ECS Sensors Plus, 2022 **1** 011601

Perspective—An Age of Sensors

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There could not be a better time to launch a new venture in sensors, and the exploration of the biological interface with physicochemical devices offers especially exciting opportunities.

[DOI: 10.1149/2754-2726/ac5523]

Manuscript received February 8, 2022. Published April 13, 2022.

The extraordinary success of electrochemical biosensors for the monitoring and control of diabetes[1] is well known amongst experts in diagnostics, but until recently it has remained the exception rather than the rule in terms of widespread adoption and use. Recent global emergencies, however, have placed specialist terms such as PCR and lateral-flow devices in common parlance, and climate change has highlighted the crucial role of measurement science in understanding potentially catastrophic shifts in the Earth's natural equilibrium. Future health emergencies, such as the continued emergence of new diseases or the decreasing effectiveness of current therapeutic agents such as antibiotics, will keep attention focussed on convenient, inexpensive and decentralised diagnostics together with improved methods for the discovery and production of pharmaceuticals. Disruption to the climate is unlikely to be halted or reversed in the near future and the consequential secondary effects, such as stresses in maintaining food and water supplies, and the defence needs associated with politcal instability, will create new sensing challenges. In this tumultuous future, sensors will play an increasing, although often somewhat concealed role. They are likely to become ever more integrated into everyday technology affecting all aspects of our lives in a highly beneficial way.

Delving into a little more detail, one can expect the relatively clumsy current generation of decentralised diagnostics used to address world health issues, to become increasingly sophisticated sensors, achieving high degrees of miniaturisation, multifunctionality and artificial intelligence. A surging trend at the moment is wearable devices,[2,3] although the challenges associated with accessing appropriately representative samples often seems to be underestimated.[4] It is crucial that innovative engineers consult carefully with physiologists before diving into the construction of devices operating on the more accessible body fluids, which may not always deliver a timely and accurate representation of key parameters. Decentralised and remote sensors are also set to play key roles, furnishing both mobility and continuous information from dispersed locations.

Biological recognition elements can confer exquisite sensitivity and specificity on sensing systems, but in their natural state they may not be sufficiently flexible, robust, or readily integrated within electronic devices. The recent challenges associated SARS-CoV-2 and its variants have predictably generated a plethora of new approaches that are readily adaptable for mutated strains, for example, cell-surface glycoproteins as coreceptors in lateral-flow devices.[5] Bioengineering of biomolecules such as proteins, peptides and nucleic acids, the creation of shielded microenvironments and the further development of biomimetic polymers[6] are some of the other routes forward to improve the stability and performance of current biosensors. Such strategies will lead to more robust decentralised, wearable and implantable sensors and further expand the range of biosensors into non-aqueous, gaseous and extreme environments, such as nuclear reactors, deep sea and space.

Electrochemical transducers have played a key role in the practical and commercial triumph of current biosensors, but optical sensors look to make an increasing contribution, building on the remarkable success of technologies such as surface plasmon resonance (SPR) for pharmaceutical development, in the hands of companies such as Biacore, and other emerging label-free nanophotonic biosensors.[7] Another notable optical example is implantable sensors based on responsive polymers, such as those reported by Mortellaro and DeHennis,[8] which have been successfully incorporated into the impressive Eversense™ continuous glucose monitoring system by Senseonics Inc. and distributed by Ascencia. Emerging transducers such as magnetic and nanopore sensors have shown us that exciting new techniques still remain to be uncovered and recent advances in both optics and electrochemistry continue to deliver improved resolution. Single molecule studies, in particular, have delivered amazing revelations and promise to uncover exciting new information about biomolecular mechanisms, along with improved measurement techniques.[9]

Effective manufacturing techniques are crucial to the future success of new sensors. This fundamental prerequisite is paid scant attention to in the academic literature, arguably with the exception of silicon-based technologies, but is absolutely core in commercial R&D. Major successes such as mediated amperometric glucose test strips for home use by people with diabetes and lateral-flow devices, initially developed for pregnancy testing, but then swiftly adapted for coronavirus detection, owe their ubiquitous adoption to inexpensive and reliable mass production technology. In the case of glucose sensors, the manufacturing technique was initially screen printing, which was then complemented with the alternative of vapour deposition in combination with laser etching. Lateral-flow devices are based on a layered membrane system which is equally well adapted to large-scale production.[10] As we move to more integrated and miniaturised sensors, innovative approaches to micropatterning various biomolecules, such as enzymes and antibodies, with good geometric alignment and while maintaining biological functionality, will be required. Approaches such as high-resolution and rapid geometric protein self-patterning using solvent-assisted protein-micelle adsorption printing to couple biomolecules onto microelectrodes, promise to deliver scalable solutions for future microarray-based diagnostics.[11]

Another important aspect of biosensor development will be integration. Multiparameter measurement with sensor arrays, possibly by creating nano-compartmentalised environments, is a given if we are to better understand living systems, but the wider exploitation of bioelectronics can yield further amalgamated benefits. Bioelectrochemical generation of energy via fuel cells is already an established route to self-powered biosensors[1] and provides interesting sustainable solutions, along with photochemical and kinetic approaches, to powering sensing systems. A further level of systems integration can be achieved by adding movement (transduction) to the energy generation and sensing functions of a device. We have shown this by integrating biofuel cells with artificial muscles[12] and others have demonstrated self-propelled nanodevices. Self-forming sensors from injectable polymers[13] and soft actuators that "grow" bone[14] have also recently been reported. Bio-logic gates[15] add an element of integrated processing capability

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to a sensor, but this is currently still dwarfed by the immense power of conventional integrated on-board electronics. However, innovative solutions to secure interconnection and communication with and between medical devices is a niche area where molecule solutions may flourish.[16] One may even speculate that nucleic acid technology or possibly even imprinting technology provides a route to self-replication by providing templates for regenerations or synthesis of new material.

Looking at all this in the round takes me back to my school days when we learnt that the essential elements of life were to be able to sense, process energy, grow, move and reproduce. Perhaps the future generations of integrated bioelectronic devices will begin to mimic rudimentary models of life itself? Speculation aside, the development of novel materials, structures and properties of sensing and detection systems, together with their characterisation and evaluation, will undoubtedly be crucial in moving us forward into an exciting new era for biosensors. When the Editors invited me to write this brief contribution, they asked me to conclude with ten 'grand challenges' and so here is my personal attempt to list the desirable features for future generations of biosensors: miniaturised, multifunctional, intelligent, wearable/implantable, stable, adaptable, sensitive, manufacturable, integrated and inexpensive.

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