

WHITE PAPER

Virus detection: Fast, sensitive, and cost-effective with electrochemical testing

With significant global viral outbreaks becoming the norm rather than generational outliers, it is imperative that fast, sensitive, and cost-effective testing is available to the masses. It is only by a concerted effort of testing and tracing that viral outbreaks can be effectively controlled before becoming global pandemics.

Screen-printed electrodes (SPEs) allow rapid, widespread testing of populations for infectious disease, without the need of skilled personnel or burdensome equipment in the field. The possibility of point-of-care (POC) testing with SPEs has been exhibited in several recent studies. Metrohm DropSens, as a manufacturer of SPEs as well as their compact measuring devices, is the right partner for virology research projects—big and small. With a high production capability, combined with a valid **ISO 13485** certification «Manufacturing of sensors for medical devices», this means testing procedures developed on DropSens SPEs can be reliably scaled up for larger operations, with easier approval by the Food and Drug Administration (FDA). As the leading brand in the market for this printing technology, Metrohm DropSens can design custommade SPEs and offers the expertise and exceptional customer support needed for complicated projects at scale.



INTRODUCTION

In our recent history, humanity has conquered agriculture, industrial manufacturing, and arguably, the final frontier of space. Due to the myriad technological, scientific, and medical breakthroughs we have made as a species (especially in the past two hundred years), we now enjoy better health than our ancestors, and with that, significantly longer lifespans. This has contributed to exponential population growth, and an increasing proportion of elderly citizens. In mid-2020, the global population rests just below 8 billion people, though this number is expected to grow by another 2 billion by 2050 [1].

However, as society grows more in size and density, we also strive to be more interconnected. In 2015, more than 54% of people lived in urban areas, and this is projected to increase to 66% in 2050 [2]. The development of megacities (defined as having 10 million people or more), as well as the explosion of affordable air travel which allowed a level of transport previously only accessible to the upper echelon, has led to an ever faster spread of disease in modern times.

The widespread epidemics of the Zika and Ebola viruses in the past decade have been overshadowed by the global pandemic of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), more commonly known as «COVID-19». Within a matter of months, COVID-19 spread from Wuhan, China across

the world. Each country's response has varied: from the tactics of encouraging normalcy to attempt quicker herd immunity, to extremely strict quarantine measures, especially for the elderly, and the closure of borders and non-essential industries. However, the most effective way to trace and contain the spread of viruses is through comprehensive testing.

Several factors leave conventional testing methods lacking when it comes to controlling the spread of highly communicable diseases. High costs limit the affordability and overall availability of tests to the general population, especially for poorer communities. Complicated analytical procedures require trained professionals, which may not be available in all areas. On top of this, the waiting time between test and result is prohibitive – sometimes taking several days, which could mean the difference between life or death.

Point-of-care testing with screen-printed electrodes allows rapid, widespread testing of populations for viral outbreaks at low cost and without the need for skilled analysts or complicated measuring equipment. Since SPEs are customizable, they can be modified and manufactured to suit the needs of all types of research groups. Metrohm DropSens SPEs, which are ISO 13485 certified, means testing procedures developed on these products require shorter times to receive FDA approval. The bulk manufacturing capability of Metrohm DropSens guarantees a stable commercial source for custom-made SPEs and their measuring devices at any order size—big or small.

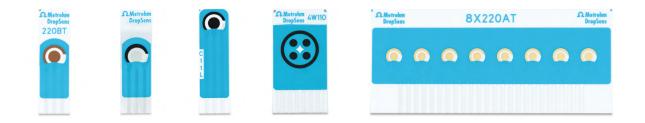


Figure 1. Assortment of screen-printed electrodes available from Metrohm DropSens.

VIRAL OUTBREAKS AND HUMAN HEALTH

Unlike the majority of bacteria, most viruses cause disease. Viruses, however, cannot survive without hosts, and therefore spread easily especially in densely populated areas. While bacterial infections can be fought with a range of antibiotics, viruses require specific vaccines, which can be extremely difficult to manufacture.

Infectious diseases are a public health concern, especially when it comes to epidemics and pandemics, where not only regional but international entities must step in and work together to stop the spread among the populace.

Several viral outbreaks have caught global attention and attracted calls for faster, more accessible testing, including Ebola [3], avian influenza virus (H5N1, H1N1, and others) [4,5], hepatitis [6], malaria [7], noroviruses [8,9], dengue [10], adenovirus [11], SARS (severe acute respiratory syndrome) [12], HIV (human immunodeficiency virus) [13], and even HPV (human papillomavirus) [14]. While some are capable of killing their human hosts in a relatively short timespan, others can linger for decades.

One commonality between these diseases is that they have all been successfully tested with disposable, custom-made SPEs from Metrohm DropSens [3–14].

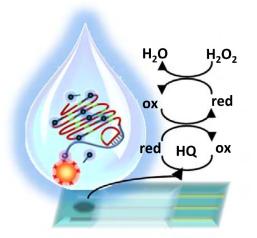


Figure 2. Representation of the electrochemical measurement of Ebola virus in a sample placed on a DropSens SPE [3].

GENERAL VIRAL TESTING METHODS

The importance of testing for the presence of harmful viruses in the population cannot be overstated. In order to stop the spread of especially communicable diseases, testing must be accurate, reliable, timely, affordable, and of course widely available.

Viral testing can be accomplished via several different methods, including virus isolation cultures, enzymelinked immunosorbent assay (ELISA), and other molecular methods like polymerase chain reaction (PCR) and reverse transcription polymerase chain reaction (RT-PCR). These techniques have drawbacks, such as requiring cumbersome, bulky instruments or special facilities, specialty chemicals, or skilled technicians. Additionally, the procedures are labor-intensive and can be time-consuming.

BENEFITS OF ELECTROCHEMICAL TESTING

Recently, initiatives for diagnostic testing methods have been launched by agencies such as the WHO to create faster, more accurate, affordable tests especially in low-resource areas. For these reasons, electrochemical testing methods have been developed on disposable screen-printed electrodes, exhibiting major promise for fast, affordable, precise testing directly at the point of care [3–14].

– SPEED

The rapid testing capabilities of electrochemical biosensors is among one of their greatest advantages. Whether through preventive measures of testing before symptoms appear (or after potential exposure), to confirm an active viral infection, or even to test for previous exposure by the presence of specific antibodies, the time from test to result is key to saving lives.

Results are obtained within minutes, rather than hours or days with other conventional techniques. Waiting for days for results can lead to further viral communication in the community, or even death in the absence of proper care. Earlier response is vital to stopping the spread of disease.

- LIMIT OF DETECTION

Specific electrochemical detection techniques (e.g., voltammetric or amperometric analysis) already allow for the detection of low analyte concentrations. The high adsorption capabilities of carbon-based working electrodes where certain recognition elements are attached play a key role in the improvement of sensitivity. To further decrease the detection limit, signal amplification by chemical or electrochemical catalytic reactions are commonly used.

- EASE OF USE

The compact size of the measuring device, not to mention the SPEs themselves, equates to complete portability for testing on the go. This allows rapid, accurate viral testing in all situations – from the point of care as well as in more remote areas without availability of larger laboratory facilities. Simply add a small volume of sample to the electrode, insert it into the measuring device, and receive results about viral exposure in minutes.

- COST

The low cost per test is a great advantage of using screen-printed electrodes for virology studies. Each SPE is meant to be disposable after a single use, ensuring a fresh substrate for every sample.

The affordability and portability of SPEs and their measuring devices makes this technique much more attractive for economically depressed areas or regions without an abundance of specialized testing laboratories and highly trained laboratory analysts.



Figure 3. Metrohm DropSens kit including DRP-STAT200 portable bipotentiostat and DRP-110 SPEs, used in Ebola virus studies [3].

- REGULATORY APPROVAL

Metrohm DropSens is certified by **ISO 13485 «Manufacturing of sensors for medical devices»**. This certification permits a simpler pathway to regulatory approval (such as by the FDA) and leads to quicker commercialization of validated tests developed on these products in the medical field.

- CUSTOMIZATION

Metrohm DropSens has the technology to develop screen-printed electrodes based on the individual needs of the customer. The configuration and dimensions of the electrodes are adapted to their specific requirements. Various types of inks can be used and combined in customized electrodes: carbon, gold, platinum, silver, silver/silver chloride, and more.

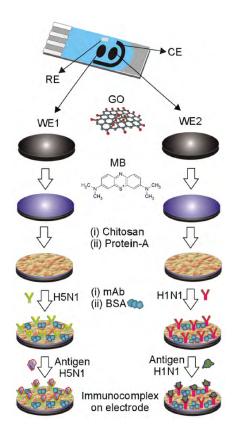


Figure 4. Surface modification of SPE for the detection of H1N1 and H5N1. WE: working electrode, CE: counter electrode, and RE: reference electrode [5].

- AVAILABILITY

The large-scale manufacturing capabilities at Metrohm DropSens guarantee a trusted, reliable source for the mass production of SPEs suitable for viral testing. With decades of electrochemical expertise, a worldwide distribution network, and top class after-sales support, the widespread commercialization of tests developed on these products is no problem.

METROHM DROPSENS: A COMPLETE SOLUTION PROVIDER

As a market leader in manufacturing reliable screenprinted electrodes as well as their measuring devices, Metrohm DropSens is the ideal partner for virology studies based on electrochemical testing, as well as for other research involving SPEs.

With a proven track record of providing custom solutions to laboratories performing virology studies on Metrohm DropSens products [3–14], combined with the ISO 13485 certification, these electrochemical biosensors can go through the regulatory approval process with less hassle than with products sourced from other manufacturers.

Large-scale manufacturing capabilities combined with a global distribution network allows for faster commercialization possibilities with a reliable source of materials.

The low cost of these products compared to other offerings on the market is an additional benefit, minimizing test development costs for research laboratories.



Portability and the simplicity of use allows rapid testing with screen-printed electrodes in all situations, not only off-site in specialized laboratories with a skilled staff. Results are both reproducible and reliable. Fast results mean quicker reaction times – for swift treatment, but also for tracing the spread of contagion and developing a concerted response before the situation gets more out of control.

For more information

Visit the Metrohm DropSens website at **www.dropsens.com** to have an overview of our products, capabilities, and additional peer-reviewed scientific literature featuring these electrodes and measuring devices.

References

[1] United Nations. Population. https://www.un.org/en/sections/issues-depth/population/index.html (Accessed May 4, 2020).

[2] World Health Organization. Global Health Observatory (GHO) data. https://www.who.int/gho/urban_health/en/ (Accessed May 4, 2020).

[3] Carinelli, S.; Kühnemund, M.; Nilsson, M.; Pividori, M. I. Yoctomole electrochemical genosensing of Ebola virus cDNA by rolling circle and circle to circle amplification. *Biosensors and Bioelectronics* **2017**, *93*, 65–71. doi:10.1016/j.bios.2016.09.099

[4] Jarocka, U.; Sawicka, R.; Góra-Sochacka, A.; Sirko, A.; Dehaen, W.; Radecki, J.; Radecka, H. An electrochemical immunosensor based on a 4,4'-thiobisbenzenethiol self-assembled monolayer for the detection of hemagglutinin from avian influenza virus H5N1. *Sensors and Actuators B: Chemical* **2016**, *228*, 25–30. doi:10.1016/j.snb.2016.01.001

[5] Veerapandian, M.; Hunter, R.; Neethirajan, S. Dual immunosensor based on methylene blue-electroadsorbed graphene oxide for rapid detection of the influenza A virus antigen. *Talanta* **2016**, *155*, 250–257. doi:10.1016/j.talanta.2016.04.047

[6] Manzano, M.; Viezzi, S.; Mazerat, S.; Marks, R. S.; Vidic, J. Rapid and label-free electrochemical DNA biosensor for detecting hepatitis A virus. *Biosensors and Bioelectronics* **2018**, *100*, 89–95. doi:10.1016/j.bios.2017.08.043

[7] Ruiz-Vega, G.; Arias-Alpízar, K.; de la Serna, E.; Neves Borgheti-Cardoso, L.; Sulleiro, E.; Molina, I.; Fernández-Busquets, X.; Sánchez-Montalva, A.; Javier del Campo, F.; Baldrich, E. Electrochemical POC device for fast malaria quantitative diagnosis in whole blood by using magnetic beads, Poly-HRP and microfluidic paper electrodes. *Biosensors and Bioelectronics* **2020**, *150*, Article 111925. doi:10.1016/j.bios.2019.111925

[8] Chand, R.; Neethirajan, S. Microfluidic platform integrated with graphene-gold nano-composite aptasensor for one-step detection of norovirus. *Biosensors and Bioelectronics* **2017**, *98*, 47–53. doi:10.1016/j.bios.2017.06.026

[9] Shionoiri, N.; Nogariya, O.; Tanaka, M.; Matsunaga, T.; Tanaka, T. Capsid protein oxidation in feline calicivirus using an electrochemical inactivation treatment. *Journal of Hazardous Materials* **2015**, *283*, 410–415. doi:10.1016/j.jhazmat.2014.09.049

[10] Cheng, M. S.; Lau, S. H.; Chan, K. P.; Toh, C.; Chow, V. T. Impedimetric cell-based biosensor for real-time monitoring of cytopathic effects induced by dengue viruses. *Biosensors and Bioelectronics* **2015**, *70*, 74–80. doi:10.1016/j.bios.2015.03.018

[11] Caygill, R. L.; Hodges, C. S.; Holmes, J. L.; Higson, S.; Blair, G. E.; Millner, P. A. Novel impedimetric immunosensor for the detection and quantitation of Adenovirus using reduced antibody fragments immobilized onto a conducting copolymer surface. *Biosensors and Bioelectronics* **2012**, *32*, 104–110. doi:10.1016/j.bios.2011.11.041

[12] Martínez-Paredes, G.; González-García, M.; Costa-García, A. Genosensor for SARS Virus Detection Based on Gold Nanostructured Screen-Printed Carbon Electrodes. *Electroanalysis* **2009**, *21*, 379–385. doi:10.1002/elan.200804399

[13] Gan, N.; Luo, N. X.; Li, T. H.; Zheng, L.; Ni, M. J. A Non-enzyme Amperometric Immunosensor for Rapid Determination of Human Immunodeficiency Virus p24 Based on Magnetism Controlled Carbon Nanotubes Modified Printed Electrode. *Chinese Journal of Analytical Chemistry* **2010**, *38*, 1556–1562. **doi:10.1016/S1872-2040(09)60076-1**

[14] Bartosik, M.; Durikova, H.; Vojtesek, B.; Anton, M.; Jandakova, E.; Hrstka, R. Electrochemical chip-based genomagnetic assay for detection of high-risk human papillomavirus DNA. *Biosensors and Bioelectronics* **2016**, *83*, 300–305. doi:10.1016/j.bios.2016.04.035

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