Graphene could one day be used to make quick, reliable tests for viruses like SARS-CoV-2

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Credit: AI-generated image (disclaimer)

Graphene is a layer of carbon only one atom thick. Since it was first isolated in 2004, it has found applications in strengthening materials, accelerating electronics, and boosting performance in batteries, among

others.

It also shows great potential for use in biosensors. These are devices used to detect small concentrations of biomarkers in biological samples, such as blood or saliva. Biomarkers are molecules that suggest the presence of disease.

In a recent review, my colleagues and I looked into the latest research to find the most exciting potential applications of graphene in point-of-care tests. This includes diagnostic tests for SARS-CoV-2, the virus responsible for COVID-19, but also detecting other viruses, bacteria and even cancerous tumours.

It's early days. The technology still needs to go through clinical trials and processes need to be developed to manufacture these tests at scale. However, in the next five years, graphene could start to play a part in healthcare technology.

A single atom layer

Because graphene is a two-dimensional material, it has a tremendously high surface-to-volume ratio, which makes it very sensitive to changes in its environment. Think of a vast, calm lake. Any tiny pebble that hits the surface creates a ripple that quickly expands across the water.

Similarly, when other substances—even single molecules—hit graphene, they generate small, measurable electrical pulses.

Relying on this phenomenon alone to detect SARS-CoV-2 wouldn't work. When used as a biosensing layer in electronic devices, graphene is sensitive down to a single molecule. Yet it can't tell the difference between coronavirus and the flu—the same way the lake would confuse a pebble and a marble.

To solve this, researchers have developed chemically modified graphene, coating it with antibodies that bind specifically to SARS-CoV-2. When the virus reaches the sensor and attaches to the antibody, it triggers an electrical signal through the thin graphene layer.

SARS-CoV-2 carries all its genetic information in a strand of RNA, which is often used in detection processes like a polymerase chain reaction (PCR). A PCR device amplifies the amount of RNA in a saliva sample until it becomes detectable under a microscope.

But this process is time consuming, requires expensive equipment and very specific and expensive reagents—substances used in the labelling and amplification process, or in the preparation of the sample.

A graphene-enabled device can detect the virus in swabs and other biological samples. It does so without any of the reagents or treatments used in other tests to extract the specific biomarker from the biological sample. It doesn't require labelling with fluorescent probes, to allow detection by optical methods, as done in PCR-based tests.

The results are quick, taking only a few seconds compared with the hours it can take for PCR tests.

Thanks to the unique electrical properties, graphene-based biosensors could detect smaller amounts of the targeted biomarker than other sensors. Graphene sensors can detect one copy of the virus RNA in 10^{18} (one followed by 18 zeroes) litres of biological sample—almost like finding our pebble if it were lost in the Mediterranean Sea. For comparison, PCR tests require around 34 billion copies of the virus in 40ml of liquid.

Graphene sensors also meet the requirements for the World Health Organization's requirements for efficient point-of-care sensors.

As well as speed and sensitivity, some graphene-based sensors bring other advantages—like being printable in a piece of paper. This means it should be simple to incorporate them into lateral-flow assays, a cost-effective technology commonly used in point-of-care diagnostics for both lab use and home testing in different areas, such as pregnancy tests and COVID-19 tests.

Beyond viruses

Featuring a mixture of graphene oxide, gold nanoparticles and antibodies, printed sensors can detect as little as ten proteins in one litre of sample. In particular, they detect a protein called CA125, a biomarker linked to ovarian, lung and breast cancers.

As well as detecting viruses, researchers have developed graphene sensors that detect harmful bacteria and tumour cells. These solutions could speed up the early detection fast-spreading infectious diseases, such as salmonella infections, *E. coli* contamination or cholera outbreaks.

Nowadays, detecting these pathogens relies on PCR methods—like the ones used for coronavirus—and other procedures based on counting bacteria colonies. The latter approaches are time consuming with low sensitivity, requiring large populations of bacteria in the biological sample. This is a problem when the presence of just one pathogen could be enough to spread the disease.

Graphene sensors overcome this hurdle and, at the same time, provide quick and reliable results. Among other devices, a graphene-based field-effect transistor can detect single cells of several *E. coli* strains in water and could be easily manufactured in large scales for areas that need a high volume of tests.

Researchers have also developed graphene-enabled devices that detect

cancer biomarkers and probes that distinguish tumour cells in blood samples—potentially saving patients from invasive procedures like biopsies.

Graphene-based diagnostics has the potential to reach commercial viability. In parallel to studies investigating graphene sensors, advances in manufacturing techniques mean graphene and related materials can be produced at large scales to a high quality.

Graphene is gradually reaching commercial viability in multiple areas. The first wave of graphene-enabled products are now on the market and commercialisation activities are moving from materials development towards building components.

Based on the outcome of initial research results, there are some challenges to overcome before graphene-based point-of-care sensors reach the market, including fulfilling all the health and safety requirements and clinical trials. But several industries and spin-off companies are already interested. Graphene and related "layered materials" will become a key player in the future of medical technologies.

More information: Ioannis Prattis et al. Graphene for Biosensing Applications in Point-of-Care Testing, *Trends in Biotechnology* (2021). DOI: 10.1016/j.tibtech.2021.01.005

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