TECHNION
Israel Institute
of Technology

LAB-ON-A-CHIP DEVICES FOR RAPID DETECTION OF CORONAVIRUS AT THE POINT OF NEED

This fast-paced emergency research program will demonstrate a working prototype for a microfluidic chip capable of rapid and early detection for coronavirus. The aim is to ensure a paradigm shift from slow and laborious central laboratory tests, to rapid and distributed testing at the point of need.

Background

It is widely agreed that one of the most effective methods of controlling/moderating the rate of spread of this pandemic (and through that preventing an overwhelming of the medical system) is to identify and isolate infected individuals as soon as possible[1].

China and South Korea achieved this, and yet in much of the rest of the world, we seem to be losing this fight, i.e., the rate of testing is far too low to cope with the rate of infection. Some countries have given up on testing, and have moved on to the next phase of equipping hospitals with sufficient beds and respirators to prepare for the coming wave of patients who require intensive care[2]. In addition, a major challenge with the current coronavirus is the number of asymptomatic carriers—people who show no symptoms and yet have an active infection and thus infect others[3]. Such individuals do not even approach the medical system for testing.

Even if this wave is overcome (e.g., complete closure for several weeks should enable exponential delay), before a large fraction of the population is infected or a vaccine becomes available, we will need to manage the virus' spread, to prevent a second wave of exponential growth.

"What we really need to focus on is finding those who are sick, those who have the virus, and isolate them, find their contacts and isolate them," said the Executive Director of the World Health Organization's (WHO) emergencies program [BBC 22/03/2020[4]]. To enable this, frequent and rapid testing of large portions of the population would be required.

The current standard for detection of the coronavirus is through a laboratory process called PCR, which is superior in its sensitivity, but its main limitation is that it requires several steps for preparation of samples, relying on trained personnel and appropriate laboratory

equipment[5]. Automated PCR machines do exist, yet are scarce, and even those cannot provide the throughput required for highly populated areas[2].

There is thus an urgent need to develop diagnostic tools that can be sufficiently simple and inexpensive to allow wide distribution, while providing the necessary sensitivity.

Our Response

We focus on two approaches for *direct detection* of the virus from throat swabs and saliva. These are the most likely to be easily adopted by the general public, as their collection is a noninvasive and non-painful process.

Focus 1 – Amplification-Free Detection of the Viral RNA (Genetic Material)

- Based on our published work [6 and 7], we will aim to use our specialized molecular probes and microfluidic technique to achieve direct detection, without RNA purification and without reverse transcription.
- The only preparation step required is inserting the sample (e.g., the swab stick) into a vial containing our probes and a chemical that breaks the virus' capsule and releases its RNA. Reaction with our specialized probes takes place immediately.

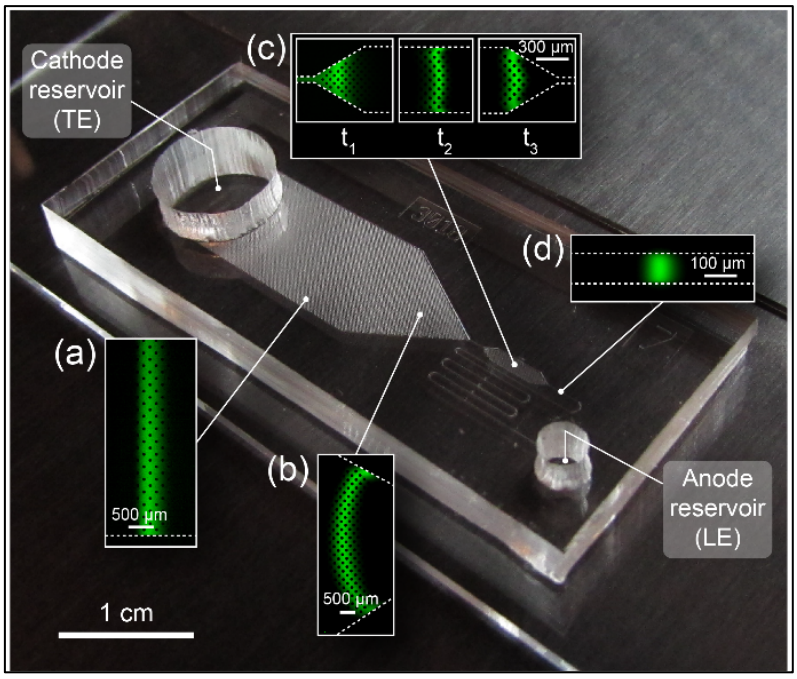

Figure 1. RNA detection device.[8] Molecular probes attach to the virus' RNA and are concentrated by more than 100,000-fold to allow rapid and highly sensitive detection.

Focus 2 – Direct Detection of Virion's Capsid Proteins (the Building Blocks of the Virus' Capsule)

- Rapid lateral flow kits (similar to pregnancy tests) exist for other respiratory viruses such as the flu. These tests are based on specific detection of proteins in the virion's capsid.
- Once effective antibodies against the coronavirus are developed (a task currently pursued by many research organizations worldwide), rapid lateral flow tests will likely be developed as well.
- The strength of lateral flow tests is that they are low cost (based on paper), simple to operate, and the result can be visually read (a colored stripe). However, the sensitivity of such tests is very limited.
- Particularly for the coronavirus, early detection of an infection is crucial. To enable such early detection, diagnostic methods should be particularly sensitive to detect very low concentrations.
- Based on our published work[9 and 10], we aim to create a paper-based device that improves the sensitivity of lateral flow tests by at least 100-fold, enabling early detection.

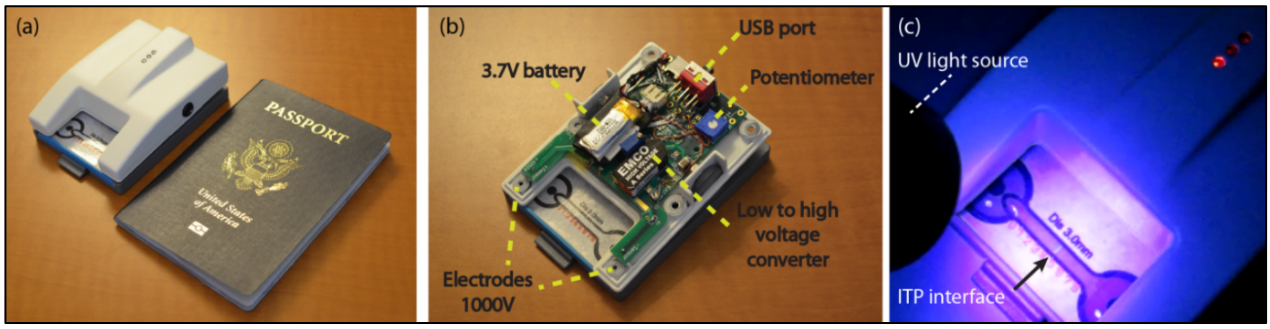

Figure 2: Our prototype hand-held device uses electric field and specialized chemistry to boost the sensitivity of paper-based tests by 100-fold.

Lifeline Workplan

We will advance both development directions simultaneously as follows:

RNA Detection:

1. Design and order specific probes based on primer designs
2. Design and fabricate microfluidic chips for detection
3. Purchase synthetic or pre-purified coronavirus RNA ("dead virus") to test and optimize the system in our lab
4. Communicate our results to colleagues at the hospital laboratory to test on real samples

Protein Detection:

1. Purchase antibodies against SARS-CoV, as well as spike proteins to serve as synthetic targets
2. Design an ITP-compatible paper device to implement a sandwich assay
3. Characterize the limit of detection of the device, compared to a lateral flow device
4. When antibodies against SARS-CoV-2 become available, adapt the system and send to colleagues at the hospital laboratory to test on real samples

Budget

$220K will provide the necessary funds to implement the Lifeline Workplan. The contribution will cover research staff salaries, research and prototyping services, and materials necessary to implement the research.

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