Technology & Health Science

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Innovation in electrochemical sensor technology: easing patient lives with hand-held portable diagnostics

In a world where time is money we believe health is a priceless investment. If properly taken care of it can be truly rewarding and help an individual live longer and better. However, disease is inevitable and every human being suffers from one or the other medical condition at some point in life. Hectic work schedules and busy lifestyles leave us with very little time to take care of ourselves and we often ignore our health issues which should ideally be a priority. 'A stitch in time saves nine', the famous idiom aptly applies in context of medical diagnosis. The timely diagnosis of any adverse medical condition or disease is the very first step towards treatment and cure. Several human deaths are caused not because the treatments are unavailable but simply because diseased conditions go undetected and undiagnosed for prolonged periods until a stage is reached where the damage becomes irreversible.

Several physiological conditions in the body such as blood pressure, temperature, pulse rate, heartbeat, glucose levels, etc are good indicators of the health status and their slight deviation from normal can be indicative of a problem. The monitoring of these simple parameters at home is usual practice and helps in detection of minor health issues which may get aggravated if left unattended over time. There are certain abnormal medical conditions and disorders that have no permanent cure but can be managed effectively. Frequent visits to clinics and path-labs are not only practically difficult but cost exhaustive too. In this regard, hand-held electrochemical sensors have played a major role in self-diagnosis and health monitoring. Diabetes is one such major example, where patients are required to monitor their blood glucose levels regularly. Electric glucometers are routinely used by millions of diabetic people across the globe to check their blood sugar levels. Although sensors are popular at-home testing devices in case of diabetes, their use has been limited in case of other conditions.

Diagnostic electrochemical sensors: the limitations in the existing technology

Electrochemical sensors based on enzymatic detection are popular commercial devices which have revolutionized the at-home diagnosis of diabetes. However very few enzymes can serve as clinical biomarkers of disease and thus this enzyme based sensor technology has remained restricted to glucometers. An alternative affinity based detection strategy has been employed which relies on the specific interaction of molecular targets with antibodies or aptamers and shows great potential. No matter how effective the detection strategy may be the success of a technology is housed in its ease of manufacture, sustainable use, durable functioning and its cost effectiveness. Electrochemical sensors fall prey to biofouling which limits the sensing functionality and hinders the commercialization of the technology. Biological fouling or 'biofouling' refers to the growth of plants, algae, small animals or microorganisms on wet surfaces of any mechanical device thus rendering them dysfunctional. Due to direct contact with biological fluids such as blood, sensors are prone to biofouling which not only spoils the detector but also spoils the equipment.

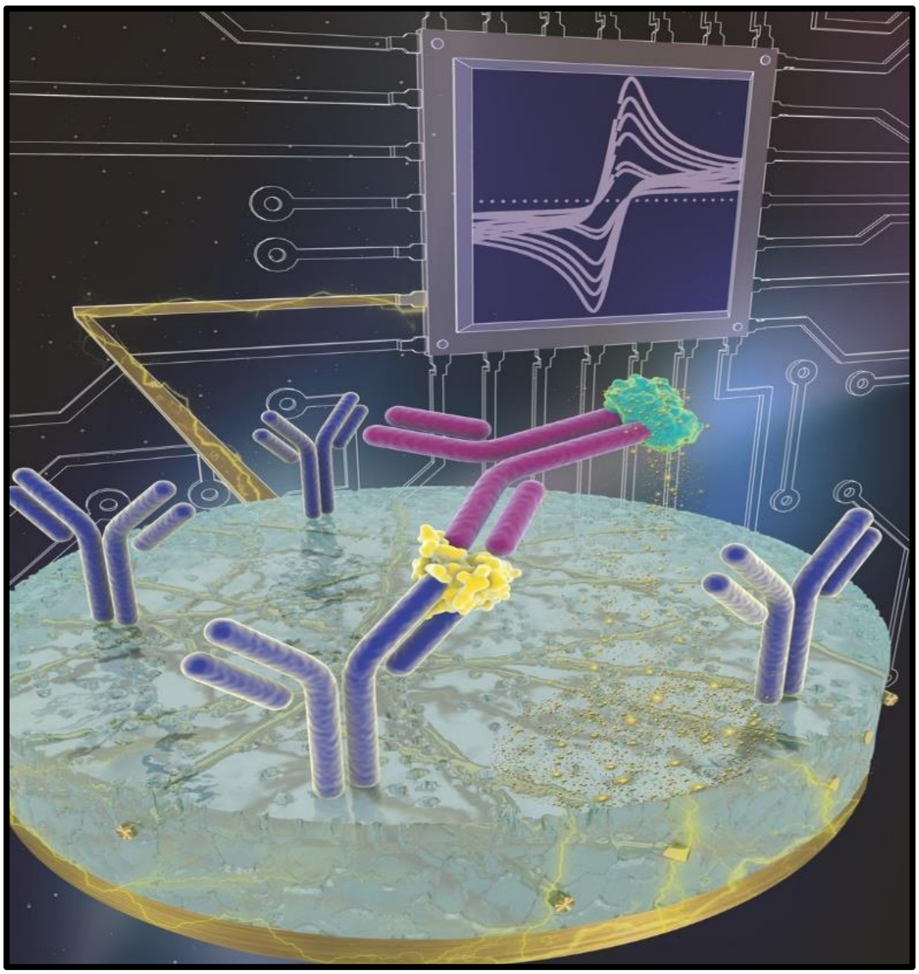

*Figure 1: The diagrammatic representation of the 'eRapid' coating. When probe (purple) and target (yellow) bind together they attract a secondary probe (magenta) that is responsible for the signal generation [**Source:** Wyss Institute at Harvard University].*

Several antifouling coatings and materials have been manufactured from time to time to overcome this problem but have failed in case of medical devices which come in direct contact with biological fluids repeatedly. Although moisture is sufficient to allow the growth of microorganisms, blood, serum, saliva, etc serve as the perfect nutrient medium to culture microbes. The currently available antifouling coatings are not very effective, difficult to mass-manufacture and have consistency and quality issues.

Researchers at the Wyss Institute for Biologically Inspired Engineering at Harvard University have developed a novel diagnostic platform technology known as "eRapid" which enables the creation of handheld electrochemical devices and sensors. These sensors are highly sensitive, can detect multiple disease biomarkers simultaneously, are effective in a variety of biological fluids and require as little as a drop of blood for efficient detection. The technology has been described in the latest issue of Nature Nanotechnology (1).

The knowhow of eRapid technology:

In electrochemical biosensing, the device along with the electrode configuration and the sample conform to a closed ionic and electrical circuit. Thus, off-target substances present in the complex biological fluids bind with the sensor's metal electrodes non-specifically and decrease the conductivity and sensitivity of the device. Conventional antifouling coatings made of poly (ethylene glycol) self-assembled monolayers (PEG-SAMs) and bovine serum albumin (BSA) also restrict the transfer of electrons and thus hinder the flow of current effectively (2, 3). To overcome the lacunae in the existing technology the research team developed a 3D nanocomposite matrix comprising bovine serum albumin (BSA) cross linked with glutaraldehyde and interlaced with a network of conducting nanomaterials such as gold nanoparticles or carbon nanotubes and gold nanowires. This simple 3D matrix allows electron transfer effectively to the underlying electrode thus improving the efficiency of the device considerably. The BSA matrix owing to its small pore size excludes proteins present in plasma and blood and the weak negative charge of BSA thwarts the strong adhesion of positively charged molecules onto the sensor.

The technology showed potential in terms of reducing the non-specific binding of the off-target substances and superior analytical quality. The newly designed coating has also been proven functionally compatible with the existing bioreceptors and antibodies. The nanomaterial-coated sensors were tested in human plasma and blood serum and it was observed that the signal detection ability was retained up to more than 90% even after storage in biofluids for more than a month. Whereas even the best anti-fouling coatings published earlier failed to protect the sensors for more than an hour after being dipped in biofluids and the devices became completely inactive within a day. This highlights the effectiveness and superiority of the 'eRapid' technology (1). The device further passed the functionality test and responded precisely when antibodies were attached to the surface of the coated electrode in a "sandwich assay" and the binding event was converted into a chemical signal. The sensor generated an accurate electric signal corresponding to the chemical signal that had precipitated onto the electrode surface. The concentration of the target was accurately measured and the device showed superior results when compared with the existing ones so far. The researchers have successfully tested the device against insulin, interleukin 6 (IL6) and glucagon in undiluted human plasma and excellent picogram-per-mL sensitivity was reported. These sensors are reusable, durable and can simply be washed and used a multiple times to detect several biomarkers serially. The ease of manufacture and the low cost has made 'eRapid' a much in demand technology with immense potential. Figure 2 describes the nanocomposite electrode (4).

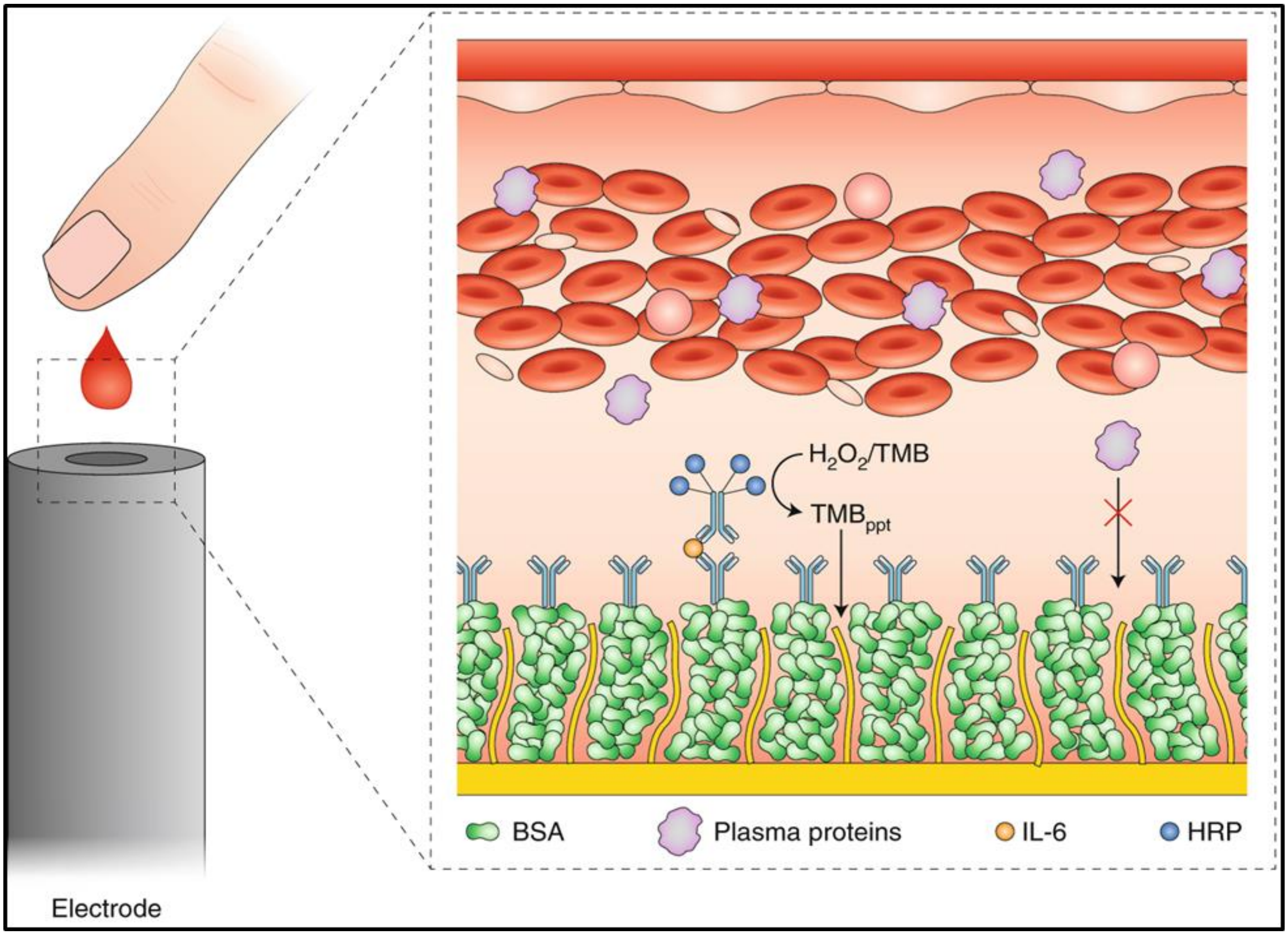

*Figure 2: The nanocomposite electrode [**Source:** Gooding JJ: Nature nanotechnology (2019)].*

The current and future prospects of the technology:

Since its conception the Wyss team has used the technology to successfully detect and test more than a dozen varied biomarkers with different molecular sizes ranging between 100 Dalton to 150,000 Dalton. Further experiments are in progress to optimize the sensitivity, conductivity and the cost of the devices further. This simple innovation in existing technology has paved way for better sensors and medical diagnostic tools which shall change the current face of self-diagnosis and at-home medical testing. Although in its infancy, 'eRapid' is capable in bringing about a revolution in the field of handheld point-of-care diagnostics and can further be used in environmental toxin sensing, implantable medical devices, small molecule detection as well as hospital diagnostics. These portable, multiplexed, innovative diagnostic tools are the next big trend in medicine which is here to stay and change our lives for the better. It is often said that self-medication is harmful but self-diagnosis and personal health monitoring are habits which we need to inculcate so that we are not only aware but also equipped to fight our health issues better. To wrap up we would just like to say take care because self-care is the first step towards living better, healthier and longer.

References:

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