CORONAVIRUS AND COVID-19 OUTBREAK: WHEN PHYSICS AND ENGINEERING GO VIRAL BROTE DE CORONAVIRUS Y COVID-19: CUANDO LA FÍSICA Y LA INGENIERÍA SE VUELVEN VIRALES

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The recent outbreak produced by SARS-CoV-2 virus has overwhelmed the world in an unprecedented way. After nearly a year of lockdowns, rampant death tolls and declining economies, the disease derived from this virus, COVID-19, has shown that the challenges to address have become more and more complex. While the scenario may look unmanageable, it poses an opportunity for revisiting ways of conducting and implementing practical research around engineering and physics aimed at virus assessment.

Despite the fact that some recent reviews and views see this crisis as a lost opportunity for micro and nanotechnology, especially for M/NEMS [1], I think that it is actually fertile ground for raising scientific arguments. In fact, I believe that the time is ripe to examine the progress made in physics and biomedical engineering with a broad perspective, following the lead of a recent review on the subject [2].

I will refer to two existing technologies that are available for virus detection and/or identification, which rely on novel engineering solutions based on physical phenomena involving material sciences, optics and acoustics and their interplay. I believe the Cuban scientists will find these approaches motivating and eventually connected to physics fields they currently work on at home and abroad.

The first approach I will focus on is related to the gold standard used to detect the SARS-CoV-2 in saliva or mucus samples: polymerase chain reaction (PCR), in this case enabled by acousto-fluidics. Combining the properties of surface acoustic waves propagating over a piezoelectric material with an engineered array of materials acting as phononic crystals, it is possible to shape the field of the waves and enable them to propagate into a liquid sample [3]. This workflow is excellently explained and detailed in some of the papers from the group of Prof. Cooper from the James Watt School of Engineering at University of Glasgow. I fully recommend the readers watching the plenary talk he tenured at SPIE Photonics West 2012 entitled "Developing Diagnostics for the Developing World". While this talk is mainly focused on bacteria and parasite detection in liquid samples with accessible instrumentation, it establishes the foundations for extending the involved techniques beyond the scope of "large" microorganisms identification and exploring their suitability in detecting nanometric sized viruses.

Now I briefly explain the working mechanism of the device, where Physics and Engineering are intimately interwoven.

The system contains a piezoelectric substrate with micro-sized electrodes patterned on top of it. When the electrodes are excited electrically they generate a vibration on the surface that produces a mechanical wave. This mechanical energy travels through the piezo material as a surface acoustic wave depending on the crystal features such as orientation and processing finishing. Given the complexity associated to processing and manufacturing of some piezoelectric substrates, in particular Lithium Niobate (LiNbO₃), Prof. Cooper's group members chose to place a superstate on top of it to produce a selective actuation. This actuation is enabled by shaping the field of the acoustic forces via the superstrate, which is designed and fabricated with custom made arrays of structures and materials that act as acoustic waveguides [3]. Taking full advantage of the phononic crystal principles, and using modeling software tools, it is possible to customize the frequency bands that are enabled for the surface acoustic wave to travel from the substrate to the superstrate by convenient shaping, thus creating a path for producing a selective actuation over targets. The liquid medium containing the bacteria, parasites or potentially viruses is placed as a small droplet over the substrate, so it is submitted to acoustic actuation [4, 5]. If the right shape of the field is achieved, then the liquid sample can be subject to streaming and heated up to certain temperature producing the breakdown of the biological material within it. Not only this heating process is possible, but also allows multiple droplets to merge and produce biochemical reactions that are necessary in the series of procedures leading to PCR. This PCR process allows DNA amplification, which ultimately leads to a clear identification of the molecular information within the droplet sample, thus accessing to the fingerprint of the pathogen (bacteria, parasite or virus).

The above technology is compatible with other techniques including, for example, micro-sized object manipulation by optical tweezers. Some work on this area was developed in Cuba in partnership with French institutions around 2008-2009 [6–8]. Using these tweezers, and with careful adaptation of the setup, it is also possible to merge solid particles with the sample droplet in order to enable other focused studies.

The second technology that I want to refer to is optomechanical sensing of mass and stiffness using microresonators. Optomechanics is currently a very active branch of research: many groups in the developed world focus on the interaction of electromagnetic fields in the optical domain with mechanical resonators. For some texts spanning the basics and applications, I refer the readers to [9–11].

Currently, a European consortium of labs in Spain, France, The Netherlands, Greece and Germany are collaborating on the ViruScan project, which searches implementing micro and nano optomechanical resonators to identify viruses. This is a very promising approach whereas there is no need to presuppose what is the virus that is attempted to be identified.

Optomechanics is at the interception of three areas that physicists and engineers have developed for decades: microelectronics, photonics and materials science. Miniaturized objects, typically micro and nanoresonators, are excited with light which drives the mechanical movement and at the same time, the optical field is varied as light goes through the resonators. As a consequence, the interplay of optics and mechanics converges to inspect the spectroscopic features of the resonators together with the mechanical features (vibration frequency and amplitude) of their motion. Now, ViruScan seeks to explore the unique features of this motion when a virus is placed on top of the resonator. The modes of the "loaded" resonator are expected to shift and differ from the natural modes of the resonator alone, thus providing information on the new frequencies related to the vibration modes of the virus, providing information on the its mass and stiffness. In this way, and given the fact that viruses are simple nanometric structures, it is expected that they can be identified. As of today, it was recently reported on the vibration modes of a single bacterium via these optomechanical resonators [12, 13]. It is the first proof of concept of how extremely small biological objects can be sensed and how their physical features can be identified.

In comprehensive recent reviews, other techniques around nanophotonics applied to biological media characterization are explained in the context of virus detection [2,14]. I strongly encourage our readers to consult these publications, which bring together many subjects plenty of contemporary and exciting physical ideas.

In the era of COVID-19 one thing is clear: the scientific

advancements, physics and engineering included, are enabling us to address a complex challenge in ways that were unthinkable only twenty years ago. For the world's physics and engineering communities, standing where we currently are is actually a privilege and a reason to feel proud of being part of the knowledge generation.

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