# Bio-Integrated Electronics

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***Abstract*—Strategies for bio-integrated electronics must overcome challenges associated with the mismatch between the hard, planar surfaces of brittle semiconductor wafers and the soft, curvilinear tissues of timely dynamic biological systems. This paper discusses the successful structural design, fabrication and bio-integration of tissue-like electronics that can intimately conform to biological tissues and deform with the tissues in a mechanically invisible manner. Examples including epidermal electronics, instrumented balloon catheters, and smart finger tubes will be discussed to manifest our multidisciplinary research at the boundary of electronics, mechanics, materials, and biomedicine.**

***Keywords—flexible electronics; mechanics; materials processing; sensing; stimulation***

## I. Introduction

Research on flexible electronics started nearly two decades ago [1, 2] with the demand for macroelectronics (i.e., large-area electronics), such as paperlike flexible displays [3]. Early research focused on organic semiconductors because their intrinsic deformability, light weight, and low manufacturing cost are appealing for large-area flexible electronics, especially when merged with roll-to-roll processes [4]. But the chemical instability of organic semiconductors and limited electronic performance have somewhat restricted their application in high-speed, low-power, or long-lasting electronics. In contrast, inorganic semiconductors represented by silicon exhibit high carrier mobility and on-off ratio as well as excellent chemical stability under ambient environments [5]. Furthermore, the electronic and mechanical properties of inorganic semiconductors have been well defined and the manufacturing processes are well established after more than 100 years of research and applications. Thus flexible electronics based on crystalline inorganic semiconductors started to emerge in the mid-2000s [6]. To overcome the rigidity of inorganic electronic materials, thin film mechanics has been applied to enhance their deformability and mechanical reliability.

## II. Mechanics: Bendability and Stretchability of Inorganic Electronic Materials

Inorganic materials such as silicon and metals are stiff and easy to rupture or yield when strains in them exceeds even very small values, such as 1%. But the mechanical limit of a structure can be offset by the geometry of the construction even for intrinsically fragile materials.

Basic beam theory predicts that the bending-induced maximum strain of a membrane is proportional to the product of membrane thickness and bending curvature. If the maximum strain is limited to a critical strain-to-rupture of the material (e.g., 1%), the maximum allowable bending curvature will be inversely proportional to the thickness of the membrane, as shown in the log-log plot of Figure 1. As the thickness of silicon decreases from millimeters to nanometers, the attainable bending curvature can be enhanced by six orders of magnitude. As a result, although bulk silicon wafers are rigid plates (Fig. 1A), silicon nanomembranes (with a thickness of ~100 nm) can be readily arched to the radius of a folded paper (~0.1 mm) without rupture, as shown in Figure 1C.

Building on this unprecedented bendability, silicon nanomembranes can be made stretchable by applying two prevailing design strategies. One strategy calls for bonding flat nanoribbons to a prestretched soft elastomeric substrate to produce wrinkled nanoribbons (represented in Figure 2A) [6-8]. When the prestretch is released, the elastomeric substrate fully retracts, inducing out-of-plane periodic sinusoidal buckling in the nanoribbons in a mechanism similar to the Euler buckling of an elastic rod under axial compression. Nanomembranes bonded to biaxially prestretched elastomeric substrates form two-dimensional wrinkled patterns as shown in Figure 2B [9]. Buckling instabilities offering large displacement out of small strains are desirable deformation mechanisms in stretchable electronics.

With the other strategy, isolated rigid islands linked by buckled linear metallic ribbons (Figure 2C) can be stretched up to 40% without mechanical failure [10-12]. When serpentine ribbons (Figure 2D) are used instead of linear ribbons, stretchability of the system can vary from 10% to 300% depending on the serpentine geometry [13-15].

Both buckling and serpentine strategies have been proven effective in keeping strains in silicon or metal below 1% when

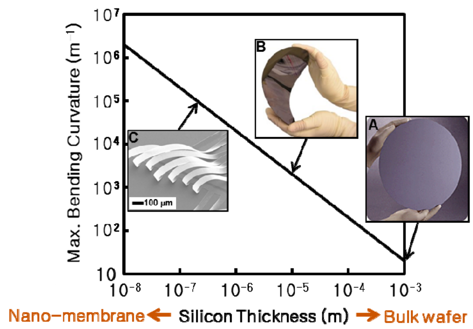


Fig. 1. Maximum allowable bending curvature as a function of silicon membrane thickness, with insets showing the bendability of (A) a bulk silicon wafer, (B) a silicon thin film, and (C) silicon nanoribbons.

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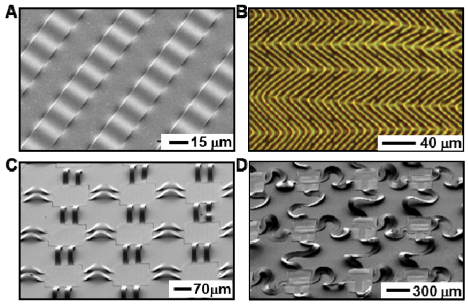


Fig. 2. Structural designs of stretchable electronics enabled by the mechanics of film-substrate interaction. (A) Silicon nanoribbons buckled on uniaxially prestretched soft elastomer. (B) Silicon nanomembrane buckled on biaxially prestretched soft elastomer. (C) Isolated device islands interconnected by popped-up linear metallic ribbons. (D) Isolated device islands interconnected by serpentine-shaped metallic ribbons.

the polymer substrate is subjected to significant bending or stretching. Thin film mechanics as such offer ways to overcome the intrinsic brittleness and stiffness of inorganic semiconductors and open the door for their applications in flexible and stretchable electronics.

## III. Materials Processing: Microtransfer-Printing

Microtransfer-printing technology developed for single crystal inorganic semiconductors [16-18] has enabled the integration of high-performance electronics on deformable substrates to create flexible displays [19], high-efficiency flexible solar cells [18, 20], bio-inspired electronic eye cameras [11, 21], and bio-integrated electronics [22-24].

Figure 3 illustrates the representative two-step microtransfer-printing method. The fabrication begins with the high-temperature process such as doping silicon nanomembranes on silicon-on-insulator (SOI) wafers. Preprocessed monocrystalline silicon nanomembranes are then released from the SOI wafer and printed onto the polyimide (PI)-coated rigid handle wafer using elastomeric stamps; the precoated PI layer serves as a support and encapsulation layer for silicon, metal, and other functional materials. Conventional low-temperature microfabrication processes (e.g., sputter, thermal, or electron beam deposition, low-temperature chemical vapor deposition of dielectrics, photolithography, wet or dry etching, and so on) can then be readily performed on the PI-coated rigid handle wafer. The circuit is eventually patterned into stretchable serpentine-meshed networks and transfer-printed from the handle wafer onto a wide variety of deformable substrates, again using elastomeric stamps, to render a fully functional flexible/stretchable system.

Because high-quality monocrystalline silicon is used as the semiconductor and low-resistance gold wires are used as the conductor in these devices, their electronic performance and long-term chemical reliability are on par with wafer-based electronics while high flexibility and/or stretchability is incorporated through the multilayer lamination and the serpentine design. Similar fabrication strategies are applicable to the fabrication of stretchable AlInGaP optoelectronics [25] as well as gallium arsenide (GaAs) photovoltaics [12].

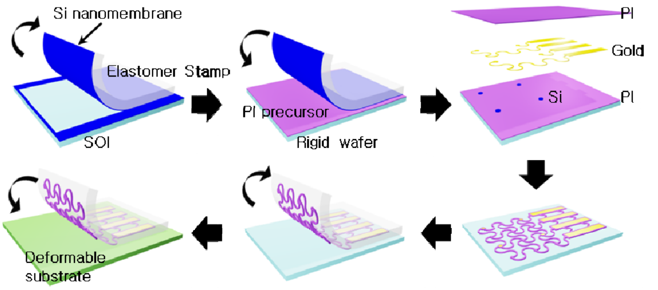


Fig. 3. Schematics of the fabrication procedures of stretchable electronics: transfer doped silicon (Si) nanomembranes from silicon on insulator (SOI) wafers onto polyimide (PI)-coated rigid handle wafer with an elastomer stamp. Silicon patterning and metallization are followed by PI encapsulation. Dry etching of PI defines the serpentine open mesh structure. Finally the well-fabricated stretchable circuit is transferred from rigid wafer to a deformable substrate.

## IV. Functionalities: Epidermal and in Vivo Sensing

With the maturity of the enabling technology for microtransfer-printing, flexible and stretchable electronics found their exemplary applications in the late 2000s with the emergence of bio-integrated electronics, a field that has greatly facilitated epidermal and in vivo sensing [26].

For conventional epidermal sensing, electrophysiological electrodes are mounted on the skin (via adhesive tape, mechanical straps, or needles) with terminal connections to separate boxes that house collections of rigid circuit boards, power supplies, and communication components [27, 28]. These systems have many important capabilities, but they are poorly suited for practical application outside of research labs or clinical settings.

The development of novel electronic systems with matching form factors and the mechanical properties with bio-tissues is essential for long-term, intimate bio-electronic interfaces. To that end, the application of filamentary serpentine structural designs and microtransfer-printing methods has enabled the development of ultrathin, ultrasoft electronics composed of high-performance inorganic materials. Such bio-integrated electronics have in turn led to exciting epidermal and in vivo bio-integrated sensors such as tattoo-like vital sign monitors [14, 29, 30], brain-computer interfaces [31, 32], electrocardiogram (ECG) mapping devices [33, 34], and smart or minimally invasive surgical tools [13, 35].

Figure 4 illustrates the use of bio-integrated electronics for epidermal and *in vivo* physiological sensing. Electroencephalograph (EEG) measurements are shown in Figure 4A, where an epidermal electronic systems (EES) is gently laminated on human forehead in a manner much like a temporary transfer tattoo, which is mechanically invisible to the wearer [14]. Because the EES is so thin, the attachment can be solely enabled by van der Waals force without any conductive gels or adhesives, these systems can function for more than two weeks at exactly the same location on the skin

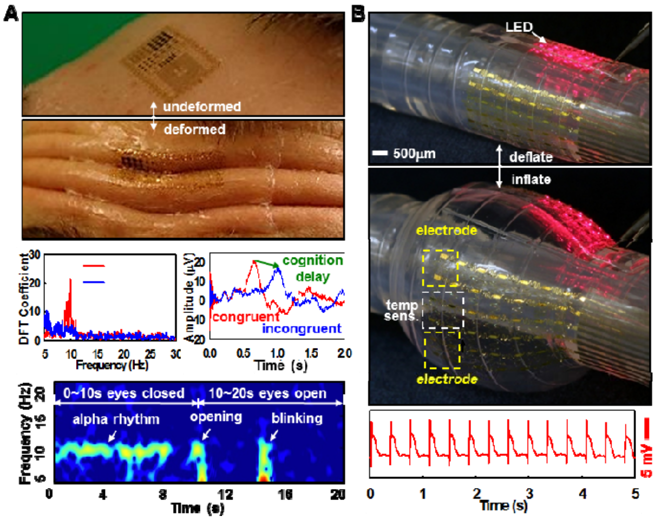


Fig. 4. Bio-integrated sensors based on stretchable electronics. (A) Ultrathin, ultrasoft epidermal electronic system (EES) laminated on a human forehead to read human electroencephalograph (EEG) (upper frames). Discrete Fourier transform (DFT) coefficients of EEG alpha rhythms (middle left), demonstration of Stroop effects in EEG (middle right), and spectrogram of alpha rhythm (bottom). (B) Multifunctional "instrumented" balloon catheter incorporating stretchable electrophysiological and radio frequency ablation electrodes, temperature sensors, pressure sensors, flow sensors, and arrays of microscale inorganic light-emitting diodes (μ-ILEDs) performing electrocardiogram (ECG) recording of a rabbit heart.

without worrying about the decomposition of the adhesives. Depending on where the electronic tattoo is placed, EEG, ECG, and EMG (electromyogram) measurements are possible with very high signal-to-noise ratios, thanks to the low impedance enabled by the intimate bio-electronics interface.

In addition to electrophysiological sensing, studies have successfully demonstrated the monitoring of skin temperature, mechanical deformation (strain), and hydration [14, 29, 30, 36]. Wireless power and data transmission coils [14] as well as stretchable batteries [15] and stretchable memory patches [37] further contribute to the standalone operation of wearable physiological sensors.

Soft electronics can integrate with not just human skin but also internal organs for *in vivo* monitoring. As an example, Figure 4B shows a multifunctional, "instrumented" balloon catheter that starts in a small initial diameter to travel through human veins and then inflates by 200% in cardiovascular cavities to perform minimally invasive surgeries such as the deployment of coronary stents or radio frequency (RF) ablations. Electrodes and sensors for temperature, contact, and flow integrated on the balloon skin provide *in vivo* endovascular and endocardial information, which used to be very difficult to access simultaneously [13]. Studies have also shown the effectiveness of other *in vivo* functionalities, such as epicardial EKG and beating amplitude sensing [33, 34] as well as the mapping of brain activities [31, 32, 34].

## V. FUNCTIONALITIES: STIMULATION AND TREATMENT

The most sophisticated version of bio-integrated electronics is a fully automated, closed-loop sensing-diagnosis-feedback device; the "feedback" that the device transmits to human can be either information or therapeutics. Although the development of closed-loop bio-integrated electronics is not yet fully realized, several types of stimulation and treatment devices are available.

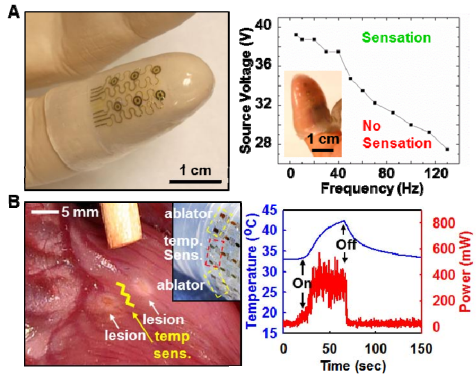


Fig. 5. Bio-integrated electrotactile stimulation and treatment tools based on stretchable electronics. (A) Wearable, conformable finger tube generates electrotactile sensation on human fingertip with suitably modulated current. (B) Lesions on a rabbit heart created by radio frequency (RF) ablators integrated on a balloon catheter (left frame). The supplied RF power and in situ tissue temperature measured by adjacent temperature sensors are shown in the right frame.

One type involves the administration of a modulated electrical current to human skin to excite cutaneous mechanoreceptors, which provide instantaneous electrotactile feedbacks to the wearer in an acute and time-controlled manner [38]. Figure 5A features a smart wearable finger tube that integrates high-performance inorganic electronics to sense finger-tip motion and provide electrotactile stimulation. The voltage-frequency combination to enable electrotactile sensation is shown in the right frame of Figure 5A [39].

As an *in vivo* example, Figure 5B shows lesions on a live rabbit heart, treated by RF ablation as a therapeutic procedure to stop heart arrhythmia. The ablation was performed using stretchable electrodes on an inflatable balloon catheter [13]. Lesion size and depth can be determined with the use of *in situ* temperature monitoring during RF ablation (right frame). *In vivo* pretreatment sensing can provide critical information to guide treatment, and *in vivo* post-treatment sensing can provide immediate data to evaluate treatment results and help guide the next treatment if any.

## VI. OUTLOOK

In the past decade, studies on mechanics, materials, and microfabrication techniques have advanced the design and manufacture of flexible and stretchable electronics, and it is likely that bio-integrated electronics will soon revolutionize personal health care and human-machine interaction.

Further progress will likely entail advances in the following areas. Maximization of the application potentials of wearable and implantable electronic systems will require the development of mechanically compatible and electronically sufficient microcontrollers, memory, power supply, and wireless data transmission modules. Multifunctional compliant systems that incorporate optical and biochemical tools would also be desirable. Another frontier of bio-integrated electronics concerns transient electronics [40], which can be bio-absorbed after performing designed functions. Roll-to-roll transfer printers for the deterministic assembly of inorganic semiconductors on polymer substrates hold the key for large-volume, low-cost manufacture of bio-integrated electronics [41]. More detailed discussion on the mechanics, materials, and functionalities of bio-integrated electronics is available in several recent review articles [22-24, 42].

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