

Signals through salt: Building machines that use the language of biology

Physiological communication relies primarily on ions to carry signals. The emerging field of bioiontronics aims to build engineered devices that can do the same.

By Yujia Zhang and Hagan Bayley

Since life began on Earth, biology has spoken the language of ions. Often called electrolytes, salt-derived ions—such as calcium, potassium, and magnesium—are used in the human body to send signals that regulate processes like nerve signaling and the beating of the heart. Scientists are only just beginning to catch up and develop devices that use ions, rather than electrons, to carry information with charge. In 2007, researchers demonstrated an ion-ejection device built from polymers that controlled the ion signaling of neurons in a petri dish. From there, the nascent field of bioiontronics—communication with living matter through ions and molecules for the detection and modulation of biological activities—has expanded.

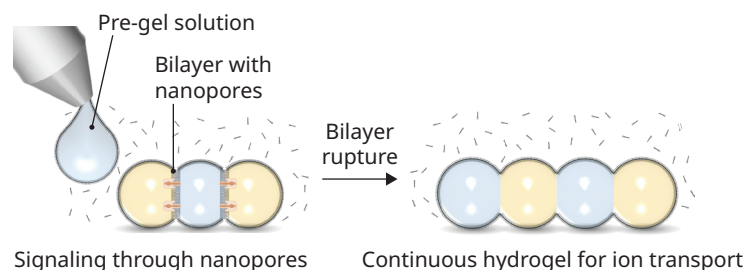
The prospect of seamlessly exchanging ionic signals with biological systems makes bioiontronic devices appealing for medical applications. You might envision, for example, using ion pumps and iontronic diodes to modulate brain activities through the one-way release of ions and neurotransmitters. Conversely, ionic signals transmitted from biological environments into bioiontronic devices could enable the detection of biological activities. Iontronic devices for targeted drug delivery are in preclinical stages of development, and certain recording devices, such as DNA sequencers, are already commercially available.

Unlike iontronic devices, conventional metal-based electrodes, such as those used to monitor brain activity or heartbeats, are commonly used for the stimulation and measurement of electrophysiological activities—action potentials from individual cells and local field potentials from groups of cells. Changes in electric fields are the composite result of assorted ion movements. Conventional electrodes, therefore, cannot be used to identify a specific ion species or read out the molecular information behind a given cellular activity. In that regard, bioiontronics offers more precise selection of ionic and molecular species and provides novel capabilities for the detection of disease markers, such as electrolyte imbalances, certain neurotransmitters, and protein biomarkers.

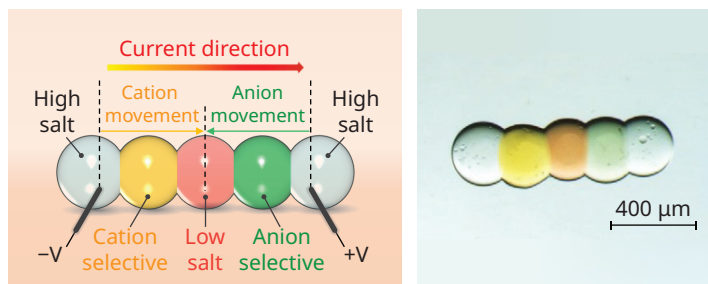
Recent advances in mechanisms, materials, device prototypes, and system designs have shown the potential of iontronic devices at biological interfaces. Below, we explore one category of devices: droplet-based devices, termed droplettronics.

Droplettronics

For minimally invasive applications in medicine, it is preferable for bioiontronic devices to be miniature, soft, and biocompatible and have the capability for both functionality and responsiveness, such as biode-



◀ **Figure 1.** To create droplettronic devices, hydrogel droplets are deposited into a surfactant-containing oil with a micropipette, and the droplets self-assemble through the formation of droplet interface bilayers. Protein nanopores (**left**) can be inserted into the bilayers to permit ionic and molecular conduction. Alternatively, photoinitiated rupture of the droplet interface bilayers can be used to form a continuous ion-conductive structure (**right**).



◀ **Figure 2.** A microscale droplet-based 125 mV power source is shown schematically (left) and in a bright-field image (right). Food dyes are used to distinguish droplets with different compositions. (Figure adapted from Y. Zhang et al., “A microscale soft ionic power source modulates neuronal network activity,” *Nature* **620**, 1001, 2023.)

gradability and remote-controlled activation. Droplettronics, which are fabricated from tiny hydrogel droplets, hold potential to meet those requirements.

To form droplettronic devices, such as the one shown in figure 1, picoliter to microliter hydrogel droplets are deposited in a surfactant-containing oil. The surfactants rapidly self-assemble on the droplets’ surfaces to form a monolayer coating. When two droplets are brought together, a metastable bilayer forms between them. Multiple droplets can be deposited to form linear, 2D, or 3D networks.

There are three key benefits of the surfactant-supported droplet assembly process. First, each droplet can contain different materials, including nanoparticles and various solutes. The droplets can therefore be used to build heterostructured, tailored devices, such as power sources, transistors, and logic gates like those used in conventional electronics.

Second, the droplet interface bilayers can incorporate nanopores or channels to allow communication between droplets. That ability has been used to investigate ion transport through membrane channels and to develop synthetic tissues. Third, external activation sources, such as temperature, light, or pressure changes, can be used to rupture the droplet interface bilayers and produce a continuous hydrogel structure without compromising the distinctness of each droplet. That hydrogel structure offers biocompatibility, strong mechanical stability, and, after bilayer rupture, high ionic conductivity.

Stand-alone droplettronic devices will require a battery to power them. With a design inspired by the electricity-producing cells in electric eels, teams (led by the authors of this article) at the University of Oxford and EPFL, the Swiss Federal Institute of Technology in Lausanne, produced a power source by depositing a five-droplet chain consisting of a low-salt droplet and two high-salt droplets separated by two charge-selective droplets, as shown in figure 2. The five droplets create a salt concentration gradient that allows cation movement in one direction and anion movement in the other, thereby producing an output ionic

current. The bilayers between the droplets enable the formation of a stable droplet network in which energy is not dissipated until a connection is made between droplets, either through nanopores or triggered rupture of the bilayers.

The design provides a soft ionic power source that is more than five orders of magnitude smaller by volume than previous hydrogel power sources. The device has been used as a biocompatible current source to modulate the electrical activities of neural tissues *in vitro* and in *ex vivo* mouse brain slices.

Other droplettronic power sources have been developed through the incorporation of various energizing materials, such as lithium-containing particles, used to form tiny lithium-ion batteries, and metabolic molecules, used for enzyme-enabled biobatteries. The inclusion of magnetic particles enables droplettronic devices to move under an external magnetic field in a way that allows them to be used as microrobots, including ones that are microscale mobile power sources. In research settings, those techniques have been used to power the movement of charged drug molecules and the defibrillation and pacing of *ex vivo* mouse hearts.

By configuring droplet combinations, the teams have developed diodes, transistors, various reconfigurable logic gates, and synthetic synapses with ionic memory effects. The various droplettronic components and their circuitry configurations represent a step forward in the development of integrated iontronic circuits with a wide range of potential applications. Already, researchers have fabricated a droplettronic device that can interface with living heart cells and record the ionic signals produced by their coordinated beating.

Outlook

Several challenges remain for developing droplettronic devices. For example, interfaces between droplets can currently undergo a one-time-only irreversible rupture that serves as an off-to-on switch for the droplettronic power source. A reversible process would be a

significant improvement for energy applications and other functionalities. In biological environments, the harnessing of endogenous energy resources, such as glucose or ATP (adenosine triphosphate), might provide a long-term energy solution for droplettronic implants. Further, enhanced robustness under biological conditions demands advances in the selection of materials, device design, system integration, and encapsulation.

Droplettronics are just one example of the variety and potential of bioiontronics. Other bioiontronic device platforms include solid-state nanofluidic chips and macroscopic polymer devices, to name but two. The future of the field lies in the fabrication of complete bioiontronic systems and the integration of those components with living tissues. Potential applications for bioiontronics include quantitative sensing, early disease detection, *in situ* drug synthesis, spatiotemporal control of drug delivery, and the motility and control of microrobots. Achieving that potential will require interdisciplinary knowledge, from fields including microtechnology, physics, chemical biology, electrochemistry, bioelectronics, and biomedical engineering.

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Additional resources

- ▶ J. Luo, A. Remy, Y. Zhang, “Iontronic devices from biological nanopores to artificial systems: emerging applications and future perspectives,” *Chem. Rev.* **125**, 11840 (2025).
- ▶ D. Wei et al., “Flexible iontronics based on 2D nanofluidic material,” *Nat. Commun.* **13**, 4965 (2022).
- ▶ M. Berggren et al., “In vivo organic bioelectronics for neuromodulation,” *Chem. Rev.* **122**, 4826 (2022).
- ▶ Y. Zhang et al., “A microscale soft ionic power source modulates neuronal network activity,” *Nature* **620**, 1001 (2023).
- ▶ J. Isaksson et al., “Electronic control of Ca^{2+} signalling in neuronal cells using an organic electronic ion pump,” *Nat. Mater.* **6**, 673 (2007).

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