



Wearable Biosensors



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Introduction

Challenges
And Future
Prospects

Type Of
Wearable
Biosensors

contents

Oral-cavity
Wearable
Biosensors

Ocular
Wearable
Biosensors

Epidermal
Wearable
Biosensors

Introduction

Schematic Representation Of Biosensor Operation Principles: Target Analyte Detection By The Corresponding Receptor Molecule Followed By Signal Transduction Method And Output

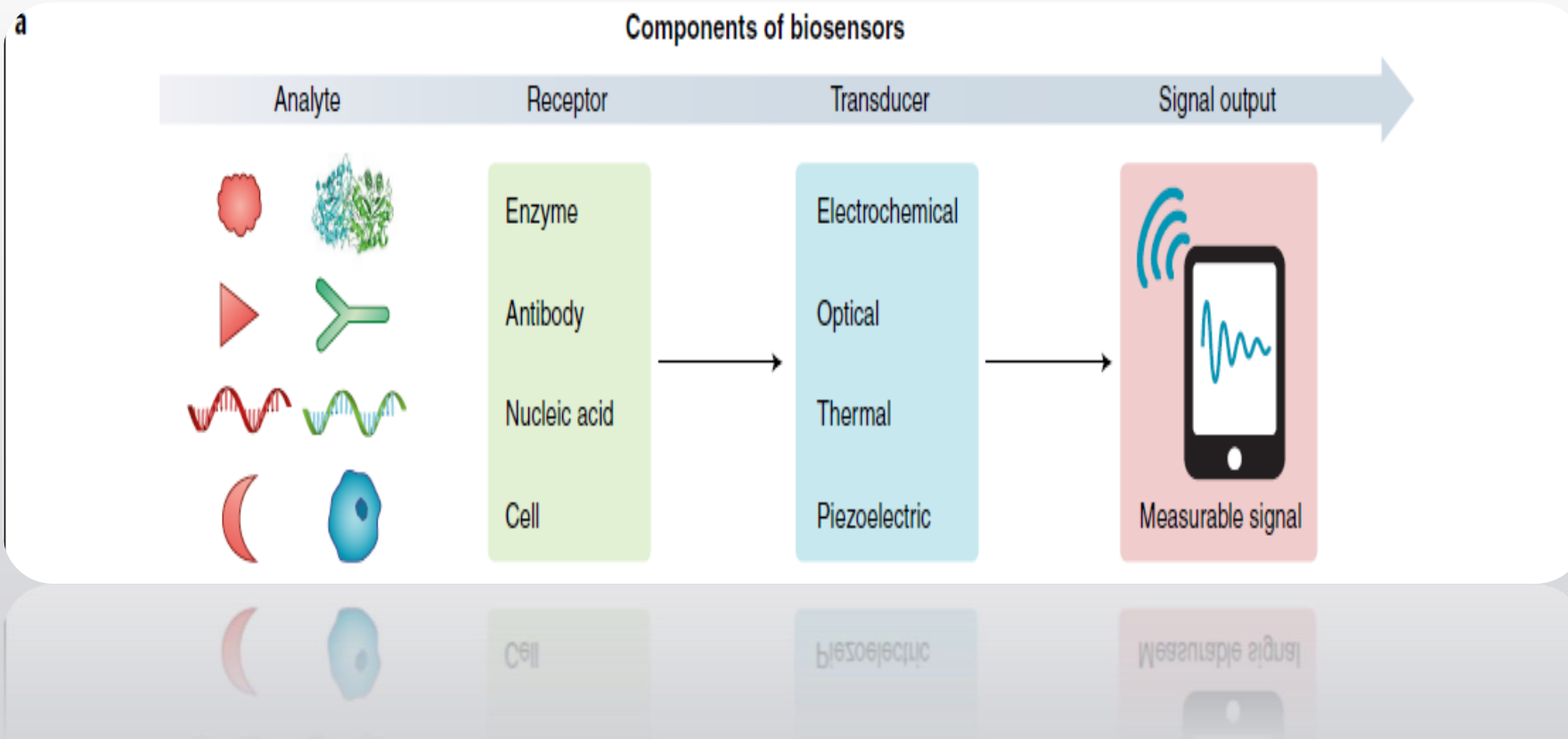


Figure Reference :Wearable biosensors for healthcare monitoring

Introduction

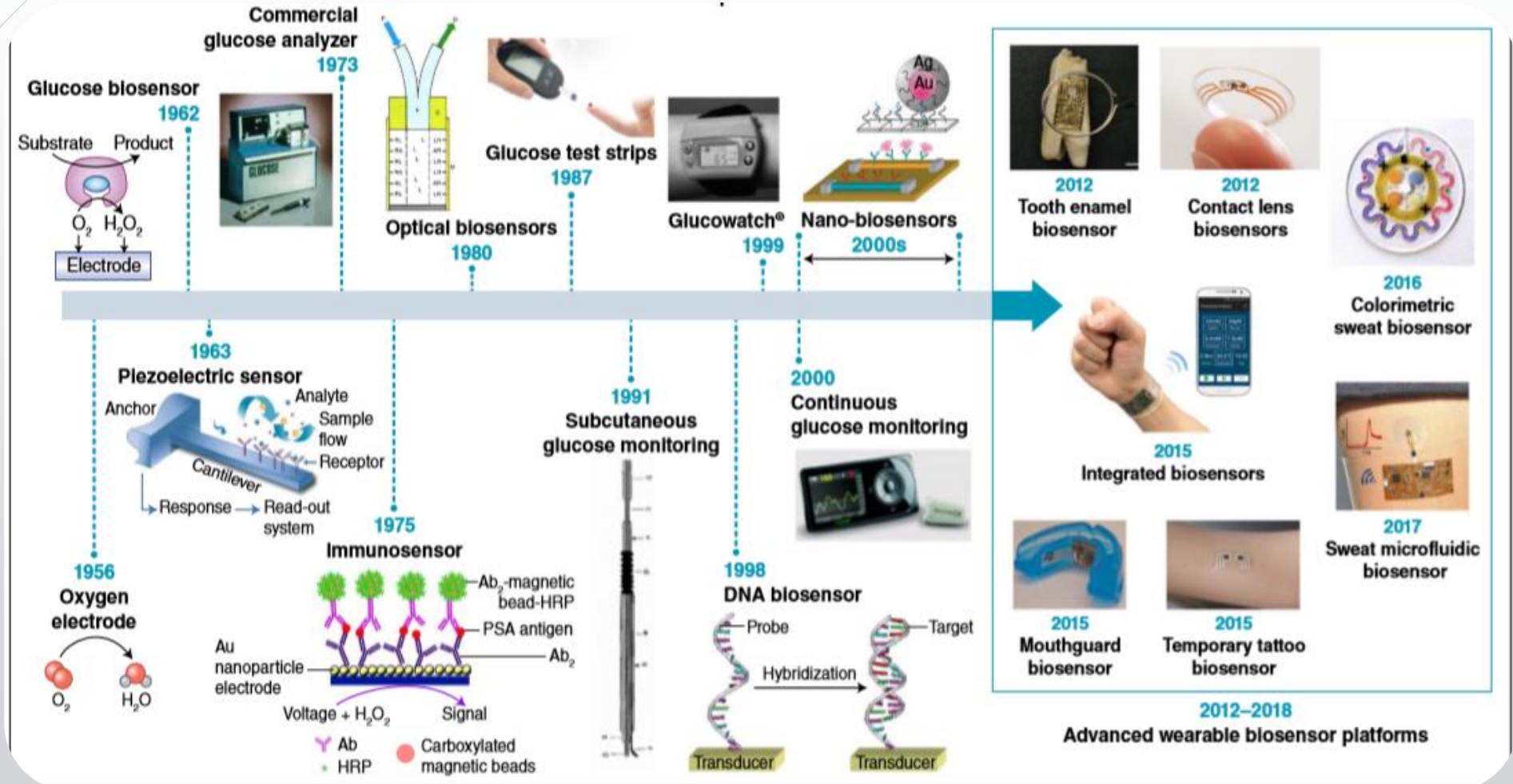


Figure Reference : Wearable biosensors for healthcare monitoring

Biosensor Developments to Wearables

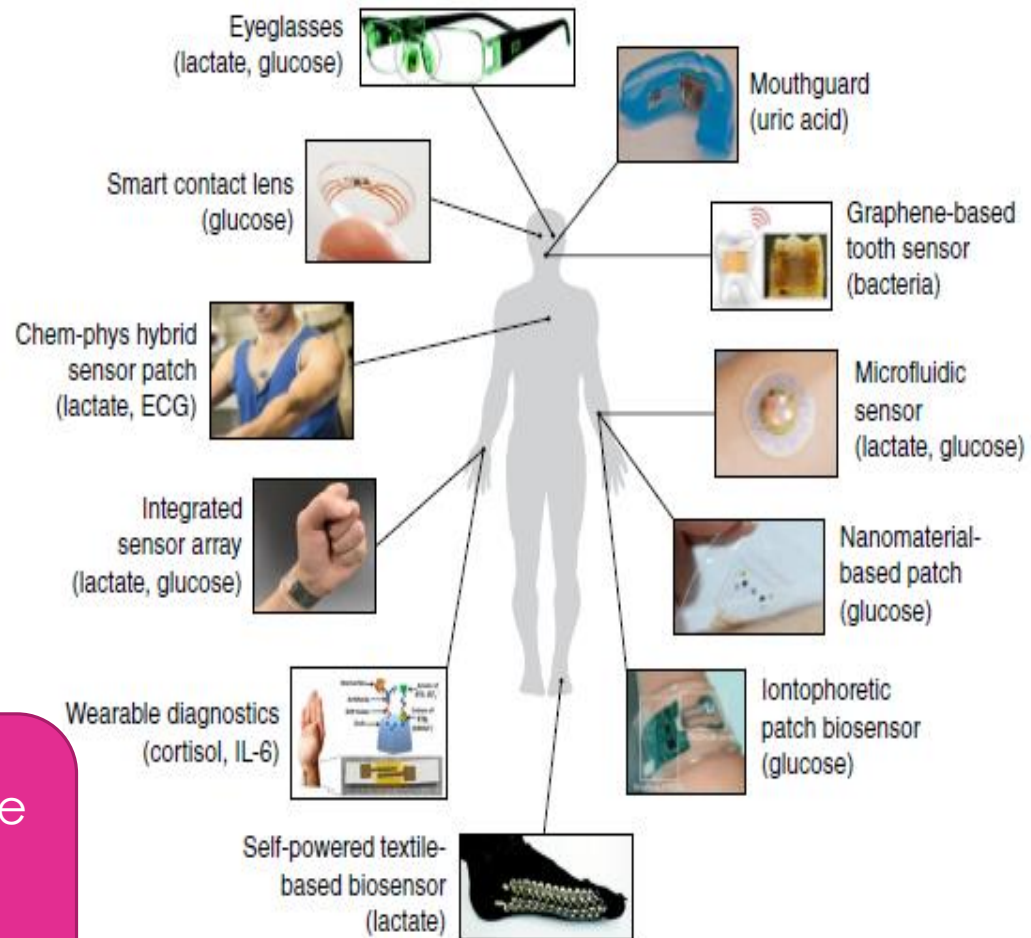
Introduction

Table 1 | Selected examples of commercial noninvasive or minimally invasive biosensors

Product, company	Analyte, sample	Wearable platform	Monitoring mechanism	Current stage	Website
Smart contact lens, Google and Novartis	Glucose in tears	Contact lens	Electrochemistry	Last update in 2018; this project is now on hold	https://verily.com/projects/sensors/smart-lens-program/
GlucoWatch, Cygnus Inc.	Glucose in ISF	Watch type	Electrochemistry	FDA approved, but retracted from market	No longer available
BioMKR, Prediktor Medical	Blood glucose	Wrist strap similar to a smart watch	Near infrared spectroscopy, bioimpedance	Under clinical testing for approval and market launch in Europe	https://www.prediktormedical.com/
GlucoWise, MediWise	Blood glucose	Finger clip	Radio frequency	Under development, running clinical trials with healthy volunteers	http://www.gluco-wise.com/
Freestyle Libre, Abbott	Glucose in ISF	Patch	Electrochemistry	FDA approved in US in July 2018	https://www.freestylelibre.us/
Dexcom G6 CGM, Dexcom	Glucose in ISF	Patch	Electrochemistry	FDA approved	https://www.dexcom.com/
GlucoTrack, Integrity Applications	Blood glucose	Finger clip	Ultrasonic, electromagnetic, thermal waves	Type 2 diabetes, approved in Europe	http://www.glucotrack.com/
Eversense, Senseonics	ISF glucose	Subcutaneous small stick implant	Fluorescence	Recently received FDA approval	https://www.eversenseddiabetes.com/
NovioSense tear glucose sensor, NovioSense	Tear glucose	Small stick (spiral type) placed under the lower eyelid	Electrochemistry	Tested in animals and human subjects	http://noviosense.com/

Table Reference :Wearable biosensors for healthcare monitoring

Wearable Biosensors



Representative examples of wearable biosensors.

Type Of Wearable Biosensors

Epidermal Wearable Biosensors

Ocular Wearable Biosensors

Oral-cavity Wearable Biosensors

Epidermal Wearable Biosensors

► Sweat-based biosensors



Figure Reference :Wearable biosensors for healthcare monitoring

Epidermal biosensors for real-time monitoring of sweat chemistry

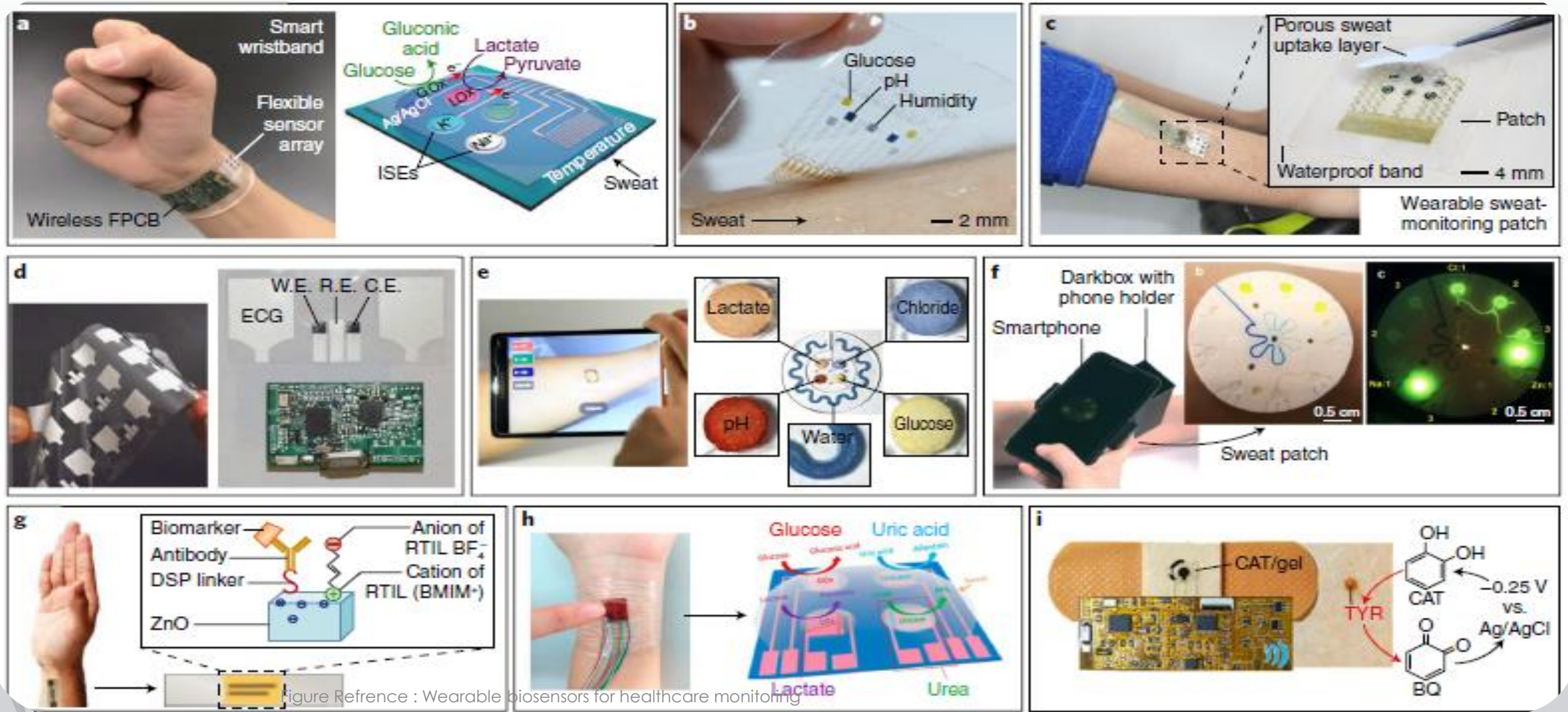


Figure Reference : Wearable biosensors for healthcare monitoring

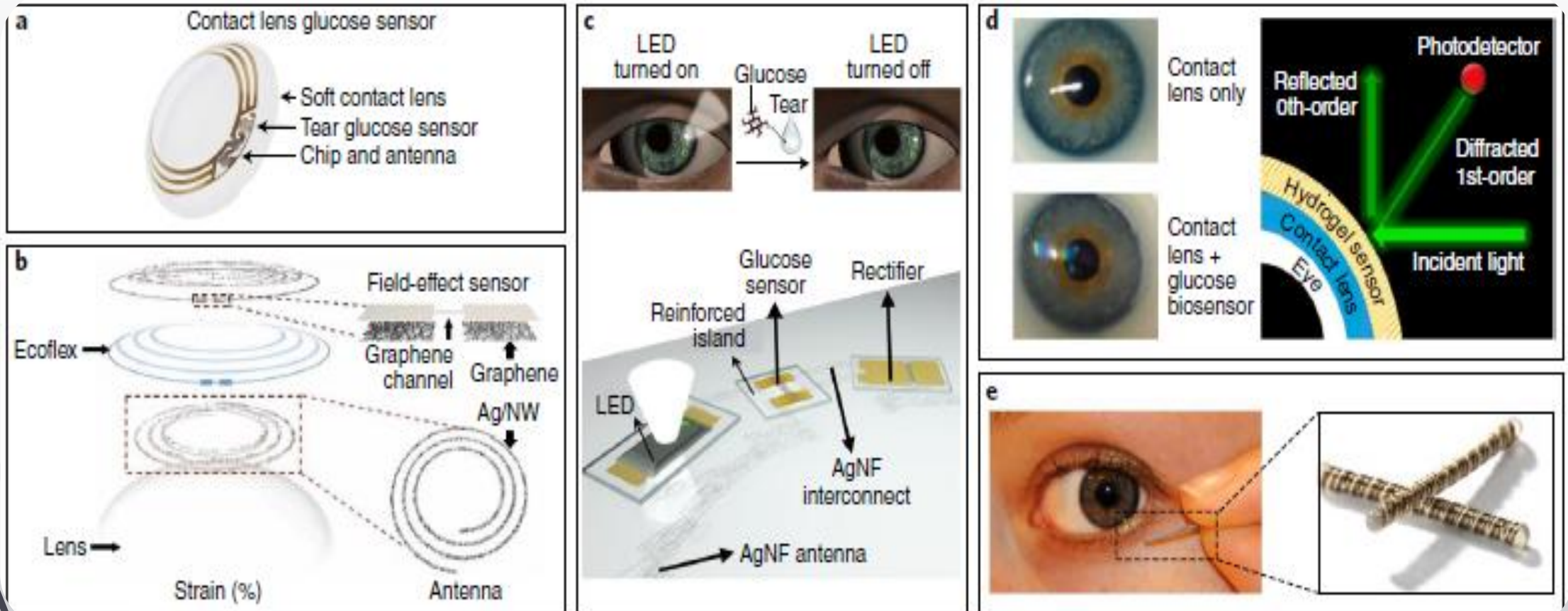
Ocular Wearable Biosensors

- ▶ Tear-based wearable biosensors



Figure Reference : <https://saednews.com/>

Tear-based biosensors



Oral-cavity Wearable Biosensors

- ▶ Saliva-based wearable biosensors



Saliva-based biosensors

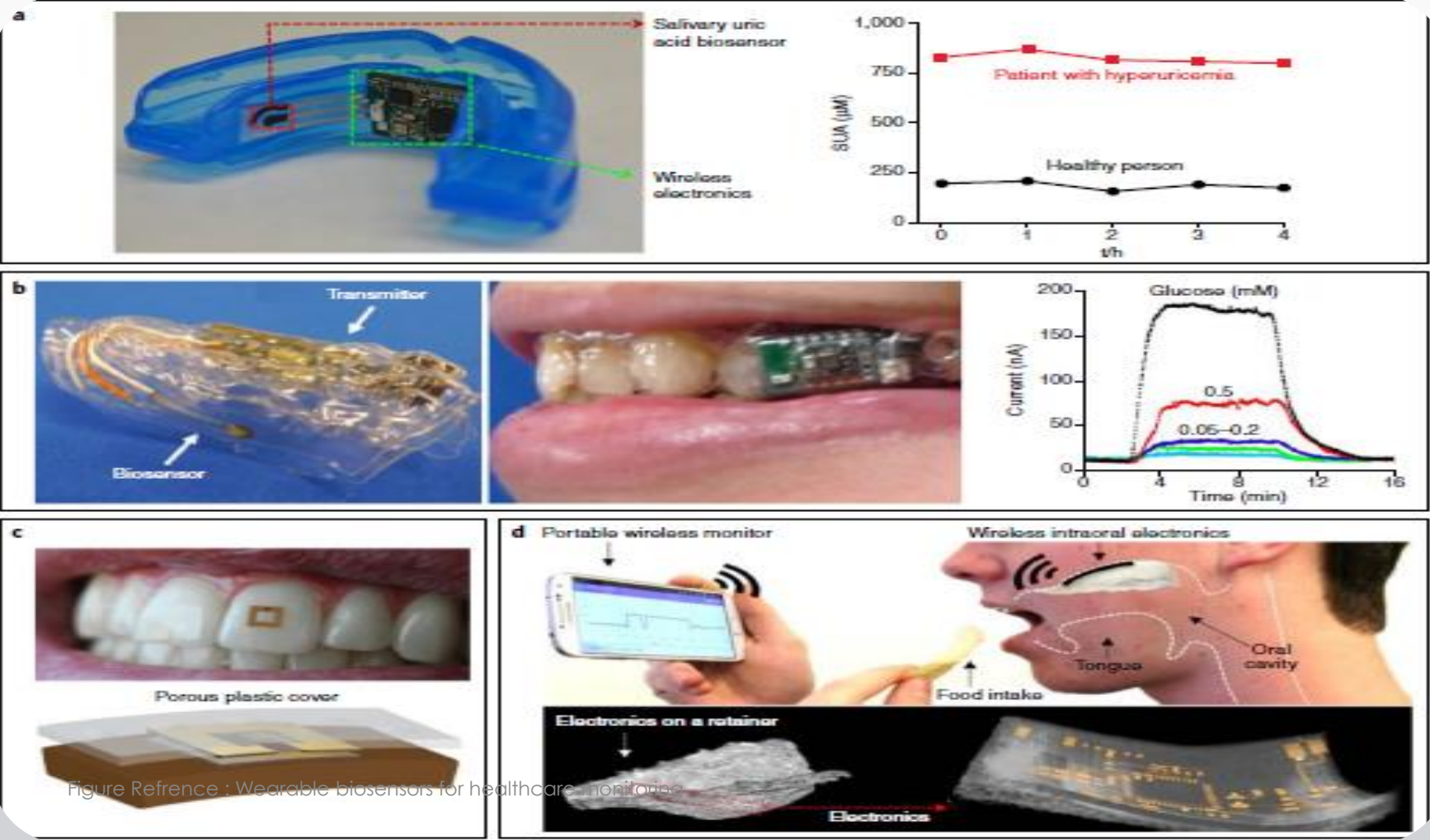
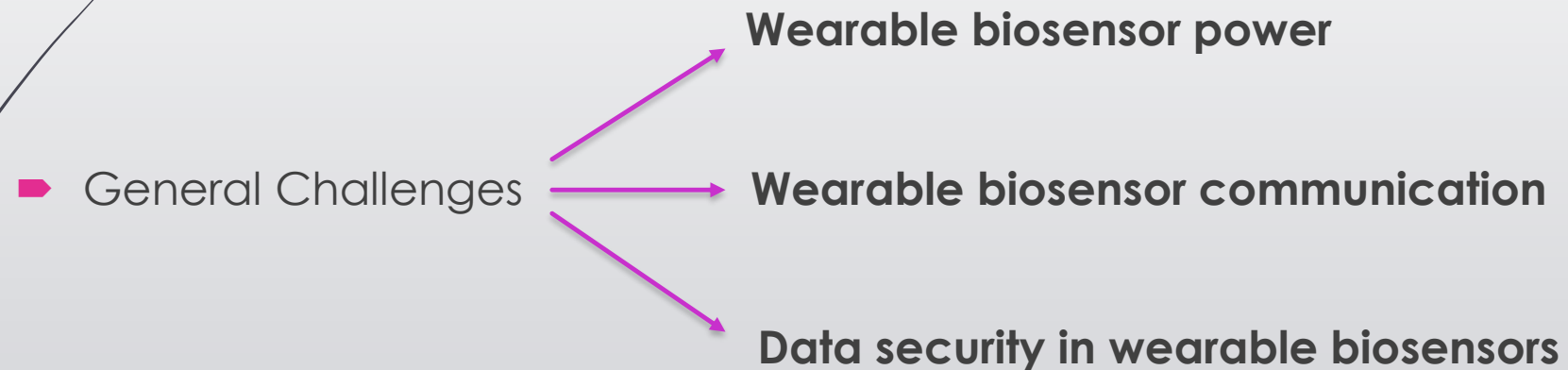


Figure Reference : Wearable biosensors for healthcare monitoring

Challenges And Future Prospects

- ▶ Epidermal Wearable Biosensors
- ▶ Ocular Wearable Biosensors
- ▶ Oral-cavity Wearable Biosensors



Wearable biosensors for healthcare monitoring

Jayoung Kim, Alan S. Campbell, Berta Esteban-Fernández de Ávila and Joseph Wang*

Wearable biosensors are garnering substantial interest due to their potential to provide continuous, real-time physiological information via dynamic, noninvasive measurements of biochemical markers in biofluids, such as sweat, tears, saliva and interstitial fluid. Recent developments have focused on electrochemical and optical biosensors, together with advances in the noninvasive monitoring of biomarkers including metabolites, bacteria and hormones. A combination of multiplexed biosensing, microfluidic sampling and transport systems have been integrated, miniaturized and combined with flexible materials for improved wearability and ease of operation. Although wearable biosensors hold promise, a better understanding of the correlations between analyte concentrations in the blood and noninvasive biofluids is needed to improve reliability. An expanded set of on-body bioaffinity assays and more sensing strategies are needed to make more biomarkers accessible to monitoring. Large-cohort validation studies of wearable biosensor performance will be needed to underpin clinical acceptance. Accurate and reliable real-time sensing of physiological information using wearable biosensor technologies would have a broad impact on our daily lives.

Wearable sensors have received much attention since the arrival of smartphones and other mobile devices, owing to their ability to provide useful insights into the performance and health of individuals^{1–4}. Early efforts in this area focused on physical sensors that monitored mobility and vital signs, such as steps, calories burned or heart rate. The face of wearable devices has changed rapidly in recent years, with researchers branching out from tracking physical exercise activity to focus on tackling major challenges in healthcare applications, such as the management of diabetes or remote monitoring of the elderly. To accomplish these goals, researchers have devoted substantial efforts to the development of wearable biosensors, which are defined as sensing devices that incorporate a biological recognition element into the sensor operation (for example, enzyme, antibody, cell receptor or organ-elle). The potential utility of wearable biosensors is evident from the rapidly increasing rate of newly reported proof-of-concept studies. Although several of these platforms are under clinical evaluation, successful translation to the commercial market has been lacking. Significant endeavors are underway toward the commercialization of noninvasive biosensors. However, these products still require further large-scale validation studies, the necessary device regulatory approvals and final marketing paths. Driven by the promise of the huge glucose sensing market, this commercial activity focuses largely on minimally invasive glucose monitoring devices, as illustrated in the representative examples given in Table 1.

A typical biosensor contains two basic functional units: a 'bio-receptor' (for example, enzyme, antibody or DNA) responsible for selective recognition of the target analyte and a physico-chemical transducer (for example, electrochemical, optical or mechanical) that translates this biorecognition event into a useful signal (Fig. 1a). Such devices were initially developed for *in vitro* measurements in controlled (laboratory or point-of-care) settings or for single-use home testing (for example, blood glucose test strips). A brief history of biosensing technologies preceding current wearable biosensors^{5–8} is provided in Fig. 1b. These past advances have paved the way to modern wearable biosensors for noninvasive biomonitoring applications as an alternative to blood monitoring biomedical devices in connection to wide range of healthcare applications.

Biosensors hold considerable promise for wearable applications due to their high specificity, speed, portability, low cost and low power requirements. Indeed, innovative biosensor platforms for noninvasive chemical analysis of biofluids, such as sweat,

tears, saliva or interstitial fluid (ISF), have already been widely applied to a variety of head-to-toe application sites, targeting an array of important diagnostic analytes in proof-of-concept demonstrations (Fig. 2)^{9,10,41–44}. Sweat, tears, saliva and ISF have been targeted as they can be sampled in a noninvasive manner, meaning that they can be readily accessed without disrupting the outermost protecting layers of the body's skin (the stratum corneum) and without contacting blood. As such, noninvasive sensing methods pose minimal risk of harm or infection and are generally more user friendly.

The wide acceptance of such wearable biosensor technology requires a deep understanding of the biochemical composition of bodily fluids, such as sweat or tears, and its relation to blood chemistry. Wearable monitoring platforms can lend insights into dynamic biochemical processes in these biofluids by enabling continuous, real-time monitoring of biomarkers that can be related to a wearer's health and performance. Such real-time monitoring can provide information on wellness and health, enhance the management of chronic diseases and alert the user or medical professionals of abnormal or unforeseen situations. Wearable biosensors can obviate painful and risky blood sampling procedures and can be readily blended with a wearer's daily routine. To accomplish this capability, the biosensing platform must provide direct contact with the sampled biofluids without inducing discomfort to the wearer. Such body compliance can be achieved through use of advanced materials and smart designs that provide the necessary flexibility and stretchability^{45–48}. Continuous multidisciplinary development of new biosensing technologies (and corresponding new materials and energy sources) has led to numerous proof-of-concept demonstrations and has driven growing efforts toward the commercialization activity of wearable sensors.

The attractive capabilities of modern wearable chemical and physical sensors and related research advances have been highlighted in several recent reviews^{2,49–51}. Unlike physical or chemical wearable sensors, the wearable biosensors reviewed here rely on highly specific bioreceptors capable of recognizing target analytes in complex samples at physiologically relevant concentrations. Despite rapid progress in wearable biosensor technology over the past 5 years, we are only at the beginning of understanding how wearable biosensor technologies can improve health and performance.

In the following Review, we provide an overview of the key advances in wearable biosensors from the past 2 years and discuss their potential as alternatives to invasive biomedical devices and

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