IMPLANTED DEVICES

Bioresorbable spectrometers

Needle-sized photonic devices that slowly dissolve in the body can spectroscopically characterize cerebral temperature, blood oxygenation and neural activity for weeks in unconstrained mice.

Sarah Forward, Sheldon J. J. Kwok and Seok-Hyun Yun

Most implantable devices that can monitor or regulate internal organs continuously on a long-term basis need to be removed from the body or replaced, and this usually involves a surgical procedure. When functionality is required only for a finite time, as is the case of sutures during wound healing[1], the devices should ideally be constructed with biodegradable or bioresorbable components that safely disintegrate after the device's intended lifetime. However, the development of resorbable implants that allow for continuous monitoring (in particular, the detection of multiple physiological inputs), or for the treatment of diseases and injuries deep in the body, has only just begun. For example, bioresorbable electronic devices have been developed for the short-term (up to a few days) continuous monitoring of internal abdominal pressure and temperature[2], and of intracranial pressure and temperature[3]. Reporting in *Nature Biomedical Engineering*, John Rogers and colleagues now demonstrate fully bioresorbable spectrometers capable of sensing physiologically relevant processes in biofluids and tissues continuously for up to seven weeks[4].

Rogers and co-authors' transient devices employ optical spectroscopy for probing the local environment of the implantation site. The entire system, which is 600-μm wide and 160-μm thick, and thus no larger than the average hypodermic needle, uses fibre optics to deliver external source light, with the implanted part of the device comprising a spectroscopic sensor made of biodegradable optical and semiconductor materials (Fig. 1). This sensing scheme circumvents the problems of light scattering by tissue typical of external optical probes, and the incorporation of optical-detection components at the system's implanted end maximizes light collection and detection. These features provide compelling advantages over previous approaches using fibre-optic light collection and delivery to an external detection instrument[5]. The embedded spectrometer, made of silicon, zinc, silica and poly(lactic-co-glycolic acid) (PLGA), naturally dissolves and undergoes clearance from the body at prescribed rates or working lifetimes (hours, days or weeks), all while maintaining high operational performance. The authors show that, after implantation in mice, the devices can monitor cerebral temperature, blood oxygenation and local neural activity in each animal's brain, with all parameters yielding comparable values to those from external bulkier probes.

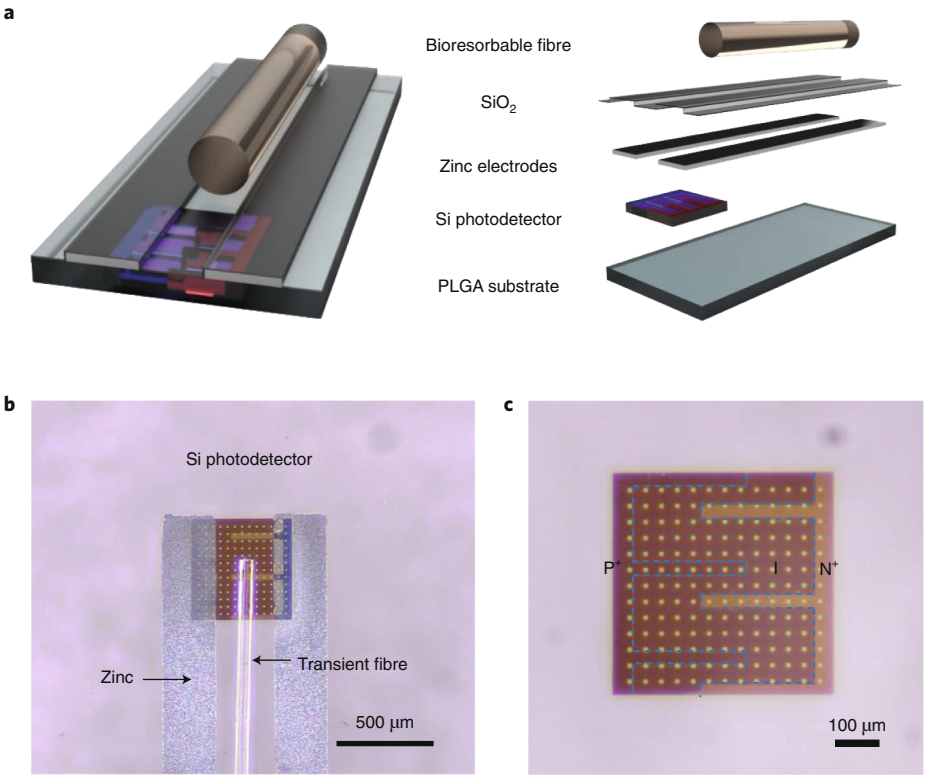

Fig. 1 | Implantable resorbable photonic spectrometer. a–c, The spectrometer (schematic in **a**; optical image in **b**) consists of a 1,500-nm-thick silicon-nanomembrane photodetector (**c**), two 400-nm-thick zinc electrodes, as well as a 150-μm-thick fibre-optic probe and a 10-μm-thick supporting substrate, both made of PLGA. The oxide layer separates the PLGA fibre from the substrate, to enhance the confinement of light in the fibre. The dashed blue lines define the n-type (N^+), p-type (P^+) and intrinsic (I) regions of the photodetector. Figure reproduced from ref. [4], Springer Nature Ltd.

The fabrication of the devices begins with the drawing of a PLGA fibre via a commercial optical fibre as the lead. This process immediately couples the two fibres together, to minimize optical-coupling losses. The fibre is then dipped into a sodium-alginate solution, which clads the PLGA core. To improve performance, the core thickness can be modulated with the addition of sputtered layers of silica and alginate hydrogel. The non-resorbable lead fibre is then connected to a broadly tuneable laser. For spectroscopic detection, a nanomembrane of doped monocrystalline silicon is used in one device as a tri-colour photodetector. Then thin zinc electrodes for electrical readout are incorporated.

The electrodes are connected to two small wires that follow the commercial fibre to the proximal optoelectronics. Light confinement is enhanced by silica, which encloses the electronics and separates the fibre from the rest of the components. Sputtering the entire device with a 200-nm layer of silica provides reliable function for up to 10 days.

Rogers and colleagues describe three different device embodiments (produced using variations of the same fabrication process): a three-wavelength photometer that simultaneously distinguishes signals at 490 nm, 570 nm and 720 nm; a system that employs a silicon-nanomembrane-based photodetection scheme with laser tuning for sensing between 400–1,000 nm; and a spectrometer created from layers of bioresorbable optical filters with alternating multi-stacks of SiO_x and SiN_y, which enable selective filtering via prescribed transmission of narrowband light. The systems boast low dark currents and high responsivities.

When the PLGA fibre was submerged in phosphate buffered saline at 37 °C, hydrolysis led to the decomposition of the zinc components into fragments by day ten, resulting in an imperceptible photocurrent. Both silicon and zinc components of the device showed the absence of abnormal accumulation in blood, brain, heart, kidney, liver, lung muscle and spleen over seven weeks post-implantation. Histological analysis showed neither signs of immune cells related to implantation in key tissue sites (heart, kidney, lung and spleen) nor tissue damage. Further blood tests did not show any signs of organ trauma, and no indication of changes in electrolyte or enzyme levels. X-ray computed-tomography imaging showed that the device completely disappeared by day 45 post-implantation. End products of the silicon component included innocuous orthosilic acid (H_4SiO_4; also known as 'dietary silicon'), which contributes to maintaining higher bone mineral density in men and premenopausal women[6].

Unlike biocompatible implants designed to withstand foreign-body responses and disintegration, biodegradable devices rely on the body's own physiological mechanisms to safely resorb the device while also maintaining adequate performance. The bioresorbable sensors developed by Rogers and co-authors accomplish this while maintaining high operational integrity over the prescribed timescales. In general, the authors' optoelectronic systems would be most relevant for applications that can harness the wide-ranging capabilities of optical technologies to fulfil unmet clinical needs, and especially impactful for applications that already require a surgical procedure, during which such a system can be implanted. Besides the biodegradability of the sensor materials, the ability to tailor the functional lifetime of sensors might enable the matching of the device's operational time to the recovery or disease-monitoring schedules of a patient. For example, the devices might find applications in the measurement of tissue oxygenation following transplantation[7], in the continuous long-term sensing of cancer cells at a biopsy site[8], in the application of photodynamic therapy following tumour resection for the prevention of cancer recurrence[9], in the monitoring of glucose concentrations in interstitial fluid, and in the control of insulin administration in diabetic patients[10]. ❐

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