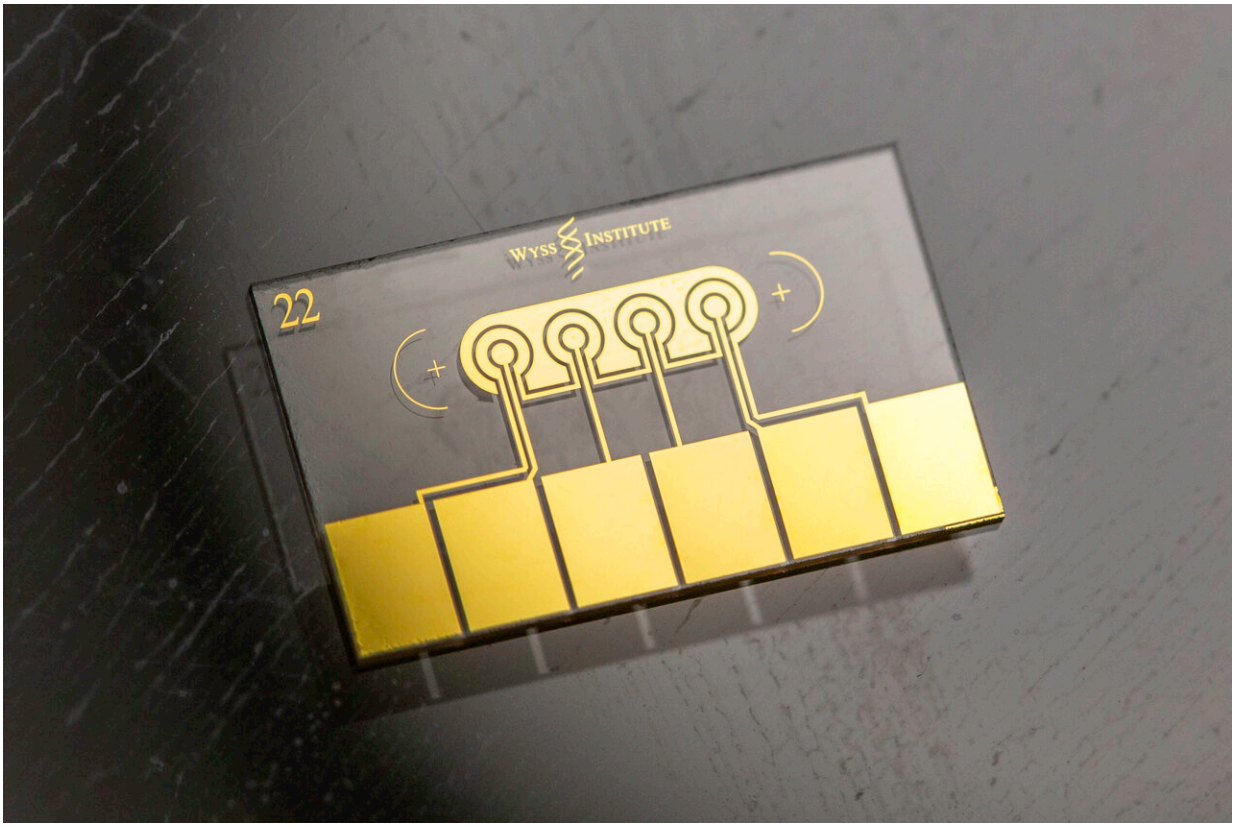
Attacking COVID-19's moving antibody target

February 2 2023, by Benjamin Boettner



The Wyss Institute's eRapid electrochemical sensor platform enables the multiplexed, fast, and inexpensive detection of biomarker molecules specific for infectious and other diseases at the point-of-care. Credit: Wyss Institute at Harvard University

Not all SARS-CoV-2 infections are created equal. We have learned this

through multiple virus waves are taking their toll on the world's population. Improving vaccines and new anti-viral therapies that target distinct viral molecules (antigens) and the changes they undergo over time have helped to soften this blow.

However, to control the disease even better and everywhere, we have to be able to assess whether and with which viral variant individuals have been infected, what kind of protective immunity they possess, and how they respond to vaccinations and therapies.

An obvious way to accomplish this is through the detection of antibodies that the immune system produces against the virus' proteins and variant-specific antigens. Importantly, currently available COVID vaccines induce the production of antibodies against the Spike (S) protein, but rarely the N protein, while natural infection produces antibodies against both proteins.

This allows the immune responses to be clearly distinguished from each other. Having a way to detect these different antibody types could inform health care and drug development decisions in a more systematic way.

However, current antibody detection technologies are time-consuming, too costly, often require clinical laboratories, are and not able to accurately measure the levels of antibodies against multiple antigens, or they suffer from a combination of these inadequacies—which prevent them from being able to rapidly and effectively generate data about antibodies across global populations.

Now, an in-depth study from a research team at the Wyss Institute for Biologically Inspired Engineering at Harvard University demonstrates that the Institute's portable electrochemical sensing technology known as eRapid could be an ideal instrument to enable the inexpensive,

multiplexed detection of different SARS-CoV-2-directed antibodies at the point-of-care.

The team, led by Wyss Founding Director Donald Ingber, M.D., Ph.D. and Wyss Senior Scientist Pawan Jolly, Ph.D., showed that specifically engineered eRapid sensors can detect antibodies targeting the virus' so-called nucleocapsid (N) protein from ultra-small samples of blood plasma and dried blood spots with 100% sensitivity and specificity within less than 10 minutes. The findings are published in *Biosensors and Bioelectronics*.

Taking aim at COVID-induced immunity

"The study's findings further validate that our much-evolved version of the eRapid diagnostic technology is capable of a fast, accurate, and differentiated assessment of antibodies against viral antigens in individuals," said Ingber. "We can obtain these results at extremely low cost using extremely small samples that individuals could easily self-collect and test at home or send to central laboratories. Thus, eRapid opens the opportunity of being used as a tool for pandemic surveillance and therapeutic monitoring, not only in the present but also for future pandemic and epidemic outbreaks."

Ingber is also the Judah Folkman Professor of Vascular Biology at Harvard Medical School and Boston Children's Hospital, and the Hansjörg Wyss Professor of Bioinspired Engineering at the Harvard John A. Paulson School of Engineering and Applied Sciences (SEAS).

The new findings build on a previous study, published in *Nature Biomedical Engineering*, that showed eRapid technology is capable of simultaneously detecting SARS-CoV-2-specific RNA and antibodies on the same electrochemical sensor chips. In their new study, the team honed further in on the N protein and virus-induced immunity.

Using specifically engineered eRapid sensors and a collection of 93 clinical samples of only 1.5 microliters in volume, they were able to distinguish 54 SARS-CoV-2 positive patients from 39 negative individuals within 10 minutes, with 100% sensitivity (all positive samples identified) and 100% specificity (all negative samples identified).

New diagnostic possibilities

"The combined features of eRapid make it an extremely useful platform for the fast and multiplexed detection of antibodies emerging in patients against a growing and fluctuating number of viral and other antigens, and for following an individual's antibody levels over time as we showed in our new study," said Jolly.

"We took the Wyss' eRapid platform through an extensive de-risking program by engineering new nanochemistry, manufacturing, and sensing abilities. At this point, we'd like to see our technology benefit as many patients in as many disease areas as possible, including, of course, infectious diseases such as COVID-19."

In 2022, the eRapid technology was licensed to the Wyss' startup StataDX for the fields of neurological, cardiovascular, and renal diseases. First author Sanjay Sharma Timilsina, Ph.D., and second author Nolan Durr, two former members of the Wyss' eRapid team who had been instrumental in advancing the novel electrochemical sensing approach as a diagnostic platform, joined StataDX.

The Wyss Institute is currently exploring additional commercial opportunities to commercialize eRapid for multiple other application areas including infectious disease diagnostics.

"With strides that we are making in parallel on developing portable

devices for housing eRapid diagnostic assays, we believe that eRapid could serve as one of the first multiplexed diagnostic platforms for a wide variety of diagnostic applications as it is based on electrochemical detection and so functions much like the glucometer that is already used world-wide for patients with diabetes," said Ingber.

More information: Sanjay S. Timilsina et al, Rapid quantitation of SARS-CoV-2 antibodies in clinical samples with an electrochemical sensor, *Biosensors and Bioelectronics* (2022). DOI: 10.1016/j.bios.2022.115037

Devora Najjar et al, A lab-on-a-chip for the concurrent electrochemical detection of SARS-CoV-2 RNA and anti-SARS-CoV-2 antibodies in saliva and plasma, *Nature Biomedical Engineering* (2022). DOI: 10.1038/s41551-022-00919-w

Provided by Harvard University