VIEWPOINT

SCIENTIFIC DISCOVERY AND THE FUTURE OF MEDICINE

Electronics for the Human Body

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The human body is soft, curvilinear, and continuously evolving; modern electronic devices are rigid, planar, and physically static. Recent research has yielded a complete set of advanced materials, manufacturing approaches, and design layouts that eliminates this profound mismatch in properties. The resulting devices can intimately integrate onto or into the human body for diagnostic, therapeutic, or surgical function with important unique capabilities in biomedical research and clinical medicine. These emerging technologies have strong potential to improve human health and to enhance the understanding of living systems. They fall into 3 categories—soft, injectable, and bioreabsorbable electronics—each demonstrated in extensive animal studies and several in initial human trials. The **Figure** presents images of bioelectronic devices.

Soft Electronics

Configuring hard, inorganic functional materials into thin, open mesh microarchitectures and embedding them in soft, elastomeric films provides a route to electronic systems, such as circuits and sensors, and optoelectronic systems, such as light-emitting diodes and photodetectors, that combine state-of-the-art operational characteristics with soft, elastic mechanical properties, even under large-strain deformations. Such devices can be bent, twisted, folded, stretched, and conformally wrapped onto arbitrarily curved objects, without significant change in performance.[1] When implemented with biocompatible interface materials, this mechanics enables intimate integration with the soft, curvilinear surfaces of major organ systems such as the brain, heart, and skin, without constraint and in ways that would be impossible using conventional wafer-based devices built and packaged on standard, rigid, printed circuit boards. Examples include balloon catheters with surface-mounted arrays of electronic sensors and actuators configured for use in high-resolution mapping of endocardial electrophysiology and in pulmonary vein ablation therapy for atrial fibrillation.[2]

Related embodiments involve 3-dimensional elastic membranes similarly instrumented and specially shaped to envelop the entire 3-dimensional surface of the heart, as an electronic artificial pericardium capable of performing spatially and temporally programmable pacing, low-energy defibrillation, and other forms of cardiac electrotherapy.[3] Thin, flexible sheets of dense collections of actively amplified sensors constructed using these same concepts can perform multiplexed electrocorticography with a resolution that far exceeds that of passive electrode arrays currently used to guide surgical interventions for treating certain forms of epilepsy.[4]

The most technically mature examples of soft electronics are in devices with thicknesses and stiffnesses that match those of the epidermis. The result enables intimate, yet imperceptible, lamination onto the surface of the skin, for applications ranging from clinical diagnostics to continuous monitors of health and wellness.[5] Proven operational modes include measurement of pressure pulse waves in near surface arteries; of thermal transport properties, stiffnesses, and hydration levels of the skin; of biopotentials associated with activity of the brain, heart, and skeletal muscles; and of full-body motion and posture. Wireless capabilities for power delivery and data communication are now available in research devices that offer measurement fidelity comparable with that of conventional, large-scale clinical apparatus.[6] Human trials in sleep studies, in assessment of wound healing, in characterization of dermatologic malignancies, and in continuous kinematic measurement of patients with motion disorders suggest a broad set of near-term opportunities.

Injectable Electronics

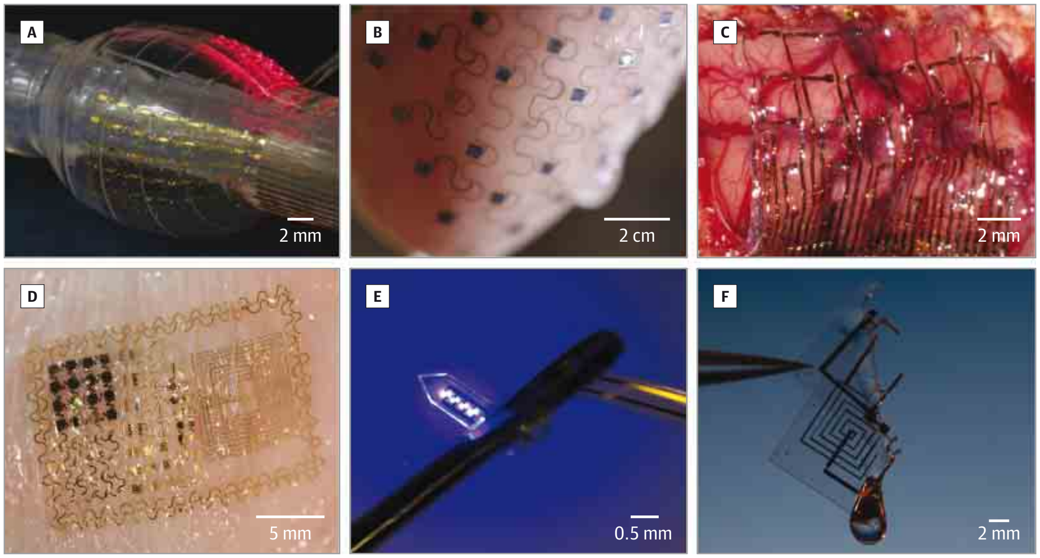
Extensions of these ideas allow for delivery of electronics not only onto the surfaces of organs but also at well-controlled locations into their depths. Here, flexible filaments serve as supports for microscale-device components that can be transported to targeted regions in a minimally invasive fashion by use of thin, releasable injection needles. The most advanced examples consist of multilayered stacks of active components, including wirelessly controlled light-emitting diodes with dimensions comparable with those of a single cell for stimulating and monitoring selected collections of neurons in the central and peripheral nervous systems via mechanisms of optogenetics.[7]

The results reveal, in one example, connections between complex behaviors and the structure and function of the brain, where wireless control of light-emitting diodes in the locus coeruleus—a brain region with known longitudinal noradrenergic cell bodies—leads to activation of dopaminergic neurons to yield salient stimuli sufficient for behavioral conditioning. The same concepts have the potential to provide new functional capabilities in deep-brain electrical stimulation through replacement of standard stimulating electrodes with full, cellular-scale integrated circuits, with additional possibilities for application in other organs.

Bioresorbable Electronics

The process of releasing the injection needles described above involves bioresorption of a thin adhesive layer upon contact with cerebrospinal fluid. Recent work demonstrates that this concept of bioresorbable materials in biointegrated electronics can be extended to entire functional systems, where all of the materials, both active and passive, dissolve completely in a controlled fashion and with programmable rates when immersed in biofluids.[8] Wide-ranging options

Figure. Images of Biocompatible Electronic Devices



A, Inflated balloon catheter equipped with arrays of sensors for pressure, flow, and contact along with actuators for ablation therapy and light-emitting diodes for optical characterization. B, Three-dimensional membrane wrapped around the entire surface of the heart for cardiac electrotherapy. C, Actively multiplexed sheet of electronics laminated onto the surface of the brain for high-resolution electrocorticography. D, Wireless electronics mounted on the skin for continuous, multimodal monitoring of physiological status. E, Injectable optoelectronic system threaded through the eye of a sewing needle and wrapped around its shaft to highlight the small dimensions and flexible mechanics. F, Bioresorbable electronic circuit, partially dissolving in a drop of water. All of the constituent materials dissolve at controlled rates into harmless end products when exposed to biofluids.

in sensing, wireless data transmission, power supply, and actuation are now available in devices that exhibit good biocompatibility in cell-level toxicity studies and animal trials. Demonstrated examples with clinically relevant utility include electronic appliques designed to eliminate infections at surgical sites, intracranial pressure, and temperature monitors for patients with traumatic brain injury, nerve stimulators that mitigate pain and accelerate regeneration, pacemakers for use during postsurgical recovery, and electronically programmable vehicles for drug release. Such devices provide high-performance, stable operation for a desired time frame, and then completely resorb to eliminate unnecessary device load on the body. Successful animal studies of these and other bioresorbable electronic systems demonstrate capabilities of relevance to unmet clinical needs.

Outlook

New opportunities afforded by biocompatible electronics have the potential to profoundly affect the future of biomedical research and clinical care. The scalability and diversity of options in multifunctional operation create a rich range of promising directions for further development and deployment. An important perspective is that the materials and device designs of many of the component building blocks align well with those found in the consumer electronics industry, thereby offering synergies for accelerated improvements in performance and scale. In this way, it is possible to realistically contemplate biocompatible transistors, light-emitting diodes, photodetectors, electrodes, and interconnects formed at submicron dimensions, in multilayered formats, with levels of integration that approach billions of devices, over areas of hundreds of square centimeters.

The most significant near-term opportunities are in surgical and diagnostic devices and in skin-mounted, continuous health monitors. Bioresorbable sensors and therapeutic devices, sometimes referred to as *bioelectronics medicines*, or *electroceuticals*, represent additional areas with significant promise. A longer-term vision involves the use of biocompatible electronics as long-term implants, for which a key additional technical challenge is in the development of thin flexible layers of materials that can serve as robust long-lived barriers to biofluids. This topic and others in chemical sensors, active microfluidics, and power-harvesting devices represent promising directions that can be pursued in parallel with more immediate efforts in translating proven technologies into clinical practice.

ARTICLE INFORMATION

Conflict of Interest Disclosures: The author has completed and submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest and reports that he has received grants and personal fees from MC10 Inc and has patents, several of which through the University of Illinois are licensed.

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