Disposable sensors

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Abstract

Device disposability is a critical feature of electrochemical sensor production, allowing complex measurements to be carried out in a low cost and efficient manner. Disposable sensors are increasing rapidly in their level of sophistication, supported by developments in materials and fabrication processing. This is, in turn, leading to greater levels of device integration and functionality and has the potential to significantly expand the number of people who can use them, where they can be deployed and how they can be used. As well as becoming more complex, there is also significant emphasis in making such disposable devices more environmentally sustainable. Current themes in the development of disposable sensors are explored here.

Introduction

Anything is potentially disposable. The predominant determining factor of disposability has, for many years been an issue of economic viability. However, it is now also increasingly linked to environmental sustainability. This holds true for sensors in applications including biomedical, industrial and environmental measurement. Disposability typically demands that devices are made from minimal quantities of materials of very low unit cost which can be rapidly manufactured in large numbers, and which are now also increasingly amenable to biodegradation. The ability to achieve very low unit costs at very high production volumes has been a key driver for the most successful commercial developments in sensors, most notably in diabetes care (glucose sensing strips) and reproductive health (pregnancy tests). While arguably no markets have come close to the glucose sensing market in terms of size, the same principles of low cost, high volume manufacture are typically applied to many new electrochemical sensing technologies to strengthen their future market potential. Thus, research, development and design concepts that facilitate disposability remain an inherent feature of the field of electrochemical sensor development. This has consequences for the nature of the materials used for fabrication, the processing methods that such materials are amenable to, and the nature of the applications to which they can be most suitably applied. An additional key feature is the increase in functional complexity which can now be achieved with increasing material and fabrication simplicity and cost. These additional requirements must all be achieved while also maintaining, improving and expanding the analytical capabilities of these devices.

Materials

The materials used for the fabrication for sensing devices can be broadly categorised as either serving a structural or functional role. Significant advancements continue to be made in both aspects of sensor materials, and the distinction between the two is becoming increasingly blurred.

The use of paper as a substrate for disposable sensors is continuing to increase in interest [1*]. Paper has many positive qualities which make it suitable for disposable electrochemical sensors. It is a very low cost, planar, mass-produced material which is naturally biodegradable and can be sourced from sustainable and recyclable sources. It generally has good mechanical strength, particularly in the dry state, is flexible, biocompatible and amenable to a wide range of processing requirements. The range of paper types available is also large and has a major bearing on how this most diverse of materials can be employed. Its properties can be either advantageous or not depending on the precise type of paper used and its application. The role of paper in sensors is typically either as a low cost, more

environmentally friendly alternative substrate to polymers, or as the basis of microfluidic systems. Porous planar substrates such as nitrocellulose have been widely used in lateral flow devices. These have demonstrated excellent mechanical strength, porosity, hydrophilicity and biomolecular interaction. However, in comparison to cellulosic paper, such materials remain costly and lack its environmental credentials. In the drive to find technological solutions to sensors in developing countries, paper has become a very attractive alternative to such substrates. However, overcoming some of its less desirable physical properties may be more or less beneficial.

Newspaper is a particularly low grade, low cost form of paper. Yang et al. applied recycled newspaper print to act as the substrate of an electrochemical sensor device [2]. Newspaper is highly absorbent and wetting brings about the rapid swelling and weakening of the short fibres. They overcame some of the issues associated with its properties through the chemical vapour deposition (CVD) of a parylene C coating (Fig. 1A). This transformed the physical properties of the paper, making it mechanically strong, flexible, deformable and hydrophilic. Metal electrodes could be deposited onto it using photolithography and CVD, and which had excellent conductivity and adhesion properties. The sensor was used in a three electrode configuration to demonstrate DNA hybridization. However, in coating the newspaper, many of the desirable properties of the newspaper are lost. Although porosity was maintained, the hydrophobicity of the material prevents it from being an effective adsorbent material. The complex CVD processing would also not lend itself easily to low cost, mass production and so it seems that a great effort has had to be made to make the newspaper a useable substrate which negates its benefits. A further illustration of an integrated paper-based device is shown in Fig. 1B and is discussed later. Disposable paper substrates have been further combined with features such as smart, electroactive materials and printed organic electronics to create a printed, disposable sensor for measuring breath alcohol [3]. The sensor employed an organic electrochemical transistor based on poly(3,4-ethylenedioxythiophene):poly(styrenesulphonate) (PEDOT:PSS) which were deposited onto ‘coated paper’ using inkjet printing. In combination with alcohol dehydrogenase, the measurement of both liquid and breath alcohol was demonstrated.

Smart, functional materials continue to play an increasingly important role in sensor development with the aim of achieving greater levels of functionality with reduced cost and increased processability. While there continues to be much recent focus on graphene, materials such as ionic liquids, carbon nanotubes, metallic nanoparticles and conducting and electroactive polymers continue to be explored and also be made amenable to flexibility, printability and disposability. Recently, He et al. combined Pt and Au nanoparticles, carbon nanotubes and graphene in an ionic liquid matrix into a printable sensor electrode film [4]. Combining zero-, one- and two-dimensional nanomaterials has potential advantages in terms of conductivity, structure and surface area and were effective for the direct, non-enzymatic measurement of glucose. However, the requirement for relatively costly materials makes it difficult to evaluate the economic viability of such devices at this time, or how and where such devices could be used that is not already addressed by current devices. Another feature of this, and other recent work, has been to use ‘graphene paper’ which acts simultaneously as device substrate, conductive layer, and into which other functional components can be embedded and integrated, so potentially integrating all three classical layers of disposable sensors into one single hybrid material [5**].

Conducting polymers such as polyaniline remain of significant interest as the basis of disposable sensor devices, particularly when in nanostructured, print-processable forms, thereby allowing mass production processing and disposability. Ink-jet printed polyaniline nanoparticles have recently been used as the basis for blood ammonia based on a polymer microfabricated sensing device [6]. Sensors were fabricated using a combination of screen and inkjet printing and integrated using polymer laminate assembly in conjunction with a gas diffusion membrane, allowing measurement of ammonia in serum to 25 μM. Effective point-of-care measurement of blood ammonia remains a clinical challenge.

Processes

A range of print fabrication processes continue to be central to the low cost, mass production of disposable electrochemical sensor devices. Screen printing remains in widespread use, while, as already illustrated, inkjet printing is seeing increased application, particularly during device prototyping typical during the earlier stages of research and technological development. However, the zeitgeist of sensor fabrication processes is 3D printing. Many of the qualities of the 3D printing process are being seen as applicable for the rapid prototyping and small-scale fabrication of complex devices at the research level in a manner that can be challenging (though not impossible) to achieve using alternative methods such as injection molding, embossing and machining. It allows layer fabrication across a broad range of length scales relevant to disposable sensor devices from nanometres to centimetres [7]. It has also freed researchers from the two dimensional paradigm and allowed them to explore new ways of addressing the structure of electrochemical devices. While most examples of the application of 3D printing have been in the rapid prototyping of polymer-based components and devices, Ambrosi et al. recently demonstrated the fabrication of metal electrodes using 3D printing [8]. They used a helical design to illustrate the ability of the technique to fabricate structures that would be either challenging or wasteful using conventional means. However, constraints remain as to the range of materials which are available. In this case, the available stainless steel was electroplated with IrO_2 to make it suitable as an electrode. Further examples of 3D printing in sensor development using polymer materials are illustrated later to illustrate how it is facilitating new applications. While 3D printing represents an exciting emerging fabrication methodology, challenges remain for it to move beyond early stage prototyping and to be the basis of a mass production process, as the unit processing time is typically high compared to other methods

Integration

Another key challenge with disposable sensor-based devices is the need for instrumentation to transduce the signals from the sensing electrode component. For obvious reasons of cost and sustainability, the parts of the sensor instrumentation have not typically been disposable. While there are examples of the disposal of silicon electronics in sensor devices such as the Clearblue® Digital pregnancy strip (an optical device), such an approach is less economical and environmentally sustainable. Many are seeking ways of integrating the wider functionality required for measurement into disposable devices in a manner that is economically and environmentally viable, particularly to address needs in very low resource environments. Such wider functionality has the potential to address power, display, data processing, and increasingly also communications requirements. Recently, significant work led by the author's own group has demonstrated the effective integration of printed biosensors, displays and battery into a single use credit-card type device for measuring total cholesterol [9**]. While the device used traditional silicon electronics for operation, the potential for both pick-and-place, 'flip-chip' hybrid silicon integration and organic circuit integration were illustrated. The device was also capable of remote communication via a camera phone interface. Such devices have the potential to make testing and management more convenient and effective (Fig. 2).

External power to drive sensors has, in the past, been achieved using batteries. The concept of self-powered sensors based on enzymatic fuel cells has been around for some time now and has recently been used to power a paper-based glucose biosensor [10**]. The fuel cell device was fabricated using a single piece of paper which was divided into hydrophilic and hydrophobic domains using wax printing and which was folded to create the final assembled device, with the paper also acting as a separation layer to confine the reaction materials while allowing proton transfer (Fig. 1B). The carbon anode and Ni/carbon cathode were deposited using screen printing. Glucose oxidase could be readily absorbed into the hydrophilic anode. The device was capable of generating in excess of 25 nW of power with 150 mV potential and a current of 175 nA at 5 mM glucose. Measurement of 1-5 mM glucose was effectively achieved. However, measurement still required the use of an external multi-meter with display and demonstrates the need for further functional integration. Glucose and lactose biofuel cells have also been integrated into stretchable devices fabricated using screen printing for integration into textile-based, wearable applications [11]. Later examples will illustrate the use of solar-rechargeable supercapacitors. Future advances are likely to demonstrate the integration of multiple features, beyond power and transduction.

Application

There are several current drivers of applications of disposable sensors. The development of new non-invasive or minimally invasive devices continues to grow in importance, as do wearable devices. In many instances, there is strong overlap between these two areas in applications such as sweat monitoring using flexible 'on-body' devices. Two groups have recently demonstrated wearable devices for analysing sweat (Fig. 3). Nie et al. have created a hybrid microfluidic device using multi-layer, laser-etched polyethylene terephthalate foils as a sweat sampling system in combination with a silicon-based pH sensor which facilitates flexible, wearable operation [12]. The silicon electrodes were bonded to the polymer with conductive paste using 'pick and place', and connected to an external voltmeter via screen-printed lead outs (Fig. 2A). The versatility of paper was again illustrated as a sample wicking material at the channel inlet. The system has been demonstrated in buffers. Glennon et al. integrated a flexible, disposable polymer microfluidic chip with screen-printed sodium sensors into a wearable electronic housing which could be strapped to the arm for sweat analysis, and preliminary on-body analysis of sweat has been demonstrated (Fig. 3B) [13*]. Both examples illustrate the challenge of integrating and reducing the size and complexity of the accompanying electronics. While it is well-established that such integration, miniaturisation and mass production of low cost silicon circuits is, in theory, possible, this tends to be very difficult to demonstrate during research and technical development, as the cost is linked to volume, which cannot be achieved at this stage. De Guzman and Morrin are employing transfer tattoo sensors to achieve non-invasive, on body analysis of skin [14]. Two concentric electrodes were screen-printed onto temporary tattoo paper and transferred to the skin (Fig. 3C). Electrochemical impedance spectroscopy yielded comparable equivalent circuit models in both hydrogel and porcine skin hydration models and has the potential to be used as the basis of disposable skin-worn sensors that can be washed off and replaced on a periodic basis.

Multi-plexing also continues to be an important driver of disposable sensor development, particularly in the area of immunodiagnostics in which small panels of biomarkers are being increasingly used to improve the sensitivity of diagnosis. Rusling's group recently employed polylactic acid 3D printing to fabricate a gravity-driven microfluidic device to measure prostate specific antigen (PSA), prostate specific membrane antigen (PSMA) and platelet factor 4 (PF4) [15]. The assay employed an antibody sandwich configuration with a secondary antibody co-immobilised to silica nanoparticles with tris(bipyridine) ruthenium (II) [Ru(BPY)] [16] immobilised onto a carbon electrode. Electrochemi-luminescence was generated by the RuBPY and co-reactant tripropylamine at 1.5 V vs. Ag/AgCl and detected by a CCD camera. The device was driven by a supercapacitor which could be recharged by a solar panel. Such a system holds the potential for future integration and disposability using printed electronic supercapacitors and light detectors.

Conclusion

The ever increasing need to access sensory information will continue to drive the development of disposable sensors and widen the availability of increasingly complex sensing and diagnostic devices. This will be achieved through the enhanced use of combinations of advanced materials, processing methods and increased levels of functional integration. This continually improving combination of cost and functionality will also continue to expand the range and mode of applications to address unmet needs. Key drivers are access to improved healthcare in low resource environments, and minimally- or non-invasive alternatives to current technologies in high resource environments. Smart functional nanomaterials in combination with print processing will facilitate greater functional integration, while still achieving mass production. While cost will continue to be a primary driver, environmental sustainability and the 'greening' of technology will grow in importance.

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An excellent demonstration of the further integration of multiple functionality into a single material with a plurality of physical and functional features. Electrochemical sensor devices typically possess multiple layers to provide distinct structural, conducting and electroactive functions. Here, a graphene oxide/gold nanoparticle/Prussian blue paper was fabricated with combined structural, conductive and electroactive properties which could be used for the measurement of hydrogen peroxide which is an important measurand in electroanalytical chemistry.

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This work illustrates the effective integration of multiple functionalities using organic and printed electronics to deliver a fully single-use, disposable, sample-to-result diagnostic device. It integrates sensors, display, and battery which are all integrated onto a single polymer substrate. The device was also able to communicate remotely via a mobile phone, which allows transmission of test results to health care providers for treatment support and compliance monitoring.

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Imaginative and effective combination of a single folded paper substrate to form a biofuel cell as the basis of electrochemical measurement of glucose. Combining elements of low-cost substrate and wax printing fabrication into a foldable fuel cell configuration, while combining power and measurement capabilities shows great potential for the future development of disposable devices for low resource environments.

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SWEATCH continues to address the practical engineering challenges of applying disposable electrochemical sensors to on-body measurements. It effectively samples sodium in sweat using a combination of disposable printed sensor and capillary microfluidics and demonstrates the remaining challenges of integrating and miniaturising silicon electronics into such systems during technological development.

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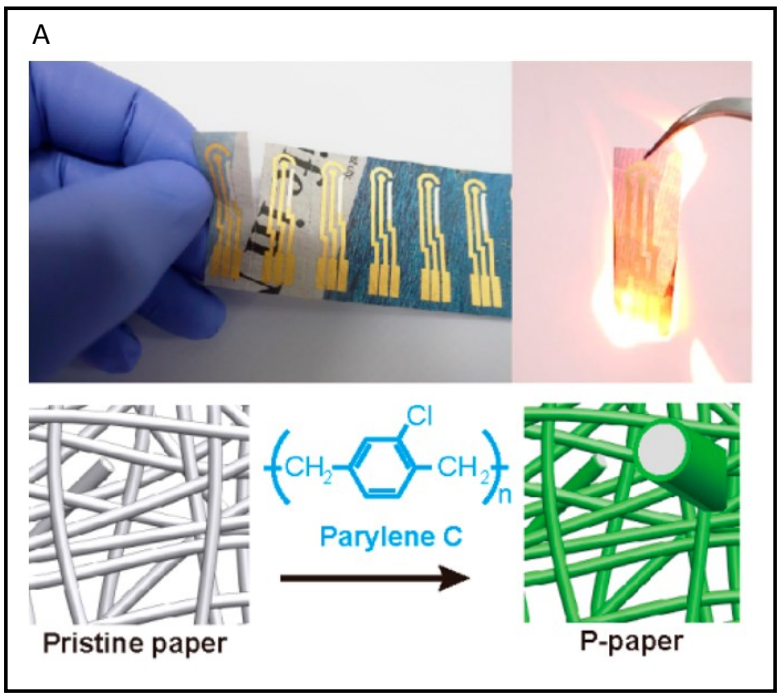
Figure Legends

Fig. 1. Disposable sensors based on paper substrates. (A) Flexible printed sensors based on newspaper modified with parylene. The newspaper was first modified with parylene using chemical vapour depiction. Electrodes were then deposited using E-beam evaporation. Reprinted with permission from M.H. Yang et al., ACS Appl. Mater. Interf. 8 (2016) 34978-34984. Copyright 2016 American Chemical Society. (B) An enzymatic biofuel cell sensor for measuring glucose. The biofuel cell sensor was fabricated from a single piece of filter paper which was divided into hydrophobic and hydrophilic regions using wax printing and folded to form a fuel cell configuration. Reprinted from C. Fischer et al. Biosens. Bioelectron. 79 (2016) 193-197, Copyright 2016, with permission from Elsevier.

Fig. 2. The Smart Integrated Miniaturised Sensor System (SIMS). (A) Graphical illustration of the 22 layer stack of display, sensor and battery. (B) Prototype device with printed battery (top), display (bottom left) and sensor (bottom right) integrated onto a single substrate, 100 mm x 80 mm. (C) Front of the prototype device with display bar on bottom left and sample application zone on right. The device can be readily reduced to the size of a credit card.

Fig. 3. Wearable applications of disposable sensors. (A) A sweat sensing device based on the integration of polymer microfluidics with a silicon chip-based pH sensor. Reprinted from C. Nie et al., Sens. Actuat. B 227 (2016) 427-437, Copyright 2016, with permission from Elsevier. (B) The 'SWEATCH' device based on screen-printed sodium sensors (2) integrated into a sweat sampling and measurement system. Reprinted with permission from T. Glennon et al., Electroanal. 28 (2016) 1283-1289, Copyright 2016 Wiley-VCH Verlag GmbH & Co. (C) Screen-printed silver transferable tattoo sensors on hydrogen (top) and porcine skin (bottom) Reprinted with permission from De Guzman et al. Electroanal. 29 (2017) 188-196, Copyright 2017 Wiley-VCH Verlag GmbH & Co.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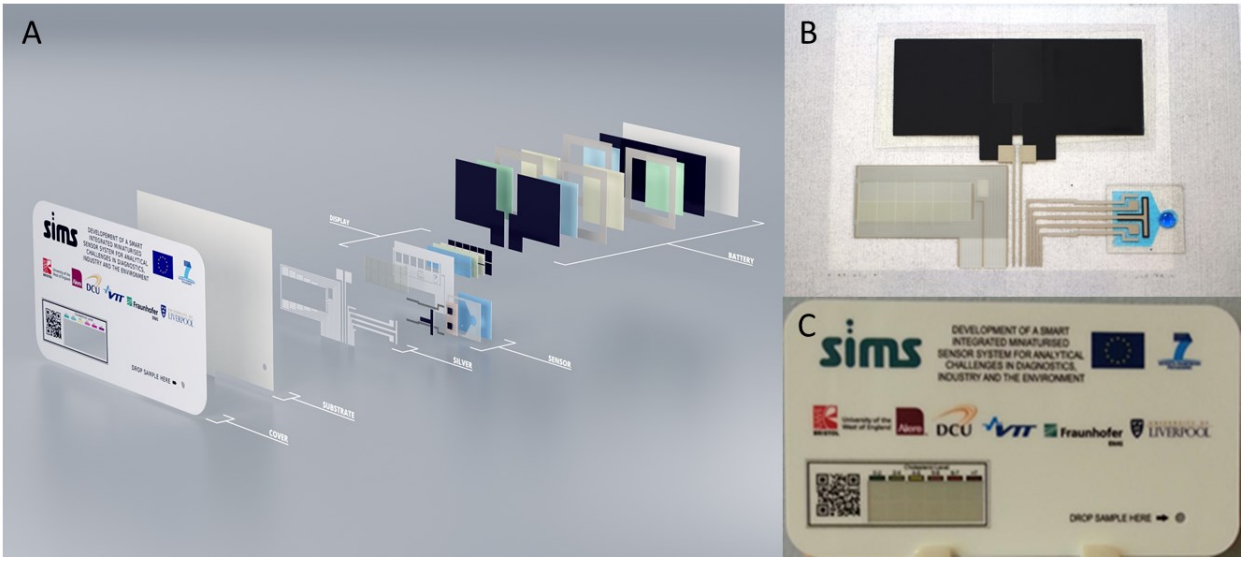
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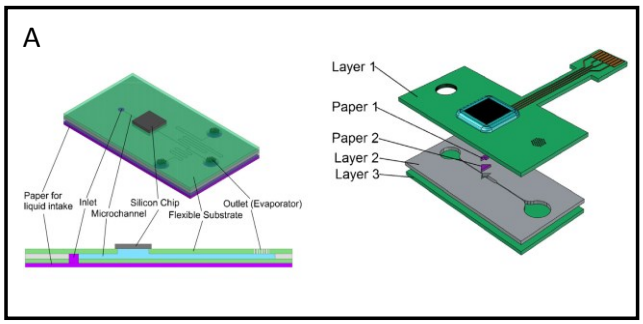
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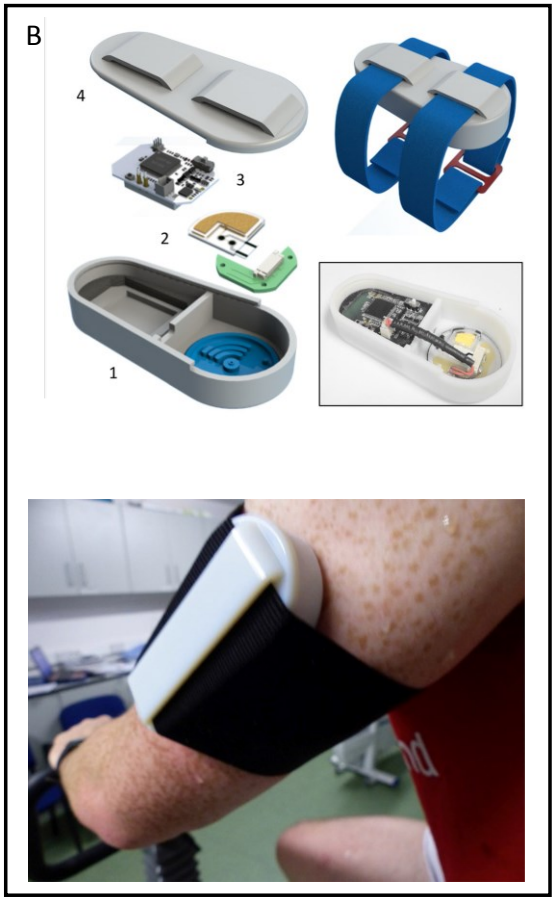
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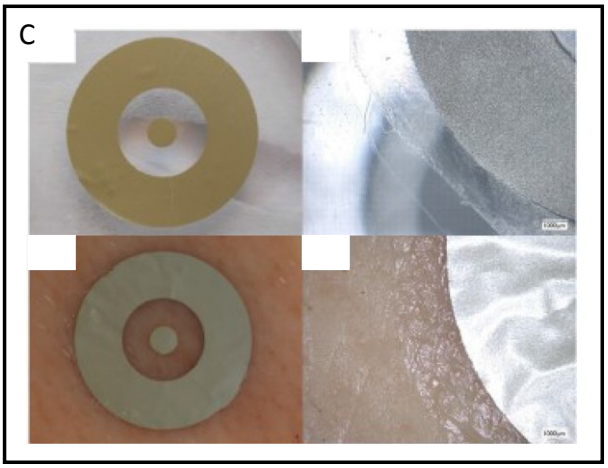
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