AION: Read + Write Bioelectricity

We are seeking adaptable engineers aligned with our mission of advancing human longevity to develop hardware at the intersection of acoustics, magnetism, and RF.

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Abstract

Cellular reprogramming through molecular and genetic interventions dominates longevity research but faces severe limitations in spatiotemporal control, organ specificity, and safety. Bioelectricity offers a powerful, underutilized framework for non-invasive, real-time cell fate modulation. **AION is developing closed-loop systems to remotely read and write bioelectric states in deep tissue through external electromagnetic and acoustic fields.** Bioelectromagnetics literature shows reproducible field-specific "windows" enabling depolarization and hyperpolarization. We argue that integrating these insights into an adaptive, feedback-driven platform establishes a new paradigm for cell reprogramming, one that surpasses molecular therapies in spatiotemporal precision. As a first application, we identify the thymus as a tractable market beachhead, where bioelectric control of proliferation and differentiation may restore immune function and extend healthspan.

Introduction

The largest longevity companies have committed to molecular approaches to cell reprogramming, which we believe is a mistake. Altos Labs raised $3B for cellular reprogramming via transcription factors. Calico, Retro Biosciences, and NewLimit follow similar strategies. These approaches face fundamental limitations in delivery and temporal control: it is difficult to target specific organs with molecules, and every organ reprograms at a different rate.

For example, the liver may reprogram in days while the brain takes weeks, and typical reprogramming cocktails cause multi-organ failure long before the slow-reprogramming organs improve. [Singh 2022] The best longevity result with Yamanaka factors thus far came from a ‘pulsed’ schedule (2 days on, 5 days off), achieving 33% median lifespan extension just by partially reprogramming the ‘fast’ reprogramming organs. [Ocampo et al. 2016] We believe, as surely Altos and the like do, that partial reprogramming of all organ systems could give a much

larger lifespan benefit. We do not believe molecules can do this due to lack of real spatiotemporal control.

The holy grail of biological spatiotemporal control is a device. External electromagnetic and acoustic fields can spatially encode effects to millimeter resolution, penetrate deep tissue, and be modulated in real time based on tissue response. However, this has been unattractive to biologists: traditional biochemistry does not tell you what field parameters produce cellular outcomes.

Bioelectricity provides the missing framework. Popularized by Michael Levin in recent years, the evidence is now clear: membrane potential changes control cell fate. All cells communicate electrically through ion channels, not just neurons. While neural networks integrate information for behavioral decisions (action space), non-neuronal cells form similar cooperative networks for anatomical decisions (morphospace), determining whether to divide, differentiate, or die. All cells behave somewhat like neurons, just on a longer timescale.

Naturally, the toolkit of neurostimulation becomes relevant. TMS, focused ultrasound, temporal interference, etc. all become general tools for modulating membrane voltage (Vmem) to direct cell fate. The engineering is actually simpler outside the brain: there are larger target structures and no skull interference.

Existing imaging technology allows us to image bioelectric states in deep tissue, enabling closed-loop read-write systems in vivo.

The space of field parameters is large, and the core scientific barrier before the ideal machine can exist is determining a narrow space of field parameters that is most effective at altering cellular membrane potential (Vmem). Our platform allows us to answer this question.

Put succinctly: **we are remotely reprogramming cells non-invasively with external electromagnetic and acoustic fields, giving us superior spatiotemporal control to drugs or gene therapies.**

Bioelectricity Background

Bioelectricity, and generally biophysics, offers a useful framework to predict interactions between external fields and cell fate.

Seminal work in the 1970s by Clarence D Cone Jr. placed cell membrane voltage as a fundamental control mechanism for the cell cycle. He published on the following:

- Hyperpolarizing cells (e.g., making Vmem more negative) inhibited cell division and stopped DNA synthesis. [Cone 1970, Cone 1971]
- Depolarizing (e.g. making Vmem less negative) mature, non-dividing neurons induced cell division and DNA synthesis. [Cone 1976]

- Reversing induced hyperpolarization or depolarization reversed the anti- or pro-cell division effects. [Cone 1971]
- Cancer cells have sustained depolarization, contributing to malignancy. For example, myosarcomas maintained -10 mV Vmem compared to -90 mV in normal cells, altering cell surface polymers and promoting proliferation. [Cone 1971]

These effects often had specificity to cell cycle stages, implying precise control over proliferation via bioelectric manipulation is possible.

Michael Levin is the modern champion of bioelectricity. His remarkable results have demonstrated that bioelectricity is not simply a lever to control proliferation, but also morphology and cell fate. Some notable examples include:

- Inducing and reversing melanoma by altering membrane potential. [Lobo 2017, Chernet 2014]
- Growing eyes outside of the head in Xenopus by altering membrane potential of a small subset of cells that became the resulting tissue. [Pai 2012]
- Deciding head vs. tail identity during regeneration in planaria with membrane potential. [Beane 2011]
- Making stable, replicating 2+ headed planaria with no genetic changes. [Durant 2017]
- Inducing complete functional limb regrowth in adult frogs via wearable bioreactor. [Murugan 2022]
- Attenuating senescence via hyperpolarization in human keratinocytes. [Sediqi 2025]

More generally, bioelectricity is a word that describes a measurement about the cell – the reading on a patch clamp; the color of a voltage reporting fluorophore. The underlying cell state that it represents is characterized by differential ion concentrations across the cell membrane, though the same voltage can have different total numbers of ions. The ionic concentration inside and outside the cell influences other biophysical properties about the cell, including, but not limited to water polarity, water activity, protein folding state, solute activity, energetics, and redox state. All of these biophysical properties are observable and correlated, making bioelectricity and all other associated biophysical readouts useful proxies of the holistic cell state. The relative ease that Levin, Cone, and others have experienced in directing cell fate by altering membrane potential through unrelated methods suggests that interventions that alter biophysical states are especially potent.

Given this, we have developed a screening platform to determine field parameters that control membrane potential and many other biophysical parameters. This enables a future of closed-loop systems that image biophysical observables in deep tissue, apply tuned fields, and repeat until the deep tissue is healed.

Neurostimulation Tools for Non-Neuronal Cells

Neurostimulation is the one of the most developed disciplines in biology that uses external fields for biomodulation (alongside energy-based tumor ablation). Non-invasive field therapies with

long-lasting effects are FDA approved, such as transcranial magnetic stimulation (TMS) for depression, OCD, smoking cessation, and migraines, and cranial electrotherapy stimulation (CES) for anxiety, insomnia, and pain.

Neurostimulation as a discipline is facing multiple difficult engineering challenges at once: sub-milimeter level precision is desired and fields must pass both the skull and intermediate brain tissue, which, as an ionic medium, acts like a faraday cage.

Using fields to stimulate non-neuronal tissue, however, likely only necessitates centimeter-level precision as structures of interest are much larger. There is also no skull in the way, so beamforming of ultrasound, for example, becomes much easier.

Neurostimulation has one advantage, though, despite being a much harder practical problem: neurons act somewhat like rectifiers. It is well known that nerves respond to AC electric fields with frequency dependency and convert the AC signal into an action potential, effectively DC. The field parameters that can polarize or hyperpolarize non-exciteable cells are yet unknown, though AION is poised to be the first to determine them.

Fields used in neurostimulation are limited by the 'focality / penetration depth tradeoff.' [Scopelitti 2020, Nurmi 2021, Deng 2012] Generally, fields that can be focused or beamformed, such as light, penetrate poorly. Fields that penetrate infinitely, such as static magnetic fields, have little ability to be focused. With the interest of deep tissue utilization at cm-precision, this restricts the practical choice of field parameters to a much smaller space. This restriction enables thorough exploration of the relevant parameter space, whereas the full space of theoretically possible fields would be prohibitively large to investigate.

Traditional biochemistry does not offer much insight into how fields can direct cell fate, but through the lens of bioelectricity, we know optimizable biophysical parameters to achieve cell level outcomes. Neurostimulation has determined some biochemical mechanisms of field-cell interactions in an electric context, such as the mechanosensitive Piezo ion channels that activate in response to ultrasound, or electric fields activating voltage-gated ion channels. Through this, bioelectricity gives the biochemical mechanism of field-cell fate interactions.

As Michael Levin said, "*you can take many neuroscience papers, do a find-replace: 'neuron' -> 'cell', & 'milliseconds' -> 'minutes', & get an interesting developmental biology paper.*"

Cell reprogramming is akin to development, so Levin's idea is extremely relevant. A reasonable prediction from the aforementioned biochemical ideas is that external fields that alter membrane potential will alter reprogramming rates and differentiation. This has now been confirmed: ultrasound has been used to reprogram fibroblasts into stem cells [Lee 2017] and endothelial cells [Kim 2019] through transient pore formation on the cell membrane.

The tools of neurostimulation exist, though no one has utilized them to gain precise control over cell fate in non-neuronal cells. AION will do this by pairing the external fields with real-time biophysical monitoring and putting an agent in the loop.

MRI as a Bioelectric Mapping Device

A fundamental problem that many in the bioelectricity field are trying to solve is the ability to image bioelectric patterns in deep tissue. This also needs to be solved to make our closed-loop bioelectricity-modifying device. Fortunately, we believe this problem is already solved.

From the start, the MRI was a bioelectricity-mapping device.

The MRI was originally created by Raymond Damadian to be a machine that could differentiate cancer tissue from healthy tissue based on a realization that electrical properties of the cells correlated with water dynamics. Damadian, in his 1971 paper proposing the MRI, stated "*My own experiments with Escherichia coli (6) suggested that altered selectivity coefficients of alkali cations in biologic tissue, such as occur in neoplastic tissue (5), can indicate alterations in tissue water structure.*" [Damadian 1971] Here, alkali cations are sodium and potassium, the prime charge carriers in bioelectricity, and tissue water structure changes are observable by the proposed MRI device.

In 2025, it was published that T2 times, a parameter that allows the MRI to have contrast between tissues based on water dynamics, correlate with experimentally altered membrane voltage. [Min 2025] Reviewers state that T2 may be altered by cell swelling from the experimental setup, though it is known that water activity and cell size are altered by depolarization without Min's intervention [Yellin 2018] and tissue size changes with bioelectric state in vivo [Rungta 2015, Shim 2025], so Min's results stand.

MRI's utilization as a bioelectric mapping device is further strengthened when considering T2 times and voltage across different tissue types. Generally, as a tissue type is more post-mitotic, it has a shorter T2 and more hyperpolarized voltage. The more proliferative or regenerative a tissue is, the longer its T2 and more depolarized the cells are. As a note of caution, the relationship is not perfect, as protein content and paramagnetic ion content can significantly influence T2 times. Regardless, longitudinal voltage changes in single tissues can be measured.

Within a single tissue type, as seen in the development of MRI, T2 times generally lengthen in cancerous vs. non-cancerous tissue, signifying less structured water -- a correlate of membrane voltage. Exhaustive work by Gilbert Ling and colleagues demonstrated that T2 differences between larger cancer tissue and smaller healthy tissue were not simply a consequence of cell size or paramagnetic ion content, but were from differences in water activity. [Ling 1990]

It is no coincidence that MRI observables are correlated to Vmem, as all biophysical parameters have crosstalk. An effective closed-loop bioelectric modulating system needs to be fast, low noise, and comfortable for patients. While low-field MRIs can help comfortability, other deep

tissue imaging modalities such as ultrasound give similar observables: tissue elasticity as measured by ultrasound, for example, is related to cell swelling. [Zheng 2006]

As Ling said in 1990, "*However, the expansive use of MRI is at present no more than a vision, a dream. It will come one day. But only after we have achieved a much higher degree of understanding of how living cells really function and malfunction. MRI can then be further engineered to tell about them in exact terms.*"

We now know the importance of bioelectricity and its correlation with MRI observables, enabling the MRI's expanded use as a key component in closed-loop bioelectric modulation, potentially alongside orthogonal deep tissue imaging techniques.

Bioelectromagnetics Literature

To gain complete control over cell fate, the membrane potential needs to be able to be controlled in both directions: both hyperpolarization and depolarization are required.

It tends to be much easier to depolarize a cell than hyperpolarize a cell. In neurons, this is because the neurons act like rectifiers and AC currents trigger action potentials. In non-exciteable cells, electroporation or sonoporation of the membrane tends to lead to potassium leakage and sodium influx, depolarizing the cell. It is not clear in the literature how to induce hyperpolarization with fields.

Outside of neurostimulation, the relevant literature to controlling cell fate with external fields falls generally under "bioelectromagnetics." The literature of this sort is mostly epidemiology regarding potential dangers of man-made radio equipment or electronics with a minority demonstrating interventional effects on cells.

There does happen to be examples of remote cell hyperpolarization in this literature. The most notable examples in a deep-tissue compatible context are the string of papers around the "ion cyclotron resonance" hypothesis by Liboff and a small amount of work on magnetoacoustics.

Biological ion cyclotron resonance (ICR) is a hypothesis proposed by Abraham R Liboff that attempted to explain 1970s data demonstrating enhanced ion flows from weak extremely low frequency magnetic fields. [Liboff 2013] In essence, it stated that an ion could resonate at its ICR frequency, where ions are accelerated in a circular path in an oscillating magnetic field parallel to a static magnetic field due to the Lorentz force. The main problem with the hypothesis is that the circle of acceleration is meters large, while the ions often have sub-nanometer distances of free movement available. A 2000 review proposing a different mechanism found the ICR hypothesis to violate Heisenberg's uncertainty principle [Binhi 2000], so the original ICR mechanism as laid out by Liboff in 1985 is not plausible. Mechanism is unsettled, but the data has been replicated and is profound: there are specific frequency and field strengths ratios, centered around ICR frequencies, that induce ion flows in living cells -- including hyperpolarizing currents.

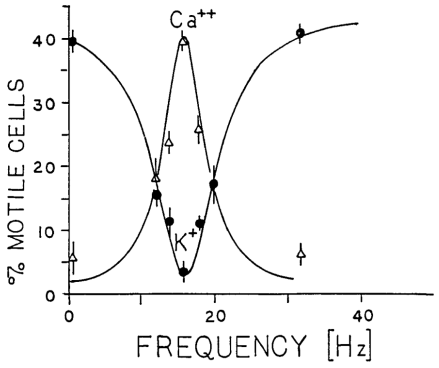

FIGURE 4. Potassium and calcium resonance curves. Two separate sets of data are shown superposed on the same frequency scale. The calcium data were obtained for diatoms exposed to minimal calcium concentrations, 0.25 mM Ca^{2+}. The potassium data were obtained for diatoms exposed to maximal calcium concentrations, 5 mM Ca^{2+}. The magnetic field B_o was adjusted to 20.9 μT for the calcium curve, corresponding to a cyclotron resonance frequency of 16 Hz at the charge-to-mass ratio for Ca^{2+}. For the potassium curve, B_o was set to 41.0 μT, corresponding to the charge-to-mass ratio for the potassium ion, again at 16 Hz. Thus, when superposed the resonance conditions for both ions occur at 16 Hz. The solid circles correspond to potassium and the open triangles to calcium. Note that whereas the Ca^{2+} resonant frequency acts to enhance cell motility, the K^+ resonant frequency acts to inhibit cell motility. Furthermore, the half-width of the K^+ resonance is about twice that of the Ca^{2+} curve.

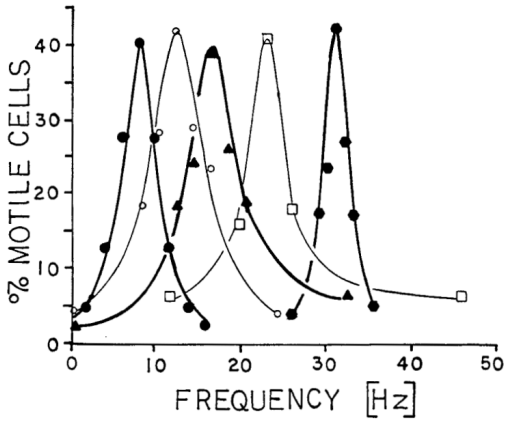

FIGURE 2. Calcium resonance curves. Fundamentals at 8, 12, 16, 23 and 31 Hz. B_o adjusted in each to maintain cyclotron resonance condition for Ca^{2+} charge-to-mass ratio. Solid circles, 8 Hz. Open circles, 12 Hz. Solid triangles, 16 Hz. Open squares, 23 Hz. Solid hexagons, 31 Hz. Error flags have been omitted, but in most cases the standard deviation is close to the symbol size for each data point. Range of standard deviations 0.2-3.0%, with the average error equal to 0.7%. Each data point represents the mean of six runs, with a minimal cell count of 600.

Figures adapted from McLeod 1987 demonstrating specificity towards biological effects at specific ICR-derived field parameters. Notably in Figure 4, K+ and Ca++ tuning give opposite effects, suggesting a plausible ability to both hyperpolarize and depolarize cells.

Inspiring Liboff's hypothesis, Ross Adey had already generated a large amount of high quality data on what would be known as "Adey windows:" bioeffects of magnetic fields not only were frequency dependent, but also amplitude dependent. [Tribute: Markov 2005] The idea of a window was somewhat controversial as biology is expected to be a warm, wet, and noisy environment and would not support resonances. Adey's data has been explored for decades and many researchers have found resonances in biology that enable potential hyperpolarization mechanisms. These resonances stand in contrast to the solely-depolarizing membrane permeabilization or neuronal action potentials -- they do not prohibit hyperpolarization.

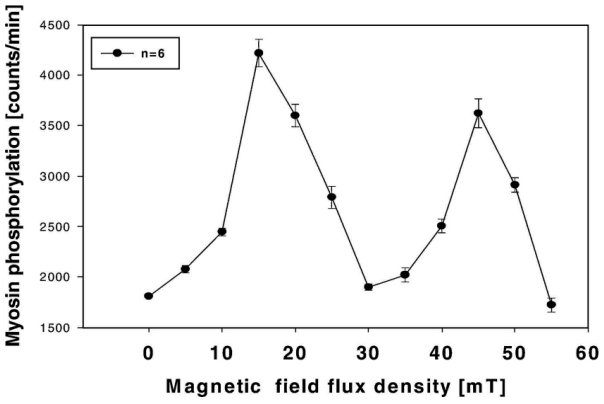

Figure 1. Myosin phosphorylation as function of applied static field.

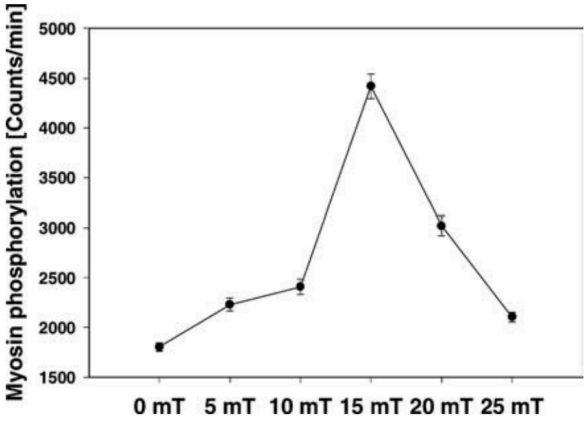

Figure 2. Myosin phosphorylation as function of applied pulsating magnetic field.

Figures adapted from Markov 2005 demonstrating magnetic field Adey windows with his ultrasensitive "biophysical dosimeter" readout of myosin phosphorylation, which is calcium dependent and has implications in bone and soft tissue healing.

Hyperpolarization is elusive in practice, though there are some success stories. Hu and colleagues achieved hyperpolarization in non-exciteable cells via magnetoacoustics in 2019. The effect appeared to require a magnetic field, which they propose synergizes with ultrasound to induce an electric field by accelerating ions through the field. However, in non-exciteable cells, the model does not explain how an electric field contributes to membrane potential as there is no clear action potential-like mechanism to rectify the field. Furthermore, the act of magnet removal may cause differences in the ultrasonic field by changing chamber geometry.

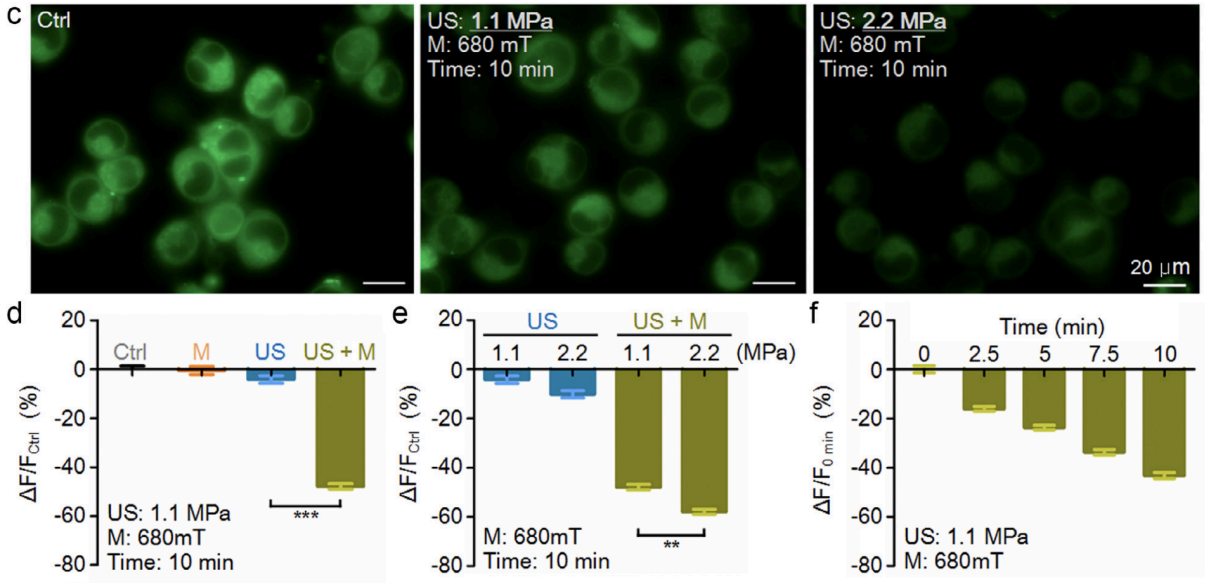

Figure from Hu 2019 demonstrating reduction in fluorescent intensity of DIBAC4(3), signifying hyperpolarization over 10 minutes only in the presence of ultrasound and a static magnetic field.

Despite encouraging data, replication is difficult in bioelectromagnetics and proposed physical models are messy and often wrong.

Mechanistic ambiguity is not a significant roadblock. Using closed-loop feedback, we can be mechanism-agnostic and let an agent determine optimal field parameters. Regardless, we can still benefit from previous mechanistic work by robustly replicating successes and testing boundaries of previous hypotheses. The record of success in the literature, even if physical models are wrong, is encouraging for discovery prospects.

Thymus as Beachhead Market

It has been robustly demonstrated by CD Cone Jr that proliferation can be controlled by bioelectricity. Novocure, which currently makes >$600M in yearly revenue, developed a device that uses electric fields to slow cancer growth: "Tumor Treating Fields." The mechanism is

somewhat unknown [Moser 2022], though it is plausible that the device alters membrane potential of cancer cells remotely. [Li 2020]

Furthermore, Michael Levin has repeatedly demonstrated that cell fate can further be controlled using bioelectricity. [Levin 2008, Levin 2013] There is therefore evidence that bioelectricity can control proliferation, differentiation, and dedifferentiation. All of these can be applicable in thymus-related indications.

Thymus regeneration post-chemotherapy is a tractable first market. Globally, ~20M new cancer cases occur each year, with about half receiving chemotherapy. Severe immunosuppression affects roughly a third of these patients, leaving ~3M individuals annually with no good solution beyond G-CSF regimens. At pricing comparable to G-CSF ($25K+ per course), the immediate oncology TAM is roughly $80B. Even priced more accessibly, the market remains substantial.

The FDA endpoints for thymus-directed therapies are organ size and T-cell counts. Thymic involution follows a defined trajectory in which thymic epithelial cells (TECs) transition into fibroblasts and subsequently adipocytes. Each step along this trajectory presents a potential point of intervention: doing virtually anything to cell fate can be useful in a thymic context.

Dedifferentiation of adipocytes back into fibroblasts may enable future TEC differentiation, while re-differentiation of fibroblasts into TECs restores the epithelial scaffold. Induction of TEC proliferation could expand thymic capacity, and enhancement of T-cell proliferation directly improves immune output. Since bioelectric modulation has been shown to influence proliferation, differentiation, and dedifferentiation, these mechanisms together suggest a range of possible strategies for restoring thymic function.

The thymus also serves as a beachhead into broader longevity. Beyond cancer recovery, age-related thymic involution drives immune decline, autoimmunity, and infection risk. A therapy that restores thymic output has applications not only in oncology but also in extending healthspan and lifespan across aging populations.

For the thymus, the flagship device will be a smaller version of what can be thought of as a “read & write MRI,” as in, a device that images bioelectricity of the thymus while applying fields. Since the thymus is located in a small part of the upper chest, portable MRIs that focus on a small part of the body represent a likely form factor (e.g., similar to Hyperfine’s Swoop).

Summary

AION is developing closed-loop systems to read and write bioelectricity in deep tissue. This addresses the shortcoming of molecular-based approaches to reprogramming and is a novel path towards bringing aging under complete biomedical control.

We are seeking adaptable engineers aligned with our mission of advancing human longevity to develop hardware at the intersection of acoustics, magnetism, and RF.