Genomic Architecture, Origins, and Conscious Experience: Evidence-First Answers to Persistent Questions in Genetics, Human Evolution, Abiogenesis, and Quantum-Level Claims

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Posted Date: 14 April 2026

doi: 10.20944/preprints202604.0879.v1

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 doi:10.20944/preprints202604.0879.v1

Article

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Running Title: Genomic Architecture, Origins, and Conscious Experience

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Abstract

Lists of "unsolved mysteries" in genetics, human origins and consciousness often mix (i) genuine mechanistic unknowns, (ii) limitations of measurement and reference quality, and (iii) category errors in which philosophical questions are treated as if they were missing molecular details. This review reframes each frequently cited "mystery" as an explicit evidence-gap and evaluates it against current data and explicit null models. A conservative information-theoretic framing is used throughout: genomes, cells, brains and societies are treated as physical systems that store, transform and transmit information under thermodynamic and evolutionary constraints. This framing helps distinguish what is open in practice (because measurement is hard) from what is constrained in principle (because population genetics, chemistry and neural dynamics limit the plausible solution space). We synthesize evidence on: (1) noncoding DNA and the "junk DNA" debate, separating biochemical activity from selected function; (2) protein folding in vivo, emphasizing energy landscapes, cotranslational folding, chaperones and quality control, and clarifying what machine-learning structure prediction does—and does not—explain; (3) Y-chromosome evolution and why complete telomere-to-telomere assemblies shift arguments about degeneration and disappearance into quantitative population genetics; (4) epigenetic inheritance, robust within individuals but constrained across mammalian generations by germline reprogramming; and (5) "dark genome" claims as annotation and callability problems increasingly addressed by long-read assemblies, proteogenomics and ribosome profiling. For human origins, we revisit chromosome-scale rearrangements (including the chromosome 2 fusion), ancient DNA evidence for branching histories and admixture, and misconceptions about "mitochondrial Eve" and the "missing link." For abiogenesis, we articulate an experimentally anchored chain from plausible prebiotic synthesis to nonenzymatic copying and protocell growth/division, while acknowledging unresolved bottlenecks (error thresholds, sustained cycles, and metabolism–genetics coupling). Finally, we evaluate quantum-level claims about consciousness with a stringent burden-of-proof: quantum biology exists in specific systems, but strong proposals in neuroscience must specify physical carriers, coupling mechanisms, coherence/error-correction arguments, computational advantages, and discriminating perturbation tests. We conclude with a falsifiability battery and an evidence hierarchy designed to separate productive hypotheses from untestable narratives.

Keywords: genomic architecture & noncoding DNA; T2T genome assembly; epigenetic reprogramming & inheritance; hominin evolution & chromosomal fusion; abiogenesis & prebiotic chemistry; quantum biology & neural decoherence; evidence hierarchy (E0-E5); scientific falsifiability

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Key Points

- Many "mysteries" in genomics reflect definitional confusion (activity vs selected function) and measurement bias (reference incompleteness), not missing physics.
- Long-read, telomere-to-telomere assemblies and pangenomes materially change what can be inferred about repeats, structural variation, and Y-chromosome evolution.
- Protein folding is constrained by energy landscapes and cell biology (cotranslational folding, chaperones, quality control); prediction advances do not eliminate open questions about dynamics and context.
- Abiogenesis remains unsolved but is increasingly constrained by experimental chemistry, nonenzymatic copying, and protocell work; key bottlenecks are explicit and testable.
- Quantum biology is established in specific systems; strong "brain as universal quantum-information receiver" claims currently lack the causal/mechanistic evidence required for acceptance noncoding DNA; genome annotation; protein folding; chaperones; telomere-to-telomere; pangenome; Y chromosome; epigenetic inheritance; proteogenomics; chromosome fusion; hominin evolution; archaic introgression; coalescent theory; RNA world; protocells; abiogenesis; FOXP2; mitochondrial Eve; mutation bias; stress-induced mutagenesis; quantum biology; consciousness

1. Premise and Method: From "Mystery" to Testable Evidence-Gap

1.1. Three Common Confusions

Public and semi-popular discussions often treat diverse questions as if they were the same kind of problem. They are not.

(i) Mechanistic incompleteness occurs when we know *that* a process exists but lack a detailed map of components and effect sizes (e.g., distal enhancers and 3D chromatin).

(ii) Measurement limitations occur when the process is understood but data pipelines are biased (e.g., short-read mapping in repeats; incomplete references; proteomics false discovery).

(iii) Category errors occur when a conceptual "why" question is framed as a missing molecular "how" (e.g., "why is there subjective experience?").

A severe review demands translation of each claim into a testable statement with a measurable discriminator. Where the discriminator is absent, the claim is explicitly marked as speculative.

1.2. An Evidence-First Information-Theoretic Framing

Biology is not "information" in the metaphorical sense alone; it is information *physically instantiated* in sequences, structures, and dynamical states. The genome is a heritable memory with error correction (DNA repair, diploidy, selection), while development and neural activity are computations constrained by energy, noise and time. An information-theoretic framing is therefore conservative: it asks what channels exist, what their capacities are, what noise sources dominate, and what causal interventions could change outcomes. This approach reduces "mysteries" to tractable categories: unknown mappings, incomplete measurement, or mis-specified questions.

1.3. Three Constraints for Stringent Review

We impose three constraints that are routinely applied by high-selectivity journals:

1. **No explanatory overreach.** Where evidence is limited, conclusions are conditional.
2. **Quantitative plausibility.** Mechanistic proposals must be compatible with known scales (copy numbers, timescales, error rates, energy budgets).
3. **Discriminating tests.** A claim is scientifically productive only if it yields predictions that could fail.

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2. Genomics and Chromosomes: What the "Mysteries" Really Are

2.1. "Junk DNA": Noncoding Does Not MEAN Nonfunctional; Functional Does Not Mean Adaptive

2.1.1. What "98% Does Not CODE for Proteins" Actually Implies

Roughly 1–2% of the human genome encodes proteins. The remaining sequence includes introns, untranslated regions, regulatory DNA, structural repeats, transposable elements, and noncoding RNAs. The phrase "junk DNA" historically captured two ideas: (a) much DNA is not under strong purifying selection, and (b) not all biochemical activity implies organism-level function. Both ideas remain relevant, but the debate is often distorted.

Two developments changed the discussion. First, large-scale functional genomics (ENCODE; Roadmap; GTEx) mapped biochemical activity—open chromatin, transcription factor binding, histone marks, transcription—across cell types (ENCODE Project Consortium, 2012; Roadmap Epigenomics Consortium, 2015; GTEx Consortium, 2017). Second, comparative genomics quantified evolutionary constraint at base-pair resolution (Lindblad-Toh et al., 2011; Ponting & Hardison, 2011). These are different kinds of evidence and answer different questions.

A second persistent confusion is to equate "noncoding" with "mysterious design." Noncoding sequence largely reflects ordinary evolutionary processes: insertion and decay of transposable elements, segmental duplications, tandem repeats, and the accumulation of nearly neutral sequence under finite population sizes. The C-value paradox—large genome sizes in some organisms without corresponding complexity—illustrates that genome bulk is not a direct proxy for organismal sophistication. Against this background, functional genomics is best seen as a map of **where regulation is possible**, not a claim that every active base is indispensable.

2.1.2. Biochemical Activity Versus Evolutionary Function

A severe review must separate **biochemical activity** from **selected function**. Biochemical activity is widespread because polymerases and binding proteins are not perfectly specific, and because the genome contains repeated motifs and mobile elements that incidentally recruit transcriptional machinery (Gingeras, 2007). Evolutionary function, in a strict sense, implies that removing or altering the element measurably changes fitness-relevant phenotypes and that constraint is detectable under an explicit null (Doolittle, 2013; Graur et al., 2013; Kellis et al., 2014; Koonin, 2016).

Current consensus among many evolutionary geneticists is that a minority of noncoding bases are under strong purifying selection, while a larger fraction can be *biochemically active* without being adaptively important. Regulatory sequences can be sparse but potent: small sequence changes in enhancers can have large phenotypic effects and can drive evolutionary divergence (King & Wilson, 1975; Levine & Tjian, 2003; Wray, 2007). For complex traits, much heritability is distributed across the genome in a way consistent with polygenic and "omnigenic" models (Boyle et al., 2017; Finucane et al., 2015; Visscher et al., 2017). This does not require that most bases have specific, selected functions; it requires that many variants have tiny effects through network coupling.

2.1.3. What is Genuinely Unknown, and How it is Being Resolved

The remaining "mystery" is not that noncoding DNA is useless, but that the causal map from sequence variation to cellular states to organism phenotypes is incomplete. Key open problems include:

- Context dependence: the same regulatory element can have different effects across cell types and developmental stages.
- Redundancy: enhancer "shadow" networks can buffer perturbations, reducing apparent effect sizes.
- Polygenicity: many small effects are hard to measure individually but matter in aggregate.

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Empirically, these gaps are being closed by: (i) perturbation screens (CRISPRi/a, base editing), (ii) single-cell multiomics, and (iii) improved reference quality for repeat-rich regions (Nurk et al., 2022; Human Pangenome Reference Consortium, 2023). Importantly, an incomplete map is not evidence of design, hidden teleology, or metaphysical causation; it is a measurement problem.

2.2. Protein Folding: Why the Cell Folds Quickly Without Brute-Force Search

2.2.1. The Computational Confusion

The "protein folding problem" is often presented as paradoxical: if a polypeptide can adopt astronomically many conformations, how can folding occur in milliseconds? This is a misreading of the search space argument (Levinthal, 1969). Proteins do not perform a random search; they descend a structured energy landscape shaped by local interactions and cooperativity (Anfinsen, 1973; Dill & MacCallum, 2012). The relevant question is not "how does the gene compute folding," but "what physical dynamics make the native state accessible and stable."

2.2.2. Cellular Mechanisms: Cotranslational Folding, Chaperones, and Quality Control

In vivo folding is aided by multiple mechanisms. Many domains fold **cotranslationally** as the chain emerges from the ribosome, reducing the effective search space. Cells deploy molecular chaperones (Hsp70, chaperonins such as GroEL–GroES) that prevent aggregation, provide isolation, and reshape kinetic traps (Hartl & Hayer-Hartl, 2002; Hayer-Hartl et al., 2016). Misfolded proteins are handled by quality control (ubiquitin–proteasome, autophagy), and folding failures underlie many diseases (Dobson, 2003). The "mystery" is therefore distributed across physics and cell biology; it is not an unexplained miracle.

2.2.3. Prediction Advances and What Remains Hard

Structure prediction has advanced dramatically (Jumper et al., 2021; Baek et al., 2021; Lin et al., 2023). Yet prediction success does not mean we have solved folding dynamics. Challenges remain for intrinsically disordered proteins, alternative conformations, folding pathways, and context-dependent states (membranes, ligands, crowding). A severe view is that the explanatory burden has shifted: the paradox is gone, but mapping sequence → ensemble → function across conditions remains open.

2.3. Y Chromosome: Degeneration Is Real in Many Lineages; Extinction Is not a Forced Conclusion

2.3.1. Why the Y is Vulnerable

The Y chromosome's nonrecombining region reduces the efficiency of selection against deleterious mutations and can promote gene loss (Bachtrog, 2013). Palindromic structures enable gene conversion, which can partially compensate for lack of recombination but can also create instability.

2.3.2. What Recent Telomere-to-Telomere Work Changed

The Y was historically under-assembled, biasing inference. Telomere-to-telomere and long-read assemblies have now produced a complete Y sequence and comparative assemblies across dozens of individuals, revealing extensive structural variation and previously missing genes (Rhie et al., 2023; Kim et al., 2023). These resources shift debates from speculation ("the Y is disappearing") to quantitative population genetics: how do mutation, gene conversion, selection, and structural rearrangements balance over time?

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2.3.3. Why "the Y Will Disappear" Is not Warranted

Some lineages have lost the Y, but others preserve it for long periods via gene conversion, dosage compensation, and selection on male fertility genes. Human data show reduced diversity on the Y consistent with linked selection (Wilson Sayres et al., 2014), but this does not imply inevitable extinction. The serious open questions are mechanistic: which Y-linked genes are essential, how structural variants affect fertility and disease, and how recombination boundaries shift (Kim et al., 2023).

2.4. Epigenetics: Robust Within Individuals, Constrained Across Generations

2.4.1. What Epigenetics can do

Epigenetic mechanisms—DNA methylation, histone modifications, chromatin structure, noncoding RNAs—regulate gene expression and enable stable cell identity during development. These mechanisms are not controversial. They are central to differentiation and plasticity.

2.4.2. Why Transgenerational Inheritance Is Limited in Mammals

A frequent claim is that environmental experiences write epigenetic marks that are then inherited for many generations. In mammals, two waves of epigenetic reprogramming (in primordial germ cells and early embryos) erase much of this information, imposing a strong constraint. Reviews emphasize that robust transgenerational inheritance is common in plants and some animals but limited and hard to establish in mammals (Heard & Martienssen, 2014; Perez & Lehner, 2019). Human studies (e.g., famine exposure) show associations consistent with developmental programming, but causal pathways and persistence are complex (Heijmans et al., 2008).

2.4.3. What Evidence Exists and What It Implies

There is credible evidence for intergenerational effects and for some multigenerational phenomena under specific conditions (Dias & Ressler, 2014; Rechavi et al., 2014). However, a severe standard requires careful separation of: direct exposure (F0 affecting F1), exposure of fetal germline (F2), and true transgenerational inheritance (F3+ in mammals). Claims that epigenetics "solves" evolution or replaces genetics typically collapse under this distinction. The real scientific task is to quantify which epigenetic information survives reprogramming, under what mechanisms (small RNAs, imprinting), and with what effect sizes.

2.5. "Dark DNA": Proteins Without Obvious Genes Usually Reflect Annotation Limits, not Missing Biology

2.5.1. Why Proteomics can "see" What Annotation Misses

Proteomics can detect peptides derived from short open reading frames, alternative splicing, and noncanonical translation. Because standard gene catalogs historically emphasized longer protein-coding genes, many peptides appear "unmapped" until annotation catches up (Kim et al., 2014; Wilhelm et al., 2014).

2.5.2. Resolution Strategies: Proteogenomics, Ribosome Profiling, and Better References

Ribosome profiling directly measures translation, revealing short ORFs and context-dependent translation (Ingolia, 2014; van Heesch et al., 2019). Proteogenomics integrates proteomic data with genome/transcriptome assemblies to refine gene models. Improved genome assemblies (including repetitive regions and segmental duplications) reduce false "dark" signals caused by missing reference sequence (Nurk et al., 2022; Human Pangenome Reference Consortium, 2023). The remaining gap is methodological rather than metaphysical: establishing stringent false-discovery rates and validating function.

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3. Human Origins and Evolution: Which Questions Are Open, and Which Are Misunderstandings

3.1. Human Chromosome 2 Fusion: The Structural Event Is Secure; Establishment and Consequences Are Quantitative

Human chromosome 2 carries strong molecular evidence of an ancestral telomere-to-telomere fusion: a head-to-head telomeric repeat region near 2q13 and a vestigial second centromere. Classic cytogenetic and sequence work supports this interpretation (IJdo et al., 1991). The "mystery" is not whether the fusion occurred; it is how the fusion arose and fixed in the ancestral population and whether it had downstream regulatory consequences.

A drift-aware quantitative treatment of establishment under underdominance, and of how reference incompleteness can masquerade as "introgression deserts," is developed in an unpublished manuscript by Mohamed Sacha, which emphasizes callability audits in the T2T era and Wright–Fisher simulations with potential transmission-ratio distortion as a sensitivity parameter (Mohamed Sacha, n.d.). While such modeling choices and datasets can be debated, the broader point is sound: for chromosome-scale events, the relevant unknowns are **quantitative** (selection coefficients, fertility costs, demography, structure), not the existence of the fusion itself.

Under population-genetic constraints, fixation of a chromosomal rearrangement can occur by drift in small populations or by selection if the rearrangement confers net advantage or reduces recombination in a beneficial way. The modern evidence base—ancient DNA, demographic inference, and improved assemblies—makes it increasingly feasible to model establishment probabilities and to test for phenotypic effects in the region.

3.2. Abiogenesis: Not Solved, but Increasingly Constrained by Chemistry and Protocell Work

"How did nonliving chemistry become the first self-replicating cell?" remains one of the deepest unsolved questions. A severe review does not pretend the answer is complete; instead it asks what minimal chain of experimentally supported steps is plausible.

Three empirically anchored pillars now exist:

4. **Prebiotic synthesis of building blocks.** Classic experiments showed amino acids can form under plausible early-Earth conditions (Miller, 1953). Modern work has expanded the menu and plausibility of nucleotide precursor synthesis (Powner et al., 2009; Patel et al., 2015; Sutherland, 2016, 2017).
5. **Nonenzymatic information copying.** RNA-world proposals suggest RNA preceded DNA and proteins, with RNA acting both as information carrier and catalyst (Gilbert, 1986; Joyce, 2002; Higgs & Lehman, 2015). Laboratory ribozymes and nonenzymatic primer extension demonstrate partial routes toward copying (Johnston et al., 2001; Szostak, 2012; Lincoln & Joyce, 2009). These are not yet full solutions: error thresholds, strand separation, and sustained cycles remain major challenges.
6. **Protocell compartments that grow and divide.** Fatty-acid vesicles can encapsulate nucleic acids and grow/divide under environmental cycles. Template-directed synthesis has been demonstrated inside model protocells (Mansy et al., 2008; Adamala & Szostak, 2013; Deamer, 2017). Environmental cycling (wet–dry, freeze–thaw, thermal gradients) can provide the physical work needed for concentration and polymerization.

A conservative synthesis is that "the first cell" likely emerged from a **continuum**: chemical networks within compartments gradually gained heredity, catalysis, and metabolic coupling. Competing scenarios (metabolism-first at hydrothermal vents; inorganic compartments) remain viable and have experimental support (Martin & Russell, 2007; Herschy et al., 2014; Lane & Martin, 2012; Koonin & Martin, 2005). What is now scientifically sharpened is the list of bottlenecks: polymerization chemistry, template copying with manageable errors, and coupling of heredity to growth/division cycles.

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3.3. The "Cognitive Explosion": Why Cultural Dynamics can Amplify Modest Biological Changes

Claims of a sudden "cognitive leap" sometimes assume that biology must have produced a large genetic mutation to explain symbolic behavior, art, and complex language. Yet gene–culture coevolution provides an alternative: modest biological changes can be amplified by social learning, cumulative culture, and demographic expansion. Once communication and learning cross a threshold, cultural information becomes a second inheritance system with high bandwidth and rapid dynamics. In this view, the "gap" is often a mismatch between expectations (a single genetic switch) and what evolutionary theory predicts (distributed changes plus cultural feedback). Fossil and archaeological evidence suggests complex trajectories rather than a single moment.

3.4. The "Missing Link": No Single Fossil can Carry the Burden of a Branching History

The fossil record is necessarily incomplete and temporally uneven. Evolution is branching, not linear, so the expectation of a single "missing link" is a category error. Paleoanthropology increasingly integrates fossils with genetics and demography, revealing structured populations, gene flow, and regional diversity (Stringer, 2016; Scerri et al., 2018; Nielsen et al., 2017). Ancient genomes document admixture between modern humans and archaic groups (Green et al., 2010; Meyer et al., 2012; Prüfer et al., 2014, 2017), further undermining linear narratives.

3.5. FOXP2 and Language: One Important Gene Within a Larger Network

FOXP2 is often misrepresented as "the language gene." In reality, FOXP2 is a transcription factor affecting neural circuits involved in speech and motor learning, and language is polygenic and networked. Human-specific changes in FOXP2 are documented (Enard et al., 2002), and pathogenic mutations can disrupt speech/language (Lai et al., 2001). But comparative and neurobiological work emphasizes that FOXP2 is part of broader pathways (Fisher & Scharff, 2009; Vargha-Khadem et al., 2005). A severe interpretation is that FOXP2 is a valuable entry point, not a complete explanation.

3.6. Mitochondrial "Eve": Coalescent Ancestry Is not a Single-Founder Bottleneck

"Mitochondrial Eve" refers to the most recent common maternal ancestor of present-day mitochondrial genomes; it does not mean that only one woman existed or that humanity descended from a single couple. Coalescent theory shows that lineages coalesce stochastically; many contemporaries leave no unbroken maternal line to the present (Kingman, 1982; Rosenberg & Nordborg, 2002; Wakeley, 2009). The empirical finding of a mitochondrial MRCA (Cann et al., 1987) is therefore consistent with large populations and with multiple ancestors in the same generation.

4. Are Mutations "Directed"? Randomness, Bias, and What Would Count as Goal-Directed Evolution

4.1. Random with Respect to Fitness, not Necessarily Uniform in Mechanism

The classic Luria–Delbrück fluctuation test showed that mutations arise before selection, consistent with randomness with respect to adaptive need (Luria & Delbrück, 1943). However, mutation processes are not uniform: sequence context, replication timing, chromatin state, and repair pathways create biases in where and how mutations occur. "Random" in evolutionary biology typically means *uncorrelated with future fitness benefit* given the organism's needs.

4.2. Stress-Induced Mutagenesis: Increased Variation Under Stress Is not Foresight

Some organisms increase mutation rates under stress (Foster, 2007). This can be adaptive at the population level because it increases exploration when current genotypes perform poorly. But it is not teleological "aiming" at beneficial mutations; it is a regulated shift in variance. Even proposals of

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reduced mutation rates in essential genes are best understood via mechanistic heterogeneity and selection on local genome maintenance (Martincorena et al., 2012) rather than foresight.

4.3. What Would Count as Strong Evidence for Truly Goal-Directed Mutation

To justify "directed evolution" in the strong sense, one would need evidence that cells preferentially generate *fitness-improving* mutations conditional on environment, beyond what can be explained by stress responses, mutational biases, and selection. Such evidence would require preregistered predictions, mechanistic pathways, and repeated demonstrations across systems. At present, mainstream evidence supports regulated mutation-rate changes and bias, not goal-directed targeting.

5. Why do We Feel Conscious Selfhood? What Neuroscience Constrains, and What Quantum Claims Must Demonstrate

5.1. What Neuroscience Already Constrains

Consciousness research has progressed by operationalizing aspects of experience (report, discrimination, confidence) and by studying changes under anesthesia, sleep, brain injury, and stimulation. Major theoretical families include global workspace accounts (Dehaene & Changeux, 2011; Mashour et al., 2020), integrated information approaches (Tononi et al., 2016), recurrent processing theories (Lamme, 2006), and predictive processing/free-energy frameworks (Friston, 2010). No single framework is universally accepted, but empirical markers have improved. For example, perturbational complexity indices correlate with level of consciousness across conditions (Casali et al., 2013), and active paradigms can reveal covert awareness in disorders of consciousness (Owen et al., 2006; Monti et al., 2010; Laureys et al., 2010). These results constrain any hypothesis: whatever consciousness is, it depends on large-scale brain dynamics and connectivity, and it is systematically modulated by physiological interventions.

5.2. Quantum Biology Is Real; Quantum Cognition Remains Unestablished

Quantum mechanics underlies chemistry; this is uncontroversial. More specifically, quantum coherence and tunneling can play functional roles in certain biological systems. Examples include excitonic energy transfer in photosynthetic complexes (Engel et al., 2007) and radical-pair mechanisms proposed for magnetoreception (Ritz et al., 2000; Hore & Mouritsen, 2016). Enzyme catalysis can involve tunneling contributions that link protein dynamics to reaction rates (Klinman & Kohen, 2013). Reviews synthesize these cases while emphasizing system-specific constraints and the importance of decoherence (Lambert et al., 2013; Brookes, 2017).

The key point for consciousness is that *existence* of quantum biology does not imply that the brain exploits long-lived coherent quantum states for cognition. Neural tissue is warm, wet, and noisy; many quantum degrees of freedom decohere extremely rapidly. This does not logically rule out all quantum contributions—some quantum effects can be robust in noisy environments—but it elevates the burden of proof.

5.3. Translating the Claim into Testable Statements: "The Human Brain Is a Superior Receiver of Universal Quantum Information"

The claim can be sharpened into a family of testable hypotheses:

H1 (weak): neural computation depends on molecular quantum effects already present in chemistry (e.g., tunneling in enzymes, stochastic ion channel behavior). This is almost certainly true but does not uniquely explain subjective selfhood.

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H2 (intermediate): the brain uses specific quantum-sensitive molecular mechanisms (e.g., radical-pair spin chemistry, nuclear-spin-dependent reactions) that modulate neural signaling in a way not reducible to classical noise terms. This is plausible in principle but currently lacks direct evidence in neural tissue.

H3 (strong): the brain functions as a *receiver* of nonlocal or "universal" quantum information and uses that input to generate consciousness. This is the strongest and most extraordinary claim and therefore demands extraordinary evidence.

For H3 to be viable under severe review, at least four requirements must be met:

7. **A physical carrier and coupling mechanism.** "Information" must be instantiated in a field or particle state that couples to neural tissue with sufficient strength and specificity to affect computation. Vague appeals to "quantum information" are not mechanisms.
8. **A coherence/error-correction story.** If the proposal requires coherent superpositions or entanglement over biologically relevant scales, it must address decoherence quantitatively. Classic estimates argue that many such states would decohere far faster than neural timescales (Tegmark, 2000). Counter-arguments must provide explicit alternative degrees of freedom, protective structures, and measurable signatures.
9. **A computational advantage.** The proposal must specify what computation is enabled that cannot be achieved classically under comparable constraints. Otherwise, "quantum" is an unnecessary label.
10. **Discriminating predictions.** The hypothesis must predict measurable effects of controlled perturbations that differ from classical theories. Without this, the claim is not empirically meaningful.

At present, requirements (1)–(4) are not satisfied for H3. Proposals such as Orch OR (Hameroff & Penrose, 2014) remain controversial partly because they have not produced widely accepted, quantitatively confirmed discriminators in vivo. A conservative scientific posture is therefore conditional: do not declare quantum reception as an explanation; instead, design tests that could support or falsify restricted versions.

Importantly, if a "receiver" claim is interpreted as sensitivity to weak environmental fields (electromagnetic or geomagnetic) that carry information, then the hypothesis becomes experimentally approachable. For example: radical-pair mechanisms predict susceptibility to specific radiofrequency perturbations in the MHz range under defined field strengths; a cognitive dependence on such mechanisms would predict reproducible modulation of neural markers or behavior under controlled RF noise, with appropriate sham conditions and blinding. Conversely, null results across adequately powered studies would place quantitative upper bounds on any such contribution. This is the kind of discipline required for extraordinary claims to become part of mainstream neuroscience rather than remaining metaphors.

5.4. Why Subjective Selfhood Is Difficult: A Realistic Division of Labor

Even if every neural mechanism were mapped, there may remain conceptual questions about "why it feels like something." However, many components of selfhood are empirically tractable: integration across modalities, memory, prediction, agency, and social cognition. These functions can be studied mechanistically and may account for much of what is called the "self." Philosophical residue should not be inflated into a gap that biology must fill with speculative physics. A severe review therefore separates the tractable (neural mechanisms of reportable experience) from the conceptual (the hard problem) and evaluates each on its own terms (Block, 1995; Seth & Bayne, 2022).

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6. Synthesis: What Remains Open, What Is Constrained, and How to Test High-Burden Hypotheses

6.1. Evidence-Status Map (Summary)

- **Noncoding DNA:** abundant biochemical activity is mapped; the causal genotype→phenotype map remains incomplete but is being resolved by perturbation and single-cell methods (ENCODE; Roadmap; GTEx; comparative genomics).
- **Protein folding:** the paradox is resolved in principle; dynamics and context-specific ensembles remain active research.
- **Y chromosome:** recent complete assemblies shift the debate to quantitative population-genetic and medical questions.
- **Epigenetic inheritance:** robust within individuals; limited but not absent across generations, with strong constraints in mammals.
- **Dark DNA:** largely annotation/measurement limitations; rapidly improving with proteogenomics and better references.
- **Human origins:** no single "missing link"; genetics and fossils show branching histories and admixture; chromosome 2 fusion is secure as an event.
- **Abiogenesis:** not solved but increasingly constrained; major bottlenecks are explicit and experimentally addressable.
- **Quantum reception and consciousness:** quantum biology exists; strong "universal receiver" claims are currently unsupported and must be framed as falsifiable hypotheses rather than conclusions.

6.2. A Conservative Falsifiability Battery for "Quantum Reception" Claims

A minimal battery that would move the field from narrative to evidence would include:

11. **Molecular identification:** identify a candidate quantum-sensitive molecular subsystem in neural tissue; show it exists at relevant abundance and location.
12. **In vitro validation:** demonstrate quantum-sensitive behavior under physiological temperature, ionic strength, and noise.
13. **Coupling demonstration:** show that manipulating this subsystem changes neural signaling in a way that cannot be accounted for by classical confounds.
14. **In vivo perturbation:** preregistered experiments where predicted perturbations (e.g., magnetic fields or RF noise, if radical-pair mechanisms are invoked) reliably modulate specific cognitive/phenomenological markers while controlling for sensory artifacts.
15. **Model comparison:** compare predictive accuracy and parsimony against classical theories.

These steps are demanding but not impossible. They define a scientific path that can either support or decisively constrain the hypothesis.

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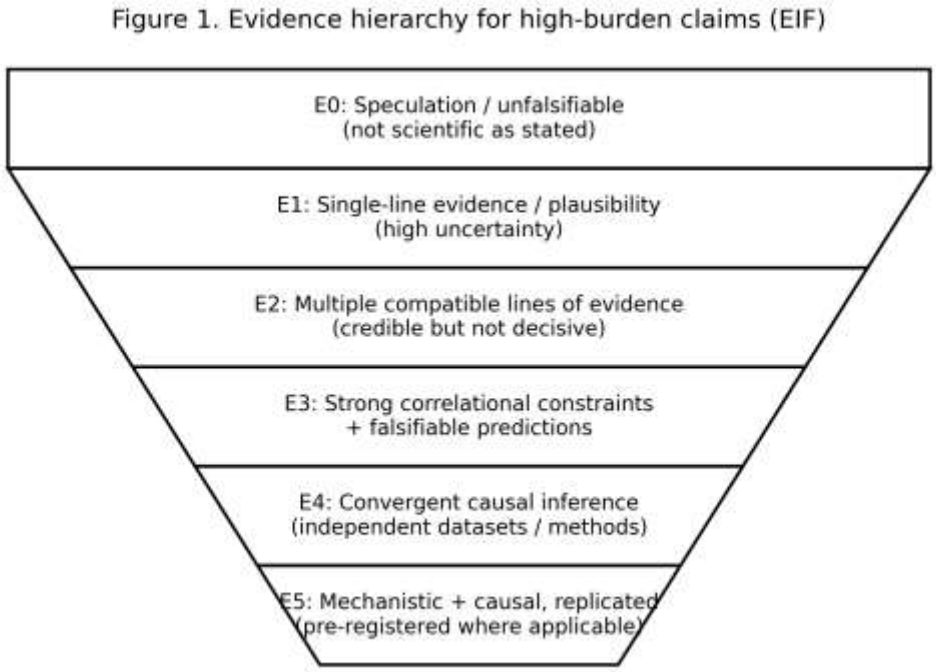

Figure 1. | Evidence hierarchy used to score high-burden claims in this review (EIF).

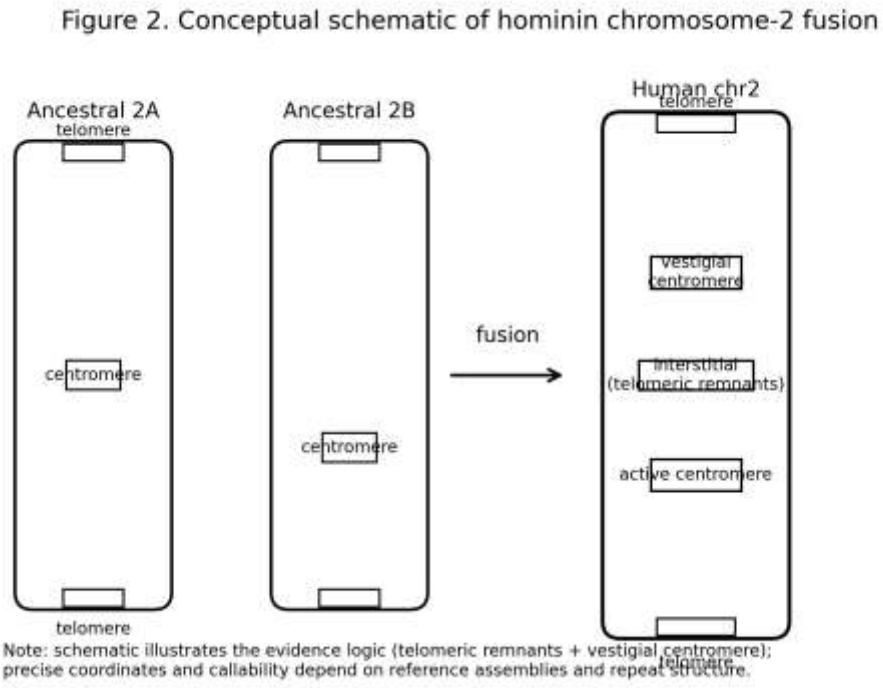

Figure 2. | Conceptual schematic of the hominin chromosome-2 fusion and the logic of sequence-level signatures.

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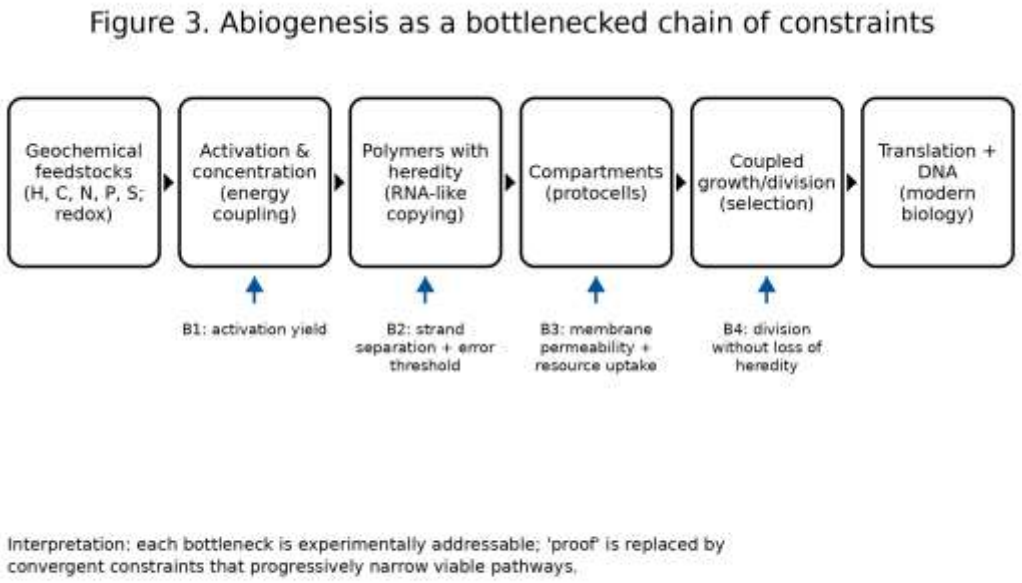

Figure 3. | Abiogenesis framed as a chain of experimentally addressable bottlenecks rather than a single 'miracle' step.

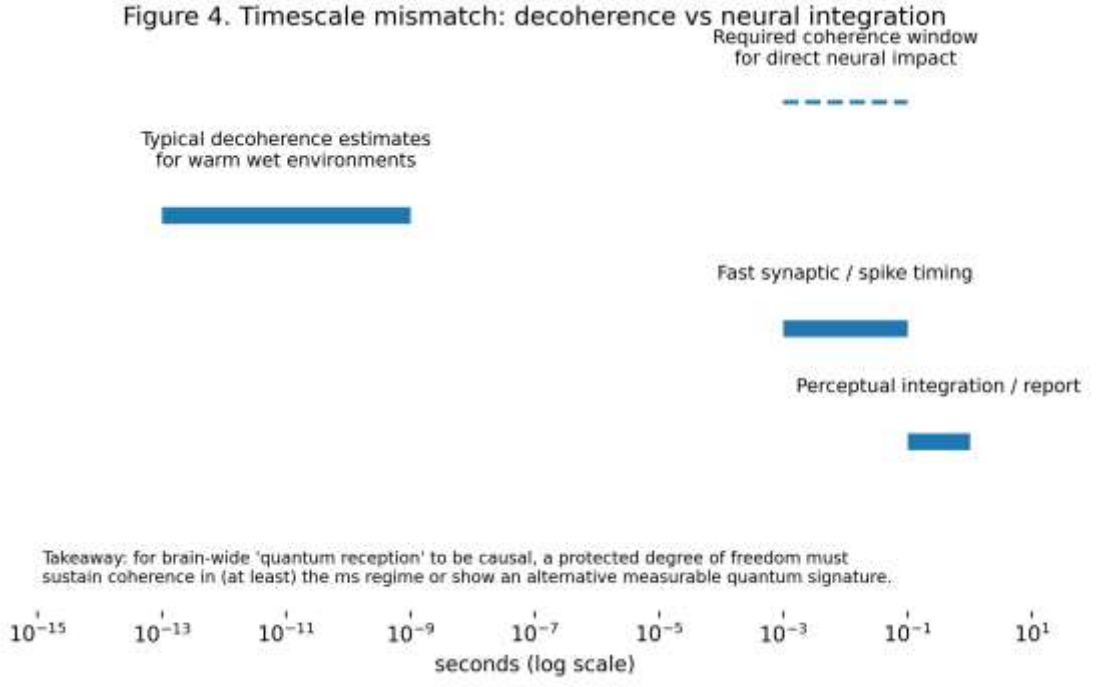

Figure 4. | Timescale comparison motivating a quantitative burden of proof for quantum-cognition claims.

Box 1 | Evidence hierarchy for claims about origins and mind

Level 1 (strongest): direct, replicated perturbation experiments with quantitative predictions and preregistered endpoints (e.g., altering a variable and measuring a causal effect with adequate controls).

Level 2: convergent mechanistic evidence across independent methods (e.g., genetics + biochemistry + structural biology, or behavior + stimulation + imaging).

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Level 3: observational correlations with strong confound control (e.g., Mendelian randomization, natural experiments, comparative genomics with explicit null models).

Level 4: plausibility arguments and toy models (useful for hypothesis generation, insufficient for acceptance).

Level 5 (weakest): narrative inference or analogy without a measurement pathway.

Throughout, claims are judged by the highest level of evidence currently available, and speculative proposals are kept separate from established constraints.

Summary tables are provided for rapid reviewer navigation and to make the evidence-status map explicit.

Table 1. | Evidence-status map for commonly cited 'mysteries' (EIF scoring).

Domain	Representative question	Status	Most reliable evidence	Key remaining uncertainty
Genome	'Junk DNA' vs function	E3–E4	comparative constraint + perturbation/CRISPR + population genetics	fraction of noncoding under selection across tissues/species
Molecular biophysics	Protein folding speed	E4–E5	biophysics + chaperone systems + structural prediction benchmarking	dynamic folding in membranes/complexes, aggregation control in vivo
Sex chromosomes	Will Y disappear?	E3–E4	T2T assemblies + comparative genomics + gene conversion models	lineage-specific trajectories; role of ampliconic evolution
Epigenetics	Transgenerational inheritance?	E2–E3	human cohorts + animal experiments + reprogramming biology	frequency/size of effects after controlling confounds
Proteogenomics	'Dark DNA' proteins	E3–E4	ribosome profiling + proteomics + improved references (T2T/pangenomes)	how many functional microproteins remain undiscovered
Human evolution	Chromosome-2 fusion	E4–E5	cytogenetics + sequence signatures (telomeric remnants/vestigial centromere)	population-genetic establishment; local introgression artifacts
Origins of life	First cell / abiogenesis	E2–E3	prebiotic synthesis + non-enzymatic copying + protocell experiments	end-to-end coupling of heredity, metabolism, and division

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Language	FOXP2 and speech	E3–E4	human genetics + neurobiology + comparative evolution	network-level genotype-to-phenotype mapping for language
Population genetics	Mitochondrial 'Eve'	E4–E5	coalescent theory + mtDNA phylogenetics	fine-scale demographic histories; selection on mtDNA
Quantum claims	Brain as 'universal quantum receiver'	E1–E2 (as stated)	quantum biology precedents + physics constraints	identifying a protected degree of freedom with causal, measurable signatures in vivo

Table 2. | Abiogenesis bottlenecks and experimentally grounded constraints.

Bottleneck	What must be achieved	Best current constraints	Open problem
B1: activation + concentration	high-yield activated monomers under plausible geochemistry	validated pathways for activated nucleotides and concentration mechanisms	robust coupling to diverse early-Earth microenvironments
B2: templated copying fidelity	non-enzymatic copying with manageable error rates	eutectic ice and chemical tuning improve copying and reduce bias	scalable strand separation without enzymes; error threshold in mixed alphabets
B3: compartmentalization	compartments that retain polymers yet allow nutrient influx	fatty-acid vesicles/coacervates support encapsulation and growth	compatibility with copying chemistry and long-term stability
B4: growth/division with heredity	cycles of growth and division that preserve informational molecules	physical division modes demonstrated in model protocells	integrating heredity with resource-driven metabolism and selection in one system

Table 3. | Referee-safe falsifiability battery for 'quantum reception' hypotheses in the brain.

Claim class	Required substrate	Quantitative requirement	Distinct prediction	Minimum decisive test
Weak quantum contribution	molecular quantum effect	effect size reproducible; parameter	specific dependence on field/isotope/temperature beyond classical models	pre-registered perturbation series with matched controls

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	influences a classical pathway	sensitivity mapped		
Protected coherence microdomain	identified qubit-like DOF in biomolecule	coherence time comparable to or functionally linked with ms dynamics	angle- or field-dependent signatures aligned with radical-pair/spin models	in situ spectroscopy or proxy readout + causal behavioral/physiology link
Brain-wide 'receiver' (strong)	distributed quantum channel	coherence and readout at neural timescale	non-classical correlations not explainable by classical noise models	simultaneous multi-site measurements showing quantum signatures + causal intervention

Supplementary Materials: The following supporting information can be downloaded at the website of this paper posted on Preprints.org.

Funding: None. .

Data and materials availability: No new datasets were generated; all statements are based on published literature and publicly available resources. .

Acknowledgments: The author thanks the broader scientific community for open datasets and critical discussion. .

Competing interests: The author declares no competing interests. .

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