Toward a Pan-Genomic Topology-Gated Photonic-Redox Control Plane

A testable ceLLM hypothesis linking mitochondrial DNA topology, nuclear noncoding receiver architecture, ultra-weak photon emission, and cellular state inference

Hypothesis manuscript draft | Revised CACNA1C edition

Prepared from source materials supplied by John Coates (RF Safe) and expanded into a literature-grounded, experimentally falsifiable framework.

Prepared for scientific discussion, critique, and collaborative experimental design.

Working thesis. The strongest version of the mtDNA-biophoton idea is not a lone-DNA antenna model, but a nested photonic-redox control plane that is experimentally falsifiable. The present revision extends that model from mitochondrial nucleoids to a broader pan-genomic receiver architecture: mitochondrial DNA topology and nuclear noncoding regulatory topology are treated as related geometry-sensitive priors through which redox, calcium, photonic, and electromagnetic variables are transformed into cellular state.

Suggested short title: Pan-genomic topology-gated photonic-redox control plane

Abstract

Ultra-weak photon emission (UPE) from living systems is an established biophysical phenomenon arising largely from oxidative metabolism and reactive oxygen species (ROS), yet its functional role in cellular signaling remains unresolved [2,5]. Mitochondria are both major generators of UPE and central integrators of redox, calcium, membrane-potential, and transcriptional signals [2,6-8]. Here we extend the original mtDNA-resonance idea into a broader, more biologically plausible framework. Cells may implement a topology-gated photonic-redox control plane in which mitochondrial redox chemistry generates structured optical and electromagnetic fluctuations. In this model, mtDNA topology, TFAM-dependent nucleoid organization, and the local hydration shell act as one geometry-sensitive transducer layer, while cytoskeletal aromatic networks, mitochondrial reticula, and nanotunnels route or stabilize local state propagation.

A recently reported CYB5B-dependent EMF-responsive calcium-coding mechanism further suggests that nucleoid-centered topology gating may be complemented by a surface-facing outer-mitochondrial-membrane interface [25]. A newly reported human sleep-EEG study provides an important nuclear-genome analogue: a single intronic variant in *CACNA1C*, rs7304986, modulated whether 3.6 GHz RF-EMF exposure accelerated NREM sleep-spindle center frequency [45]. Because *CACNA1C* encodes the α_{1C} subunit of L-type voltage-gated calcium channels, this finding suggests that nuclear noncoding regulatory architecture can act as a receiver-state variable, shaping how electromagnetic and bioelectric inputs are transformed into physiological outputs [45].

Organelle contact sites amplify weak perturbations into Ca^{2+}, membrane-potential, and retrograde signaling events, while condensates plus transcriptional programs store the resulting update to cellular state [2,6-29]. Within the cellular Latent Learning Model (ceLLM), these processes are interpreted as a multiscale state-inference architecture rather than literal transformer-like computation. Human mtDNA provides useful dimensional heuristics for experimental design: a 16,569-bp circular genome has a contour length of about 5.633 μm, a relaxed-circle diameter of about 1.79 μm, and is typically packaged into nucleoids near 100 nm, mapping to free-space guideposts near 53 THz, 167 THz, and 3 PHz, respectively [1,9-15]. These values are not asserted as classical in vivo antenna resonances inside hydrated organelles; instead, they define physically motivated search windows for testing whether geometry and topology modulate mitochondrial sensitivity to narrow-band optical or terahertz perturbations [8,14,15].

The paper reframes the central question from same-frequency resonance to cross-scale frequency conversion: optical excited-state chemistry may be converted at hydrated DNA-protein and membrane interfaces into lower-frequency electrochemical envelopes that cells can amplify, integrate, and remember. The CACNA1C sleep-EEG result motivates a parallel nuclear-genome question: whether noncoding sequence, local DNA shape, and chromatin topology act as physical weighting layers for how native bioelectric hardware is deployed and how external electromagnetic inputs are resolved into cellular or organismal state [45-50]. We present falsifiable predictions and a concrete experimental program spanning TFAM and topoisomerase perturbation, rho0 depletion and rescue, quartz-versus-glass optical isolation, narrow-band THz exposures with thermal controls and Ca^{2+} uptake blockade, cytoskeletal perturbation, MERC disruption, CYB5B perturbation, CACNA1C genotype-stratified RF-EEG studies, regulatory profiling, and spectral-entropy analysis of photon bursts. If supported, the framework would not merely rehabilitate a biophoton-signaling hypothesis; it would define a systems-biology problem at the intersection of mitochondrial organization, nuclear noncoding topology, redox physics, intracellular communication, bioelectricity, and cellular decision-making.

Keywords: mitochondrial DNA; nuclear noncoding DNA; CACNA1C; biophotons; ultra-weak photon emission; terahertz; nucleoid topology; TFAM; ceLLM; mitochondria-ER contact sites; cytoskeleton; redox signaling; CYB5B; calcium oscillations; sleep spindles; bioelectricity

Box 1. A disciplined map of what is known, what is proposed, and what would most directly falsify the model

What is established	What is proposed here	What would most directly falsify it
UPE exists and is tightly linked to oxidative metabolism. Mitochondria are major UPE sources and signaling hubs. mtDNA is circular, topological, TFAM-packaged, and structurally heterogeneous. MERCs, retrograde signaling, actin dynamics, and mitochondrial subnetworks are real control layers. Nuclear noncoding variants can alter regulatory binding and gene expression, and 3D genome organization shapes transcription and development [46-50].	mtDNA topology plus its hydration shell acts as a geometry-sensitive mitochondrial transducer. Nuclear noncoding sequence and chromatin topology act as related receiver-state variables for native bioelectric hardware. Weak optical events are converted into lower-frequency electrochemical envelopes. Cells implement a nested photonic-redox-bioelectric control plane rather than a lone-DNA antenna.	No shift in optical / THz sensitivity after TFAM or topology perturbation. No dependence on mtDNA abundance or organization in rho0/rescue designs. No added predictive value from structured UPE variables beyond standard redox readouts. No association between CACNA1C regulatory state and RF-induced spindle effects after genotype, CaV1.2 modulation, and chromatin profiling.

1. Introduction

A century after Gurwitsch proposed that dividing tissues might exchange ultraviolet signals, the existence of ultra-weak photon emission from living systems is no longer the main controversy; the unresolved question is whether any biologically useful information is embedded in those emissions, and if so how cells could physically transduce it [2-6]. UPE is now widely interpreted as a consequence of oxidative chemistry, especially excited species generated during ROS-producing metabolism. That baseline interpretation is important because it keeps the problem anchored to known chemistry rather than mysticism. At the same time, it leaves open a serious systems question: whether metabolic light is merely waste, or whether evolution exploited it as a state variable in already existing signaling architectures.

Mitochondria are the natural place to ask that question. They generate and respond to redox signals, shape calcium microdomains, regulate membrane potential, communicate with the nucleus, form extended subnetworks, and sit at the center of many cell-fate decisions. They are also major sources of UPE and have shown both light-responsive behavior in isolated preparations and frequency-selective responses to narrow-band terahertz irradiation [2,6-8]. A framework that links mitochondrial organization to weak optical signaling therefore has a plausible empirical foothold, even if stronger historical claims about coherence or long-range photonic control remain unsettled [4,5].

The original mtDNA-antenna formulation is valuable because it treats mitochondrial DNA not only as a sequence archive but as a physical object with contour, circularity, topology, packaging, and hydration. Those properties matter. Human mtDNA is a 16,569-bp circular genome [1]. Its contour length is about 5.633 μm, its relaxed-circle diameter is about 1.79 μm, and in mammalian cells it is usually compacted into TFAM-organized nucleoids near 100 nm that vary in accessibility and activity [9-13]. The key correction made here is that these are not grounds to claim a literal classical loop antenna operating inside a water-rich organelle. They are grounds to ask a sharper question: can mtDNA geometry and topology change how mitochondria couple to the local optical, terahertz, and electrochemical microenvironment?

The present revision adds an equally important nuclear-genome question. If mtDNA topology can be treated as a physical receiver state, then nuclear noncoding architecture should not be ignored. A 2025 randomized, double-blind, sham-controlled human 5G sleep-EEG study found that an intronic *CACNA1C* variant, rs7304986, modulated whether a controlled 3.6 GHz RF-EMF exposure accelerated NREM sleep-spindle center frequency [45]. This result is important because *CACNA1C* encodes native calcium-channel hardware and because the variant lies in the regulatory/noncoding region rather than a straightforward protein-substitution site. In ceLLM language, this is a human example of the broader principle: the same electromagnetic input does not produce a fixed biological output; the output depends on the receiver architecture.

To make the question publishable and testable, this paper broadens the scope from mtDNA alone to a pan-genomic topology-gated photonic-redox control plane. mtDNA remains central, but as one transducer layer embedded in a richer architecture that includes ETC chromophores, hydration-shell physics, cytoskeletal aromatic networks, mitochondrial reticula, organelle contact sites, nuclear noncoding regulatory topology, chromatin structure, and slower transcriptional memory. The ceLLM concept is used here as a systems metaphor for cellular state inference: cells integrate fast variables and slower structural priors to update state, rather than responding as purely local chemical switches. The aim is not to declare a paradigm shift by rhetoric. The aim is to define a coherent hypothesis that can be broken by experiment.

2. Empirical foundation

2.1. UPE is real; the signaling question is still open

UPE is experimentally well established. Modern reviews describe it as a low-intensity broadband emission spanning approximately ultraviolet to near-infrared wavelengths and arising from electronically excited species generated during oxidative metabolism and stress [2,5]. Claims that all UPE is coherent or laser-like remain unsupported by the strongest critical reviews [5], but the existence of the emission itself is not in doubt. That matters because a candidate signaling variable does not need to be perfectly coherent in order to be biologically sampled; it only needs to covary with internal state strongly enough that a cell can integrate it with other channels.

Mitochondria are unusually well positioned to generate such variables. Oxidative phosphorylation produces ROS, excited carbonyls, singlet oxygen, redox oscillations, and membrane-potential fluctuations in a physically confined geometry. Recent isolated-mitochondria experiments suggest that mitochondria can influence one another in non-chemical ways that depend on shielding and ambient-light conditions [6]. Separate photobiomodulation work shows that isolated mitochondria respond directly to 810-nm light [7]. Most strikingly, a 2026 ACS Nano study reported a frequency-selective terahertz effect in which 34.5 THz irradiation promoted mitochondrial biogenesis via calcium influx and the PGC-1alpha-NRF1/2-TFAM axis, whereas a nearby tested frequency did not produce the same effect [8]. None of these findings proves photonic computation. Together, however, they justify a serious search for topology-sensitive mitochondrial coupling mechanisms.

The detected external UPE intensity is extremely low, which is precisely why the signaling question remains open [2,5]. External counts, however, need not equal local intramitochondrial flux, because many emitted photons may be reabsorbed or scattered before they escape the cell; that possibility remains a plausible inference rather than a settled measurement. In this regime the relevant question is not whether a single photon triggers a deterministic switch, but whether structured fluctuations in burst timing, spectral mix, or entropy bias an already noisy redox/Ca^{2+} decision landscape. That is the regime in which stochastic resonance becomes physically relevant: in nonlinear threshold systems, added noise can improve detection of weak signals rather than merely degrade it [34]. The present model therefore relies on downstream amplification at contact sites, mitochondrial network junctions, and retrograde pathways rather than on a high-fidelity optical command channel. Hydration-shell dynamics and biomolecular-condensate phase transitions may provide one route across the timescale gap by trapping ultrafast optical or THz perturbations into longer-lived conformational or electrochemical states that millisecond calcium machinery and slower transcriptional programs can sample [14,15,21].

2.2. mtDNA geometry and nucleoid organization provide a physically meaningful substrate

mtDNA itself is not static packaging. Super-resolution work showed that mammalian nucleoids are relatively uniform in size and often contain a single mtDNA molecule [9]. Subsequent studies showed that only a minority of nucleoids are transcriptionally or replicatively active at a given moment, and that inactivity correlates with high TFAM-to-mtDNA ratios consistent with stronger compaction [10]. More recent structural work found that single-nucleoid architecture is heterogeneous rather than monolithic [11], while mechanistic studies demonstrated sequence-specific DNA bending in TFAM-mediated packaging and transcription initiation [12]. Topology control by mitochondrial topoisomerases provides yet another layer of physical regulation [13]. In other words, the mtDNA system already behaves like a tunable structural state variable before any photonic hypothesis is imposed on it.

Hydration adds an underappreciated physical bridge. Terahertz spectroscopy studies show that the DNA hydration shell differs measurably from bulk water [14], while long-range DNA-water interaction studies indicate that hydrated DNA supports low-frequency collective modes sensitive to temperature and hydration state [15]. This does not demonstrate information-bearing resonance. It does suggest that the relevant coupling problem is not simply a bare DNA loop in vacuum. The physically interesting object is the DNA-protein-water interface, where excited-state chemistry, local field fluctuations, and structural dynamics coexist.

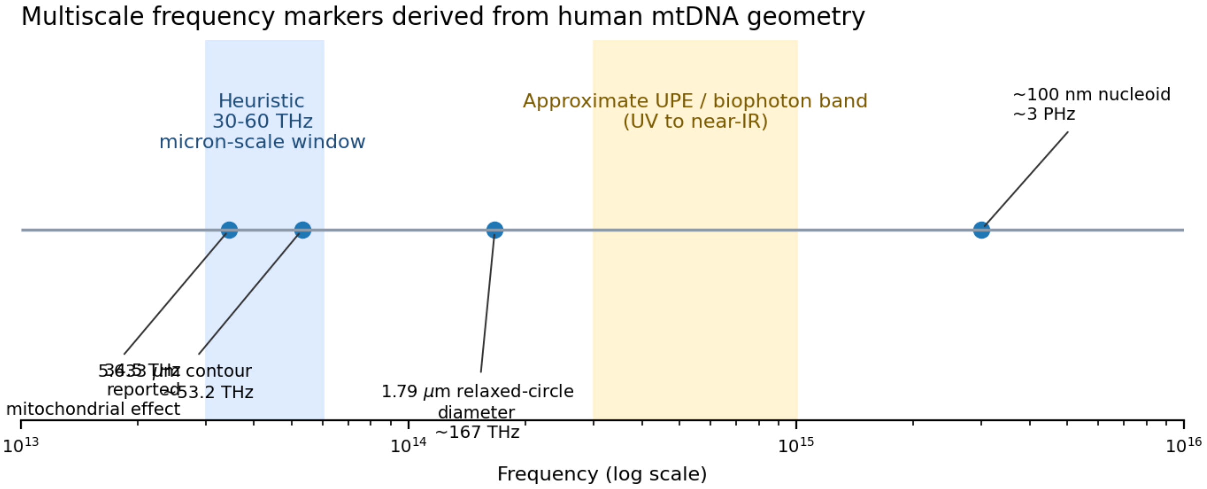

Figure 1: Multiscale frequency markers derived from human mtDNA geometry. The plotted values are dimensional guideposts only: a 5.633 μm contour maps to about 53.2 THz, a 1.79 μm relaxed-circle diameter to about 167 THz, and a 100 nm nucleoid scale to about 3 PHz. The shaded 30-60 THz band highlights the micron-scale window emphasized in the original engineering argument, while the broad UPE band spans the approximate UV-to-near-IR range reported in the biophoton literature. These are not asserted as classical in vivo resonant peaks.

2.3. Candidate routing and amplification layers already exist in mainstream cell biology

The intracellular context also offers credible routing and amplification partners. Electronic energy migration has been measured in microtubules over a scale comparable to a tubulin dimer [16], and ultraviolet superradiance has been proposed and experimentally probed in large tryptophan-rich biological architectures including tubulin systems [17]. These findings do not prove long-range optical waveguiding inside cells, but they make aromatic cytoskeletal networks plausible short-range relays or sinks for optical excitation. Actin, meanwhile, appears particularly important as a state-distribution system: an interphase actin wave has been shown to promote mitochondrial content mixing, maintain polarization and oxygen consumption, and suppress excess ROS [18]. That makes actin a powerful candidate for converting local optical-redox perturbations into spatially distributed mitochondrial state changes.

Finally, mitochondria already participate in established mesoscale signaling networks. Mitochondria-ER contact sites regulate exchange, calcium coupling, redox homeostasis, and metabolic transitions [19]. Mitochondria also form sites of contact with the nucleus that help organize retrograde signaling [20]. In muscle, the mitochondrial reticulum behaves like a subcellular energy-distribution network [22], and nanotunnels may provide another route for inter-mitochondrial interaction under constrained motility [23]. Beyond the single cell, connexin-43-associated contacts and other mechanisms can support intercellular mitochondrial transfer [24]. Even biomolecular condensates have been shown to reshape electrochemical equilibria and membrane-associated state variables [21]. These observations together motivate a layered framework in which weak optical events need not carry the full signaling burden themselves; they may simply bias, trigger, or synchronize networks that already have powerful classical amplifiers.

2.4. A newly identified mitochondrial surface mediator sharpens the problem

A timely addition to this landscape comes from a 2026 Cell study that engineered an EMF-inducible in vivo gene switch and identified cytochrome b5 type B (CYB5B) as an essential mediator, likely acting as an EMF sensor. Importantly, activation depended on rhythmic oscillatory calcium dynamics rather than generic calcium influx. This does not prove that CYB5B is the endogenous receiver for ultra-weak photon emission or for environmental electromagnetic exposures. It does, however, establish that a named mitochondrial-surface protein can couple controlled field stimulation to patterned calcium coding and gene expression [25].

CYB5B is biochemically well placed for such a role. It is a tail-anchored outer-mitochondrial-membrane hemoprotein with a heme-binding redox domain and established functions in sterol C4-demethylation/cholesterol biosynthesis and the mitochondrial amidoxime-reducing component (mARC) system; related work also links the mARC-CYB5B-CYB5R axis to nitrite/NO chemistry [26-28]. Within the present framework, CYB5B is best treated as a candidate surface-facing transducer or code-shaping interface that may complement, rather than replace, a nucleoid-centered topology-gated layer.

2.5. A human nuclear-genome analogue: CACNA1C rs7304986 gates RF-to-bioelectric coupling

A randomized, double-blind, sham-controlled human study of 5G RF-EMF exposure in *CACNA1C*-genotyped volunteers provides a striking nuclear-genome analogue to the topology-gated control-plane hypothesis [45]. Thirty-four participants, including 15 T/C and 19 matched T/T carriers of rs7304986, underwent 30-minute pre-sleep exposure to 700 MHz, 3.6 GHz, or sham. Only T/C carriers showed a significant acceleration of NREM sleep-spindle center frequency after 3.6 GHz exposure, with effects distributed across central, parietal, and occipital cortex [45].

The relevance to ceLLM is not merely that an RF exposure altered a brain rhythm. The critical point is that the response was gated by a single variant in the third intron of *CACNA1C*, a gene encoding the α_{1C} subunit of L-type voltage-gated calcium channels [45]. *CACNA1C* is native bioelectric hardware: its channels regulate voltage-dependent calcium entry, neuronal firing, gene transcription, sleep EEG oscillations, learning, memory, and development [45].

Because rs7304986 is intronic, the result points toward regulatory architecture rather than a simple protein-substitution explanation. In ceLLM terms, this is consistent with the idea that noncoding DNA contributes to the weights and biases of cellular state inference: it helps determine how a cell or tissue deploys calcium-channel hardware and how the same electromagnetic input is resolved into a physiological output. The CACNA1C finding therefore extends topology-gated inference beyond mtDNA nucleoids into nuclear noncoding regulatory architecture.

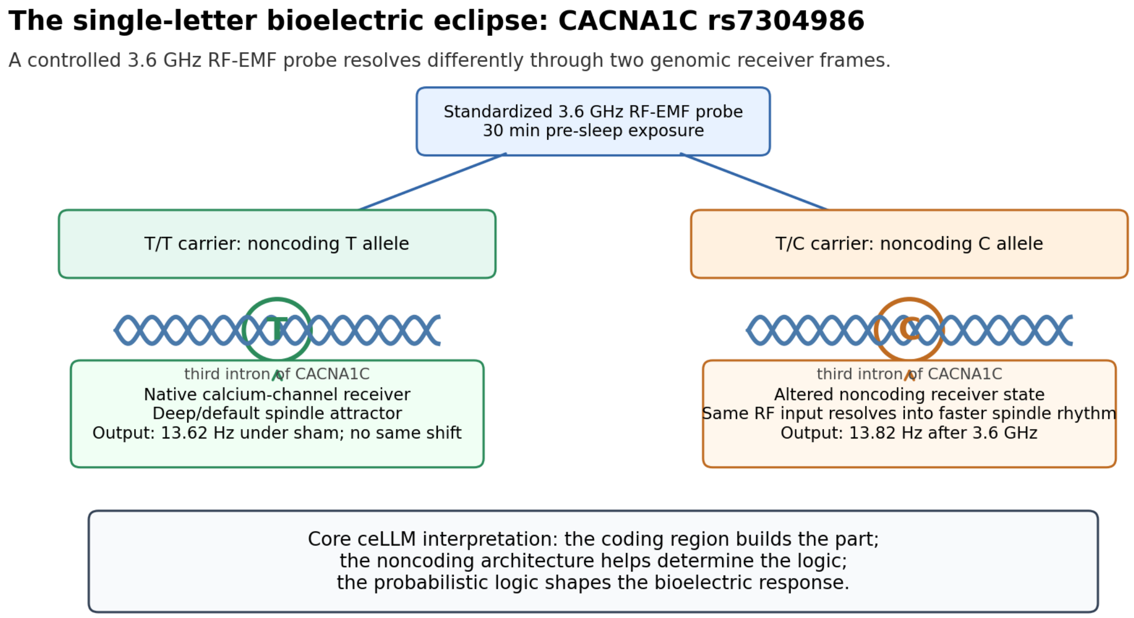

Figure 2: The single-letter bioelectric eclipse. A controlled 3.6 GHz RF-EMF input acts as a probe. In T/T carriers, the receiver state remains associated with the default spindle attractor. In T/C carriers of the intronic CACNA1C rs7304986 variant, the same probe resolves into a faster NREM spindle center frequency. The figure is a conceptual summary of Sousouri et al. [45], not a claim that the exact microscopic mechanism is already known.

2.6. Noncoding sequence as atomic receiver architecture

The CACNA1C result clarifies that topology should not be limited to hydration shells or organelle-scale DNA packaging. A single nucleotide substitution changes the actual atomic structure of DNA at that locus: base chemistry, hydrogen-bonding context, stacking interactions, local groove geometry, electrostatic potential, and the binding grammar available to regulatory proteins. Foundational structural work showed that DNA shape can be a major mode of protein-

DNA recognition, especially through sequence-dependent minor-groove geometry and electrostatic potential [47]. Machine-learning and genome-scale studies further show that DNA shape features improve transcription-factor binding prediction and that noncoding variants can alter transcription-factor binding [46,48-50].

Thus, the noncoding genome can be interpreted as a physical receiver architecture. Its letters do not merely encode proteins; they encode local mechanical and geometric constraints that determine how regulatory complexes assemble, how chromatin folds, and how bioelectric hardware is deployed. In ceLLM terms, noncoding DNA is a candidate substrate for biological weights and biases: a sequence-defined atomic lattice that shapes the probability with which a given input becomes a cellular or physiological output. The hydration shell is not the weight matrix by itself. It is the coupling medium. The aligned atoms of DNA - their base chemistry, shape, electrostatic surface, stacking geometry, and regulatory folding grammar - are part of the mechanical probability architecture.

Table 1: Empirical status of the major components used in the hypothesis.

Component	Status	Role in this model	Key uncertainty
UPE from living cells	Strong	Fast optical/redox state variable	Whether UPE is ever functional rather than byproduct
Mitochondria as major UPE sources	Moderate to strong	Primary emitter and integrator	Relative contribution by context and cell type
Circular mtDNA and nucleoid organization	Strong	Physical substrate for topology-sensitive transduction	How geometry couples in hydrated organelles
TFAM compaction affects nucleoid activity	Strong	Slow prior controlling transducer state	Exact coupling between compaction and field sensitivity
Nuclear noncoding regulatory architecture	Strong biology; new ceLLM extension	Candidate receiver-state layer controlling how native bioelectric hardware is deployed	Whether specific noncoding architectures predict field-to-bioelectric coupling
CACNA1C intronic variant rs7304986	Emerging human evidence	Nuclear noncoding receiver variable gating RF-to-bioelectric coupling in sleep EEG	Whether causal mechanism is chromatin topology, expression, splicing, channel density, tissue electrical properties, or combined regulatory architecture
Narrow-band THz mitochondrial effects	Moderate	Experimental foothold for frequency selectivity	Whether mtDNA is the critical mediator
Microtubule energy migration / aromatic networks	Moderate	Possible short-range routing or excitonic relay	Distance, specificity, and biological relevance in vivo
Actin-dependent mitochondrial mixing	Strong	Spatial distribution of local perturbations	Whether it carries optical-state information specifically
MERCs / NAMs / retrograde signaling	Strong	Classical amplification layer	Which hubs are necessary for any optical leg
Condensate electrochemistry	Emerging	Memory / persistence layer	Extent of generalization to mammalian mitochondrial signaling
Intercellular mitochondrial transfer / Cx43 contacts	Moderate	Hybrid amplifier across cells	When direct hardware exchange dominates over optical leakage
Large-scale UPE coherence claims	Weak / disputed	Not required by core model	Whether any nonclassical statistics survive rigorous testing

Component	Status	Role in this model	Key uncertainty
CYB5B-mediated EMF-responsive calcium oscillations	Emerging	Candidate surface transducer / calcium-code interface	Exact sensing physics and relevance outside engineered platform
S1-S4 voltage-sensing domains / VGIC route	Strong biology; disputed EMF coupling	Candidate plasma-membrane flood / noise entry route	Whether physiologically relevant weak-field or envelope structure perturbs gating in vivo

3. Hypothesis: from lone antenna to pan-genomic control plane

The central claim of this paper is narrower, stronger, and more testable than a literal loop-antenna narrative. The claim is that mitochondrial redox chemistry generates structured optical and electromagnetic microfluctuations; that mtDNA topology, TFAM-dependent nucleoid organization, and the local hydration shell form a topology-gated transducer layer sensitive to those fluctuations; that nuclear noncoding regulatory architecture can function as a related receiver-state layer for native bioelectric hardware; and that downstream mitochondrial, nuclear, and cellular signaling networks amplify the resulting perturbations into stable state updates. The newly identified CYB5B pathway suggests that this architecture may include both a nucleoid-centered interface and a surface-facing outer-mitochondrial-membrane interface for writing or shaping downstream calcium codes [25]. The CACNA1C sleep-EEG result suggests that nuclear noncoding architecture can likewise shape how electromagnetic input is resolved into brain-wide bioelectric rhythm [45].

This model is easiest to understand in layers. The source layer is conventional mitochondrial biophysics: ETC activity, ROS production, excited-state chemistry, membrane-potential oscillation, and UPE generation [2,6-8]. The transducer/receiver layer includes the mtDNA-nucleoid complex, including circular geometry, supercoiling and topological control, TFAM compaction, DNA bending, and the hydration shell, as well as nuclear noncoding regulatory topology and candidate surface-facing redox interfaces at the outer mitochondrial membrane such as CYB5B [1,9-15,25-28,45-50]. The routing layer includes candidate short-range relays such as microtubules, actin-dependent mitochondrial rearrangement, mitochondrial reticula, and nanotunnels [16-18,22,23]. The amplification layer includes MERCs, calcium microdomains, membrane-potential changes, retrograde signaling to the nucleus, and any CYB5B-linked calcium-code interface that sits at the transducer-amplification boundary [19,20,25]. The memory layer includes condensate state, transcriptional reprogramming, nucleoid accessibility, chromatin topology, and other slow variables that preserve the consequences of brief perturbations [10-12,21,45-50].

Within this architecture, the most plausible physics is not same-frequency resonance across all components. A more interesting possibility is cross-scale frequency conversion. Optical excited-state chemistry may be converted at hydrated DNA-protein and membrane interfaces into lower-frequency structural or electrochemical envelopes, which then propagate through calcium, redox, and membrane-potential networks. One plausible bridge is non-radiative relaxation: optically excited states produced by ROS chemistry can dump energy through internal conversion and vibrational energy redistribution into low-frequency collective modes and solvent-coupled phonons in the THz band, providing a candidate route from UV/visible UPE chemistry to THz-scale structural dynamics [14,15,37]. In engineering language, the cell may behave less like a narrowband radio and more like a heterogeneous mixer, envelope detector, and adaptive controller.

The ceLLM language offers a disciplined systems interpretation. Let x_t denote the latent cellular state at time t. Let r_t encode redox variables, p_t encode structured photon variables such as spectral mix and burst entropy, c_t encode calcium and membrane-potential variables, and g_t encode slowly varying genomic or topological priors. In the original mtDNA-centered formulation, g_t included nucleoid compaction, contact-site density, and condensate organization. In the revised pan-genomic formulation, g_t includes a broader receiver-state tensor:

$$g_t = \{g_{mtDNA}, g_{nuclear}, g_{noncoding}, g_{chromatin}, g_{hydration/interfacial}\}.$$

Thus a minimal update rule becomes:

$$x_{t+1} = F(x_t, r_t, p_t, c_t, g_{mtDNA}, g_{nuclear/noncoding}).$$

This need not be computationally exotic. It simply states that cells update state by integrating fast fluctuating inputs through slower structural constraints. In that sense, ceLLM is a language for probabilistic state integration, not a claim that cells implement software large language models.

A key implication of the CYB5B result is that the relevant intracellular variable may be signal structure, not just dose. The EMF-inducible platform responded to rhythmic oscillatory calcium dynamics rather than generic calcium influx [25]. In ceLLM terms, this sharpens the distinction between bulk stress variables and patterned state variables: cells may update state not only from how much Ca^{2+} enters a compartment, but from whether that Ca^{2+} arrives in the right frequency, phase, or burst architecture to be interpreted as informative rather than noisy. The CACNA1C result adds a second implication: receiver architecture is not only mitochondrial. A single noncoding nuclear variant can gate how a controlled RF input is resolved into a physiological rhythm [45].

A second distinction is now important for mechanistic clarity. The CYB5B result concerns rhythmic oscillatory calcium dynamics rather than generic influx [25]. Classical ion-channel biology, by contrast, identifies S1-S4 voltage-sensing domains as the membrane modules that convert transmembrane electric fields into channel opening, with positively charged S4 residues moving across a focused hydrophobic constriction site [42]. Within the present framework, this suggests a reviewer-safe contrast between calcium code and calcium flood: CYB5B-like outer-mitochondrial-membrane interfaces may help write patterned, information-bearing Ca^{2+} oscillations, whereas inappropriate opening of plasma-membrane voltage-sensing channels would inject bulk, weakly structured Ca^{2+} load. Whether weak environmental fields can access that plasma-membrane route remains contested [43,44], but the distinction itself is experimentally useful because it predicts that downstream state transitions should depend on calcium structure, not calcium quantity alone.

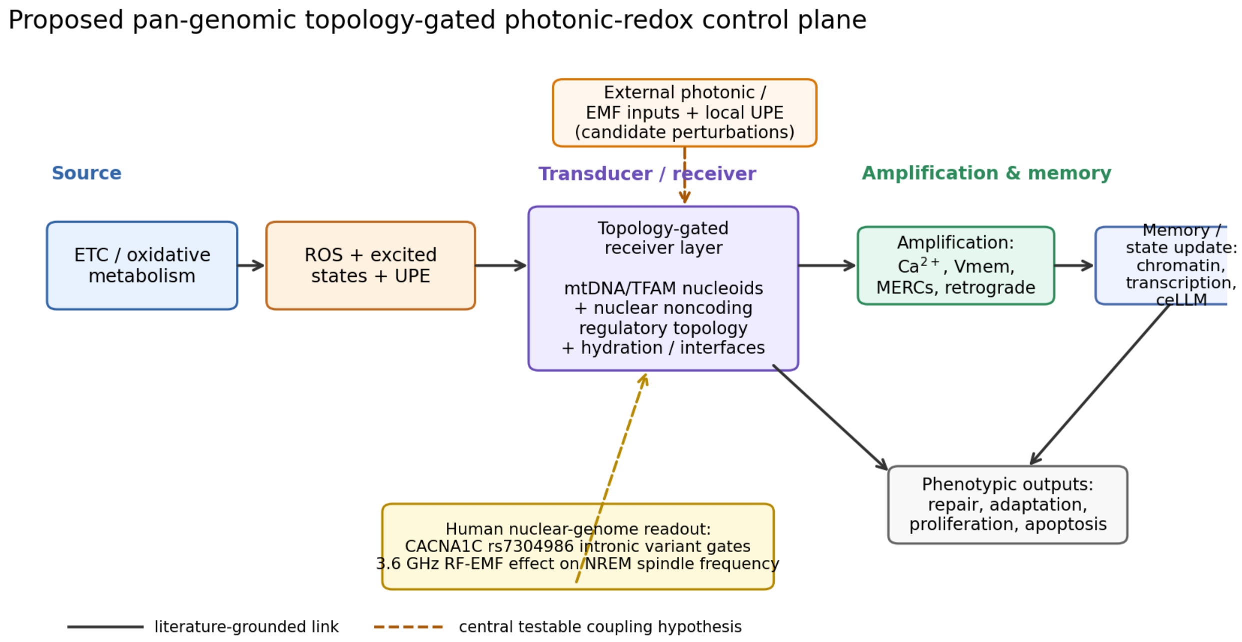

Figure 3: Proposed pan-genomic topology-gated photonic-redox control plane. Solid arrows indicate links grounded in mitochondrial, contact-site, nuclear regulatory, and transcriptional biology. Dashed arrows mark central testable coupling hypotheses. The revised central receiver layer includes mtDNA/TFAM nucleoids, nuclear noncoding regulatory topology, and hydration/interfacial structure. The CACNA1C rs7304986 sleep-EEG result provides a human nuclear-genome readout for the receiver-architecture principle [45].

This framing also places the hypothesis inside current bioelectricity research rather than outside it. Emmons-Bell et al. showed that transient gap-junctional blockade in planaria can stochastically induce species-specific head morphologies that persist for weeks before remodeling back toward the native state, illustrating how fast membrane-level perturbations can be transduced into longer-lived, yet still reversible, morphological memory without changes in DNA sequence [39]. Likewise, depolarization of resting membrane potential is increasingly treated not merely as a downstream consequence of oncogenic transformation but as an instructive bioelectric variable that can regulate proliferation, migration, and metastatic state switching [40,41]. In that light, the proposed control plane is not meant to replace classical bioelectric circuits. It offers candidate subcellular mechanisms by which fast photonic-redox fluctuations and noncoding genomic priors could bias the distributed electrochemical envelopes that cells already use as actionable summaries of internal state.

4. Intercellular extension and relation to circadian / photobiomodulation narratives

The model also suggests a restrained but important intercellular extension. A pure free-space biophoton-communication thesis is physically difficult because photon counts are low and tissue environments are lossy. A hybrid network is more plausible. Local UPE may provide synchronization, directional bias, or state leakage over short distances, while gap junctions, calcium waves, direct contacts, tunneling nanotubes, and mitochondrial transfer amplify or stabilize the effect [6,19,20,24]. In this reading, Gurwitsch's onion-root experiments become historically provocative but not dispositive: they motivate the search for an optical leg in cell-cell communication without proving the modern mechanism.

This hybrid framing also helps place the model alongside established external-light pathways rather than against them. In mammals, circadian photoentrainment is initiated primarily by retinal photoreceptors, especially melanopsin-containing intrinsically photosensitive retinal ganglion cells, while cryptochromes remain core clock flavoproteins and blue-light photoreceptors in other taxa [31,32]. Likewise, photobiomodulation literature often treats cytochrome c oxidase as a principal mitochondrial photoacceptor, or at minimum a central node, for red/near-IR responses [7,33].

The present framework operates at a different scale and with different inputs. It asks how endogenous ultra-weak photon emission generated by mitochondrial ROS chemistry might be sampled by the nucleoid-cristae-cytoskeletal architecture inside the organelle and then amplified into redox, Ca^{2+}, membrane-potential, and transcriptional updates. It also asks how nuclear noncoding receiver state changes the way native bioelectric hardware is deployed and how electromagnetic inputs are translated into physiological timing. External photons, internally generated UPE, and external RF probes need not be rival stories; they may converge on related receiver architectures.

Brown adipose tissue, for example, need not possess a unique signaling chemistry for its putative biophoton role. Its heightened thermogenesis may simply raise ROS-linked photon output and thereby increase local coupling opportunities within the same general architecture.

5. Falsifiable predictions and experimental program

A credible hypothesis paper must make itself vulnerable. The present model can be falsified, narrowed, or strengthened by a focused experimental program that distinguishes source, transducer, receiver, routing, amplification, and memory layers.

First, topology dependence should be tested directly. TFAM overexpression, TFAM depletion, and topoisomerase perturbation should alter nucleoid compaction or topology without necessarily abolishing respiration outright [10-13]. If the model is correct, such perturbations should shift the relationship between optical or terahertz input and mitochondrial readouts such as ROS, membrane potential, calcium handling, and transcriptional activation. A null result across well-controlled perturbations would weigh against the transducer claim.

Second, mtDNA itself should be made experimentally dispensable and then restored. rho0 or mtDNA-depleted systems, followed by rescue where feasible, can test whether the candidate coupling layer depends on mtDNA abundance or organization rather than only on membranes and canonical photoacceptors. If narrow-band or optical effects survive complete loss of mtDNA with unchanged magnitude and structure, the strongest version of the mtDNA-centered hypothesis would fail; such persistence would instead implicate alternative chromophores such as flavins, porphyrins, or cytochrome c oxidase [33,35].

Third, routing candidates should be separated from sources. Microtubule perturbation and actin perturbation should be combined with simultaneous imaging of UPE, ROS, calcium, membrane potential, and mitochondrial morphology [16-18]. The key question is not merely whether the cytoskeleton changes emission intensity, but whether it changes propagation, anisotropy, synchronization, or the spatial spread of downstream state changes. A routing role predicts altered correlation structure even when mean emission changes are modest.

Fourth, amplification hubs should be attacked. MERC disruption, altered calcium-handling proteins, and perturbation of retrograde signaling should test whether any weak optical coupling requires classical organelle-contact amplification to become functionally relevant [19,20]. If disrupting amplification abolishes a candidate effect while source emission persists, the theory gains a mechanistic foothold: photons may bias a control plane whose biological meaning is created downstream by established signaling circuits.

An additional layer-specific test is now available. CYB5B knockdown, rescue, or heme-/anchor-mutant complementation should be combined with controlled low-frequency field stimulation and live-cell imaging of rhythmic calcium dynamics, reporter activation, ROS, membrane potential, MERC organization, and TFAM-linked transcriptional readouts [25-28]. If CYB5B functions as a genuine control-plane entry point, disrupting it should abolish patterned field-induced calcium coding more than generic ionophore-driven Ca^{2+} influx. Combined TFAM/topology perturbation can then determine whether a surface-facing CYB5B interface and a nucleoid-centered topology gate operate in series, in parallel, or redundantly. Because the Ei platform depended on field structure rather than dose alone, waveform, duty cycle, and low-frequency envelope architecture should be treated as first-class experimental variables rather than collapsed into average intensity.

A complementary orthogonality test should explicitly compare calcium code against calcium flood. Controlled stimulation protocols that vary carrier, low-frequency envelope, burst structure, and duty cycle should be combined with compartment-resolved calcium imaging, voltage-gated calcium-channel blockade, and CYB5B perturbation [25,43,44]. If the proposed signal-to-noise architecture is correct, CYB5B disruption should preferentially erase rhythmic mitochondrial-linked oscillations, whereas channel blockade should preferentially suppress any bulk plasma-membrane influx component. Downstream transcriptional state changes should then track calcium structure more strongly than calcium quantity alone.

Fifth, the known 34.5 THz mitochondrial-biogenesis result provides a ready-made frequency window to separate transducer from amplification layers. Co-application of targeted mitochondrial Ca^{2+} uptake inhibitors - for example Ruthenium Red, Ru360, or MCU inhibitors such as DS16570511 - during narrow-band THz exposure should abolish downstream PGC-1alpha-NRF1/2-TFAM induction and biogenesis if the effect requires the Ca^{2+} amplification node [8,36]. If the topology-gated transducer hypothesis is correct, the same Ca^{2+} blockade should leave any upstream changes in UPE statistics or nucleoid-localized coupling intact, whereas TFAM or topoisomerase perturbation should shift the THz sensitivity window even when Ca^{2+} influx is permitted. This experiment directly leverages existing mechanistic detail and creates a clean double dissociation between amplification and transducer layers.

Sixth, intercellular optical claims should be forced into competition with classical explanations. Quartz-versus-glass or other optical-isolation assays should be paired with chemical diffusion controls, optical shielding, gap-junction blockade, TNT inhibition, and Cx43 perturbation [3,6,24]. A hybrid-network hypothesis predicts partial separability: some effects should survive chemical isolation and depend on optical transmission, whereas others should disappear when classical contact-mediated amplification is disabled.

Seventh, signal structure should be tested against simple intensity metrics. UPE research often reduces measurements to photon counts, but a control-plane model predicts that burst timing, spectral composition, entropy, and cross-correlation with ROS or calcium events may outperform raw counts as predictors of state transitions [2,29]. The decisive question is whether mtDNA-nucleoid variables - topology, TFAM compaction, hydration-shell state, or their perturbation history - add predictive power beyond standard redox, Ca^{2+}, and membrane-potential readouts. If TFAM or topoisomerase perturbation shifts the relationship between structured UPE variables or narrow-band THz input and downstream state transitions while respiration and bulk ROS remain controlled, the topology-gated transducer claim gains support. If no such shift occurs, the model narrows toward a simpler redox/membrane-only mechanism. This is where AI-enabled analysis can contribute immediately: state-space models, sequence models, and graph-temporal models can determine whether structured photon variables plus topology state improve prediction beyond conventional metabolic measurements.

Eighth, the CACNA1C human finding should be converted into an explicitly mechanistic follow-up program. Genotype-stratified sleep-EEG experiments should combine controlled RF waveforms with CaV1.2 pharmacological modulation, CACNA1C expression assays, splice-isoform analysis, methylation profiling, chromatin accessibility, and contact mapping. The decisive question is whether RF-induced spindle shifts track noncoding receiver state better than SAR alone, and whether CaV1.2 modulation alters or suppresses the genotype-gated response. This program would test whether rs7304986 is merely a marker or whether CACNA1C regulatory architecture is a causal component of RF-to-bioelectric coupling [45].

Finally, the computational program should run in parallel with wet-lab work. Multiscale electrodynamic and molecular simulations can bound plausible coupling regimes for hydrated nucleoids, membrane interfaces, and noncoding regulatory DNA. At the systems level, latent-state models can ask whether including UPE-derived variables and genomic receiver-state variables improves forecasting of mitochondrial or cellular fate. Such modeling will not prove mechanism, but it will sharpen experimental priors and identify which observables are worth expensive measurement.

Table 2: Decisive experiments, readouts, and what their outcomes would mean.

Perturbation	**Core readouts**	**Prediction if the model is correct**	**If negative, the model narrows to**
TFAM up/down perturbation; topoisomerase perturbation	UPE spectrum, ROS, membrane potential, Ca^{2+}, transcription, nucleoid imaging	Sensitivity to optical / THz input shifts with nucleoid topology or compaction	No change implies weak support for topology-gated transducer
rho0 depletion and rescue	Same readouts plus mtDNA abundance / organization controls	Specific coupling effects weaken or disappear without mtDNA and recover on rescue	Persistence without mtDNA points to membranes or protein chromophores
CYB5B knockdown / rescue / heme- or anchor-mutant complementation during controlled low-frequency field stimulation	Rhythmic Ca^{2+} oscillations, reporter activation, ROS, membrane potential, MERC imaging, TFAM-linked transcription	CYB5B perturbation abolishes patterned field-induced Ca^{2+} coding more than generic ionophore responses; combined TFAM/topology perturbation separates surface and nucleoid contributions	Field response points to other membrane/cytosolic sensors, or CYB5B role is limited to engineered platform
CACNA1C rs7304986 genotype stratification +/- CaV1.2 pharmacological modulation +/- CACNA1C regulatory profiling	Sleep spindle center frequency, CaV1.2 expression, CACNA1C chromatin accessibility/contact mapping, methylation/splicing, EEG response to controlled RF waveforms	RF-induced spindle shifts track noncoding receiver state; regulatory/topological differences predict response better than SAR alone; CaV1.2 modulation alters or suppresses genotype-gated spindle response	Effect unrelated to CACNA1C regulatory architecture and reflects another tissue/network variable
Microtubule and actin perturbation	Spatial anisotropy, correlation length, timing, mitochondrial mixing	Routing metrics change more than source intensity alone	Pure transport/mechanics explanation becomes more likely
MERC disruption / altered Ca^{2+} handling	Ca^{2+} microdomains, dehydrogenase activity, retrograde signals, phenotype	Weak optical effects require classical amplification hubs	Optical observations without downstream dependence may be epiphenomenal

Perturbation	Core readouts	Prediction if the model is correct	If negative, the model narrows to
34.5 THz exposure +/- mitochondrial Ca^{2+} uptake inhibitors +/- TFAM/topology perturbation	PGC-1alpha-NRF1/2-TFAM induction, mitochondrial biogenesis markers, UPE statistics, nucleoid imaging, Ca^{2+} microdomains	Ca^{2+} blockade abolishes downstream biogenesis while preserving any upstream UPE or nucleoid changes; topology perturbation shifts THz sensitivity independently of Ca^{2+} influx	Effect is purely Ca^{2+}-channel mediated with no topology dependence
Quartz-vs-glass optical isolation plus gap-junction / TNT / Cx43 blockade	Intercellular respiration, ROS, UPE, fate markers	Partial separability of optical and contact-mediated components	Loss of all effects under diffusion/contact controls argues against an optical leg
Sequence or state modeling of photon bursts with vs. without TFAM perturbation	Spectral mix, entropy, burst timing, cross-correlation with ROS / Ca^{2+}	Structured UPE variables plus topology state outperform raw counts or standard redox readouts for state prediction	No added predictive value weakens topology-gated control-plane framing
Controlled waveform comparison +/- CaV blockers +/- CYB5B perturbation	Cytosolic vs mitochondrial Ca^{2+} time series, phase structure, ROS, membrane potential, reporter activation	CaV blockade preferentially suppresses bulk influx; CYB5B perturbation preferentially erases rhythmic coding; downstream state changes track Ca^{2+} structure more than Ca^{2+} load	No separable code-vs-flood regimes weakens distinct S4/CYB5B signal-to-noise architecture

6. Physical constraints and alternative explanations

Several constraints need to be stated plainly. Hydrated cytoplasm and the mitochondrial matrix are lossy, screened, thermally noisy environments. Early validation will therefore rely on isolated mitochondria, 2D cultures, and tightly controlled optical-isolation assays, because intact tissues are highly scattering and absorptive media in which photonic effects are difficult to separate cleanly from diffusion, heating, and contact-mediated signaling in vivo [38]. Terahertz fields couple strongly to water and collective vibrational modes, so any in vivo effect is more likely to involve dielectric, hydration-shell, interfacial, or channel-gating physics than classical free-space antenna behavior. The free-space dimensional markers used here - 5.633 μm contour length to about 53 THz, 1.79 μm relaxed-circle diameter to about 167 THz, and 100 nm nucleoid scale to about 3 PHz - are therefore experimental search windows rather than direct predictions of in vivo resonant peaks [8,14,15]. The recent frequency-selective THz result is consistent with this caution: 34.5 THz, but not 36.1 THz, promoted mitochondrial biogenesis through calcium influx and the PGC-1alpha-NRF1/2-TFAM axis rather than through demonstrated direct mtDNA absorption [8].

Alternative explanations are also real. Reported terahertz effects may act primarily through water, membranes, ion channels, or canonical chromophores such as flavins, porphyrins, and cytochrome c oxidase rather than mtDNA specifically [33,35]. Cytoskeletal perturbations may alter mitochondrial behavior through transport or mechanics rather than optical routing. UPE may remain a passive byproduct in many contexts. The coherence question remains unresolved, and the field has a history of overinterpretation [4,5]. These are not reasons to avoid the problem; they are reasons to design experiments that distinguish mechanisms rather than merely accumulating suggestive correlations.

The CYB5B result sharpens one longstanding objection to weak-field mitochondrial biology - the absence of a named surface mediator - but it does not yet settle environmental relevance. The Ei platform used controlled low-frequency EMF stimulation and identified CYB5B as an essential mediator, likely sensor, of rhythmic calcium coding [25]. It did not demonstrate direct responses to everyday wireless carriers, nor did it resolve whether the coupling physics arises from heme spin chemistry, altered electron-transfer kinetics, membrane-potential effects, or some combination thereof. The disciplined conclusion for the present manuscript is therefore narrow and important: a real outer-mitochondrial-membrane hemoprotein can sit upstream of structured Ca^{2+} and gene-expression change under controlled field conditions.

The same caution applies to S4/VGIC hypotheses. Modern wireless systems are not defined by carrier frequency alone; they also contain low-frequency temporal structure arising from burst repetition, framing, beaconing, and duty cycle. Reviews advancing an IFO/VGIC account argue that modulation structure and polarization are the biologically relevant variables [43], whereas critical reviews conclude that induced currents at guideline limits are far too small and that no validated rectification mechanism has yet been shown for RF-driven Ca^{2+} gating [44]. For the present manuscript, the practical implication is methodological rather than rhetorical: carrier frequency, envelope frequency, waveform structure, and duty cycle should be manipulated explicitly in experiments rather than inferred from carrier frequency alone.

The CACNA1C sleep-EEG result provides a stronger human physiological anchor for receiver-dependent EMF biology, but it should still be treated as an entry point into mechanism rather than as the final mechanism. The key fact is that one intronic regulatory difference gated an RF-to-bioelectric output [45]. The mechanism may involve CACNA1C expression, splicing, chromatin topology, tissue electrical properties, channel density, or combined regulatory architecture. That uncertainty is an opportunity for direct testing, not a weakness of the broader receiver-state principle.

7. Discussion

If the model proves partly correct, the payoff is substantial even without any appeal to exotic coherence. A demonstration that nucleoid topology modulates sensitivity to optical or terahertz perturbations would establish mtDNA organization as an active physical control variable rather than merely a genetic repository. A demonstration that structured UPE variables outperform simple intensity in predicting mitochondrial state would transform biophoton measurements from curiosity to systems-biology readout. A demonstration that weak optical effects require MERCs or retrograde signaling would reveal how fragile physical perturbations are translated into robust biological meaning. A demonstration that noncoding nuclear variants predict RF-to-bioelectric coupling would establish a parallel receiver-state layer in the nuclear genome [45-50].

7.1. The Biological Eclipse: noncoding DNA as receiver logic

The CACNA1C sleep-EEG finding provides a human biological eclipse for the ceLLM framework. In the 1919 eclipse, starlight revealed invisible spacetime geometry by bending around the sun. In the CACNA1C study, a controlled 3.6 GHz electromagnetic probe revealed hidden genomic receiver architecture by producing a genotype-gated shift in NREM sleep-spindle frequency [45]. The same external field passed through different genomic frames and produced different bioelectric outputs.

The result is important because the variant is intronic. It is not a simple coding substitution that replaces one calcium-channel part with another. It is a noncoding regulatory difference in a gene whose product is central to voltage-dependent calcium signaling. The observation is therefore naturally interpreted as a change in receiver logic: the same external RF input is transformed differently because the genomic and bioelectric frame of the receiver has changed.

This is precisely the role assigned to genomic topology in ceLLM. Noncoding DNA is not inert filler. It is part of the physical control architecture that determines how channels, redox systems, transcriptional programs, and oscillatory states are deployed. In this sense, the CACNA1C variant functions as a natural perturbation of the cell's probability landscape. It shows that the response to electromagnetic input depends not only on field strength or tissue heating, but on the genomic receiver architecture through which the signal is interpreted.

The old protein-dictionary model cannot fully explain why a single intronic letter should gate an RF-induced sleep-spindle shift. ceLLM can: noncoding DNA is part of the regulatory geometry that determines how native bioelectric machinery is deployed and how external fields are interpreted. The coding region builds the part. The noncoding architecture helps determine the logic. The probabilistic logic shapes the bioelectric response.

7.2. CYB5B, calcium code, and bioelectric dissonance

The newly reported CYB5B pathway also changes the map of what can now be asked plausibly. A longstanding mechanistic objection to weak-field mitochondrial biology was the absence of named hardware at the mitochondrial surface. The Ei study does not prove that endogenous CYB5B is the universal sensor of physiological or environmental electromagnetic cues, but it does show that a real outer-mitochondrial-membrane hemoprotein can sit upstream of structured calcium coding and transcriptional change under controlled field conditions [25]. In the logic of the present hypothesis, this is important not because it displaces nucleoid-centered topology gating, but because it suggests a nested architecture: surface-facing CYB5B-like transducers may write fast calcium codes, while the nucleoid-cristae-hydration system filters, amplifies, and stores the consequence of those codes [25-28].

One disease-relevant extension follows naturally from this nested architecture. If CYB5B-like interfaces write structured mitochondrial-linked Ca^{2+} codes while plasma-membrane S4-containing voltage sensors admit bulk Ca^{2+} load, then pathology may arise not from calcium elevation alone but from collapse of calcium signal quality. In that framing, patterned oscillatory coding is the signal and unpatterned influx is the noise; when noise dominates, downstream transcription reads disordered electrochemical envelopes rather than informative state summaries [25,42]. The framework refers to this potential loss of pattern-to-noise ratio as bioelectric dissonance. The term is only useful if it stays falsifiable: the decisive question is whether equal or comparable total Ca^{2+} loads produce different state outcomes when delivered as rhythmic mitochondrial-linked oscillations versus unpatterned cytosolic influx.

7.3. Morphological memory and structural priors

The multi-timescale architecture of the proposed control plane offers a physical lens for macroscale phenomena such as morphological memory. Emmons-Bell et al. showed that transient gap-junctional blockade in *Girardia dorotocephala* can induce temporary species-specific head morphologies in genetically wild-type animals [39], a result that fits Levin's broader view of bioelectric networks as reprogrammable morphogenetic circuits [40]. Within the present framework, the induced state can be interpreted as a fast, bioelectrically maintained short-term memory, whereas reversion toward the native morphology could reflect reassertion of deeper, genetically canalized priors reinforced by coordinated nuclear and mitochondrial retrograde signaling [20,40]. Future in vivo studies could test this bridge directly by asking whether controlled structured electromagnetic perturbations accelerate the decay of such transient bioelectric memories, thereby degrading the fidelity of the electrochemical envelopes normally integrated by the proposed photonic-redox network.

More broadly, the framework offers a way to merge several literatures that currently talk past one another: mitochondrial redox biology, photobiomodulation, biophoton emission, nucleoid organization, cytoskeletal energy transport, organelle-contact biology, nuclear noncoding regulatory topology, sleep EEG genetics, and AI-style state inference. The important discovery may not be that cells communicate by light alone. It may be that cells possess a nested photonic-redox-bioelectric control plane in which light, redox chemistry, topology, noncoding regulatory architecture, and classical signaling are inseparable parts of one regulatory architecture.

The hypothesis presented here is therefore ambitious but not unconstrained. It asks the field to move beyond the false choice between "biophotons are mystical" and "biophotons are meaningless waste." A more rigorous middle position is available: ultra-weak optical events may be biologically relevant when, and only when, they are embedded in geometry-sensitive mitochondrial and nuclear receiver networks with strong downstream amplifiers. That proposition can be tested. If it fails, the field becomes sharper. If it succeeds, cellular biology will have acquired new physical control variables.

8. Conclusion

This manuscript proposes that the most defensible expansion of the mtDNA-biophoton idea is a pan-genomic topology-gated photonic-redox control plane. In this framework, mitochondrial redox chemistry generates weak but structured optical and electromagnetic fluctuations; mtDNA topology, TFAM, and the hydration shell form a candidate mitochondrial transducer; nuclear noncoding regulatory architecture forms a parallel receiver-state layer for bioelectric hardware; cytoskeletal and mitochondrial subnetworks distribute local perturbations; organelle contact sites amplify them into canonical signaling variables; and slower transcriptional, chromatin, and condensate states store the update. The ceLLM concept enters as a state-inference description of that multiscale integration, not as a claim of literal machine-learning hardware in the cell.

The CACNA1C rs7304986 sleep-EEG finding provides a human nuclear-genome analogue of the topology-gated control-plane hypothesis: a single intronic variant in native calcium-channel regulatory architecture changed how a controlled RF-EMF input was resolved into brain-wide bioelectric rhythm [45]. This does not replace the mitochondrial hypothesis. It strengthens and broadens it. It suggests that DNA topology, whether mitochondrial or nuclear, may act as a geometry-sensitive receiver layer that shapes how electromagnetic, redox, calcium, and photonic signals are transformed into cellular state.

The paper is intentionally written so that its core claims can be broken. The decisive issues are whether nucleoid topology changes coupling, whether mtDNA is required, whether routing and amplification layers can be separated experimentally, whether structured UPE variables carry more state information than simple photon counts, and whether nuclear noncoding receiver architecture predicts RF-to-bioelectric outputs better than field intensity or SAR alone. Those are tractable questions. Answering them cleanly would move the discussion from metaphor to mechanism.

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