quantum states in an external probe to measure radicals in cells. Such a measurement can help test an endogenous mechanism; it is not evidence that the cell uses the probe's coherence. The University of Chicago's Berggren Center describes quantum sensing for biology and medicine in this instrumental sense.[4] UCLA's Quantum Biology Center explicitly connects nanoscale investigation with cellular and organismal scales, while Surrey's doctoral centre organizes work around defined biological systems and physicist–biologist collaboration.[5] This monograph shares the field's concern with causal links across scale. It concentrates on the specific question of whether local mechanisms change the feasible joint performance of work, replacement, fidelity, and persistence under matched resources.

Scholes and Fleming have asked how microscopic quantum or quantum-like events can be amplified into biological function, what measurements would establish a quantum contribution, and how convincing classical mimics should be tested. Their agenda is closely related to the methodological argument here. The distinct emphasis of this book is to organize those questions around recurring capacities of living matter and to measure their common deadlines and renewal costs. This synthesis is a proposed research framework, not an experimental discovery of a general biological advantage. [176]

Appendix D. The Extended-Coherence Frontier

The frontier literature asks questions beyond the local-mechanism account. They require an explicit state, a scale over which correlations persist, the preparation and readout under native conditions, and a functional perturbation. The pairs below indicate why an optical or magnetic signal cannot by itself settle a biological claim.

Photosynthetic Coherence

Two-dimensional spectroscopy of the Fenna–Matthews–Olson complex helped establish coherent features in prepared photosynthetic pigment–protein systems. Subsequent work found that electronic dephasing at ambient conditions can be rapid and that longer-lived oscillations may have substantial vibrational character. These studies do not cancel one another: they examine distinct states and assignments. Their unresolved biological comparison is productive transfer under natural light and a matched classical or stochastic alternative. [28,35,36,178]

Spin Dynamics

Cryptochrome radical-pair chemistry has a defined spin-dependent reaction mechanism, plausible sensitivity to weak fields, and molecular tests. The QuantumBirds programme describes demonstration of the primary retinal detection event as an active research aim.[6] A field-dependent reaction in purified protein and field-dependent orientation in an animal are two measurements; connecting them requires

[4] Berggren Center for Quantum Biology and Medicine, University of Chicago, https://berggrencenter.uchicago.edu/.

[5] California NanoSystems Institute, UCLA, https://cnsi.ucla.edu/project/september-21-2021-cnsi-launches-quantum-biology-center-at-ucla/; University of Surrey Quantum Biology Doctoral Training Centre, https://www.surrey.ac.uk/leverhulme-quantum-biology-doctoral-training-centre/research.

[6] QuantumBirds, https://www.quantumbirds.eu/.

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native preparation, signaling, and selective rescue. Spin coherence in the radical pair need not imply an organism-wide coherent state.

Collective Optics and Neural Proposals

Reports of collective tryptophan fluorescence and energy migration in microtubule preparations motivate quantitative models of coupled chromophores. Optical response can have collective classical analogues and must be measured at relevant concentrations, excitation conditions, and lifetimes. Fröhlich-type driven condensation, long-lived nuclear-spin proposals, and MRI-based claims of nonclassical brain correlations make different physical assertions. They should be assessed separately, with the conventional electromagnetic, chemical, and instrumental alternatives specified for each. None follows from the observation that neurons contain proteins or spins. [73,74,179–181]

An experiment supporting a stronger claim would demonstrate a nonclassical witness under physiological preparation, independently determine spatial extent and lifetime, perturb the witnessed quantity while maintaining ordinary chemistry and energy supply, and prospectively predict a functional readout. An outcome that can be reconstructed from the full classical record process establishes a model of downstream behavior; it does not show that the corresponding physical source is cheap or available. Conversely, a striking functional change after a nonspecific perturbation does not identify the state responsible. Independent replication and an adversarial reference model are essential.

Appendix E. Protocol for a Constrained Comparison

For each proposed quantum contribution, the study record should specify

$$\mathfrak{C} = (M, F, R, \mathcal{C}, \mathcal{I}, H, \varepsilon).$$

M is the microscopic mechanism; F the functional task and readout; R the set of permitted alternative mechanisms; $\mathcal{C}$ the resource and geometry constraints; $\mathcal{I}$ the interventions, preparation, and observation procedures; H the observation horizon; and ε the tolerated error or failure. This tuple is a reporting convention, not a physical law. The focal unit—molecule, cell, organism, or lineage—must also be stated.

Mechanism and Intermediate

Measure the state, transfer, or reaction product assigned to M under the relevant environmental conditions. Report uncertainty in the attribution: isotope substitution can change more than tunneling, magnetic fields can affect several radical reactions, and mutations can alter expression or assembly. Specify the intermediate record by which the microscopic change could affect F. A simultaneous change in mechanism and function does not establish the intermediate chain without its own perturbation and rescue.

Reference and Constraints

At least four useful reference classes can be distinguished: a mechanistic approximation that removes one term while holding other parameters as nearly fixed as possible; a quantum-calibrated stochastic network retaining local outcome probabilities but not explicit collective coherence; a collective quantum model retaining the proposed correlations; and an alternative physical architecture allowed to reorganize the task under the same resource limits. The last can defeat an advantage found against a dephased copy of the original design. An optimizer's best candidate is not an upper bound on all possible alternatives.

Account for available molecules, expression burden, volume, input power, geometry, memory, reset, preparation, waste, construction, and replacement. A synthetic cell with a preloaded enzyme has received a resource that the purported autonomous mechanism did not make. An alternative with extra parallel machinery must pay for that machinery and its renewal. If an exact match is impossible, bound the unmatched quantity and test whether the conclusion survives its plausible range.

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Function and Persistence

Record completion distributions, not only mean rates, whenever loss or a deadline matters. Measure useful output at a stated load, accuracy, turnover of essential components, and persistence through serial dilution or other specified stress. Vary one constraint at a time when identifying a boundary, then test joint operation under a shared budget. Separate a molecular rate improvement from a shift in the viable region of the complete apparatus.

Predictions and Stopping Rules

Freeze the mechanism model, its parameters, comparison architectures, endpoints, and planned exclusions before the decisive downstream experiment. Keep discovery data separate from withheld conditions. Randomize and blind where feasible, include off-target controls, and seek rescue through a different physical route. Publish negative links in the proposed chain. If the intermediate does not transmit the perturbation, narrow the causal claim. If an admissible alternative attains the same work, fidelity, and renewal within the matched budget, withdraw the claimed necessity at that constraint level. A positive result in another regime may still remain valid.

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