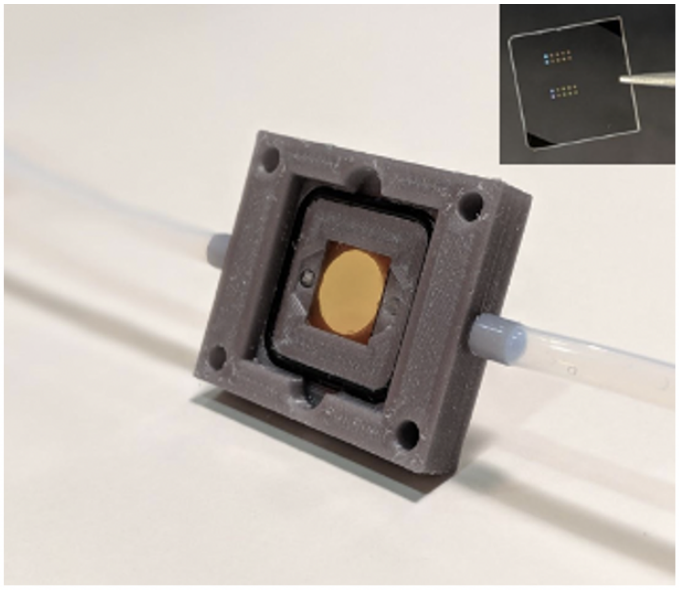
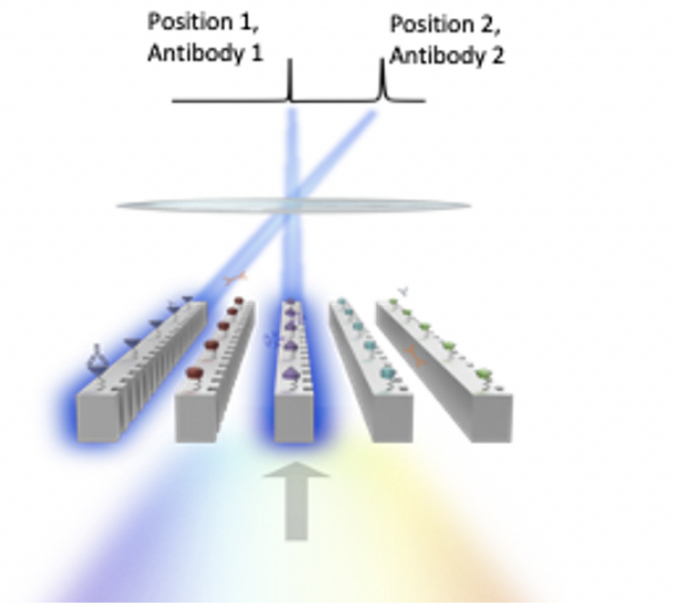
Docket #: S20-284

COVID-19 diagnostics: direct optical detection of viruses and antigens with nanofabricated surfaces

Stanford researchers at the Dionne Lab have developed a new hand-held technology that uses optical characterization to rapidly and quantitatively measure extracted viral-RNA target binding or antibody binding to nanofabricated platforms. Importantly, this invention can detect extracted viral-RNA gene sequences from the SARS-CoV-2 genome encoding for different proteins, including envelope proteins, RNA-dependent RNA polymerase, and proteins that form viral nucleocapsids simultaneously and without amplification. We can also detect antibodies, including IgG, IgM, and IgA from serological samples. This technology could be readily extended to other viral or bacterial infections.

The platform relies on high-quality-factor (high Q) nanostructured dielectric substrates, known as metasurfaces. By relying on free-space resonant metasurfaces, this invention overcomes the typically low signal-to-noise ratio of lateral flow assays. Consisting of hundreds or thousands of independent and highly environment sensitive image pixels, each metasurface facilitates an unprecedented number of simultaneous measurements to be performed at cutting edge detection limits using off-the-shelf consumer electronics-grade camera sensors. Using the nanopatterned Si surfaces also guarantees the scalability and cost-effectiveness of this assay, by using well-established CMOS fabrication processes. Additionally, unlike fluorescent-based assays, this platform does not suffer from bleaching or photoblinking. These optically resonant substrates will allow measurement of antigen binding at the point-of-care within an hour. Clinicians can detect multiple nucleic acid sequences on a single chip for assay multiplexing, improving sensitivity and specificity, and enabling detection of multiple viruses simultaneously.





Stage of Development

- Working prototype
- Optimizing surface functionalization for maximum sensitivity and long-term stability
- Testing the assay on multiple RNA and DNA sequences

Applications

- COVID-19 diagnostics
- Analysis, diagnosis, monitoring, and treatment of infectious diseases

Advantages

- Near-instantaneous read-out (we currently use 30ms acquisitions); therefore, combined with sample processing (viral gene fragmentation), our assay can provide antigen results in 15 minutes at the point of care.
- Extremely low limit of detection, owing to the chips laser-sharp scattering spectra.
- By relying on nanopatterned Si, we capitalize on the low-cost and scalable fabrication of established high-throughput CMOS fabrication processes.
- Fluorescent tagging or secondary antibodies are not required; therefore, no reagents are required by users after receiving our product.
- No bleaching or photoblinking, unlike fluorescent-based assays.
- Massive multiplexing is possible on a single chip, without sacrificing sensitivity, owing to the "free-space" illumination of the surfaces and our bioprinted functionalization.
- Our substrates are reusable after washing.
- Minimal training for use is needed, unlike PCR which requires a lab technician or health care professional.
- Can be extended to other viral or bacterial infections.

Publications

- Lawrence, M., Barton, D.R., Dixon, J. et al. High quality factor phase gradient metasurfaces *Nat. Nanotechnol* (2020).

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