# The Electrome: A Comprehensive Analysis of Bioelectric Field Topography in Biological Systems

## The Foundations of Bioelectricity: From Ion Flux to Morphogenetic Fields

The architecture of life is sculpted by forces both visible and invisible. While the twentieth century was dominated by the elucidation of the chemical and genetic codes that specify the molecular components of living systems, a parallel and more ancient regulatory layer is now being recognized as fundamental to biological organization. This layer is not chemical in its primary language but biophysical, encoded in the dynamic patterns of electric fields and currents that permeate all living tissues. This endogenous bioelectricity, far from being mere epiphenomenal noise or a specialized property of excitable nerve and muscle cells, constitutes a primary information-bearing medium that guides the development, maintenance, and regeneration of complex anatomical structures. The study of this phenomenon, termed Bioelectric Field Topography (BFT), involves mapping and interpreting this "electrome"—the complete spatiotemporal pattern of bioelectric fields within an organism—to understand its instructive role in health and disease. This section establishes the foundational principles of BFT, tracing its intellectual history from early observations of "animal electricity" to its modern conceptualization as a sophisticated, multi-scale regulatory system.

### Defining the Bioelectric Landscape: A Multidisciplinary Synthesis

To comprehend Bioelectric Field Topography, one must adopt a multidisciplinary perspective that integrates biophysics, electrophysiology, systems theory, and even quantum biology.1 At its most intuitive, the concept can be understood through the metaphor of a "Bioelectric Terrain," an unseen energetic landscape that animates and organizes the physical structures of an organism.1 Much like a garden's vitality depends on a complex, subterranean network of roots and nutrients, the visible form and function of a living being are supported by a dynamic orchestra of subtle electrical currents and fields. This terrain is not static; it is a responsive matrix influenced by physiological state, environmental inputs, and even emotional conditions, forming an energetic blueprint for health.1

This intuitive framework finds its rigorous scientific footing in the measurable biophysical phenomena of developmental bioelectricity. The "terrain" is, in fact, the collective result of endogenous ion fluxes, transmembrane and transepithelial voltage gradients, and the electric currents and fields that are actively produced and sustained in all living tissues.3 Cells and tissues communicate not only through chemical signals but also through these electrical impulses, creating a constant flow of bioelectricity that forms a coherent, information-rich field.1 This field is a fundamental layer of the complex signaling environment that impinges upon every cell, regulating its interactions during pattern formation and maintenance throughout an organism's lifespan.3

Elevating this definition to a formal academic level, BFT is the study of a sophisticated biophysical field that functions as a primary regulatory system, integrating the chemical, electrical, and informational strata of biological organization.1 It is crucial to understand that this field is not merely the linear summation of individual cellular membrane potentials. Rather, it is a coherent, macroscopic field that exhibits emergent properties, acting as a non-genetic template for biological form and function.1 This perspective posits that the bioelectric field guides cellular differentiation, orchestrates tissue organization, and maintains homeostatic stability. Some theories even extend its role to the regulation of organismal behavior and the substrate of consciousness.1 The concept of the "Bioelectric Terrain," therefore, serves as a vital semantic bridge, connecting the holistic, qualitative understanding of an energetic blueprint for health with the quantitative, biophysical reality of a morphogenetic field. This dualism highlights a central challenge for the discipline: to maintain scientific rigor while effectively communicating its paradigm-shifting implications to a broader scientific and clinical audience that may be more accustomed to purely biochemical models of life.

### The Biophysical Engine: Molecular Mechanisms of Field Generation

The generation of the bioelectric landscape is a testament to the elegant harnessing of fundamental physics by molecular machinery. The process begins at the most basic unit of life, the cell, with the establishment of a charge separation across its boundary. The lipid bilayer of the plasma membrane, an indispensable structure for the origin of life itself, acts as a biological capacitor, creating an inside/outside discontinuity.3 Across this membrane, a complex array of molecular machines—ion channels, pumps, and transporters—work ceaselessly to orchestrate a dynamic exchange of ions, establishing an uneven distribution of charge.5

The cornerstone of this system is the establishment of the cellular resting membrane potential (Vmem​), the fundamental "battery" that powers bioelectric signaling. This potential arises from the maintenance of steep electrochemical gradients, most notably a high intracellular concentration of potassium ions (K+) and a low intracellular concentration of sodium ions (Na+) relative to the extracellular environment.6 The primary engine maintaining this state is the Na+/K+ ATPase, a pump that actively expels three

Na+ ions for every two K+ ions it imports, a process that consumes a significant portion of a cell's energy budget.6 The resulting resting potential, typically in the range of -50 mV (inside negative) for non-excitable cells, is a dynamic equilibrium of these active pumping processes and the passive leakage of ions through various channels.7

A single cell's membrane potential is but the first step in constructing the organism-wide electrome. The propagation and integration of these potentials across vast cellular collectives are achieved through specialized intercellular connections. Electrical synapses, known as gap junctions, form conductive pathways between adjacent cells, allowing them to directly share ions and small molecules. This coupling enables cells to share their Vmem​ with their neighbors, creating local domains of isoelectric cells that can act as coordinated functional units.3 This long-range communication is essential for patterning tissues over distances far greater than a single cell's diameter. Conversely, tight junctions act as resistors, mitigating the paracellular leakage of ions and preventing the short-circuiting of these crucial voltage gradients, particularly in epithelial sheets.3

When cells with polarized distributions of ion transporters, such as those in an epithelium, align themselves, they generate larger, tissue-level electrical phenomena. These aligned cells function like batteries connected in series, creating significant transepithelial potentials that can drive steady, long-range ionic currents through the tissue.3 Together, these cellular resting potentials, gap-junctional communication networks, and transepithelial potentials form the rich and dynamic patterns of voltage and current that demarcate anatomical features. These patterns are not mere byproducts of cellular activity; they are a causal architecture of life, a physical information flow that constructs and maintains the organism. This architecture follows a clear causal hierarchy, originating from quantum-level charge transport phenomena, which are harnessed by molecular pumps to create cellular

Vmem​, which are then integrated into tissue-level fields that, in turn, provide the instructive cues for large-scale morphogenesis.3 BFT, therefore, is not simply a descriptive tool but a map of this fundamental causal chain.

### Historical Perspectives on the "Fields of Life"

The recognition that electricity is intrinsic to life is not a recent development. The field of electrophysiology was born in 1791 with the seminal experiments of the Italian physician Luigi Galvani, who observed that the legs of a dissected frog would twitch when touched with metal probes, leading him to coin the term "animal electricity".3 While his contemporary Alessandro Volta correctly argued that some of these effects were due to the electrochemical interaction of dissimilar metals, Galvani later demonstrated muscle contraction without any external metal source, definitively proving that living tissue generates its own electricity.3 In the 1840s, the German electrophysiologist Emil du Bois-Reymond used sensitive galvanometers to measure not only the rapid action potentials of nerve and muscle but also the steady, weaker currents that flow from wounded tissues—the first characterization of the "current of injury".3

Despite these early discoveries, the idea that steady bioelectric fields could play an instructive role in shaping the organism was most rigorously pursued, and subsequently most thoroughly ignored, by Harold Saxton Burr, a neuroanatomist at Yale University School of Medicine. From the 1920s through the 1950s, Burr and his colleagues developed highly sensitive vacuum-tube voltmeters to systematically map what he termed the "Fields of Life," or "L-Fields," across a vast array of organisms, from slime molds to humans.9

Burr's decades of meticulous research, published in dozens of papers in peer-reviewed journals, produced a series of remarkable findings. He demonstrated that the primary developmental axis of a frog embryo—the line that would become its head and tail—invariably aligned with the plane of the greatest voltage drop measured across the unfertilized egg, suggesting the electric pattern was a primary blueprint for the future anatomy.9 In studies on mice bred to be susceptible to cancer, he discovered that abnormal voltage gradients could be detected long before any physical tumor became apparent, proposing that bioelectric measurements could serve as an early diagnostic tool.9 He conceptualized the L-Field as a "blueprint for immortality," an electrodynamic matrix that guides the constant process of cellular replacement, ensuring that new cells and molecules arrange themselves into the same stable pattern as the old ones, thus preserving the organism's form through ceaseless metabolic turnover.9

The marginalization of Burr's work can be attributed to several historical factors. His field-centric worldview ran counter to the ascendant gene-centric and biochemical paradigms of the mid-20th century, which offered more readily dissectible molecular components. Furthermore, the rise of a pharmaceutical-focused model of medicine, solidified by influential reports like the 1910 Flexner Report, created an institutional environment less receptive to biophysical or "energetic" therapeutic approaches.10 Burr's work languished in relative obscurity until the 1970s, when the field was revitalized by a crucial technological innovation: the vibrating probe. Developed by Lionel Jaffe and Richard Nuccitelli, this non-invasive device could measure the minute, steady extracellular ion currents flowing around developing and regenerating tissues with unprecedented sensitivity.3 This invention provided the missing link, allowing researchers to connect Burr's macroscopic field measurements with the underlying molecular-level ion fluxes, thereby grounding the concept of "Fields of Life" in modern cell and developmental biology and sparking the current renaissance in the field.

## Mapping the Invisible Architecture: Technologies for Visualizing Bioelectric Patterns

The conceptual leap from acknowledging the existence of bioelectric fields to understanding their functional role as an information-bearing system depends critically on the ability to visualize their spatiotemporal dynamics. The history of the field is inextricably linked to the development of instruments capable of detecting these often subtle and complex electrical phenomena. Modern research in Bioelectric Field Topography employs a diverse toolkit of technologies, each with its own principles, capabilities, and limitations, spanning scales from the single ion channel to the entire organism. These methods can be broadly categorized into direct electrophysiological measurements, macroscopic field imaging, molecular and optical visualization techniques, and a range of novel emerging systems that push the boundaries of sensitivity and resolution.

### Electrophysiological Probes and Sensors: Direct Measurement

The most direct way to assess bioelectric activity is to measure electrical potentials and currents using electrodes. These techniques form the bedrock of classical electrophysiology and continue to provide essential ground-truth data for foundational research.

**Microelectrodes** are designed for high-resolution measurements at or within the cellular level. They are typically fabricated as either fine metal needles insulated to their tip or as glass micropipettes filled with an electrolyte solution.11 By carefully inserting a microelectrode into a cell, one can directly measure its transmembrane potential (

Vmem​). While indispensable for characterizing the electrical properties of individual cells, this method is highly invasive, technically demanding, and impractical for mapping the coordinated activity of large cell populations in intact tissues.11

**Surface and Needle Electrodes** are the workhorses of clinical diagnostics, used for electrocardiography (ECG), electroencephalography (EEG), and electromyography (EMG). Surface electrodes are non-invasive metal discs placed on the skin, typically with a conductive electrolyte jelly to ensure a low-impedance electrical contact.11 They measure the summed electrical potentials generated by large ensembles of cells (e.g., cardiac muscle or cortical neurons). While clinically robust, their spatial resolution is limited by the distance from the source and the smearing effect of intervening tissues. Needle electrodes, which are inserted through the skin to a target muscle or near a nerve, offer improved spatial localization at the cost of being invasive.11 A common challenge for both types is their sensitivity to motion, which can generate electrical noise known as artifacts.11

**The Vibrating Probe**, developed in the 1970s, represented a major technological advance for developmental biology. This non-invasive instrument measures the minute, steady extracellular ion currents that constitute the electric fields around living tissues. It consists of a tiny platinum-black microelectrode that is vibrated at a known frequency between two points in the extracellular medium.3 If an electric field is present, the probe will oscillate through a voltage gradient, generating a sinusoidal alternating current (AC) signal. A phase-sensitive lock-in amplifier is used to detect this tiny AC signal amidst the background noise, allowing for the calculation of the steady direct current (DC) field strength with high sensitivity. The vibrating probe was instrumental in mapping the "current of injury" at wounds and the developmental currents around embryos, providing the first direct evidence of these guiding fields in vivo.3

**The Bioelectric Field Imager (BFI)** is a more recent innovation that enables non-contact mapping of the surface potential of tissues. Based on a principle first proposed by Lord Kelvin, the BFI uses a small, flat vibrating probe that forms a parallel plate capacitor with the tissue surface.12 The vibration creates an oscillating capacitance, which in turn generates a measurable oscillating current if there is a voltage difference between the probe and the skin. By applying a series of known backing voltages to the probe and identifying the voltage at which the oscillating current becomes zero, the instrument can precisely determine the skin's surface potential at that point without physical contact. The entire apparatus is mounted on a motorized manipulator that scans the probe across the tissue surface, generating a high-resolution 2D map of the bioelectric field, making it a powerful tool for studying wound healing and skin physiology.12

### Macroscopic Field Imaging: EEG and MEG

For studying the collective bioelectric activity of the human brain, two non-invasive techniques are paramount: electroencephalography (EEG) and magnetoencephalography (MEG). Both offer the exceptional temporal resolution necessary to track neural processes that unfold on the millisecond timescale, a capability that metabolic imaging techniques like functional magnetic resonance imaging (fMRI) lack.13

**Electroencephalography (EEG)** records the electrical potentials on the scalp that result from the synchronized postsynaptic currents of large populations of cortical neurons.13 A cap fitted with dozens or even hundreds of surface electrodes detects these tiny voltage fluctuations. EEG is a mature, relatively inexpensive, and portable technology, making it a widely used tool in both clinical neurology (e.g., for diagnosing epilepsy) and cognitive neuroscience.14 Its primary limitation is its relatively poor spatial resolution. The electrical signals are smeared and distorted as they pass through the tissues of the brain, cerebrospinal fluid, skull, and scalp—a phenomenon known as volume conduction. This makes it challenging to precisely localize the deep brain sources of the signals recorded at the scalp.14

**Magnetoencephalography (MEG)** provides a powerful complement to EEG. According to Maxwell's equations, any electrical current—including the ionic currents in neurons—generates a corresponding magnetic field.17 MEG uses an array of extremely sensitive detectors called superconducting quantum interference devices (SQUIDs) to measure the incredibly weak magnetic fields (on the order of femtoteslas) produced by the brain that emerge outside the head.13 The great advantage of MEG is that magnetic fields are not significantly distorted by the skull or scalp. Consequently, MEG can localize the sources of neural activity with much greater spatial accuracy than EEG, while retaining the same excellent temporal resolution.13 However, MEG systems are extremely expensive, require a magnetically shielded room to operate, and are less sensitive to radially oriented neural sources (those perpendicular to the scalp) compared to tangential sources.14 Often, EEG and MEG are recorded simultaneously to combine their complementary strengths, providing a rich, dynamic picture of large-scale brain function.16

The relationship between these measurement techniques and their therapeutic counterparts, transcranial electric and magnetic stimulation (TES and TMS), is governed by a profound physical principle known as the Helmholtz reciprocity theorem.13 This theorem states that the spatial sensitivity pattern of a sensor configuration (its "leadfield") is identical to the electric field pattern that would be produced if that same configuration were used to apply a current. This means, for example, that brain regions from which it is difficult to record a strong EEG signal are also inherently difficult to stimulate effectively with TES. This deep connection provides a unifying theoretical framework for bioelectromagnetism, demonstrating that the ability to measure and the ability to manipulate are two sides of the same physical coin, where the limitations of one directly predict the limitations of the other.13

### Molecular and Optical Visualization: High-Resolution Mapping in Vivo

While electrophysiological probes provide direct electrical measurements and EEG/MEG capture macroscopic brain dynamics, the most significant recent advances in BFT have come from technologies that allow for the visualization of bioelectric patterns in living tissues with cellular resolution. This technological progress is the primary driver of the current renaissance in developmental bioelectricity, transforming the field from one of correlation to one of direct functional investigation.

**Voltage-Sensitive Fluorescent Dyes and Reporters** are molecules that change their optical properties in response to changes in the electric field across the cell membrane. These tools enable the creation of dynamic, high-resolution "maps" of the bioelectric landscape in intact, developing organisms.19 Early versions were chemical dyes that could be loaded into tissues, while more recent advances have produced genetically encoded fluorescent voltage indicators (GEVIs)—proteins that can be expressed in specific cell types to report their membrane potential.3 Using advanced microscopy techniques like fluorescent lifetime imaging (FLIM), researchers can now visualize the subtle but crucial Vmem gradients that act as pre-patterns for morphogenesis, revealing, for example, the hyperpolarized domains that presage gene expression during craniofacial development in a frog embryo.20

**Optogenetics** has revolutionized the ability not just to observe, but to actively manipulate bioelectric states with unparalleled precision. This technique involves the genetic expression of light-gated ion channels, such as Channelrhodopsin (a cation channel) or Halorhodopsin (a chloride pump), in target cells.19 By illuminating the tissue with specific wavelengths of light, researchers can precisely depolarize or hyperpolarize these cells at will, in any desired spatial or temporal pattern. This provides a powerful method for functionally testing the causal role of bioelectric signals. For example, by using optogenetics to artificially create a specific Vmem pattern in an embryonic tissue, researchers can determine if that pattern is sufficient to induce the formation of a complex structure, such as an eye, thereby directly linking the bioelectric code to its anatomical consequence.20

### Novel and Emerging Measurement Systems

The frontier of BFT is being pushed by the development of novel sensor technologies and imaging modalities that offer new ways to probe the electrical properties of biological systems.

**Interdigitated Capacitance Sensors (IDCS)** represent a highly sensitive in vitro method for detecting minute bioelectrical signals from cell cultures or tissue samples.23 An IDCS consists of a pair of interlocking, comb-like electrodes fabricated on a substrate. A biological sample is placed on the sensor, and an AC excitation voltage is applied. Perturbations in the local electric field caused by the sample's bioelectric activity induce phase shifts in the resulting voltage signal. Using a digital lock-in amplifier to filter out noise, this system can achieve nanovolt-level sensitivity, allowing for the real-time monitoring of processes like neurotransmitter release or the spontaneous contractions of cardiac cells.23

**4D-Scanning Precession Electron Diffraction (4D-SPED)** is a technique adapted from materials science that has the potential for ultra-high-resolution mapping of electric fields in biological samples.24 In this method, a focused electron beam is scanned across a sample in a transmission electron microscope (TEM). The local electric field within the sample deflects the transmitted beam due to the Lorentz force. By recording a complete diffraction pattern at each point of the scan, a 4D dataset is created from which the magnitude and direction of the local electric field can be calculated, offering a way to visualize fields at the nanoscale.24

Other emerging modalities, often supported by research initiatives like the National Institute of Biomedical Imaging and Bioengineering (NIBIB) Bio-Electromagnetic Technologies program, are expanding the imaging toolkit.25

**Electric Field Imaging (EFI)**, developed by NASA, uses an array of solid-state sensors to reconstruct a 3D image of an object based on its dielectric properties without direct contact.26

**Electrical Impedance Tomography (EIT)** maps the conductivity of tissues by applying small currents through surface electrodes and measuring the resulting voltages, a technique used to monitor lung function or detect cancer. **Magnetic Particle Imaging (MPI)** is a new modality that tracks the location of magnetic nanoparticles injected into the body, with potential applications in cell tracking and angiography.25 These diverse and innovative approaches promise to provide an increasingly comprehensive view of the body's electrome.

| Technology | Principle of Operation | Spatial Resolution | Temporal Resolution | Invasiveness | Key Applications |
| --- | --- | --- | --- | --- | --- |
| **Microelectrode** | Direct measurement of intracellular potential via a penetrating glass or metal probe. | Sub-cellular (~1 µm) | High (µs to ms) | High (penetrates cell) | Single-cell electrophysiology, patch-clamp studies. 11 |
| **EEG** | Measures electric potentials on the scalp from synchronous neural activity. | Low (~cm) | Very High (<1 ms) | Non-invasive | Clinical neurology (epilepsy), cognitive neuroscience, brain-computer interfaces. 13 |
| **MEG** | Measures magnetic fields outside the head from neural currents using SQUIDs. | Medium (~mm) | Very High (<1 ms) | Non-invasive | Epilepsy focus localization, mapping brain dynamics, pre-surgical planning. 17 |
| **Vibrating Probe** | Measures extracellular ion currents by detecting voltage changes of an oscillating electrode. | Medium (~10-50 µm) | Low (seconds to minutes) | Non-invasive | Mapping developmental currents, wound healing fields. 3 |
| **Voltage-Sensitive Dyes** | Optical imaging of fluorescent reporters that change intensity or lifetime with Vmem. | High (cellular, ~µm) | Medium (ms to seconds) | Minimally invasive | Mapping bioelectric pre-patterns in embryos, real-time Vmem imaging. 19 |
| **Optogenetics** | Genetic expression of light-gated ion channels to control Vmem with light. | High (cellular, ~µm) | High (ms) | Invasive (genetic modification) | Functional testing of bioelectric signals, precise neural circuit manipulation. 19 |
| **EIT** | Reconstructs tissue conductivity maps from applied currents and measured surface voltages. | Low (~cm) | Medium (seconds) | Non-invasive | Lung ventilation monitoring, cancer detection. 25 |

## The Bioelectric Code: Instructive Signals in Development, Regeneration, and Physiology

The ability to map the electrome reveals that bioelectric patterns are not random but constitute a veritable code—a system of instructive signals that orchestrates cellular behavior on a vast scale. This code functions as a layer of physiological software that directs the deployment of the genetic hardware, providing essential positional information and coordinating the complex processes of morphogenesis, regeneration, and physiological homeostasis. By deciphering this code, researchers are uncovering fundamental principles of biological organization and identifying novel points of control for therapeutic intervention.

### The Blueprint for Morphogenesis: Bioelectric Pre-patterns

The prevailing model of embryonic development has long been centered on the concept of chemical morphogen gradients, where diffusing molecules provide positional information to cells, instructing them on their developmental fate. However, a growing body of evidence demonstrates that bioelectric gradients often act as primary "pre-patterns" that exist prior to, and serve to organize, subsequent biochemical and genetic patterning events.20

In developing embryos, distinct spatial domains of resting membrane potential (Vmem​) demarcate the future locations of complex anatomical structures. For instance, in the early frog embryo, a specific pattern of hyperpolarized and depolarized cell groups in the facial ectoderm precedes and is required for the correct formation of the eyes, mouth, and jaws.20 These bioelectric landscapes are not merely correlated with development; they are causally instructive. The most dramatic proof of this principle comes from experiments where these endogenous patterns are deliberately altered. By misexpressing a specific human ion channel in a small group of embryonic cells, thereby creating an artificial bioelectric state that mimics the one normally found in a developing eye, researchers can induce the formation of a complete, correctly structured ectopic eye on the gut or tail of a tadpole.6 This remarkable result demonstrates that a specific bioelectric signature can act as a master-regulator, a trigger sufficient to initiate the entire complex, downstream genetic cascade for organogenesis. This finding fundamentally challenges a purely gene-centric view of development, suggesting that the genome encodes the protein "hardware" (the channels, pumps, and receptors), but the physiological software—the dynamic pattern of bioelectric fields—provides the high-level instructions for how to build an organ.

Cells "read" and interpret these bioelectric cues through a variety of transduction mechanisms. Voltage-gated ion channels, for example, can open or close in response to changes in Vmem​, leading to fluxes of signaling ions like calcium (Ca2+), which in turn activate a host of downstream biochemical pathways.3 Recent work has uncovered an elegant mechanism that integrates mechanical, electrical, and chemical signaling during the migration of neural crest cells—a crucial process for forming the vertebrate face and peripheral nervous system. During development, mechanical stretching of the neural fold tissue activates specific ion channels, generating a local electric field. This field is sensed by an enzyme in the migrating neural crest cells called voltage-sensitive phosphatase 1 (Vsp1), which transduces the electrical signal into a directional cue, guiding the collective migration of the cell population.28 This illustrates the sophisticated interplay of physical forces and molecular machinery that underlies bioelectric control of morphogenesis.

### The Electrophysiology of Regeneration and Repair

The instructive role of bioelectricity is not confined to embryonic development; it is redeployed throughout an organism's life to orchestrate the processes of wound healing and tissue regeneration. When an epithelial tissue, such as the skin, is wounded, its integrity is breached. This breach short-circuits the normally robust transepithelial potential, creating a steady, laterally oriented DC electric field that points towards the center of the wound.30 This phenomenon, known as the "current of injury," can persist for hours or days and serves as a primary guidance cue for the cells involved in repair.31

Cells exhibit a remarkable ability to sense and migrate directionally within these weak physiological electric fields, a process termed **galvanotaxis** or electrotaxis.30 Keratinocytes, fibroblasts, endothelial cells, and even immune cells essential for the healing cascade all respond to the current of injury by migrating into the wound bed to close the defect, proliferate, and restore the damaged tissue.31 The electric field appears to be a dominant cue, capable of overriding other potential guidance signals.31 The failure of chronic wounds, such as diabetic ulcers, to heal properly has been linked to an inability to generate or maintain a sufficiently strong current of injury, highlighting the clinical importance of this endogenous electrical system.31

In organisms with more dramatic regenerative capabilities, such as planarian flatworms and salamanders, bioelectric signals play an even more profound role. They are not only involved in the cell migration of wound closure but also in the large-scale pattern regulation required to rebuild entire, complex appendages. For example, a specific bioelectric signature—a depolarized region at the amputation site—is required to initiate limb regeneration in amphibians.20 Furthermore, by experimentally manipulating the bioelectric gradients across a planarian's body using pharmacological agents, it is possible to override the organism's normal anatomical polarity. A fragment that would normally regenerate a tail at the posterior cut site can be induced to regenerate a head instead, resulting in a two-headed worm. Conversely, a fragment that should regenerate a head can be forced to regenerate a tail.3 These experiments demonstrate that bioelectric circuits store critical information about large-scale body plan organization, and that this information can be rewritten to control regenerative outcomes.

### Bioelectric Regulation of Cancer and Cellular Plasticity

The connection between bioelectricity, proliferation, and pattern control has profound implications for understanding and treating cancer. A consistent and striking finding is that cancer cells across many different tumor types exhibit a distinct bioelectric signature: a chronically depolarized resting membrane potential compared to their healthy, terminally differentiated counterparts.27 This depolarized state is not an epiphenomenon but is functionally linked to the hallmarks of cancer, particularly uncontrolled proliferation and the block of differentiation. The

Vmem​ of a cell acts as a key regulator of the cell cycle, with depolarization being a permissive signal for mitosis.34

Furthermore, the same galvanotactic mechanisms that guide cells during development and wound healing can be hijacked by cancer cells to facilitate metastasis. Some metastatic breast cancer cells, for example, respond to weak electric fields, which can guide their migration and invasion into surrounding tissues.35 This suggests that the bioelectric landscape of the tumor microenvironment may play a crucial role in promoting or suppressing cancer progression.

Perhaps the most transformative insight from this area of research is the concept of cancer as a disorder of tissue-level pattern control, a kind of "bioelectric amnesia." In this view, cancer is not solely a cell-intrinsic problem caused by genetic mutations, but also a failure of the surrounding tissue's collective bioelectric field to impose the correct anatomical "pattern memory" on its constituent cells. When this field-level control breaks down, cells can revert to a more ancient, single-cell-like agenda focused on proliferation, losing their context within the larger organismal plan.20 This framework is supported by stunning experiments in which the cancerous phenotype can be suppressed without altering the cancer cells' genome. By manipulating the bioelectric state of nearby "instructor" cells—forcing them to express ion channels that normalize the local bioelectric environment—researchers have been able to induce highly metastatic, genetically-encoded melanomas in tadpoles to cease their invasion, normalize their morphology, and reintegrate functionally into the host tissue.20 This suggests a revolutionary therapeutic paradigm: instead of simply trying to kill cancer cells, it may be possible to "re-educate" them by re-imposing the correct bioelectric context, coaxing them back into a quiescent, cooperative state.

## Clinical Translation: Bioelectronic Medicine and Therapeutic Interventions

The growing understanding of the electrome is not merely an academic exercise; it is the foundation for a new class of diagnostics and therapeutics that leverage the body's endogenous electrical signaling. This emerging field, broadly termed bioelectronic medicine, uses sophisticated devices to interface with the body's electrical systems to treat a wide range of diseases and injuries.38 These interventions operate on a principle of "exogenous mimicry," where therapeutic success is achieved by designing technologies that restore, amplify, or mimic the natural bioelectric signals that govern a given physiological process. This approach marks a departure from purely pharmacological interventions, offering the potential for therapies with greater precision and fewer side effects. The applications span a wide spectrum of specificity, from highly targeted neural interfaces that speak the body's electrical language to broader biophysical therapies that apply an external force to modulate cellular behavior.

### Modulating the Nervous System: The Core of Bioelectronic Medicine

The most established applications of bioelectronic medicine involve interfacing with the nervous system, the body's primary electrical communication network. These therapies use electrical stimulation to modulate neural circuits that have gone awry in disease states.

**Vagus Nerve Stimulation (VNS)** is a prime example of a circuit-targeted therapy. The vagus nerve is a major information highway in the autonomic nervous system, playing a key role in regulating organ function and inflammation.38 Researchers have discovered a specific neural pathway, the "inflammatory reflex," through which the brain senses inflammation and sends signals down the vagus nerve to suppress it. By implanting a small device that delivers electrical pulses to the vagus nerve in the neck, clinicians can artificially activate this reflex.38 VNS is an FDA-approved treatment for epilepsy and depression and is showing remarkable efficacy in clinical trials for inflammatory conditions like rheumatoid arthritis and Crohn's disease. Preclinical studies have also demonstrated its potential to control bleeding in hemophilia by triggering a "neural tourniquet" effect.38

**Transcranial Magnetic and Electric Stimulation (TMS/TES)** are non-invasive techniques used to modulate the activity of the cerebral cortex. TMS uses a powerful, focused magnetic field pulse to induce a small electrical current in a targeted brain region, while TES applies a weak electrical current directly to the scalp via electrodes.13 These methods can be used to excite or inhibit cortical activity, and repeated sessions of TMS have been approved as a highly effective treatment for major depressive disorder that is resistant to medication. Both techniques are being actively investigated for a wide range of other neurological and psychiatric conditions.13

**Brain-Computer Interfaces (BCIs)** represent the most information-rich and specific form of bioelectronic medicine. These systems involve implanting microelectrode arrays directly into the brain to record the electrical activity of neurons. These signals, representing a person's intentions (e.g., the desire to move a limb), are then decoded by sophisticated AI algorithms and used to control external devices or even the person's own body. In a landmark clinical trial, researchers successfully implanted microchips into the motor cortex of a man paralyzed from the neck down. The system was able to re-link his brain to his body and spinal cord via a computer, allowing him to regain movement and the sense of touch in his hands for the first time in years.38 This demonstrates the transformative potential of technologies that can read and write the neural code with high fidelity.

### Electric Field-Based Oncotherapies

Beyond modulating the nervous system, electric fields are now being applied directly to the body as a novel modality for cancer treatment. These therapies exploit the unique biophysical vulnerabilities of rapidly dividing cancer cells.

**Tumor Treating Fields (TTFields)** is an FDA-approved therapy for glioblastoma, one of the most aggressive forms of brain cancer, and for mesothelioma.34 The therapy is based on the discovery that low-intensity (1-3 V/cm), intermediate-frequency (100-300 kHz) alternating electric fields can specifically disrupt the process of mitosis in cancer cells while leaving non-dividing healthy cells largely unaffected.39 During cell division, the electric fields exert forces on highly charged molecules like tubulin and septin, interfering with the proper formation of the mitotic spindle. This leads to abnormal cell division and ultimately triggers cell death.40 The treatment is delivered non-invasively via transducer arrays that the patient wears on their shaved scalp for at least 18 hours per day. Clinical trials have shown that adding TTFields to standard chemotherapy significantly improves survival for glioblastoma patients.39

**Electroporation-Based Therapies** use short, high-voltage electrical pulses to dramatically increase the permeability of cell membranes. In **electrochemotherapy**, these pulses are used to transiently open pores in cancer cells, allowing for a much greater uptake of cytotoxic drugs, thereby enhancing their local efficacy.22 In

**irreversible electroporation (IRE)**, the electrical pulses are stronger and longer, designed to permanently destroy the cell membrane, causing the tumor cells to die through necrosis. IRE has been approved for soft tissue ablation and is particularly useful for treating tumors near critical blood vessels, as it does not rely on thermal effects that could damage adjacent structures.22 A newer variant,

**Nano-Pulse Stimulation**, uses even shorter, nanosecond-duration pulses that not only porate the outer cell membrane but also the membranes of internal organelles, inducing a more controlled form of regulated cell death.22

### Accelerating Wound Healing with Electrical Stimulation

Building on the fundamental understanding of the endogenous "current of injury," a large body of clinical research has demonstrated that applying exogenous electrical stimulation (ES) can significantly accelerate the healing of chronic wounds. These wounds, such as diabetic foot ulcers, venous leg ulcers, and pressure sores, are a major clinical challenge, often failing to heal for months or years due to impaired natural healing processes.41

Numerous randomized controlled trials (RCTs) have investigated various forms of ES, including direct current (DC), pulsed current (PC), and high-voltage pulsed current (HVPC). The overwhelming consensus from these studies is that ES, when added to standard wound care, leads to a significantly greater reduction in wound size and a faster rate of complete healing compared to sham treatment or standard care alone.31 The applied electrical fields are thought to work by mimicking and augmenting the body's natural healing currents, promoting the directional migration (galvanotaxis) of keratinocytes and fibroblasts, increasing local blood flow and angiogenesis, and exerting bactericidal effects.31

The future of this therapy lies in the development of "smart" bioelectronic dressings. These are flexible, wearable devices that integrate sensors for monitoring key wound parameters—such as pH, temperature, oxygenation, and infection biomarkers—with electrodes for delivering therapeutic ES.43 Such a closed-loop system could provide adaptive, personalized wound care, delivering stimulation only when and where it is needed based on real-time feedback from the wound bed. Despite the strong clinical evidence, a regulatory gap remains; as of now, no ES device has been specifically approved by the FDA for the indication of promoting wound healing, although some are approved for other uses like antimicrobial action, which hinders its widespread clinical adoption.31

## Synthesis and Future Horizons

The study of Bioelectric Field Topography is catalyzing a fundamental shift in the life sciences. It compels a move beyond a purely chemical and genetic view of life to one that embraces the essential role of biophysics, information processing, and field-based organization in shaping living systems. This emerging paradigm does not seek to replace the biochemical worldview but to integrate with it, revealing a richer, more complete picture of biological regulation. As the technologies for mapping and manipulating the electrome become more sophisticated, the field is poised to revolutionize regenerative medicine, oncology, and neuroscience. However, this progress also brings with it significant conceptual challenges and profound ethical considerations that must be addressed by the scientific community and society at large.

### Reconciling Paradigms: Bioelectricity and the Biochemical Worldview

For much of the 20th century, the concept of "morphogenetic fields" was viewed with skepticism by mainstream biology, often relegated to the realm of theoretical or even esoteric science due to a lack of a clear physical basis and tractable experimental tools.44 The modern science of bioelectricity has changed this. It has firmly grounded the morphogenetic field in measurable, physical reality: the integrated, dynamic pattern of cellular resting potentials and ion flows that constitutes the electrome.4 The persistent underappreciation of bioelectricity's instructive role in non-excitable tissues represents a significant conceptual blind spot, a legacy of the overwhelming success and dominance of the molecular genetics paradigm.10

The current challenge is not to prove that bioelectricity exists—the clinical utility of the ECG and EEG has made that undeniable for decades—but to demonstrate its causal, instructive role in patterning and physiology outside of the nervous system. The data presented throughout this report make a compelling case that bioelectric signals are not just one cue among many but often serve as a primary layer of positional information, acting upstream of and in concert with genetic and biochemical pathways.27 Reconciling these paradigms requires an interdisciplinary approach, one that equips molecular biologists with the conceptual and experimental tools of electrophysiology and physics.

It is also critically important to draw a firm line between the rigorous science of bioelectromagnetism and the unsubstantiated claims of some forms of "energy medicine" or "biofield therapies." Scientific BFT is rooted in well-understood physical principles (Maxwell's equations), generated by known molecular machinery (ion channels and pumps), measured by validated instruments (voltmeters, SQUIDs, fluorescent reporters), and applied therapeutically through FDA-regulated devices.45 It deals with measurable phenomena like ion flows and voltage gradients, distinguishing it from vague, pseudoscientific notions of vitalistic "energy fields".46

### The Next Frontier: Quantum Biology, AI, and the Future of Electrophysiology

The future of BFT is dynamic and multifaceted, with several key research directions promising to deepen our understanding and expand our capabilities.

**Deeper Mechanistic Understanding:** A primary goal is to fully elucidate the intricate interplay between the electrome and the genome. This involves systematically mapping the downstream genetic and proteomic cascades that are triggered by specific bioelectric signals and, conversely, understanding how genetic networks build and regulate the ion channel and pump machinery that generates the fields in the first place.48

**Quantum Biology:** An exciting and speculative frontier is the exploration of non-trivial quantum effects in bioelectric phenomena. Life operates at the interface of classical and quantum physics, and processes like electron and proton tunneling are already known to be vital for enzyme function and metabolism.4 It is plausible that quantum coherence or other quantum effects play a more significant role in the generation and perception of bioelectric signals than is currently understood, potentially providing a mechanism for the remarkable coherence and information processing capabilities of biological fields.48

**Artificial Intelligence and Automation:** The convergence of BFT with artificial intelligence and laboratory automation promises to accelerate discovery dramatically. A visionary proposal involves creating a closed-loop system where advanced microscopy and voltage reporters provide real-time data on the bioelectric state of a regenerating tissue. This data would be fed to a Deep Reinforcement Learning (DRL) algorithm, which would then "learn" to control a spatial light modulator to deliver precise optogenetic stimulation. The AI's goal would be to manipulate the bioelectric signals in real time to guide the tissue towards a desired target morphology, such as the perfect regeneration of a limb. Such a system would not only be a powerful tool for regenerative medicine but also a scientific instrument for discovering the fundamental rules of the bioelectric code.19

**Next-Generation Technologies:** Progress in the field will continue to be driven by technological innovation. This includes the development of more sensitive, higher-resolution, and less invasive tools for measuring weak bioelectromagnetic fields, as well as the engineering of more sophisticated, targeted, and biocompatible bioelectronic devices for therapeutic neuromodulation and tissue regeneration.48

**Environmental and Ethical Considerations:** As we gain the ability to manipulate the electrome, it becomes imperative to understand the potential effects of the anthropogenic electromagnetic fields that now saturate our environment—from power lines to wireless communication—on biological systems.49 Furthermore, the power of these technologies, particularly in the realm of neuromodulation and brain-computer interfaces, raises profound ethical questions. The ability to read and write to the brain's electrical circuits forces us to confront issues of cognitive liberty, privacy, enhancement versus therapy, and the very definition of personal identity. The mastery of BFT will necessitate the development of a new field of "electr-ethics" to navigate this complex territory.48

### Concluding Remarks: The Dawn of the Electrome

In biology, the suffix "-ome" denotes a totality of some kind: the genome is the entirety of an organism's genetic information; the proteome is the full complement of its proteins. It is now appropriate to formally define the **electrome**: the integrated, dynamic totality of endogenous electric fields, currents, and potentials within a living organism.

The electrome is not a metaphor; it is a physical entity that serves as a crucial medium for information storage and processing. It is a master regulator of growth and form, a blueprint for anatomy, and a key determinant of physiological state. Understanding and learning to manipulate the electrome represents a true paradigm shift in biology and medicine. It moves us beyond an exclusively chemical description of life to a more holistic view that integrates the fundamental principles of physics. The dawn of the electrome heralds a future where we may be able to repair birth defects by correcting embryonic pre-patterns, treat cancer by re-imposing healthy tissue organization, regenerate complex organs, and communicate directly with the nervous system to heal the mind and body. The continued exploration of this invisible architecture promises not only to yield transformative new therapies but also to deepen our fundamental understanding of what it means to be alive.

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