

Electricity Before Anatomy: The Bioelectric Language of Repair

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Abstract (original summary). Cells generate membrane potentials, and injured epithelia can establish electrical gradients that influence migration and healing. This essay evaluates tissue bioelectricity as one potential input into repair coordination. It distinguishes well-supported electrical physiology from speculative claims about instructing whole-organ anatomy and identifies the controls needed for credible therapeutic studies.

Endogenous voltage is not a metaphor

Cells maintain transmembrane potentials, and epithelia can generate electrical fields when their normal barriers are disrupted. These phenomena can influence cell migration and wound responses. The provocative extension is that patterns of electrical activity might participate in directing some developmental or regenerative events. But 'bioelectricity' refers to many distinct mechanisms: ion-channel activity, gap junctions, extracellular fields and tissue-scale voltage gradients. Conflating them turns a research field into a slogan.

How a signal might become spatial information

Ion channels and pumps alter membrane voltage; gap junctions permit exchange of small ions and metabolites; epithelial injury can establish local directional cues. Cells may migrate along electric fields, while electrical changes can alter downstream signaling and gene expression. Electrical context can therefore modulate repair without being a complete anatomical instruction set. In a complex tissue, direction, magnitude, timing and cell identity all matter. A field that encourages epithelial closure might not specify cartilage shape or nerve branching.

A credible research hypothesis

The Institute proposes examining electrical state as one component of regenerative competence, especially where conventional biochemical assays fail to capture spatial organization. Tissue electrical measurements might eventually complement imaging and gene-expression data in some injury models. The correct experiment would link a precisely measured or manipulated electrical variable to a reproducible structural outcome, with controls for heat, mechanical disruption and unintended chemical effects.

Why caution matters

Human applications remain highly condition-specific. An electrical intervention that improves one type of wound closure is not proof that all scarred organs can be regenerated. Manipulating tissue bioelectric patterns can also disturb excitability or growth. Any claim of therapeutic precision must specify cell type, field strength, exposure duration, intended endpoint and adverse effects. Bioelectric regulation is interesting precisely because it can be investigated mechanistically rather than invoked as an invisible life force.

A clinical thought experiment

A healing corneal or skin epithelial surface generates electrical gradients as its barrier is disrupted. The existence of these gradients is credible physiology; the leap to instructing complex anatomy is much larger. A designed

wound-healing device might change epithelial migration without supplying the information needed to rebuild a severed tendon. The paper should make this distinction concrete rather than hide it under the word 'energy.'

What would discriminate among explanations

Useful evidence would link a defined electrical perturbation to controlled cell migration, improved structure and durable function, ideally with dose–response and polarity controls. If changes vanish when heat or chemical gradients are controlled, the electrical account weakens. Safety evaluation must also test unwanted changes in cellular excitability and proliferation.

Electrical gradients are ordinary wound physiology

Epithelia maintain voltage differences through ion transport and barrier properties. When an epithelial surface is wounded, the interruption of that barrier can generate endogenous electric fields that influence cell movement and orientation. Directed cell migration in response to electrical cues is known as electrotaxis or galvanotaxis. These are experimentally tractable phenomena, not evidence of an invisible mystical force. Their existence nevertheless complicates a purely chemical account of wound repair: cells experience electrical as well as biochemical and mechanical information.

The difficulty is scale. A cultured keratinocyte moving toward an electrode under controlled conditions is one thing. Reconstructing a multilayered, vascularized, innervated human organ is another. Electric fields may help orient migration without specifying complete anatomy. They can interact with receptor signaling, cytoskeletal polarization and local ion transport, but their contribution must be measured against other constraints such as oxygen delivery, matrix composition, infection and mechanical stress.

A proposed signaling hierarchy

One hypothesis is that injury-related electrical signals help provide an early directional cue before more elaborate tissue organization develops. A disrupted surface creates a local field; responsive cells polarize and migrate; subsequent cytokine, growth-factor and mechanical signals govern proliferation and matrix remodeling. This ordering is deliberately provisional. It may vary by tissue, and the evidence does not justify claiming that electricity universally precedes chemical communication in development or healing. The term 'electricity before anatomy' should be read as a provocative question about information flow, not an established temporal law.

A further possibility is that impaired ion-channel function changes how cells interpret a wound environment. But this requires specificity: which ion channel, in which cell type, under which electrochemical conditions, and with what functional effect? Simply measuring a change in a local potential would not show it is causal. For clinical interpretation, abnormalities in systemic serum electrolytes must also be distinguished from micrometer-scale extracellular electrical fields.

Why clinical stimulation trials are not proof of a universal repair code

Electrical stimulation has been investigated for particular wound types and neuromuscular indications, but efficacy depends on the condition, device, waveform, treatment protocol and quality of evidence. A positive finding in one wound-healing context cannot be extended to organ regeneration or systemic rejuvenation. Conversely, an ineffective stimulation protocol does not falsify every possible role of endogenous bioelectric signaling. The stimulus delivered by an external device may not reproduce the spatiotemporal pattern generated by injured tissue itself.

To make progress, studies would need to measure local fields, identify responsive cell populations, demonstrate that selective perturbation changes repair, and show that restoring the signal rescues a functional endpoint. The sequence matters because electrical changes may be consequences rather than causes of tissue injury. Injury itself changes membrane integrity and extracellular ion composition; a detected field could be a passive marker of damaged tissue rather than an actionable instruction.

The safety and interpretation problem

The claim that bioelectric signaling regulates some cellular behaviors should not be transformed into claims that magnets, consumer electrical devices or unspecified frequency therapies regenerate organs. External currents can cause irritation, burns, rhythm-related risks with certain applications and interference with implanted devices. A mechanistic finding requires a defined clinical protocol before it supports treatment advice.

The profound scientific question is how cells integrate multiple classes of information. An epithelial cell does not receive an isolated 'healing message'; it responds to gradients of ligands, matrix attachments, mechanical stresses and electric potentials. Understanding that integration may reveal why a signal is helpful in one wound but insufficient in another. The frontier lies in reconstructing control systems, not attributing all repair to an electrical master switch.

Information is encoded in geometry as well as voltage

A local electric field has direction and magnitude; a pattern of fields can potentially convey spatial information. But different cell types may respond in different directions, and their responses are modified by receptor expression, ion transport, matrix adhesion and the microenvironment. Thus the existence of an electrical gradient does not establish that a tissue possesses a complete electrically encoded blueprint. One could observe robust electrotaxis while still needing separate positional signals to determine a cell's ultimate identity.

A convincing multi-scale experiment would first measure endogenous electrical gradients at a wound, then perturb them without broadly injuring tissue, and finally restore the pattern to see whether directional cell movement and anatomical recovery normalize. Recording only accelerated closure would leave open whether the result came from altered inflammation, cell proliferation or barrier function. Those processes can all affect the wound's electrical measurements in the opposite causal direction.

A mature field of bioelectric medicine will need reproducible maps of specific tissue states, not device-centered promises detached from biology. Its most interesting questions concern how electrical cues cooperate with known developmental and wound signals.

A challenge for studies of exogenous stimulation

When an externally delivered field changes wound closure, a useful trial should compare it with appropriate sham conditions and standard wound care. The study must report wound characteristics, stimulation parameters, treatment duration and adverse effects. Without those details, apparently contradictory studies cannot be meaningfully compared. The delivery device is part of the intervention, not merely a neutral carrier of an established natural signal.

A particularly revealing design would measure whether stimulation restores the spatial organization of cell migration or only changes the overall rate of closure. Accelerated surface closure might be useful clinically but could coexist with fragile tissue or poor later remodeling. Bioelectric explanations should therefore be evaluated at the same functional standard as chemical and mechanical therapies.

Selected scientific readings

- Molecular basis of positional memory in limb regeneration. Nature (2025). <https://www.nature.com/articles/s41586-025-09036-5>
- López-Otín C et al. (2023). Hallmarks of aging: An expanding universe. Cell. <https://doi.org/10.1016/j.cell.2022.11.001>

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Editorial status: substantially revised conceptual article. Evidence-informed, not peer-reviewed, not a systematic review or clinical treatment guidance.