WHAT ARE BIOSENSORS?

HOW DO BIOSENSORS WORK AND WHAT ARE THEIR APPLICATIONS IN THE WATER SECTOR?

During the Covid 19 pandemic Biosensors have been in the spotlight as a method for detecting the presence of the virus. Biotechnology including biosensors has been predicted to be a key industry during the 21st century with huge innovation potential. So what are biosensors? How do they work and what are their applications in the water sector? Why and when would you choose to use a biosensor over other monitoring technologies? What new developments are there in biosensors and how can they be commercialised?

Water quality monitoring is traditionally achieved through a grab sample and then lab analysis, which could involve growing microbiology for 24 or 48 hours, and/or analytical chemistry such as mass spectrometry, liquid chromatography or colorimetric chemistry which all take time and can be costly. However, a biosensor can be dipped into water to provide a near instant result of a water quality parameter such as the presence of bacteria, viruses, algae, or pollutants. Biosensors have potential applications in monitoring drinking water supply systems, wastewater systems and raw water in catchments for early detection of water quality issues.

"A 'biosensor' can constitute biological molecules integrated with electrical components right through to technology monitoring whole organisms", explains Richard Luxton a Professor at the Institute of Biosensing Technology at the University of the West of England. Typically, a biosensor will detect the presence of a target molecule in a sample, through the use of a specific bioreceptor (e.g. an antibody) which sends a signal of the specific biological binding event via a transducer, which is then processed further and ultimately displays a result to the user (figure 1).

One potential application of a biosensor is for monitoring the growth of biofilms inside drinking water distribution systems. The presence of biofilms is related to drinking water quality since biofilms can release pathogenic microorganisms into water (Figure 2). However, accessing buried drinking water pipelines to monitor biofilm growth can be difficult without disrupting the water supply. Dr Frances Pick and colleagues within The Water Distribution Research Group at the University of Sheffield have been working in collaboration with South Staffordshire Water on a proof-of-concept biosensor for this purpose. An innovative sampling technique comprises articulated pipe sections which can be added onto existing pipework with minimal disruption, combined with flow cytometry (analysis of cells as they flow past a laser). Research conducted by Dr Pick and colleagues has shown that the rate of biofilm growth is different between operational drinking water distribution systems, and that biofilms are likely to be a function of water quality. If water companies started monitoring biofilm growth, they could use this information to prioritise networks in terms of risk return, assess the outcome of network interventions, including operational maintenance (such as mains conditioning, flushing etc) or treatment changes, and ultimately justify maintenance or investment resources to minimise customer dissatisfaction.

Another application is a biosensor to help optimise wastewater treatment plant (WWTP) operation. This time the biosensor comprises a microbial fuel cell which is installed and naturally colonised by the local microorganisms present. Given some time to acclimatise, the normal microbial growth rate can be established for the site, which is measured via the electrical potential on the fuel cell (Microbial Electron Transfer or MET) (Figure 2). A change in MET can provide an early warning of a toxic event which will inhibit anaerobic digestion processes at the WWTP. A time series of MET data can help identify the source of the toxic events e.g. disinfection of breweries on certain days and times was determined at a plant in Canada, and the data used to charge industries for wastewater processing at the plant. Measuring MET has also been used at a WWTP in Canada to help optimise carbon dosing for denitrification, since during the Covid pandemic the plant was not getting as much carbon from wastewater as it was originally designed and calibrated for. In Arizona this biosensing method has been used to give confidence to WWTP operators that the first flush after a heavy rainfall event was diluted enough to release stormwater and avoid overloading the plant.

Biosensors have been developed to monitor Covid 19 in wastewater. Dr Zhugen Yang at Cranfield University has developed a microfluidic paper-based device, for rapid detection of SARS-CoV-2 in the field (with results in less than one hour compared with the much slower lab-based PCR test), through detection of nucleic acids specific to Covid 19. Since the virus can be detected in wastewater before people are symptomatic this could be used as an early warning system of an outbreak. A sample of wastewater was processed with a syringe-membrane and is then added to the microfluidic device and an indicator panel changes green if the sample is positive or blue if the sample is negative for the virus. The device is low cost at less than £1 per test, and would be easy to scale up for mass production as it simply comprises wax printed paper, cassette, with some biochemical reagents. It is manufactured with laser cutting and is easy to assemble. Other benefits are that it is user-friendly without technical knowledge. Cranfield University partnered with water companies to test the device in WWTP to develop an early warning system for Covid 19 detection, as part of the UK National Wastewater Epidemiology Surveillance Programme (N-WESP). Next steps will be to improve the data science and add telemetry e.g. through the Internet of Things (IoT). The platform can be adapted to detect different

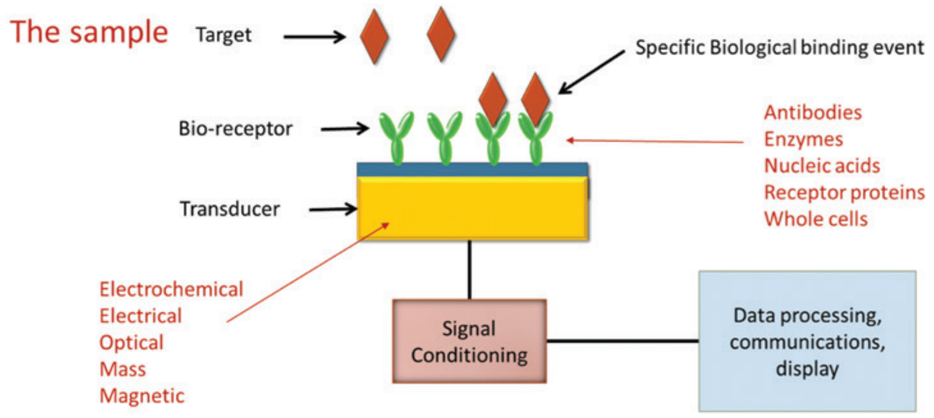

Figure 1: Components of a biosensor (© Richard Luxton, UWE, 2021)

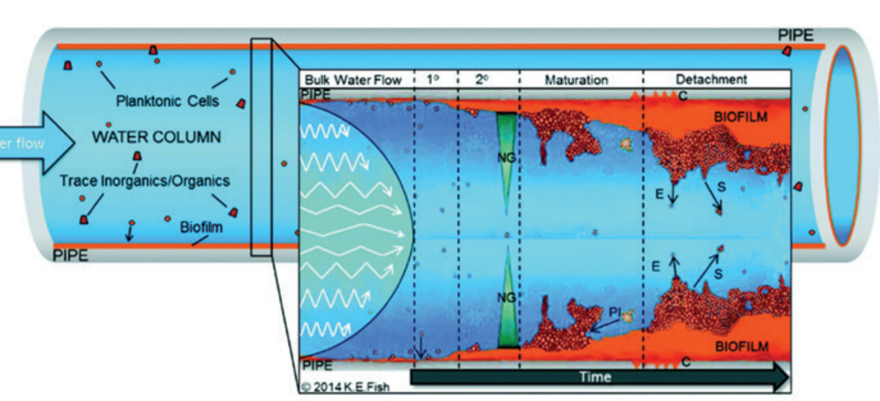

Figure 2: Biofilm development and interaction with the water flow within a drinking water pipe. © Dr Katherine Fish, 2014 (published within Fish et al. 2016).

pathogens such as malaria and sexual transmitted infectious disease. For example, the device was used to test the blood from a local school in Uganda to detect malaria and in a local Indian farm for rapid veterinary diagnosis.

Biosensors can also be used for monitoring catchments. A whole cell biosensor is under development to detect mercury from illegal gold mining in the River Nanay, Peru, through a collaboration between Open BioLab Brussels (Erasmushogeschool Brussel) and the laboratorio de Manipulación y Visualización de Moléculas Individuales (UPCH). Mercury is toxic to humans and other organisms. A natural detoxification system in bacteria uses metal pumps to pump heavy metals out of the bacterial cell. This system has been genetically engineered in a plasmid (bacterial DNA) and transferred into E coli, so that if mercury is present a reporter gene is expressed to produce a blue pigment (Amil CP blue). In a cell pellet, this blue pigment can be seen when the E coli bacteria are grown for 16 hours into water contaminated with mercury. The reporter gene is expressed in proportion to the amount of mercury present, and the amount of blue pigment produced has a linear correlation with the concentration of mercury present in a water sample. At present the blue pigment can be seen at 10 nM mercury concentration, whereas the safety limit is 5 nM for drinking water, so the sensitivity needs to be improved for detection of mercury at levels relevant for human health. With further development, this represents a cheap (once engineered), easy to handle technology with no need for high tech equipment – just glassware and the naked eye, and users do not need to be highly skilled. A further step would be to combine this whole cell biosensor with electronics for measurement of the blue pigment produced.

Many biosensing technologies are very young and getting new technologies to the point where they are adopted by industry represents a massive hurdle. "Typically, universities get engagement from the market for research and development, but to present the full commercialised product with repeatable results to the market is a much bigger step." Says Tom Williams of Enebio "that takes time, patience, investment and is a matter of spreading your risks."

Dr Martin Peacock of Zimmer and Peacock agrees, "In order to survive you need to have a range of products to support your business, not rely on developing just one product," explains Dr Peacock, "obviously funding helps you to cross the well-known 'valley of death' of product development, but I would strongly recommend anyone to get their product to market early to sell it to early adopters otherwise you will miss the boat and someone else will get there first."

This is an exciting time for new technologies, with significant investment forecast in the immediate future for the water sector. Therefore, the future looks bright for biosensors for water.

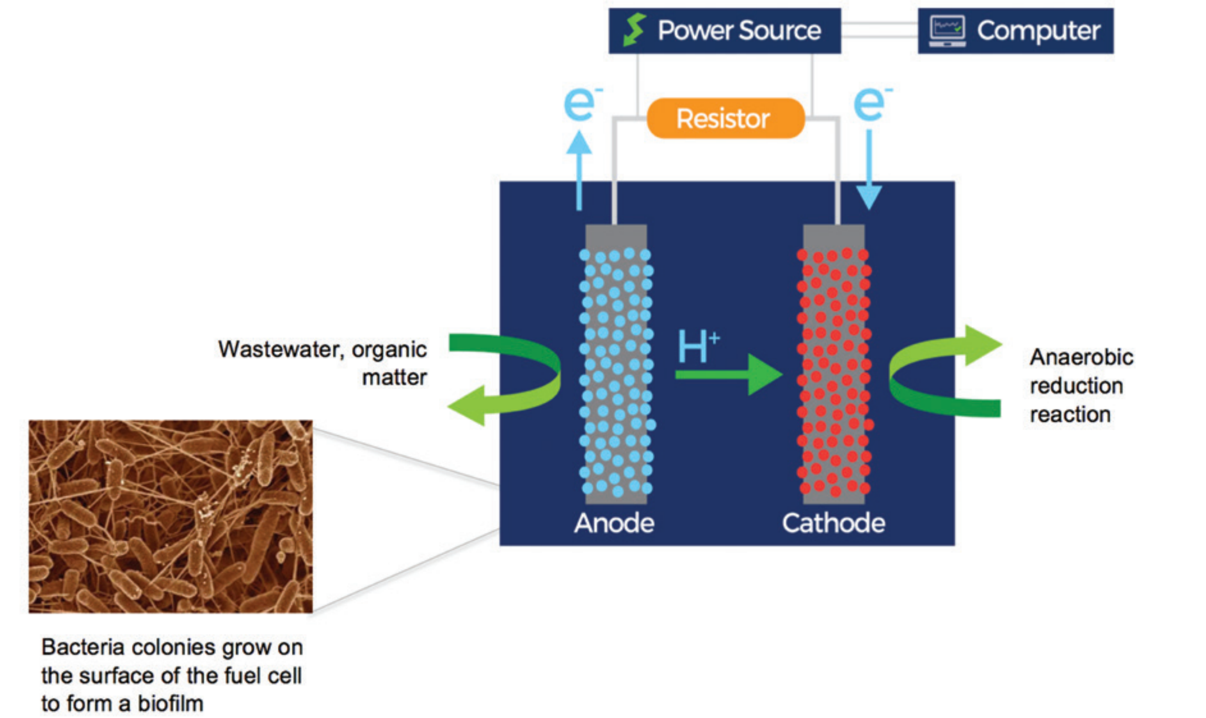

Figure 2: A microbial fuel cell biosensor can detect changes in environmental conditions in real-time (© Tom Williams, Enebio, 2021)

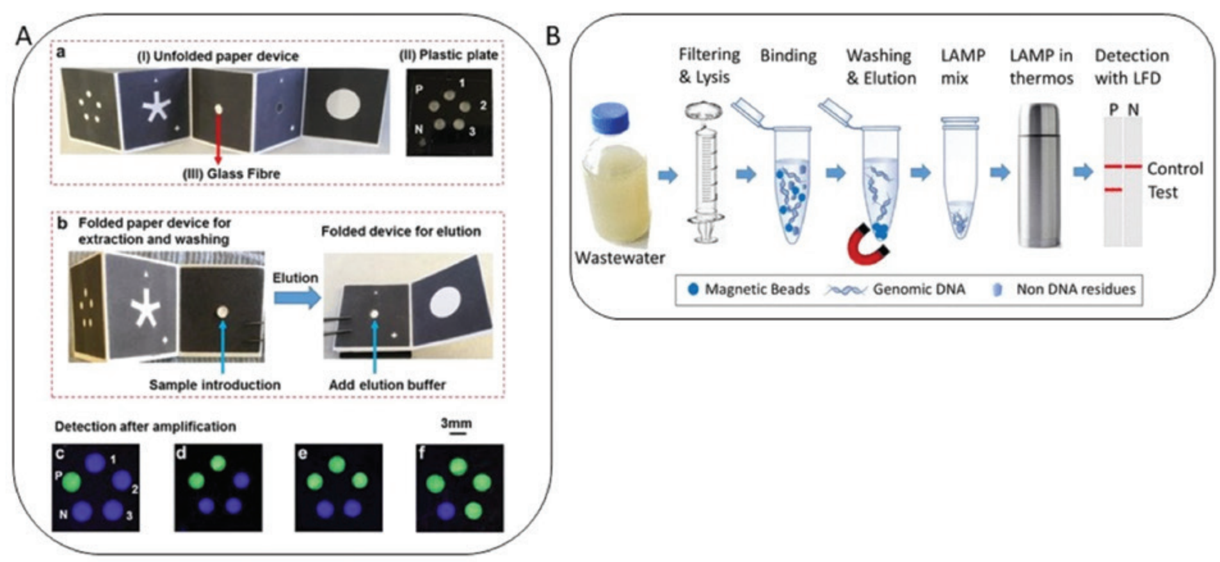

Figure 3: (A) The schematic diagram of the origami-paper device for the detection of three pathogens (BoHV-1, Brucella and Leptospira), (B) Illustration of the wastewater analysis using paper-based lateral flow device © Dr Zhugen Yang, 2018

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