The use of biosensors in forensic science

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Background. Biosensors have emerged as indispensable tools with vast applications in diverse fields. In recent years, their potential has been increasingly recognised in the area of forensic science, where they offer significant advantages in terms of sensitivity, specificity and rapid detection.
Objectives. To review the use of biosensors in forensic science.
Methods. A review of the use of biosensors in forensic science was conducted, using publications within the past 15 years. The publications were reviewed for relevance. The complete text was therefore examined for data on biosensors.
Results. A total of 21 publications were reviewed, of which 81% were journal articles and 9% were books; 1 (5%) was a book chapter and 1 (5%) an obituary. The most common uses discussed in the literature were forensic applications (27%). Health applications were discussed in 21%, environmental and security applications in 18% each, food applications in 11% and agricultural uses in 5%. The forensic uses or potential applications discussed were drug or toxicology screening (21%), biological trace screening, including body fluid detection, identification, sweat and blood analysis (21%), pathogen detection (17%), body detection (12.5%), chemical analysis (12.5%), latent fingerprint detection (8%) and alcohol detection (8%).
Conclusion. Despite their potential, routine use of biosensors in forensic science remains limited. Current research and technological advances in biosensor technology hold promising prospects for the continued evolution and integration of these analytical devices into forensic sciences and beyond. Future developments are expected to focus on multiplexing capabilities, nanotechnology integration for portability, and the exploration of newly discovered Cas proteins for bacteria and virus detection.

Undergraduate Res Health 2025;3(1):e2018. https://doi.org/10.7196/URHJ.2024.v3i1.2018

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A biosensor is an analytical device that can measure biological or chemical signals proportional to the concentration of the analyte, transduce them into a measurable signal, and then display the results.[1,2] A biosensor usually consists of four components, as illustrated in Fig. 1.

The analyte is the substrate or substance of interest. A multitude of analytes can be detected using biosensors, including but not limited to glucose, pathogens, toxins, etc.[3]

The bioreceptor is a biological entity that reacts to a specific analyte. Common examples of bioreceptors include enzymes (proteins), aptamers (short single-stranded sections of DNA or RNA that fold into a three-dimensional structure when interacting with the target analyte), antibodies (protein molecules produced by the immune system in response to an antigen), nucleic acids (DNA or RNA), and molecular imprinted polymers (polymer matrices where template-shaped cavities are imprinted with the cavities matching the specific analyte being tested).[2]

Biosensors are classified according to the type of transducer they use. A transducer is a device that converts energy or signals from one form to another. For example, it takes the strength of a chemical reaction and converts it into an electrical impulse that can be interpreted. Common types of transducers are magnetic, optical (fluorimetric, chemiluminescence, optical fibre, surface plasmon resonance), electrochemical (amperometric, potentiometric, conductometric, impedimetric), mass-based (pizoelectric, magnetoelastic, quartz crystal microbalance) and thermal.[4]

Important characteristics that good biosensors need in order to be functional include selectivity, reliability, sensitivity, and limit of detection (LOD). The selectivity refers to the biosensor's ability to identify and react with a specific analyte within a mixture of different substances.

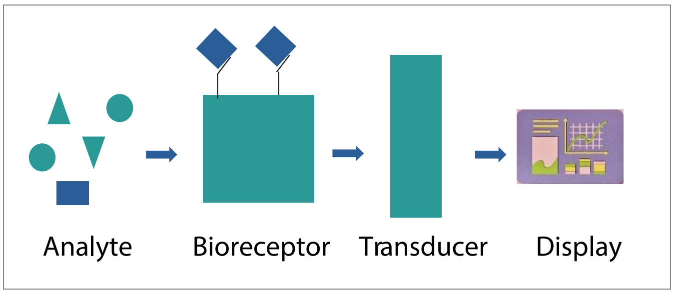

Fig. 1. Common components of a biosensor.

When constructing a biosensor, the bioreceptor must be very specific for the target analyte. Reliability is the ability of the biosensor to replicate and reproduce the same results multiple times using the same analyte and bioreceptor. This reproducibility will indicate that the results (and therefore the biosensor) are reliable. The sensitivity and LOD are also of paramount importance in the construction of a biosensor. The LOD is the minimum amount of the analyte that can be found within a substance that can be successfully detected by the biosensor. For a biosensor to be useful, it needs to be able to detect trace amounts of analyte.[2]

The concept of biosensors dates back to the early 20th century, when M Cremer proved that the concentration of an acid suspended in a liquid generates a proportional electric potential when this acid suspension is separated by a glass membrane. This finding led to the production by W S Hughes of an electrode that could measure the pH (hydrogen ion concentration) of a solution.[2]

In the 1960s, the father of biosensors, Leland C Clark Jr, worked on the development of a heart-lung machine, during which he developed an oxygen meter that is also known as a Clark electrode.[5] This was possible by reducing oxygen at a platinum electrode (after wrapping the electrode in a gas-permeable piece of cellophane for protection). In turn, he calibrated this electrode by deoxygenating his test solutions by adding glucose oxidase and glucose to the solution, which removed the oxygen from the test solution and formed hydrogen peroxide as a by-product. His work on the oxygen meter soon resulted in the first known biosensor for glucose, when Clark immobilised the glucose oxidase on his oxygen electrode and realised that the glucose would decrease proportionately to the oxygen in the solution and the hydrogen peroxide would increase.[5] In 1969, Guilbault and Montalvo developed the first potentiometric biosensor to detect urea.[2] The first commercial biosensor was developed in 1975.[5,6] A timeline of the major developments is shown in Fig. 2.[2,6]

Biosensors are used in a multitude of industries and areas, such as health monitoring and diagnosis, water quality monitoring, agriculture, environmental monitoring, security, food safety, drug development and monitoring, and forensic analysis. There are, however, limited reviews on the use of biosensors in forensic science. This article will give a broad overview of the use of biosensors in the above areas, but the main focus will be on their use in forensic science.[6]

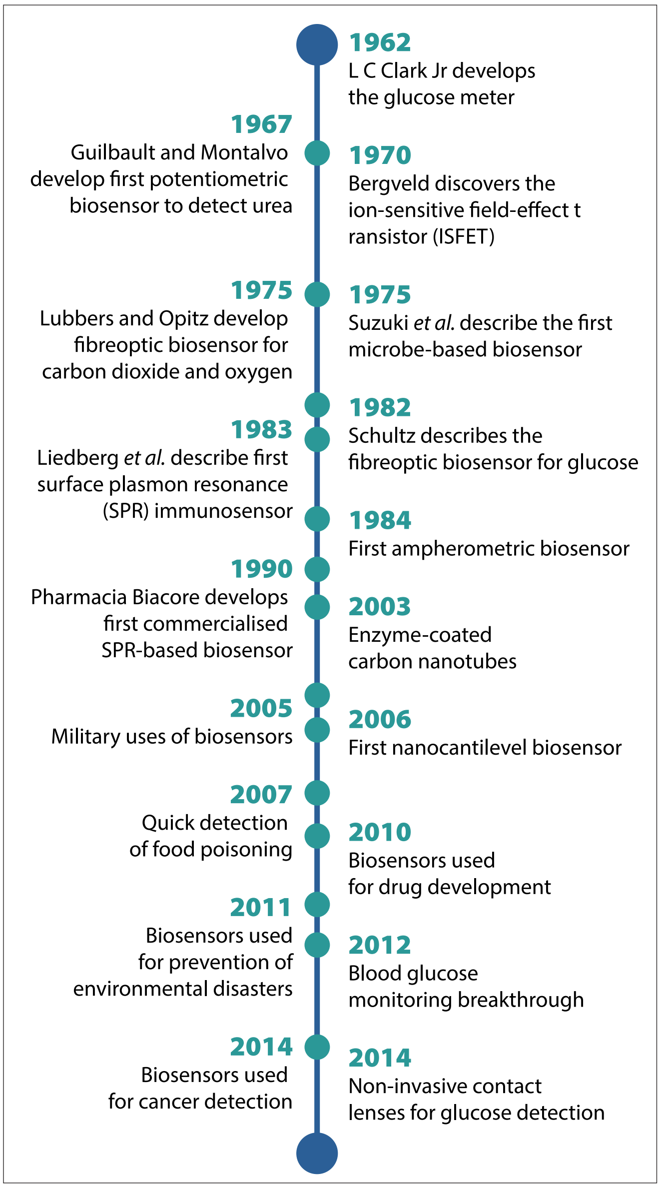

Fig. 2. Timeline of the development of biosensors.

Methods

A review of the use of biosensors in forensic science was conducted, and articles published within the past 15 years were used. The articles were reviewed for relevance. The complete text of the articles was therefore examined for data on biosensors.

Data were collected from well-known web search engines and databases, including PubMed, Google Scholar and Science Direct. References for selected articles were assessed so as not to miss any relevant information.

The following keywords were used for this research: biosensors, biological sensors, biological devices, forensic science and medicine, application and use, and limitations. Words were connected using Boolean operators with 'AND' as an example.

The data collected were sorted in terms of different categories, as ordered in historical developments in which similarities and differences were observed. Secondly, the data were sorted in terms of types of biosensors and applications, and data on current research on biosensors were analysed.

The study aimed to review the use of biosensors in forensic science, as there are limited reviews on their use in this area. The objectives were to provide a brief history of biosensors, to review the literature around the use of biosensors in forensic science, to explain where and when they are used, and to explore current areas of research on biosensors in forensic science and their future uses using journals, manuals and books.

Ethics approval for this study was obtained from the Sefako Makgatho University Research and Ethics Committee (ref. no. SMUREC/M/60/2023:PG).

Results

A total of 21 publications were reviewed, of which 81% (n=17) were journal articles, 9% (n=2) were books, 5% (n=1) was a book chapter and 5% (n=1) was an obituary. As shown in Fig. 3, the publications were from a range of countries, with 20% (n=4) each from the US and the UK, 14% (n=3) from India, and 10% (n=2) from China. The remainder, each

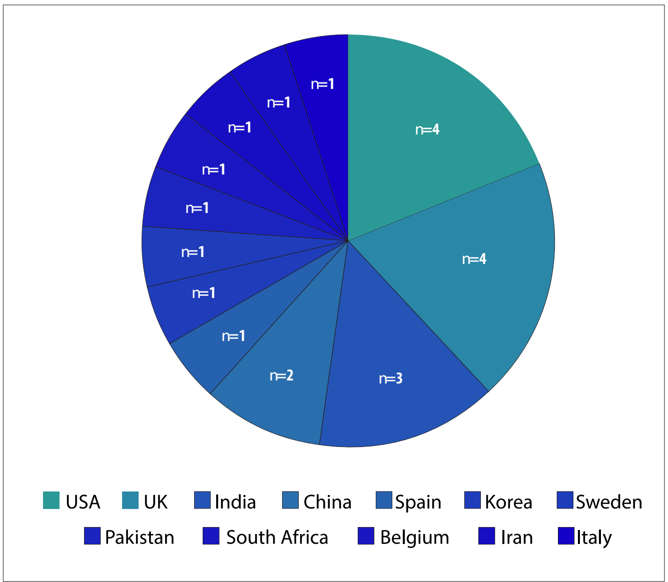

Fig. 3. Countries in which the articles reviewed were published.

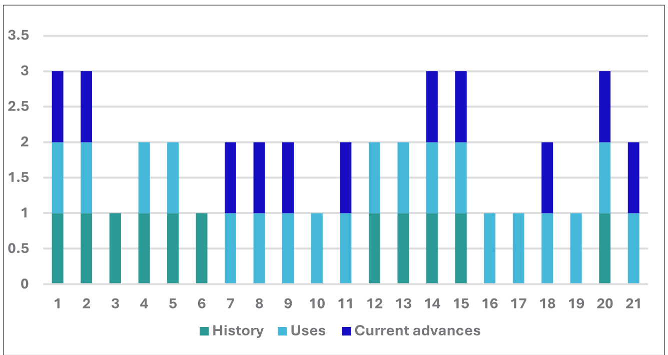

Fig. 4. Representation of areas of study covered by the literature analysed.

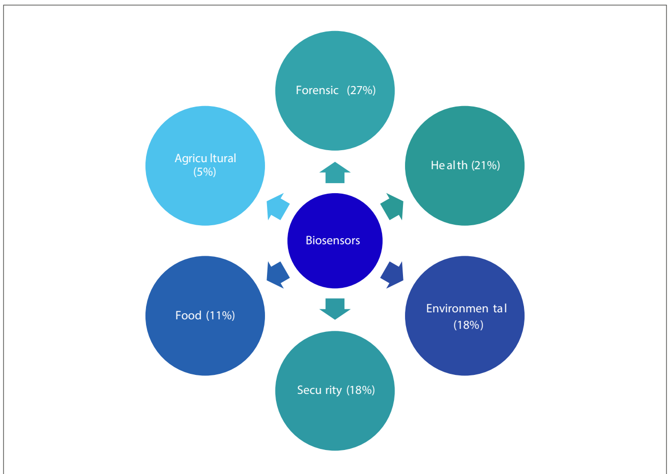

Fig. 5. Current uses and applications of biosensors across different industries and sectors.

comprising 5% (*n*=1), were from Belgium, Iran, Italy, Korea, Pakistan, South Africa, Spain and Sweden.

The literature collected was limited to include only the past 15 years. Most (14%; *n*=3) was published in 2022; 2010, 2012, 2014, 2020 and 2021 had 2 publications each year (48%; *n*=10); and the remaining publications were from 2006 - 2008, 2011, 2016, 2017, 2019 and 2023 (38%; *n*=8).

Of the literature reviewed, 52% (*n*=11) discussed the history of biosensors and their development. Two publications, accounting for 9.5% of the reviewed literature, focused solely on the history and development of biosensors. The majority, 90.5% (*n*=19), explored and discussed the various applications of biosensors, while 52% (*n*=11) also examined the current and future advances in the field (Fig. 4).

The most common uses of biosensors in the literature reviewed were forensic applications. Around 27% of applications (*n*=12) were purely forensic, 21% (*n*=9) were in health, 18% each (*n*=8 and *n*=8) were in the environmental and security fields, 11% (*n*=5) were food applications, and 5% (*n*=2) were agricultural uses. This breakdown (Fig. 5) highlights the limited number of reviews on the use of biosensors in forensic sciences, as forensic applications were favoured in the literature selection for this review.

The forensic uses or potential applications and uses that were discussed in the literature reviewed were drug or toxicology screening (21%),[1,7,8] biological trace screening (including body fluid detection, identification, sweat and blood analysis) (21%),[1,8-10] pathogen detection (17%),[1,7] body detection (12.5%),[8,11] chemical analysis (12.5%),[7] latent fingerprint detection (8%)[10] and alcohol detection (8%).[7,12]

The future developments discussed were nanotechnology, the CRISPR-Cas system, multiplexing biosensors, label-free biosensors and LOC (lab-on-a-chip) capabilities. These innovations and technologies were discussed across 29% of the literature reviewed (*n*=6).[1,2,4,6,13,14]

Discussion

Since the humble beginnings of the biosensor, major developments have occurred across all industries and sectors.[15] The earliest publication in which the term biosensor was used was in 1966. Then the number slowly increased as new innovations were developed, with ~3 000 articles published between 1984 and 1990.[16] The same number of publications appeared in the early 1990s, but with double the amount of patent applications, before exponentially increasing in the later 1990s and 2000s.[16,17] Currently, ~55 000 scholarly publications on biosensors can be found on PubMed.[16] This is illustrated by Olson and Bae,[16] who examined the trends in biosensors throughout the years.

The commercial use of biosensors also increased at an astonishing rate. According to strategic business reports and forecasts, the global market for biosensors increased from USD6.1 billion in 2004 to USD8.2 billion in 2009.[18] The vast majority of the revenue, 99%, comes from applications in the biomedical and life sciences.[18] Currently, the global biosensor market is estimated to be worth USD15.7 billion, with projections that it will be worth USD28.9 billion by 2029.[19]

As mentioned above, most biosensors are applied in the medical field and healthcare.[18,19] Biosensors can be used as diagnostic, screening and monitoring tools for medical conditions.[1,14,20] The advantages of tools of this type are that they are non-invasive, relatively cheap and easy to use, and with the assistance of smartphones, trends can be recorded and stored for easy record keeping.[6] Screening and monitoring tools can take various forms, including wearable biosensors, such as those currently available on the market, which can be worn around the wrist, ankles or chest.[6] Wearable biosensors can measure vital signs such as the heart rate, blood pressure, temperature and cardiac activity.[6] Epidermal biosensors worn on the skin or clothing or even in the form of a tattoo can monitor sweat for alcohol, glucose, lactate and a host of electrolytes.[6,20] Biosensors are available in the form of contact lenses that can monitor the components of the tears for glucose levels, and can detect pressure changes within the orbit of the eye to monitor glaucoma progression.[6,20] Saliva can also be monitored for certain proteins and uric acid levels.[6]

Disease detection is also possible with the use of biosensors. Cancer detection has been described in the literature, where biosensors can screen for certain proteins secreted by tumour cells and even detect whether the tumour cells are benign or malignant.[3] Cardiovascular disease can also be diagnosed and monitored by detecting cardiac markers in the blood.[13] The importance of pathogen detection was once again demonstrated during the COVID-19 pandemic, and rapid pathogen detection tools have become an integral part of healthcare.[14]

Other areas in which biosensors have made a significant contribution include environmental, agricultural and food screening. This screening is mostly applied to avoid serious health hazards to humans and animals and to detect dangerous pollutants and pathogens in the air, water and ground.[3] The pollutants screened for include heavy metals (lead, mercury, copper, etc.) and pesticides (organophosphates), as well as micro-organisms that live in wastewater (*Salmonella*, *Listeria*, *Monocytogenes*, *Campylobacter jejuni*, *Escherichia coli*). These pesticides and heavy metals are known to build up over time, and cause serious health issues.[21] The pathogens can lead to widespread outbreaks with harmful outcomes.[21]

The forensic and security sectors are catching up on the uses of biosensors. The most common uses for biosensors include drug or toxicology screening, biological trace screening, pathogen detection, body detection, chemical analysis, latent fingerprint detection and alcohol detection.

Drug and toxicology screening is of importance in both the forensic field, as drugs and toxins are a common cause of sudden death and contribute to a large number of unnatural deaths, and the security sector, where illicit drugs are of particular importance.[7] Various types of biosensors have been developed that can identify the presence of arsenic. These include an electrochemical device that uses the inhibitory effect of arsenic on acetylcholinesterase.[7] Many biosensors for the detection of cyanide have been proposed, including one using its inhibitory effect on the horseradish peroxidase enzyme.[7] The detection of illicit drugs is currently still mostly laboratory bound, with the gold standard being mainly gas chromatography-mass spectrometry. Unfortunately, this is expensive and time-consuming, and requires expert equipment and expert analysis.[7] As an alternative, biosensors are more cost-effective and faster, and can be used in the field as a screening tool. Another advantage of biosensors is that they are highly sensitive and specific and can pick up trace amounts of drugs that would be impossible with traditional methods.[16] Various biosensors have been developed for the detection of cocaine, codeine, opiates, methamphetamine, gamma-hydroxybutyric acid (GHB) and ecstasy.[1]

Biological biosensors are a unique type of biosensors mainly used in the forensic and security sectors. These use the olfactory capabilities of various vertebrates, and even invertebrates, to identify a certain substrate. The downside of using trained animals as biological sensors is that they use the principles of associative learning and conditioning, and training can take a long time. Secondly, canines especially are linked to a specific handler and can only work with them. Canines are used in search and rescue teams to identify survivors of mass disasters, but also to pick up the scent of decay. They are also invaluable in the detection of various substances, including illicit drugs, narcotics, explosives and flammable fluids.[8,11] Rats are used for the detection of explosives and landmines in certain African countries. The advantages of using rats are that they can operate independently of a handler and their movements can be observed remotely, thus reducing the risk of a handler being involved in a landmine explosion.[8] Invertebrates such as certain honeybees, wasps and moths are also used for the detection of bodies and explosives. Pavlovian conditioning is used with invertebrates, to teach them to associate certain odours with food resources. The advantages of using invertebrates include that training can be completed in as little as 15 seconds.[8]

Another important aspect of forensic investigation is the detection of biological traces.[9] According to Locard's principle of exchange, which states that a perpetrator will bring something into a crime scene and take something with him, it is imperative to be able to detect bodily fluids and tissues that can be transferred through touch.[9] Biological trace detection through biosensors includes human semen, prostate-specific antigen, glycophorin A (a protein found in the red blood cell membrane), and acid phosphatase (found in prostatic epithelial cells).[1] The chemical content of fingerprints can also be analysed, and saliva can be used to screen for the presence of tetrahydrocannabinol (THC).[10]

Lastly, alcohol is of immense importance in the forensic field, as it is involved in a myriad of forensic scenarios. Luo *et al.*[12] describe a disposable biosensor that provides an accurate serum alcohol level that is fast, cost-effective and reliable. While the disposable biosensor could be advantageous in drunk driving cases, it is not yet applicable to postmortem samples, as the sensor cannot differentiate between alcohol and aldehydes, which are produced endogenously during the postmortem period.[12] Biosensors for determining alcohol concentration in exhaled air are also being tested.[7] Even sweat is a viable option for blood alcohol level determination.[7]

Biosensors have come a long way since their initial development, and the industry is expanding at a rapid rate. Unfortunately, the routine use of biosensors has not yet been established in forensics, despite their numerous advantages. Rigorous research is required to adapt biosensors for medicolegal applications, as many reported uses have not been validated as admissible evidence in court. Additionally, the application of biosensors to postmortem samples will require further intensive research in the future.[7,9,10] Current advances in biosensors, however, are focusing on multiplexing capabilities, which make it possible for one biosensor and one analyte to be screened for multiple substances/enzymes simultaneously.[7] Nanotechnology has been widely incorporated in the medical field, but it has not been established in the forensic field. Future developments will therefore be certain to focus on nanotechnology, as biosensors in forensics need to be small and portable.[1] Lastly, newly discovered Cas proteins have opened the field for bacteria and virus detection using biosensors.[14] This development is exciting for the field of forensic pathology, as viral and bacterial detection is currently complex and time consuming. However, studies will have to be done specifically on postmortem samples for the application to be viable, as no such studies currently exist.[14]

Conclusion

This study reviewed 21 articles published over the past 15 years, with a focus on diverse applications of biosensors across different countries. Forensic applications emerged as a prominent area, encompassing drug and toxicology screening, biological trace screening, pathogen detection, body detection, chemical analysis, latent fingerprint detection and alcohol detection.

Despite advances, the routine use of biosensors in forensic science is still underdeveloped. Rigorous research is essential to establish their applicability in the medicolegal field. Future developments are expected to focus on multiplexing capabilities, nanotechnology integration for portability, and the exploration of newly discovered Cas proteins for detection of bacteria and viruses.

In summary, biosensors have emerged as indispensable tools with vast applications in diverse fields. The ongoing research and technological advances hold promising prospects for the continued evolution and integration of these analytical devices into forensic science and beyond.

Declaration. The research for this study was done in partial fulfilment of the requirements for KRM's MB ChB degree at Sefako Makgatho Health Sciences University.

Acknowledgements. The authors would like to express their gratitude to their families, friends and colleagues for their invaluable contributions to this research. Special thanks are extended to the Department of Forensic Pathology at Sefako Makgatho Health Sciences University.

AI declaration. The authors acknowledge that AI-assisted tools may have been used for language editing and refinement in the preparation of this manuscript, in accordance with the journal's policy on AI usage.

Author contributions. KRM conceptualised the research, drafted and submitted the protocol for ethics approval, collected the data and did the data analysis. He submitted a research report to the Department of Forensic Pathology as part of the requirements for his degree. KKH was the supervisor and CvW was the co-supervisor. KKH, CvW and YB edited the research report for journal submission and made reviewer corrections as suggested.

Funding. None.

Data availability statement. The datasets generated and analysed during the current study are available from the corresponding author (CvW) upon reasonable request.

Conflicts of interest. None.

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Received 11 March 2024. Accepted 3 February 2025. Published XXXX.