Silicon electronics on silk as a path to bioresorbable, implantable devices

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Many existing and envisioned classes of implantable biomedical devices require high performance electronics/sensors. An approach that avoids some of the longer term challenges in biocompatibility involves a construction in which some parts or all of the system resorbs in the body over time. This paper describes strategies for integrating single crystalline silicon electronics, where the silicon is in the form of nanomembranes, onto water soluble and biocompatible silk substrates. Electrical, bending, water dissolution, and animal toxicity studies suggest that this approach might provide many opportunities for future biomedical devices and clinical applications. © *2009 American Institute of Physics*. [doi:10.1063/1.3238552]

Advanced implantable biomedical devices have great potential in clinical applications.[1] Systems that allow insertion into the body to establish conformal contact with the curvilinear surfaces of various organs must be flexible and biocompatible. The conformal and flexible characteristics could be enabled by recently reported organic, inorganic, and nanomaterial based electronics.[2–4] Achieving biocompatibility, on the other hand, can be challenging, due to the complex nature of the biological response to many organic and inorganic materials. An ideal solution to this problem that largely avoids the longer term issues involves the construction of the electronics out of materials that are soluble and biodegradable; here the device simply disappears, or resorbs, over time. Alternatively, a large fraction of the device can be designed to resorb, such that a sufficiently small amount of material remains that its induced biological response is negligible. This approach has the advantage that it does not require the development of an entire set of biogradable electronic materials, but still yields an overall system that dissipates bulk material features at a rate suitable for the application. Here we report the combination of silicon electronics, based on nanomembranes of silicon, with biodegradable thin film substrates of silk protein, to yield a flexible system and device that is largely resorbable in the body. The use of silicon provides high performance, good reliability, and robust operation. Silk is attractive, compared to other biodegradable polymers such as poly(glycolic acid), poly(L-lactic acid), and collagen, because of its robust mechanical properties, the ability to tailor the dissolution, and/or biodegradation rates from hours to years, the formation of noninflammatory amino acid degradation products, and the option to prepare the materials at ambient conditions to preserve sensitive electronic functions.[5,6]

Figure 1 shows the schematic fabrication process. We used single crystalline nanomembranes of silicon (thickness ~260 nm p-type, SOITEC, France) to construct transistors on ultrathin sheets of polyimide (PI), using procedures similar to those described previously.[7,8] Briefly, the doped silicon nanomembranes were transfer printed onto a film of PI (PI, ~1.2 μm, Sigma Aldrich, USA) cast onto a thin sacrificial layer of poly(methylmethacrylate) (PMMA, ~100 nm, A2 PMMA, MicroChem, USA) on a silicon wafer (i.e., carrier

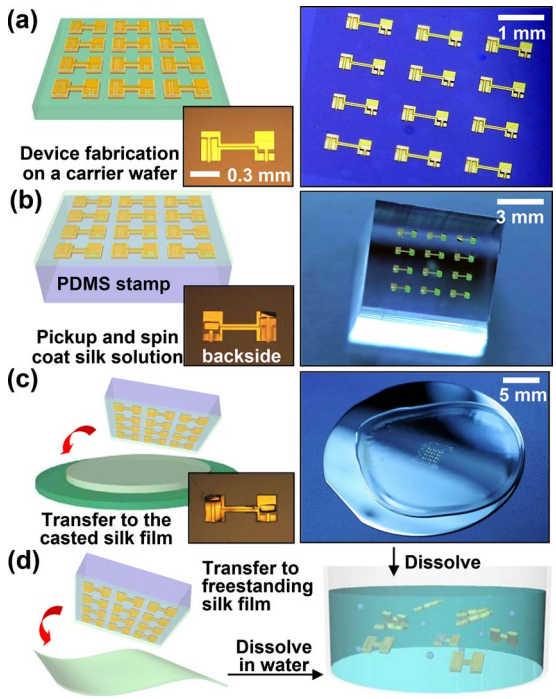

FIG. 1. (Color online) Schematic diagram (left), corresponding high resolution image (right) and microscope image (inset) of (a) ultrathin devices on a carrier wafer, (b) devices lifted onto the surface of a PDMS stamp, and (c) process for transfer printing onto a silk film cast on a silicon wafer. (d) Schematic diagram of transfer printing onto a freestanding silk film (left) and dissolution (right).

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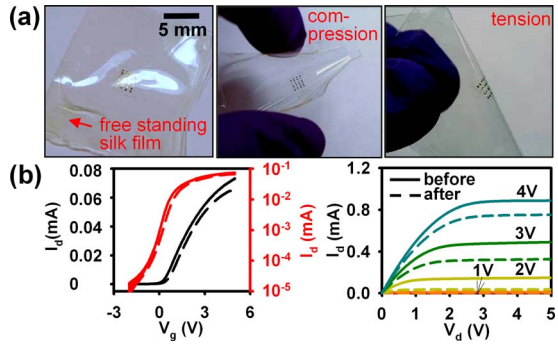

FIG. 2. (Color online) (a) Ultrathin devices on a flexible silk substrate, in flat (left) and bent (center and right) configurations. (b) Transfer curves (left) and *IV* curves (right) before (solid curve) and after (dotted curve) dissolution, where I_d, V_g, and V_d represent the drain current, gate voltage, and drain voltage, respectively. The voltage for each *IV* curve in the right frame denotes the gate bias voltage.

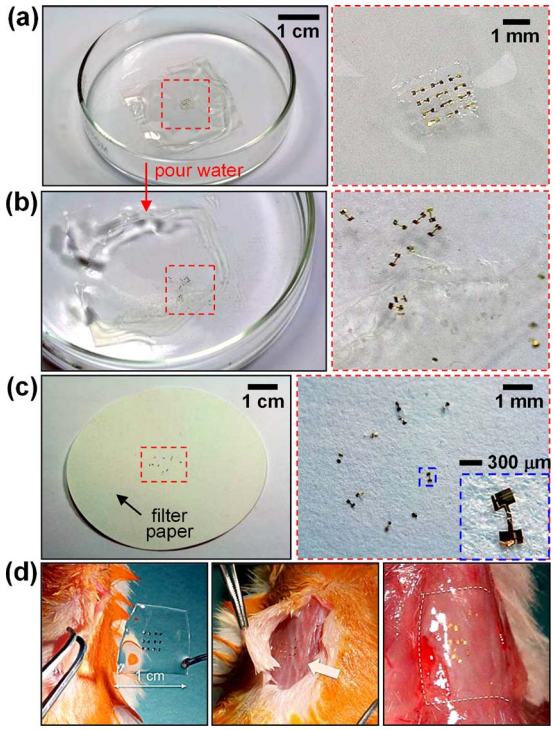

FIG. 3. (Color online) Images of the water dissolution of a system of silicon electronics on silk, at various time stages (left) with magnified views (right): (a) start and (b) after 3 min. (c) Image of devices recovered on filter paper after complete dissolution of the silk (left) with magnified view (right). (d) Procedure and result of the animal toxicity test: image before (left) and shortly after (center) and two weeks after (right) implantation.

wafer for processing). After printing, a series of fabrication processes, including photolithography, reactive ion etching, plasma enhanced chemical vapor deposition of oxides, and electron beam evaporation of metals, formed silicon metal oxide field effect transistors connected by metal lines. Next, spin coating a layer of PI (~1.2 μm) encapsulated the active devices and located them near the neutral mechanical plane. Dry etching the polymer layers completed the fabrication of an array of isolated devices on PMMA, as shown in Fig. 1(a). Next, dissolving the PMMA with acetone released the devices from the carrier wafer. These devices were lifted onto the surface of a transfer stamp of poly(dimethylsiloxane) (PDMS, Sylgard 184, Dow Corning, USA), as shown in Fig. 1(b). Transfer printing delivered the devices to either a spin cast film of silk on a silicon substrate [Fig. 1(c)] or a freestanding silk membrane [Fig. 1(d)]. To accomplish transfer at high yield, we spin coated a ~7% aqueous silk solution on the backsides of the devices while on the PDMS stamp, at spin rates between 2000 and 3000 rpm for 30 s. This layer of silk served as an adhesive for a transfer, which involves first establishing conformal contact with the silk substrate while on a hot plate (~110 °C) and then slowly retrieving the stamp. This process yielded a system in which the substrate is water soluble, and resorbable, but the devices are not, as shown in the schematic diagram in Fig. 1(d). An important point is that the devices can be constructed in very small dimensions (interconnected or not, depending on the application), with very small total amounts of material, thereby offering the possibility to minimize their effects on the biology. Further, the mode of processing the silk can be designed to yield rapid dissolution rates, as is the case here, or to degrade over years.[5]

Figure 2(a) shows a freestanding silk film with transfer printed silicon devices. The center and right frames of Fig. 2(a) demonstrate the mechanical flexibility of the system. Under bending at these levels (radius of curvature, R, as ~5 mm), we observed no mechanical or adhesive failure. We estimate that the bend induced strains at the top surface of the silk film (~25 μm, ~5 mm bending radius) are in the range of ~0.25%. Electrical measurements of a typical *n* channel device show expected properties [solid line of Fig. 2(b)]. Here, the channel length and width was 13 and 100 μm, respectively, and the gate oxide thickness was 50 nm. The electron mobility, threshold voltage, and on/off ratio calculated from the transfer curve in the left frame of Fig. 2(b) are ~500 $cm^2/V\,s$, ~0.2 V, and $>10^4$, respectively. The current-voltage characteristics at different gate biases are shown in the right frame of Fig. 2(b). The gate leakage current was less than tens of picoamperes. We also characterized the *n*MOS transistor after dissolving the silk substrate in water and then filtering out the devices onto filter paper [dotted line of Fig. 2(b)]. Even after dissolution, the transistors functioned with only modest changes in properties. The electron mobility, threshold voltage, and on/off ratio were estimated from the transfer curves to be ~440 $cm^2/V\,s$, ~0.5 V, and $>10^4$.

This dissolution process relies on the capability of silk to disintegrate in water, leaving proteins as the products that are then degraded by proteolytic activity.[9] The resulting silk fibroin protein is a Food and Drug Administration (FDA) approved biocompatible material that generates noninflammatory amino acid degradation products usable in cell metabolic functions. Further, the mechanical properties of the silk substrate can be tailored, based on the mode of processing, to match the level of toughness required.[10,11] To illustrate the process, we collected images at various times after dipping a typical device into a petri dish filled with water, at room temperature. With a ~25 μm thick silk substrate, we observed complete dissolution within 3 min, as shown in Figs. 3(a) and 3(b). Figure 3(c) shows devices recovered onto a piece of filter paper. Since the vast majority of this type of implantable device consists of the substrate and because the sizes of the active devices can be reduced even further by using standard microelectronic technology, very tiny or negligible residues of nonresorbable materials can remain after dissolution.

We implanted similar types of devices into animals to determine the inflammatory response. Here, the devices consisted of doped silicon, silicon dioxide, and metal layers encapsulated with PI, similar to those described previously. Since PI and gold are known to be biocompatible,[12] the main concerns were for the silicon and silicon dioxide. Recent reports on the biocompatibility of porous nanoparticles of silicon and silicon dioxide[13] suggest the possibility of biocompatibility in the Si/SiO_2 components used in the transistors. To examine this issue directly, samples were implanted subcutaneously in mice [left and center frame of Fig. 3(d)] and retrieved after two weeks. The results show the partial dissolution of the film in this time frame, as well as the lack of any inflammation around the implant site. The mice did not exhibit any sign of abscessing or liquid buildup, and initial integration of the silk carrier into the subcutaneous layers could be observed. The size of the implant is estimated to be between 15%–20% smaller than the originally implanted device and detachment of a few transistor structures can be observed, as shown in the right frame of Fig. 3(d). Although additional studies are required, these initial *in vivo* tests suggest some promise for this form of biodegradable electronics.

In conclusion, we developed unconventional material processing and device fabrication procedures for a class of implantable biomedical device that is largely, but not completely, bioresorbable.[14] The systems combine an FDA approved biomaterial substrate, silk, and with silicon nanomaterial electronic devices. Preliminary *in vivo* toxicity and inflammatory evaluations showed no harmful effects on a living animal. A technology of this type could open various possible applications for insertion of high performance flexible electronics into implantable biomedical devices. Further, since silk is the toughest known natural biopolymer in fiber form, this substrate provides a suitable base substrate upon which to develop a family of such implantable devices, where *in vivo* lifetime of components can be tailored from short to long term, hours to years.

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