BIOELECTRIC FIDELITY

IN EARLY HUMAN DEVELOPMENT

A mechanistic plausibility framework linking time-structured electromagnetic exposure to calcium-waveform distortion, chromatin/BET dysregulation, NDEL1-linked neurogenesis, and developmental vulnerability

> *"The question is not whether one exposure causes one diagnosis. The question is whether developing cells can lose the timing fidelity required to execute their instructions."*
>
> — John Coates

JOHN COATES

Founder, RF Safe

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DOCUMENT STATUS

This is a falsifiable mechanistic synthesis, not a systematic review, clinical conclusion, or proof that radiofrequency exposure causes autism, neural-tube defects, or any individual diagnosis. Its purpose is to define what is known, identify the untested bridges, and specify the experiments capable of confirming or rejecting the proposed pathway.

Prepared for scientific discussion, replication, and research prioritization

Author's Note: Why This Question Matters

I lost my first daughter, Angel Leigh, to anencephaly, a devastating neural-tube disorder. Her condition is not offered here as evidence that radiofrequency radiation caused her death. No retrospective exposure story can establish that. Her life is the ethical reason I continue to ask whether preventable disturbances of developmental signaling have been overlooked, and whether the scientific tools now exist to test those disturbances directly.

The focus of this paper is therefore narrower than the most forceful language in some of my public posts. I am not claiming that wireless exposure is a sole cause of autism, neural-tube defects, cancer, autoimmunity, attention disorders, or any other diagnosis. I am arguing that early development depends on high-fidelity biological timing; that calcium waveforms are part of that timing language; that several recent studies identify experimentally measurable points at which electromagnetic fields, calcium rhythms, chromatin readers, progenitor-cell decisions, and developmental regulators intersect; and that the full chain should now be tested rather than dismissed or assumed.

> *"Life can compensate for many insults. The research question is whether it can compensate for chronic timing noise during the brief windows in which tissues are being instructed how to form."*
>
> **— John Coates**

Personal motivation is not causal evidence

This paper keeps the author's personal loss separate from the evidentiary chain. The motivation is certain. The cause is not assigned. The scientific task is to define a pathway that can be independently confirmed, narrowed, or rejected.

Abstract

Embryonic development depends on precisely coordinated signals that regulate proliferation, differentiation, migration, cytoskeletal contraction, gene expression, and tissue morphogenesis. Calcium is central to this coordination, but cells do not read calcium only as an average concentration. They decode frequency, amplitude, duration, phase, localization, burst structure, intercellular coherence, and recovery kinetics. This paper calls the preservation of those parameters bioelectric fidelity and the measurable degradation of them low-fidelity biology. The concept is explicitly multifactorial: genetic susceptibility, nutrient status, maternal illness, inflammation, hypoxia, pollutants, pharmaceuticals, metabolic stress, and physical environmental inputs can interact, and no single contributor is presumed sufficient or universal.

Three recent findings provide complementary empirical anchors. Cakir et al. reported that a defined 2.4-GHz radiofrequency exposure altered radial-glia differentiation, chromatin programs, retroelement expression, and neuronal phenotypes in human cortical organoids, with rescue of multiple effects by BET bromodomain inhibitors. Kim et al. used a CRISPR screen in an engineered 60-Hz electromagnetic-field-responsive gene-switch system to identify CYB5B as an essential mediator likely acting as an EMF sensor; critically, activation depended on rhythmic calcium oscillations rather than generic calcium influx. Courchesne et al. reported that autism-derived brain cortical organoid growth and accelerated neurogenesis were associated with reduced NDEL1 activity and expression and with later social-symptom severity in the donor toddlers. Separate developmental studies show that calcium flashes, calcium channels, and calcium homeostasis are required for apical constriction and neural-tube closure.

These studies do not establish an end-to-end causal chain from ambient wireless exposure to autism or neural-tube defects. They were conducted in different systems, with different field conditions and endpoints. Their integration nevertheless supports a coherent and falsifiable research hypothesis: time-structured electromagnetic exposure may, under some conditions, perturb CYB5B-dependent and/or voltage-sensitive calcium machinery; altered calcium-waveform fidelity may then change kinase/phosphatase activity, histone acetylation, BET recruitment, and kinase-sensitive developmental regulators such as NDEL1; during critical windows, those changes could shift cell-state transitions or morphogenesis. The paper distinguishes direct findings from established biological bridges, proposed mechanistic bridges, and downstream interpretations, and specifies the experiments and falsification criteria required to evaluate the pathway under realistic exposure and developmental conditions.

Keywords: *bioelectric fidelity; calcium oscillations; CYB5B; S4 voltage sensors; BET proteins; NDEL1; radial glia; cortical organoids; neural-tube closure; RF modulation; developmental windows*

Contents

Page numbers are generated from the rendered manuscript. Entries are grouped by the paper's evidence-to-experiment logic.

The DOCX remains fully editable. The PDF is the fixed-layout sharing version.

Executive Summary

Central conclusion

The complete causal chain from everyday wireless exposure to autism, neural-tube defects, or any other human developmental disorder has not been demonstrated. The constituent biology is nevertheless sufficient to define a coherent, mechanistically grounded, and directly falsifiable research pathway. The next scientific step is not declaration of causation; it is coordinated testing of the missing links.

Seven propositions supported at different evidence levels

1. Calcium signals encode information through waveform and location, not merely through average concentration. Frequency and duration can select different transcriptional outputs, and channel-specific microdomains can signal selectively to the nucleus. [5-8]
2. Developmental morphogenesis is timing-sensitive. Calcium flashes, T-type calcium channels, distinct calcium-transient classes, and secretory-pathway calcium homeostasis participate in neural-tube closure and radial-glia proliferation in experimental models. [9-13]
3. A defined low-power 2.4-GHz RF exposure altered corticogenesis-relevant biology in Cakir et al.'s human cortical organoid system, and BET inhibition rescued multiple RF-associated phenotypes. [1]
4. A separate engineered 60-Hz EMF system required CYB5B and a rhythmic calcium pattern for gene-switch activation, establishing a candidate endogenous electromagnetic transduction route. [2,3]
5. Autism-derived cortical organoid growth and accelerated neurogenesis were associated with reduced NDEL1 activity and expression in the Courchesne study, but NDEL1 was not shown to be an RF target or a sole cause of profound autism. [4]
6. The calcium-to-chromatin bridge is biologically plausible because calcium-dependent kinases and phosphatases regulate transcription factors, histone acetylation machinery, and chromatin state, while BET proteins read acetylated lysines and recruit transcriptional elongation machinery. [14-17]
7. No experiment has yet combined realistic RF dosimetry, CYB5B manipulation, high-resolution calcium-waveform analysis, BET occupancy, NDEL1 state, and neurodevelopmental outcomes in one blinded model. That missing experiment is the central priority of this paper.

What this paper claims - and what it does not

POSITION	SUPPORTED STATEMENT	BOUNDARY	STATEMENT NOT MADE
CLAIMS	Calcium timing is an information-bearing developmental variable.	DOES NOT CLAIM	A calcium disturbance observed in one model proves human disease.
CLAIMS	Defined EMF/RF exposures can engage biological pathways in specific experimental systems.	DOES NOT CLAIM	The Kim 60-Hz system is equivalent to Wi-Fi, Bluetooth, or 5G.
CLAIMS	Cakir, Kim, and Courchesne can be connected into a testable hypothesis.	DOES NOT CLAIM	Those studies already demonstrate an unbroken causal chain.
CLAIMS	Modulation and waveform deserve independent study in addition to average power.	DOES NOT CLAIM	A low-frequency envelope is physically identical to a standalone ELF field.
CLAIMS	EMF may be one contributor within a multifactorial developmental load.	DOES NOT CLAIM	EMF is a sole or universal cause of autism, NTDs, or population-wide decline.

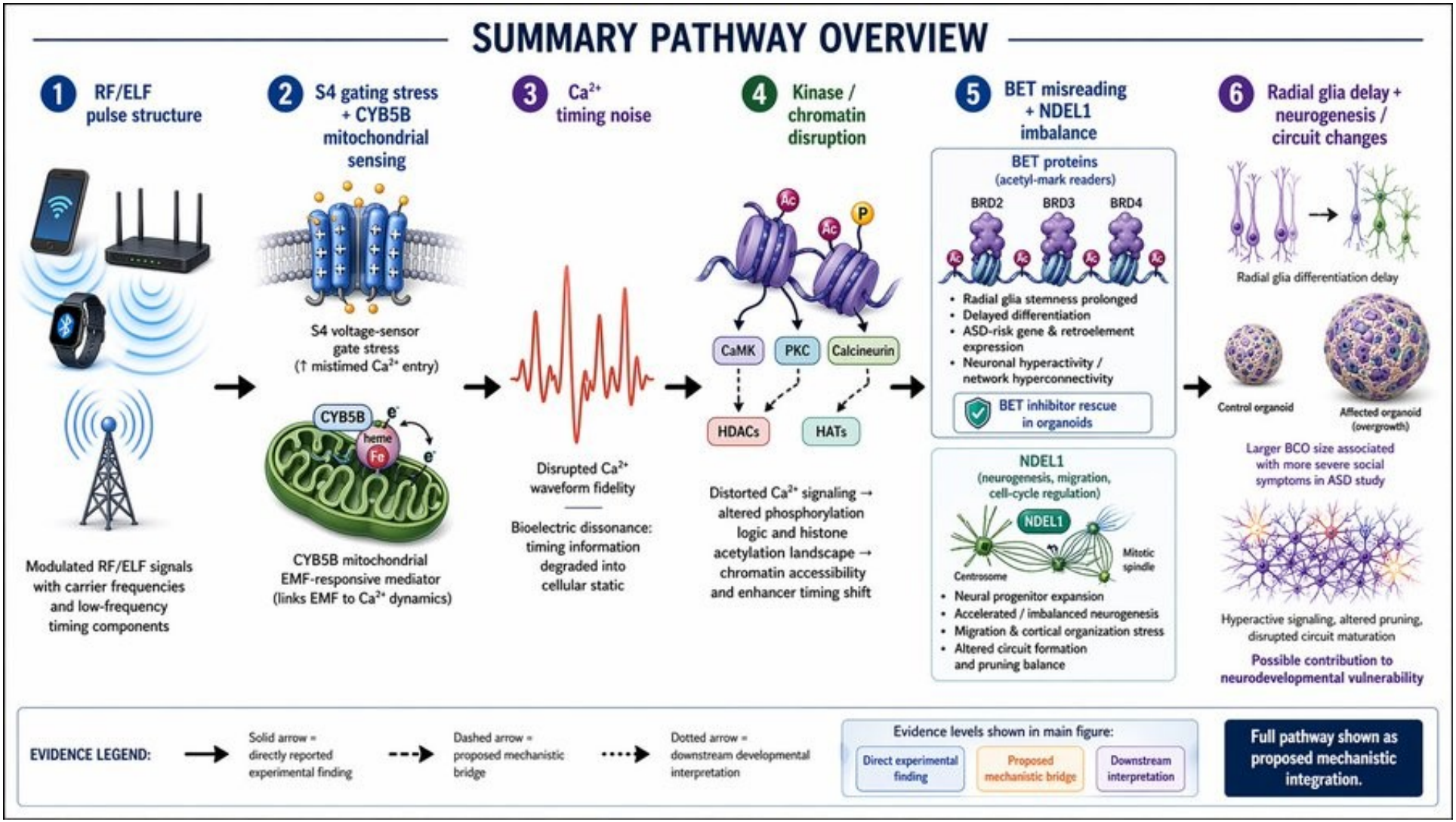

Figure 1. Summary pathway overview. The illustration integrates findings from different experimental systems. Solid arrows represent directly reported findings within a cited model; dashed arrows represent proposed bridges; dotted arrows represent downstream developmental interpretations. No single experiment has tested the complete pathway. ***Conceptual illustration supplied by the author.***

Reading rule: Cakir et al. directly support the RF-to-BET/radial-glia branch in their organoid model; Kim et al. support a CYB5B-dependent EMF-to-calcium branch in a distinct engineered 60-Hz system; Courchesne et al. support the NDEL1/organoid-growth association in ASD-derived organoids. The links connecting those studies are the research hypothesis.

1. Scope, Claims, and Evidentiary Boundaries

1.1 Purpose

This paper is a mechanistic plausibility synthesis and research agenda. It asks whether time-structured electromagnetic exposure can contribute to a measurable loss of developmental signaling fidelity and whether that loss can be traced through calcium waveforms, kinase/phosphatase decoding, chromatin state, BET-family readers, and developmental-control proteins such as NDEL1. It does not calculate population risk, estimate an attributable fraction, or establish a clinical diagnosis.

Mechanistic plausibility is not a synonym for proof. It means that the proposed chain is compatible with known physics and biology, contains experimentally supported nodes, does not require an impossible step, and generates predictions that distinguish it from competing explanations. A strong plausibility paper must therefore show both the supporting trail and the discontinuities in that trail.

1.2 Method of synthesis

The analysis prioritizes primary experimental studies relevant to five domains: calcium waveform coding; embryonic morphogenesis; RF effects in human cortical organoids; CYB5B-dependent EMF transduction; and NDEL1-linked organoid growth. Foundational work on BET proteins, chromatin regulation, sterol C4 oxidation, and the mARC electron-transfer system is used to define possible bridges. The review is narrative rather than systematic: no comprehensive database search, preregistered protocol, formal risk-of-bias instrument, or meta-analysis was performed. Consequently, the paper should be treated as a hypothesis architecture, not as a quantitative evidence grade for human risk.

1.3 Four evidence categories

To prevent a conceptual diagram from being mistaken for a proven causal chain, every link is assigned one of four statuses: direct experimental finding, established biological bridge, proposed mechanistic bridge, or downstream interpretation. Direct findings remain model-specific. Established bridges are well-supported relationships in biology but may not have been tested under RF exposure. Proposed bridges are the precise missing experiments. Downstream interpretations are potential outcomes, not observations.

DIRECT	ESTABLISHED BRIDGE	PROPOSED BRIDGE	INTERPRETATION
Reported in the cited experimental model	Accepted biology, not tested in the combined pathway	Mechanistically plausible and experimentally testable	Downstream implication, not a demonstrated outcome

1.4 Ethical and clinical boundaries

Autism is heterogeneous, and autistic people are not evidence of moral, social, or evolutionary decline. This paper does not treat neurodivergence, identity, empathy, or gender expression as measures of biological worth. It focuses on developmental mechanisms, high-support-needs outcomes, and preventable impairment without assigning blame to families or individuals.

The framework does not establish that vaccination causes autism or regression, and it should not be used to discourage routine vaccination, prenatal care, medically indicated treatment, or acetaminophen use under professional guidance. An acute immune response, a medication exposure, and a radiofrequency exposure are not interchangeable stressors. Each interaction requires direct evidence.

> **Disclosure of perspective**
>
> The author is an RF-safety advocate and supports expanded use of wired, fiber, and optical communications. That perspective motivates the research question and makes explicit falsification criteria especially important. The paper should be independently reviewed before journal submission or use as expert evidence.

2. Development Is Time-Coded Biology

2.1 Calcium is a waveform, not a bucket

Cytosolic calcium is often summarized as an increase or decrease in concentration. That shorthand discards the variables cells actually use. A calcium event can be described by its frequency, peak amplitude, rise time, duration, duty cycle, inter-spike interval, phase relative to other oscillators, subcellular location, spatial propagation, and return-to-baseline kinetics. Two signals with the same time-averaged calcium can therefore activate different transcription factors or produce different cell fates. Classic experiments demonstrated that oscillation frequency can alter transcriptional efficiency and specificity and that CaMKII can act as a frequency decoder. [5,6]

The spatial origin of calcium also matters. Calcium entering through an L-type channel can communicate with a channel-bound calmodulin complex and signal selectively to nuclear pathways. [8] A global calcium rise produced by an ionophore is not necessarily biologically equivalent to a local microdomain repeatedly generated near a channel, endoplasmic-reticulum contact site, mitochondrion, or nuclear pore.

2.2 Development requires ordered transitions

Embryogenesis is a sequence of branching decisions. A progenitor must divide at the right time, stop dividing at the right time, acquire polarity, migrate, differentiate, contract, adhere, and respond to neighboring tissues. Developmental robustness does not mean unlimited tolerance. It means that feedback, redundancy, and repair usually keep trajectories within a viable corridor. When several perturbations act during the same narrow window, small timing deviations can interact nonlinearly.

Radial glial cells illustrate this principle. They are progenitors, structural scaffolds, and signaling units. Calcium waves propagate through radial glia and modulate proliferation in the developing neocortex. [7] A field-associated change in calcium dynamics would therefore be relevant not because calcium is generically “important,” but because the same variable helps determine whether a radial-glia population remains proliferative, differentiates, or coordinates with neighboring cells.

2.3 Information loss can occur without gross toxicity

A developmental signal can be degraded without producing immediate cell death, tissue heating, or a large change in average calcium. Timing jitter, loss of phase coherence, altered burst spacing, or mislocalization can be consequential even when bulk measurements appear normal. This is the engineering intuition behind bioelectric fidelity: an information channel can fail through noise and timing error before it fails through energy overload.

Conceptual signal model (not a validated clinical equation)

$$\text{Developmental instruction: } S(t, x)$$

$$\text{Observed calcium waveform: } C(t, x) = H[S(t, x), E(t, x), G, M] + N(t, x)$$

H = cellular transfer function; E = external input; G = genotype; M = metabolic state; N = endogenous noise

Low fidelity = increased error between the expected and observed temporal-spatial code

3. Operationalizing Bioelectric Fidelity

3.1 Definition

Bioelectric fidelity is the accuracy and reproducibility with which a cell or tissue generates, propagates, and decodes voltage- and ion-dependent signals appropriate to its developmental state. Low-fidelity biology is a condition in which those signals become noisier, less coherent, mistimed, mislocalized, or incorrectly coupled to downstream effectors. The definition is agnostic about cause and diagnosis.

3.2 Measurable dimensions

DIMENSION	EXPERIMENTAL MEANING
Frequency fidelity	Difference between expected and observed oscillation frequency; missed or extra bursts.
Amplitude fidelity	Peak-height error, baseline drift, saturation, or excessive cell-to-cell dispersion.
Phase coherence	Loss of coordination among cells, organelles, or coupled signaling pathways.
Spatial fidelity	Calcium appearing in the wrong microdomain or failing to propagate through the intended tissue path.
Recovery fidelity	Delayed clearance, incomplete return to baseline, or altered refractory period.
Spectral order	Increase in broadband irregularity or entropy relative to a developmental reference state.
Decoder fidelity	Mismatch between waveform and kinase, phosphatase, transcription-factor, or chromatin response.
Developmental output	Shift in proliferation, differentiation, migration, contraction, closure, or network maturation.

3.3 Why average power and average calcium are insufficient

Average absorbed power remains essential for dosimetry and thermal control, but it does not describe every biologically relevant temporal parameter. Likewise, average intracellular calcium does not describe waveform content. A properly designed experiment must report both: exposure physics at the tissue and cellular level, and the biological signal in the time and frequency domains.

> **Key distinction**
>
> The hypothesis is not “weak fields contain a hidden large dose.” It is that a nonlinear biological transducer might respond to timing or waveform features at doses that do not cause appreciable heating. Whether that occurs under realistic telecom exposure is an empirical question.

4. Critical Windows: Calcium Timing and Neural-Tube Closure

4.1 Why neurulation is the clearest test case

Neural-tube closure occurs early and depends on coordinated changes in cell shape, adhesion, cytoskeletal force, convergent extension, and tissue-tissue mechanics. Neural-tube defects have established genetic, nutritional, metabolic, and pharmacologic risk factors; folate prevention remains a major public-health success. [29] The existence of established causes does not exclude additional modifiers, but any new claim must be tested against that well-developed evidence base.

4.2 Calcium flashes drive pulsed contraction

Live-imaging work in Xenopus showed that cell-autonomous calcium flashes elicit pulsed contractions of a medioapical actin network during neural-tube closure. The contractions are not simply a monotonic squeeze. Their timing, distribution, and ratcheting contribute to apical constriction and tissue bending. [9] This directly supports the premise that morphogenesis can depend on temporally patterned calcium events.

4.3 Channel and pump dependence

T-type calcium-channel loss or inhibition reduced neural-tube calcium transients and produced failure of anterior closure in Ciona and Xenopus, with altered EphrinA/EPHA signaling. [10] Distinct classes of intracellular calcium dynamics contribute differently to apical constriction and closure. [11] In mice, loss of the secretory-pathway calcium ATPase SPCA1 disrupted myosin localization, actin dynamics, apical constriction, and neural-tube closure. [12] These studies establish a calcium-dependent developmental vulnerability, not an electromagnetic cause.

4.4 What an EMF-neurulation experiment must show

A valid test cannot stop at counting malformed embryos. It must record calcium flashes and contraction pulses before the morphological endpoint, quantify whether exposure changes their frequency, amplitude, spatial distribution, or phase, and show that manipulating the same waveform reproduces or rescues the closure phenotype. It must also separate direct effects on the neural plate from indirect effects on mechanically coupled tissues, maternal physiology, temperature, oxygenation, and culture conditions.

> **Personal relevance without retrospective attribution**
>
> Angel Leigh's anencephaly demonstrates the human stakes of neural-tube closure. It does not identify an exposure cause. The proper scientific response is a prospective, blinded, mechanistic neurulation experiment.

5. Evidence Anchor I: RF, BET Proteins, and Human Cortical Organoids

5.1 Experimental system

Cakir et al. used human cortical organoids derived from human embryonic stem cells, together with nonhuman-primate neural progenitor models, to examine radiofrequency exposure during early corticogenesis. The study used a 2.4-GHz Bluetooth V2.0+EDR source reported at 4 dBm output, with a reported maximum measured power density of approximately 2.5 mW/m2. Exposure began during early organoid development and included 12-hour-per-day and continuous conditions. [1] Source output and external power density should not be confused with absorbed dose inside each organoid; replication requires complete field mapping and thermal characterization.

5.2 Directly reported findings

- RF exposure altered radial-glia differentiation and maintained stem-cell identity for longer in the studied model.
- The exposure changed transcriptional and chromatin-accessibility programs, including expression of ASD-associated genes and endogenous retroelements.
- Neurons that developed under exposure showed altered morphology, synaptic features, electrophysiology, and spontaneous calcium activity.
- Low-dose BET inhibitors, including JQ1 and iBET762, rescued multiple RF-associated morphological, transcriptional, differentiation, and neuronal phenotypes.
- Related effects were observed across human and nonhuman-primate progenitor systems, strengthening model generality while not establishing human pregnancy risk.

5.3 Why the BET rescue is mechanistically important

A rescue experiment helps distinguish a functional node from a passive biomarker. If blocking BET bromodomains reverses several RF-associated changes, BET-family activity participates in maintaining those downstream states. The rescue does not identify the initial sensor. BET proteins bind acetylated lysines and regulate transcriptional machinery; they are better interpreted as downstream readers of an altered chromatin context than as primary RF antennas.

5.4 What the study does not show

- An organoid does not contain a placenta, maternal metabolism, skull, vasculature, endocrine system, complete immune system, or normal fetal thermoregulation.
- Direct culture exposure cannot be translated to fetal dose without maternal-fetal dosimetry.
- The study does not identify CYB5B or an S4 voltage sensor as the upstream RF transducer.
- The study does not demonstrate autism, profound autism, or a neural-tube defect as an outcome.
- The findings require independent replication with blinded exposure, sham equivalence, preregistered endpoints, and detailed dosimetry.

Defensible interpretation

Cakir et al. provide direct evidence that a defined 2.4-GHz RF exposure altered BET-dependent corticogenesis-relevant biology in their organoid system. The study does not establish that ordinary household exposure produces the same effect in a fetus.

6. Evidence Anchor II: CYB5B and EMF-Induced Calcium Rhythm

6.1 What Kim et al. built

Kim et al. engineered an electromagnetic-field-inducible gene switch for remote control of gene expression in cells and animals. The optimized exposure was a defined 60-Hz, 2.0-mT field - an ELF magnetic-field condition, not a telecom RF carrier. A CRISPR-Cas9 screen identified cytochrome b5 type B (CYB5B) as an essential mediator likely acting as an EMF sensor. CYB5B loss abolished the engineered response and re-expression restored it. [2] An erratum published in July 2026 corrected supplementary material and did not withdraw the central conclusions. [3]

6.2 Rhythm rather than generic influx

The most relevant result for this framework is that gene-switch activation depended on rhythmic oscillatory calcium dynamics rather than on generic calcium entry. This narrows the biological variable from "calcium changed" to "a particular calcium waveform was generated and decoded." It aligns with decades of calcium-signaling work showing that frequency, duration, and channel location select downstream outputs. [5,6,8]

6.3 What CYB5B is - and what remains unknown

CYB5B is an outer-mitochondrial-membrane heme protein involved in electron transfer. Separate work shows that CYB5A and CYB5B can compensate in sterol C4 oxidation and that CYB5B participates with CYB5 reductase and mARC proteins in an N-reductive electron-transfer system. [18-20] Those ordinary functions justify measuring sterol intermediates, redox state, and mARC activity in RF experiments. They do not show that wireless exposure impairs those functions.

The direct physical coupling remains unresolved. The Cell paper supplies a necessary mediator in its engineered 60-Hz system, but it does not establish that CYB5B heme iron undergoes the proposed spin bias under Wi-Fi or Bluetooth exposure. Heme redox spectroscopy, electron-transfer kinetics, field-orientation experiments, and mutant rescue are required before a spin mechanism can be stated as observed.

6.4 The "huge frequency gap" problem

The Kim exposure cannot simply be equated to a GHz wireless signal because both contain low-frequency timing. A 60-Hz magnetic field and a 2.4-GHz field with a low-frequency envelope differ in carrier, electric-to-magnetic ratio, polarization, induced-current distribution, penetration, near-field geometry, and molecular coupling. Conversely, it is also incomplete to compare only the GHz carrier and ignore modulation or packet timing. The correct research question is whether a nonlinear biological transducer responds to the envelope, the carrier, their interaction, or neither.

> **Defensible interpretation**
>
> Kim et al. establish that a defined electromagnetic field can be converted through CYB5B-dependent endogenous machinery into a biologically decoded rhythmic calcium signal. They do not establish harmful responses to ambient telecom RF.

7. Candidate S4/VGIC Route: Plausible, Important, and Unproven

7.1 Why S4 domains are relevant

Voltage-gated ion channels contain charged voltage-sensing structures, commonly including S4 helices, that move in response to changes in membrane potential. Because channel opening controls calcium microdomains and downstream transcription, an exposure mechanism acting at voltage sensors would be biologically consequential. The S4/VGIC proposal therefore identifies a physically and biologically specific target rather than invoking an undefined "stress response."

7.2 Status of the ion forced-oscillation model

Panagopoulos and colleagues have proposed that polarized and coherent anthropogenic fields can drive forced oscillation of membrane-associated ions and perturb voltage-gated channels, with downstream oxidative and DNA effects. [21,22] This is a published mechanistic model, not a consensus demonstration that ordinary wireless exposure forces S4 gates open. The force calculations, membrane boundary conditions, noise environment, channel-specific effects, and reproducibility remain actively contestable.

7.3 How to test S4 without assuming it

The clean test is genetic and biophysical. Use cells or organoids expressing voltage-sensor mutants with altered gating charge, compare channel-null and rescue conditions, perform voltage-clamp measurements during precisely characterized exposure, and determine whether the RF-associated calcium waveform depends on a specific channel. The hypothesis gains strength only if channel manipulation changes exposure sensitivity while preserving baseline viability and if wild-type rescue restores the response.

7.4 Dual-transducer model

CYB5B and S4/VGIC mechanisms need not be mutually exclusive. One could alter mitochondrial redox/electron transfer and the other membrane excitability; both could converge on calcium timing. But "dual hardware jam" remains a proposed bridge until the two systems are manipulated in the same experiment. The model should predict whether effects are additive, synergistic, redundant, or cell-type-specific.

> **Language rule**
>
> Use "candidate S4/VGIC transduction route" or "proposed ion forced-oscillation mechanism." Do not write that environmental RF has been proven to mechanically force S4 gates open.

8. Translating Calcium Timing into Chromatin and BET Recruitment

8.1 Calcium decoders

Calcium-dependent enzymes have characteristic activation and deactivation kinetics. CaMKs, calcineurin, PKC, calpain, and related pathways can therefore act as temporal filters. CaMKII is a classic frequency decoder. Calcineurin/NFAT integrates repeated calcium events through dephosphorylation and nuclear residence. Different waveform shapes can favor competing transcriptional programs even at similar average calcium.

8.2 Histone acetylation as the translation layer

Calcium-dependent signaling can alter the balance and localization of histone acetyltransferases and histone deacetylases. CaMKII-dependent phosphorylation of HDAC4, for example, regulates its nuclear export in a well-characterized system. [17] The exact enzymes in radial glia may differ, but the general bridge is established: calcium-responsive kinases can change chromatin-regulatory state.

8.3 BET proteins read the resulting landscape

BET-family proteins - BRD2, BRD3, BRD4, and BRDT - contain bromodomains that recognize acetylated lysines. JQ1 competitively occupies that recognition pocket. [14] BRD4 can recruit P-TEFb and facilitate productive RNA polymerase II elongation. [15] The coherent model is therefore not “RF directly hits BET.” It is: an upstream physical input changes calcium/redox timing; calcium-dependent enzymes alter acetylation and accessibility; BET proteins faithfully read a mistimed chromatin landscape; transcriptional timing and cell-state decisions shift.

Proposed calcium-to-BET bridge

```
                    Time-structured field input
          -> candidate CYB5B and/or VGIC transduction
        -> altered Ca2+ frequency / phase / localization
          -> kinase-phosphatase and HAT-HDAC imbalance
             -> altered acetylation / accessibility
   -> altered BET occupancy and transcriptional elongation
             -> altered progenitor-cell state
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8.4 The decisive hierarchy test

If BET proteins are downstream readers, BET inhibition should rescue transcriptional and differentiation phenotypes without necessarily normalizing the upstream CYB5B redox state or calcium waveform. Conversely, restoring the normal calcium waveform should normalize BET occupancy and cell-state transitions even without directly inhibiting BET. This directionality is a critical prediction.

9. The NDEL1 Branch: Developmental Control, Not a Proven RF Target

9.1 What Courchesne et al. reported

Courchesne et al. generated 4,910 brain cortical organoids from deeply phenotyped autistic toddlers and controls. Across two batches, ASD-derived organoids were larger, grew nearly three times faster on average, and the largest organoids were associated with more severe social symptoms and accelerated neurogenesis. NDEL1 oligopeptidase activity and expression were reduced in ASD-derived organoids and inversely associated with organoid size and growth rate. NDEL1 activity was not significantly correlated with symptom severity itself. [4]

9.2 NDEL1 is kinase-sensitive developmental machinery

NDEL1 participates in centrosomal function, mitosis, dynein regulation, neuronal migration, neurite outgrowth, and morphogenesis. Sequential phosphorylation by DYRK2 and GSK3beta promotes neuronal morphogenesis, while Aurora-A-mediated phosphorylation is required for centrosomal maturation, separation, and mitotic entry. [16,17] This makes NDEL1 a reasonable downstream node in a timing-sensitive kinase network.

9.3 Why “NDEL1 suppression causes profound autism” is too strong

The Courchesne study was powerful in its within-donor linkage but small in the number of human donors. It identified association and biological stratification, not a single initiating cause. Reduced NDEL1 activity may contribute to growth, reflect another upstream abnormality, or participate in a network of dysregulated cell-cycle processes. The study did not expose organoids to RF and did not test calcium-waveform manipulation.

9.4 A parallel branch, not a forced linear chain

The most defensible architecture places NDEL1 in a parallel developmental-control branch downstream of kinase and cell-cycle timing, alongside the chromatin/BET branch. The branches may converge on radial-glia self-renewal, neurogenesis, migration, and cortical organization. Direct measurement is required to determine whether RF-associated calcium changes alter NDEL1 expression, phosphorylation, localization, enzymatic activity, or binding partners.

> **Defensible interpretation**
>
> Courchesne et al. identify NDEL1-associated embryonic growth dysregulation in ASD-derived organoids. NDEL1 is a candidate downstream reporter and rescue target in an RF organoid experiment, not an already demonstrated RF mediator.

10. The Integrated Adverse-Outcome Pathway

The proposed pathway is best represented as an adverse-outcome pathway with explicitly graded links. This format prevents evidence from one model being silently transferred into another.

PATHWAY LEVEL	PROPOSED EVENT	EVIDENCE STATUS	INTERPRETATION
Molecular initiating interaction	Time-structured EM input interacts with a susceptible cellular transducer.	DIRECT in Kim system; PROPOSED for telecom RF	CYB5B dependence shown at 60 Hz; S4/VGIC route remains proposed.
Key event 1	Calcium waveform fidelity changes.	ESTABLISHED importance; partial DIRECT evidence	Rhythmic Ca required in Kim; altered neuronal Ca activity in Cakir; full waveform bridge untested.
Key event 2	Kinase/phosphatase decoding changes.	ESTABLISHED BRIDGE	Calcium decoders are known; not mapped under Cakir exposure.
Key event 3A	Histone acetylation/accessibility and BET recruitment change.	DIRECT downstream support in Cakir	BET rescue shown; upstream CYB5B/Ca causality untested.
Key event 3B	NDEL1 expression/activity/phosphorylation changes.	DIRECT association in Courchesne; PROPOSED RF bridge	Must be measured in exposed organoids.
Key event 4	Progenitor self-renewal, differentiation, migration, or contraction shifts.	DIRECT in model-specific studies	Radial-glia effects in Cakir; neurulation effects in calcium perturbation models.
Organ/tissue outcome	Cortical organization, neural-tube closure, or circuit maturation changes.	DIRECT only in separate models	No unified exposure experiment.
Human outcome	Change in risk or severity of a developmental condition.	INTERPRETATION	Requires realistic dosimetry, in vivo replication, and human epidemiology.

10.1 The core mechanistic sentence

Core hypothesis

Under some exposure and susceptibility conditions, time-structured electromagnetic fields may perturb CYB5B-dependent and/or voltage-sensitive calcium machinery; altered calcium timing may then change kinase/phosphatase decoding, histone acetylation, BET recruitment, and NDEL1-linked developmental control; during a critical window, those changes may shift progenitor-cell decisions or tissue morphogenesis.

10.2 Why this is stronger than a generic oxidative-stress claim

Oxidative stress is common to many insults and can be downstream of injury. The present framework is more discriminating because it predicts a temporal sequence and directionality: an exposure-specific calcium waveform should precede defined kinase/chromatin changes; CYB5B or channel manipulation should alter exposure sensitivity; BET inhibition should rescue downstream transcription but not necessarily the upstream waveform; and waveform replay should reproduce the phenotype. These predictions can fail.

FIGURE 2 | PROPOSED BIOELECTRIC DISSONANCE PATHWAY

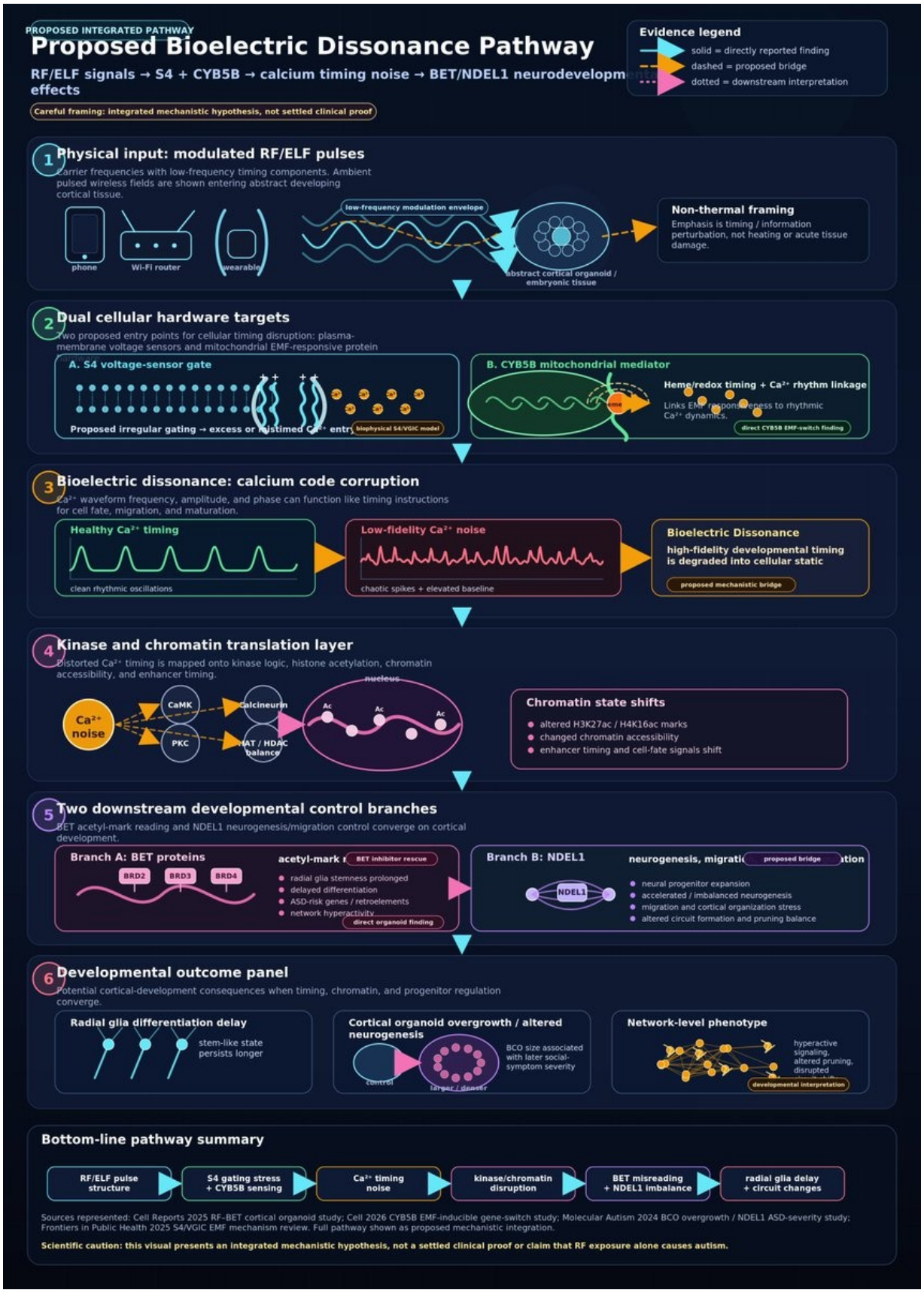

Figure 2. **Full proposed pathway. The central claim is not that this complete chain has been demonstrated; it is that each node can be measured and the connecting bridges can be tested in one coordinated experimental program.** ***Conceptual illustration supplied by the author.***

11. A Multifactorial Model of Low-Fidelity Biology

11.1 EMF is proposed as one input, not the entire system

Developmental biology integrates genetics, nutrition, oxygenation, maternal metabolism, infection and inflammation, endocrine state, pollutants, medications, sleep and circadian timing, mechanical forces, and physical environmental inputs. A fidelity model should therefore predict interaction effects and variable susceptibility rather than a one-exposure/one-disease rule.

Multihit statistical model

```
                    Developmental error probability during window w:
P(error_w) = logistic(beta0 + betaE*E + betaG*G + betaM*M + betaN*N + interactions)
    E = electromagnetic exposure; G = genotype; M = metabolic/immune state; N =
                            nutrition/toxicant context
      The equation is a study-design template, not a clinical risk calculator.
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11.2 Reserve, threshold, and interaction

A developing system may tolerate one mild perturbation but fail when several converge. That does not mean every stressor is interchangeable. The interaction must be specified: for example, whether hypoxia changes CYB5B redox state, whether folate deficiency alters closure reserve, whether inflammation changes calcium-channel expression, or whether a genetic variant reduces buffering capacity. A catch-all “toxic load” explanation is not sufficient.

11.3 Transgenerational claims require a higher evidence bar

The statement that society is witnessing degradation of transgenerational traits is not established by the evidence reviewed here. During maternal gestational exposure, the mother, fetus, and fetal germ cells can all be directly exposed; persistence into a later unexposed generation is required before a true transgenerational mechanism is inferred. [30] A credible program would track exposure, germline epigenomics, fertility, developmental phenotypes, and replication through the appropriate unexposed generation.

11.4 Why broad behavioral claims should be separated

Attention, social communication, cognition, empathy, identity, and physical health arise from different biological and social pathways. They should not be bundled as proof of a single population-wide “devolution.” The fidelity framework is most scientifically useful when it predicts a measurable cellular phenotype in a defined developmental window and then tests the corresponding functional outcome.

12. Exposure Physics: Carrier, Envelope, Modulation, and Dose

12.1 Four variables that must not be collapsed

VARIABLE	WHY IT MATTERS
Carrier frequency	The rapid electromagnetic oscillation, such as 2.4 GHz.
Temporal envelope	Packet, beacon, frame, burst, and duty-cycle structure that changes signal amplitude over time.
Field vector and geometry	Electric and magnetic components, polarization, orientation, near/far field, gradients, and induced currents.
Internal dose	The field and absorbed power inside the biological target, including local hotspots and temperature.

12.2 An envelope is not a second standalone carrier

A recurrent 10-Hz timing pattern in a Wi-Fi beacon is not physically the same thing as a uniform 10-Hz magnetic field. It is a low-frequency feature of a high-frequency waveform. For that feature to become biologically operative, a nonlinear transducer must detect or demodulate it. The existence, efficiency, and cell-type specificity of such transduction cannot be assumed from the spectrum alone.

12.3 Why the envelope still deserves study

Biological systems are nonlinear and contain thresholds, rectifying membranes, voltage-sensitive proteins, redox reactions, and coupled oscillators. It is therefore scientifically reasonable to test whether a modulated RF waveform and a continuous-wave carrier at the same average power produce different calcium dynamics. A modulation-specific result would challenge an exclusively average-power model; a null difference would weaken the timing hypothesis.

12.4 Required exposure controls

- Field-free sham with indistinguishable handling, sound, vibration, airflow, and electronics.
- Continuous-wave RF at the same average absorbed power as each modulated condition.
- Matched thermal control reproducing any measured temperature change without RF.
- Pure ELF condition reproducing the selected envelope frequency.
- RF plus independently applied ELF to test interaction.
- Multiple modulation patterns, duty cycles, polarizations, orientations, and developmental windows.
- Blinded exposure coding, preregistered endpoints, and independent dosimetry audit.

Power versus time is not an either/or choice

Chronic low-level exposure cannot be assumed equivalent to an acute high-field experiment, and acute high-field results cannot be dismissed solely because the environment is lower. Dose, duration, waveform, adaptation, and nonlinear response must be mapped experimentally.

13. Epidemiological and Temporal Context

13.1 The rise in identified autism prevalence is real

CDC surveillance estimated autism prevalence at 32.2 per 1,000 eight-year-old children - about 1 in 31 - across 16 U.S. sites in 2022, with wide variation among sites and in identification practices. [23] The increase in identified prevalence over recent decades is therefore a legitimate public-health fact requiring explanation.

13.2 A temporal co-trend is a hypothesis generator, not a causal test

The expansion of household wireless technology and the rise in identified autism prevalence occurred over overlapping decades. That temporal coexistence is sufficient to justify asking a question, but not to answer it. Diagnostic criteria, awareness, service access, ascertainment, survival, parental age, genetic and environmental factors, and true incidence changes can all influence observed prevalence. Ecological timing cannot distinguish among them.

13.3 What an informative human study would require

A useful prospective study would measure personal maternal exposure across preconception and gestational windows rather than infer exposure from residence or self-report alone. It would record carrier and modulation features, device-body distance, nighttime exposure, occupational sources, and fetal dosimetry; collect genetic, folate, metabolic, infection, medication, air-pollution, and socioeconomic covariates; and prespecify developmental outcomes. Biomarkers should include calcium-signaling or chromatin signatures capable of connecting epidemiology to mechanism.

13.4 Autism is not one endpoint

The pathway may be more relevant to specific developmental subtypes, windows, tissues, or genetic backgrounds than to autism as a whole. The Courchesne work itself argues for biologically distinct organoid-growth subtypes. [4] Pooling all autism into one outcome could obscure a real susceptible subgroup or produce a misleading average.

14. Evidence Matrix: What Exists and What Is Missing

LINK	STATUS	CURRENT SUPPORT	DECISIVE NEXT STEP
Ca waveform -> gene selection	Direct foundational evidence	Frequency/amplitude/duration select transcriptional pathways.	Replicate in radial glia and neuruloids with developmental endpoints.
Ca waves -> radial-glia proliferation	Direct developmental evidence	Waves propagate through radial glia and modulate proliferation.	Determine whether RF changes wave statistics before cell-state changes.
Ca dynamics -> neural-tube closure	Direct animal evidence	Flashes, channels, and pumps regulate apical constriction/closure.	Expose neuruloids/embryos with blinded waveform-specific conditions.
2.4-GHz RF -> BET-dependent organoid phenotype	Direct in Cakir model	Differentiation/chromatin/neuron changes; BET inhibitor rescue.	Independent replication, dosimetry, CYB5B and Ca directionality.
60-Hz EMF -> CYB5B -> rhythmic Ca	Direct in engineered Kim system	CRISPR dependency and rhythmic Ca requirement.	Test under RF carriers and nonengineered developmental promoters.
RF -> CYB5B heme/redox change	Proposed	Biologically specific candidate.	Spectroscopy, mutants, electron-transfer kinetics under RF.
RF -> S4/VGIC gating	Proposed/model-based	Voltage sensors are plausible targets.	Patch clamp, gating-charge mutants, channel knockout/rescue.
Altered Ca -> histone acetylation -> BET	Established bridge, untested in chain	Ca-responsive kinases/HDACs and BET acetyl-lysine reading are known.	Time-resolved Ca, phosphoproteomics, CUT&RUN, rescue.
Ca/kinase -> NDEL1 change	Proposed	NDEL1 is phosphorylation-sensitive developmental machinery.	Measure NDEL1 state and rescue in exposed organoids.
Full chain -> human autism/NTD	Not established	No end-to-end evidence.	Realistic dosimetry, in vivo validation, prospective epidemiology.

14.1 The strongest inference currently justified

The literature supports the existence of a biologically meaningful route by which calcium-waveform perturbation could alter developmental decisions, and it identifies experimentally tractable RF/EMF-associated entry points and downstream chromatin nodes. It does not yet show that ordinary wireless exposure engages that route at a magnitude that changes human developmental risk.

15. Decisive Experimental Program

15.1 Phase I - Replicate the Cakir phenotype

Before extending the pathway, independent laboratories should reproduce the 2.4-GHz organoid findings with identical and independently constructed exposure systems. The protocol should be preregistered, exposure-coded, and analyzed blind. Temperature, incubator position, vibration, power-supply noise, airflow, and culture handling must be monitored. Primary endpoints should be fixed before data collection: radial-glia markers, differentiation timing, organoid morphology, calcium dynamics, BET occupancy, and transcriptomic state.

15.2 Phase II - Test CYB5B necessity and specificity

- Wild-type organoids from multiple independent stem-cell lines.
- Inducible partial CYB5B knockdown to avoid nonspecific developmental failure.
- CYB5B knockout, if viable and interpretable.
- Wild-type CYB5B rescue.
- Heme-binding, electron-transfer, membrane-anchoring, and partner-interaction mutants.
- CYB5A manipulation to test compensation in sterol C4 pathways.

If CYB5B is necessary for the RF-BET phenotype, reducing it should alter or eliminate the RF-specific calcium and chromatin response, and wild-type rescue should restore sensitivity. If mutants fail selectively, the required molecular function is identified. If the phenotype persists unchanged, CYB5B is unlikely to be the necessary upstream mediator in the Cakir system.

15.3 Phase III - Measure calcium as a waveform

- Oscillation frequency, amplitude, burst duration, inter-burst interval, phase, and recovery.
- Spectral entropy, autocorrelation, and signal-to-noise ratio.
- Cell-to-cell synchronization and propagation velocity.
- Cytosolic, mitochondrial, ER, and nuclear calcium using compartment-specific sensors.
- Coupling to membrane voltage and channel opening with simultaneous electrophysiology.
- Single-cell heterogeneity and developmental-stage dependence.

The decisive condition is one in which average calcium remains similar but temporal organization changes. If that condition alters BET recruitment and cell fate, it directly supports the low-fidelity calcium-code model.

15.4 Phase IV - Map the calcium-to-chromatin hierarchy

- Phosphoproteomics for CaMK, calcineurin, PKC, CREB, MEF2, NFAT, HDACs, and HATs.
- H3K27ac, H3K9ac, H4K16ac, and related marks by CUT&Tag or ChIP-seq.
- BRD2, BRD3, and BRD4 occupancy by CUT&RUN/CUT&Tag.
- ATAC-seq for accessibility and P-TEFb/RNA polymerase II pausing/elongation assays.
- Single-cell RNA-seq and retroelement expression.
- Waveform replay or optogenetic calcium control to reproduce or normalize the RF-associated pattern.

15.5 Phase V - Test the NDEL1 branch

Measure NDEL1 RNA, protein, oligopeptidase activity, phosphorylation sites, centrosomal localization, dynein interactions, mitotic spindle orientation, cell-cycle duration, neuronal migration, and morphogenesis. Test whether NDEL1 restoration rescues organoid growth or differentiation without correcting upstream calcium, and whether normalizing calcium restores NDEL1 state.

15.6 Phase VI - Neural-tube and assembloid models

Use human neuruloids or neural-tube organoids and validated Xenopus or other vertebrate systems to record calcium flashes, apical actomyosin pulses, closure velocity, neuropore dynamics, and tissue mechanics during exposure. For later cortical refinement, use microglia-containing assembloids rather than standard cortical organoids before making claims about pruning or immune-neural interactions.

15.7 Exposure comparison matrix

CONDITION	DESIGN	QUESTION
Sham	No field; identical apparatus state	Baseline and artifact control
Continuous-wave RF	Same carrier and average absorbed power	Tests whether modulation adds an effect
Bluetooth-like RF	Replicate Cakir waveform and geometry	Direct replication
Wi-Fi beacon/traffic patterns	Prespecified packet and duty structures	Tests protocol-specific temporal structure
Legacy GSM-like 217-Hz structure	Matched average power	Tests a distinct envelope frequency
Pure 60-Hz magnetic field	Kim-like and lower-dose series	Separates standalone ELF from RF envelope
RF plus ELF	Independent phase-controlled fields	Tests interaction or entrainment
Matched thermal	No RF; reproduce measured heating	Excludes thermal explanation

15.8 Decisive predictions

PREDICTION	SUPPORTIVE RESULT	RESULT THAT WEAKENS MODEL
CYB5B dependency	Knockdown changes RF-specific Ca/BET response; WT rescue restores it.	No change with CYB5B manipulation.
BET downstream	BET inhibitor rescues transcription/differentiation but not necessarily upstream Ca/redox.	BET inhibition normalizes the initial physical/Ca event or has no rescue.
Waveform specificity	Same mean Ca, different timing -> different chromatin/cell fate.	Only total Ca predicts outcome.
Modulation specificity	Modulated RF differs from CW at matched absorbed power.	CW and modulated conditions are indistinguishable.
Developmental window	Effects peak during defined progenitor/closure windows.	No timing dependence or only nonspecific toxicity.
NDEL1 branch	RF/Ca manipulation changes NDEL1 state and targeted rescue modifies outcome.	NDEL1 is unchanged or rescue is irrelevant.

16. Falsification Criteria

The framework is scientific only if negative results can meaningfully reduce confidence. The following findings would substantially weaken or reject central parts of the model:

1. Independent laboratories cannot reproduce the Cakir RF-associated organoid phenotype.
2. Active and sham exposures differ in temperature, incubator conditions, vibration, or handling, and correcting those differences removes the effect.
3. High-resolution imaging shows no reproducible calcium-waveform change before downstream transcriptional effects.
4. CYB5B manipulation does not alter RF sensitivity in the replicated organoid model.
5. Voltage-channel manipulation does not alter the exposure response and electrophysiology shows no exposure-associated gating effect.
6. BET changes precede or occur independently of the proposed calcium disturbance, invalidating the stated directionality.
7. Continuous-wave and modulated RF produce the same outcome whenever absorbed power and temperature are matched.
8. There is no developmental-window, dose, field-orientation, or waveform relationship, and outcomes track only nonspecific toxicity.
9. Realistic maternal-fetal dosimetry places internal fields far below the threshold for any replicated cellular effect.
10. In vivo developmental models and well-designed prospective human studies fail to show the predicted biomarkers or subtype-specific associations.

> **A negative result is progress**
>
> Rejecting CYB5B, S4, modulation specificity, or the NDEL1 branch would narrow the search and prevent a broad concern from becoming an unfalsifiable theory. The objective is to identify the true transfer function of the developing cell, not to preserve a preferred narrative.

17. Regulatory and Research-Governance Implications

17.1 Mechanism is not a prerequisite for every protective action

Regulators commonly act under uncertainty when exposure is widespread and susceptible populations cannot meaningfully consent. At the same time, mechanistic specificity improves hazard identification, dosimetry, causal inference, and engineering control. The proper response to an incomplete pathway is neither to declare safety nor to declare causation, but to fund the decisive work.

17.2 Relevance to the D.C. Circuit remand

In Environmental Health Trust v. FCC, the D.C. Circuit held that the FCC had not adequately explained its determination regarding non-cancer effects below existing limits and identified children, long-term exposure, pulsation or modulation, ubiquity, Wi-Fi, and 5G among the issues inadequately addressed. [24] The proposed CYB5B-calcium-BET experiment speaks directly to those research questions without requiring the agency to assume the hypothesis is correct.

17.3 Minimum federal research package

- Independent replication of the Cakir organoid study with open dosimetry and raw data.
- A CYB5B knockout/rescue RF organoid study with calcium-waveform and BET endpoints.
- A modulation-versus-continuous-wave comparison at matched absorbed power.
- Human neuruloid/neural-tube experiments focused on calcium flashes and closure mechanics.
- Maternal-fetal computational and physical dosimetry for common devices and use positions.
- Prospective pregnancy cohorts with personal exposure measurement and mechanistic biomarkers.
- Public repositories for exposure waveforms, calibration files, code, negative findings, and replication attempts.

17.4 Standards should report waveform as well as power

Even if modulation ultimately proves biologically irrelevant, reporting it costs far less than rediscovering it after years of inconsistent experiments. Exposure studies should archive the full time-domain waveform, spectrum, duty cycle, pulse rise/fall characteristics, polarization, field vector, internal dose distribution, and temperature. “2.4 GHz at X power” is not a complete exposure description.

18. Engineering Implications: Reduce Uncertainty by Design

18.1 A research-compatible precautionary hierarchy

Engineering controls can reduce exposure without asserting that a specific disease has been proven. The hierarchy is straightforward: eliminate unnecessary transmitters; substitute wired or fiber connections where practical; increase distance and reduce duty cycle; schedule transmissions; and use shielding only when it is designed and verified not to increase device output or create new hotspots.

18.2 Optical wireless and Li-Fi

Optical wireless communication is a serious infrastructure alternative because it can move indoor data traffic out of the microwave band and confine coverage spatially. It should not be advertised as biologically inert by definition. Optical systems must be assessed for wavelength, irradiance, retinal and skin exposure, flicker, modulation depth, photosensitive populations, and cybersecurity. At typical communications power, many optical systems may offer a favorable exposure profile, but safety is an engineering specification, not a slogan.

18.3 The “140-year mistake” reframed

The author's phrase “a 140-year mistake” is best understood as an engineering thesis rather than a settled historical conclusion: electromagnetic technologies have often been evaluated primarily as energy-transfer systems, while living tissues also operate as information-processing systems. Heating and average power remain indispensable variables; the proposed correction is to add temporal information fidelity, not to discard dosimetry.

18.4 Clean Aether/Clean Ether policy concept

A credible clean-communications policy would not ban connectivity. It would establish technology-neutral performance goals: wired/fiber backbones, optical-wireless compatibility where suitable, low-power and low-duty operation, exposure transparency, waveform reporting, child-sensitive design, and continuous biological research. The policy case is strongest when it is tied to measurable engineering outcomes rather than to claims of settled disease causation.

19. Conclusion: A Pathway That Exists as a Testable Scientific Question

The scientific literature does not presently justify the statement that household wireless radiation has been proven to cause profound autism, neural-tube defects, or a general transgenerational decline. It does justify a more precise and consequential statement.

Final scientific statement

Defined EMF and RF exposures have been shown, in separate experimental systems, to engage CYB5B-dependent calcium signaling, BET-dependent cortical-development programs, and developmental phenotypes involving radial glia, neuronal activity, and tissue morphogenesis. Calcium waveforms are established information-bearing signals, and NDEL1 is established kinase-sensitive developmental machinery associated with organoid growth in an ASD subtype study. The complete chain is unproven, but it is coherent, biologically specific, and falsifiable. It therefore warrants direct investigation under realistic exposure and developmental conditions.

The most important conceptual advance is the shift from asking only whether exposure produces enough energy to heat tissue to asking whether it alters the fidelity of biological timing. That question cannot be answered by rhetoric on either side. It requires synchronized exposure physics, live calcium imaging, molecular genetics, chromatin mapping, developmental models, in vivo validation, and human dosimetry.

The pathway will become stronger if CYB5B dependence, calcium-waveform distortion, BET directionality, NDEL1 involvement, modulation specificity, and developmental-window sensitivity are reproduced. It will become weaker if those predictions fail. Either outcome would be valuable. The urgent task is to perform the experiment capable of deciding.

> *"We are not asking science to accept a conclusion. We are asking it to stop leaving the decisive experiment undone."*
>
> **— John Coates**

Editorial note: AI-assisted drafting and formatting were used in preparing this discussion paper. Scientific responsibility, interpretation, and any future submission remain with the author. This paper is not medical advice.

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Appendix A. Proposed Bioelectric Fidelity Index

A fidelity index would allow the framework to be tested quantitatively rather than described metaphorically. The following is a proposed analysis architecture, not a clinically validated score.

Candidate Bioelectric Fidelity Index (BFI)

```
BFI = 1 - [wf*Df + wa*Da + wp*Dp + ws*Ds + wr*Dr + wh*Dh]
Df = frequency divergence; Da = amplitude divergence; Dp = phase divergence
Ds = spatial divergence; Dr = recovery divergence; Dh = heterogeneity/entropy divergence
Weights w are preregistered and sum to 1. BFI approaches 1 as fidelity approaches the
reference waveform.
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A.1 Reference state

The reference cannot be a single idealized sine wave. It should be a developmental-stage-specific distribution learned from sham cultures across multiple stem-cell lines and batches. Each endpoint should be normalized to within-line baseline variability before pooling.

A.2 Recommended signal analyses

DOMAIN	METHOD	INTERPRETATION
Frequency	Peak detection, wavelets, power spectral density	Missed/extra bursts; dominant-frequency shift
Phase	Phase-locking value, cross-correlation	Loss of cell-cell or organelle coordination
Entropy	Sample/spectral entropy	Broadband irregularity or loss of ordered oscillation
Propagation	Optical flow, wavefront velocity	Abnormal spatial spread or stalled waves
Recovery	Decay constants, baseline drift	Impaired clearance or refractory timing
Coupling	Voltage-Ca, mito-Ca, nucleus-Ca coherence	Decoupling of compartments

A.3 Developmental validation

A useful index must predict a later developmental endpoint and respond to rescue. It should change before altered differentiation or morphogenesis, correlate with the magnitude of the downstream phenotype, normalize when the waveform is restored, and remain stable when only imaging noise changes.

Appendix B. Exposure and Experimental Design Matrix

DESIGN ELEMENT	CORTICAL ORGANOID	NEURULOID	EMBRYO	IN VIVO
Model	Human cortical organoids	Human neuruloids/neural-tube organoids	Xenopus/vertebrate embryo	Maternal-fetal in vivo model
Primary window	Radial-glia expansion/differentiation	Neurulation and closure	Live closure mechanics	Gestational exposure windows
Field conditions	Cakir replication; CW; multiple modulations; sham	Same plus pure ELF	Scaled, mapped field geometry	Realistic devices and calibrated chambers
Genetic tests	CYB5B KD/KO/rescue; channel mutants	SPCA1/CaV3 interaction	Channel and cytoskeletal perturbation	Susceptibility genotypes
Live endpoints	Compartmental Ca, voltage, growth	Ca flashes, actomyosin pulses	Closure velocity and tissue strain	Maternal physiology and fetal signals
Molecular endpoints	BET occupancy, acetylation, NDEL1	Closure gene networks	Ephrin/EPHA, cytoskeleton	Placenta, fetal brain, germline
Critical controls	Temperature, position, handling, blinded code	Oxygen, media, geometry	Developmental staging	Stress, restraint, maternal heating
Decision rule	Mechanistic dependency and rescue	Waveform precedes closure effect	Reproducible dose/window relation	Internal dose overlaps in vitro active range

B.1 Reproducibility requirements

- At least three independent laboratories and multiple biological lines.
- Exposure systems built by independent engineering teams.
- Preregistered analysis code and locked primary endpoints.
- Raw waveform, dosimetry, temperature, and imaging data deposited publicly.
- Positive biological controls that alter calcium timing without RF.
- Negative controls that change average calcium without reproducing the waveform.
- Publication of null and contradictory results.

Appendix C. Hypothesis-Generating Extensions and Excluded Claims

Several extensions in the author's public posts may be worth testing, but they should not be merged into the core pathway as if demonstrated. This appendix preserves the ideas while marking the missing evidence.

EXTENSION	BIOLOGICAL ANCHOR	CURRENT GAP / BOUNDARY
CYB5B -> sterol C4 intermediates -> RORgammat/Th17	CYB5A/B participate in sterol C4 oxidation; dimethyl sterols have regulatory activity.	No evidence reviewed here shows RF inhibits this pathway, produces the proposed sterol profile, or drives pathogenic Th17 differentiation.
Th17/B-cell response -> folate-receptor-alpha autoantibodies	FRalpha autoantibodies and cerebral folate deficiency are studied in some neurodevelopmental contexts.	No demonstrated RF-CYB5B-Th17-FRalpha chain; target selection and tissue specificity are unexplained.
“Density gating” at choroid plexus	High-energy transport epithelia have distinctive mitochondrial and barrier biology.	Density gating is a proposed concept, not an established exposure law. Requires tissue-resolved dosimetry and vulnerability mapping.
CYB5B/mARC impairment + acetaminophen	CYB5B participates in mARC electron transfer; acetaminophen metabolism can create oxidative stress at toxic dose.	No evidence reviewed here shows RF paralyzes mARC or that the combination causes autism. Clinical use should not be changed from this hypothesis.
Vaccination as a regression trigger in an RF-stressed child	Immune activation changes metabolism and cytokine signaling.	No evidence reviewed here establishes an RF-vaccine interaction causing autism or regression. This claim is excluded from the core paper.
One pathway causes autism, cancer, autoimmunity, and metabolic syndrome	Calcium/redox signaling is shared across tissues.	Shared machinery does not establish one upstream cause. Each disease requires its own adverse-outcome pathway and evidence.

C.1 Minimum standard for promoting an extension into the core model

An extension should move into the main pathway only after an exposure-specific upstream change is reproduced, temporal ordering is demonstrated, genetic or pharmacologic intervention establishes necessity, rescue establishes reversibility, and realistic internal dose is shown. A plausible biochemical route without those tests remains hypothesis-generating.

Appendix D. Terminology and Claim-Language Guide

TERM	WORKING DEFINITION
Bioelectric fidelity	Accuracy and reproducibility of voltage- and ion-dependent signaling appropriate to a developmental state.
Low-fidelity biology	Measurable temporal, spatial, or decoding error in those signals; not a diagnosis.
RF	Radiofrequency electromagnetic field; in this paper, usually a MHz/GHz carrier.
ELF	Extremely low frequency. A standalone ELF field is not identical to a low-frequency envelope on an RF carrier.
CYB5B	Outer-mitochondrial-membrane heme electron-transfer protein identified as essential in Kim et al.'s engineered EMF gene-switch system.
S4 voltage sensor	Charged transmembrane structure in many voltage-gated channels; proposed exposure target, not established here.
BET proteins	Bromodomain and extra-terminal chromatin readers that bind acetylated lysines and regulate transcription.
NDEL1	Kinase-sensitive centrosomal/cytoskeletal developmental protein associated with organoid growth in the Courchesne study.
Mechanistic plausibility	A coherent, biologically possible, falsifiable chain with supported nodes; less than causal proof.
Critical window	Developmental period in which a particular signaling process has disproportionate influence on later structure or function.

D.1 Recommended claim language

LANGUAGE	EXAMPLE
Use	“Cakir et al. reported RF-associated BET-dependent developmental effects in their organoid model.”
Avoid	“Cakir proved Wi-Fi causes autism.”
Use	“Kim et al. identified CYB5B as an essential mediator likely acting as an EMF sensor in an engineered 60-Hz gene-switch system.”
Avoid	“CYB5B is proven to be the Wi-Fi sensor in every human cell.”
Use	“The combined studies support a testable CYB5B/Ca/BET/NDEL1 hypothesis.”
Avoid	“The complete mechanism is settled and denial is no longer possible.”

LANGUAGE	EXAMPLE
Use	"Modulation may matter and should be compared with continuous wave at matched absorbed power."
Avoid	"A 10-Hz RF envelope is physically the same exposure as a 10-Hz magnetic field."
Use	"Optical and wired alternatives can reduce microwave exposure and should be safety-engineered."
Avoid	"Li-Fi is biologically native and therefore automatically harmless."

D.2 One-sentence public summary

Shareable summary

Recent organoid and gene-switch studies do not prove that wireless radiation causes autism, but they reveal a testable pathway by which electromagnetic exposure could alter the timing fidelity of calcium signals that control chromatin, progenitor-cell decisions, and early brain development - a pathway that now warrants direct, independent testing.