Biological and Environmental Sensors Based on Lensfree Microscopes

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Abstract: Lensfree microscopes offer an ultra-large field of view together with high resolution and cost-effective, compact hardware. This makes them well suited for the COVID-19 and airborne nanoparticulate matter sensing applications we present here.

1. Introduction

Lensfree microscopes (Fig. 1a) combine a light source, image sensor, and computational processing to image a transparent sample. When the light source is partially coherent, an interference pattern is recorded on the image sensor, which is equivalent to an in-line hologram when the sample is relatively sparse. The image of the sample can be computationally reconstructed with submicron resolution using digital holography [1]. Compared to traditional microscopes, lensfree microscopes offer a significantly larger field of view at comparable resolution and simpler, more compact hardware, making them well-suited for deployment in low resource settings. Here we present two examples where lensfree microscopy has been combined with automated image processing to achieve sensing tasks: sensing COVID-19 [2] and sensing ultrafine airborne particulate matter.

2. Materials and Methods

We sense SARS-CoV-2 by imaging an agglutination assay that we developed inside a microfluidic chip (Fig. 1b) [2, 3]. Microspheres (2 µm diameter) are coated with ACE-2 protein, which is the same cellular receptor to which SARS-CoV-2 binds during infection. We mix these beads with various concentrations of a noninfectious pseudovirus that bears the same spike protein as infectious SARS-CoV-2. In the presence of the virus, the beads will cluster around viral particles. We use holographic reconstruction combined with a convolutional neural network to identify and count the number of beads in each cluster. This is used to compute the fraction of beads that are bound together, which serves as our sensing signal.

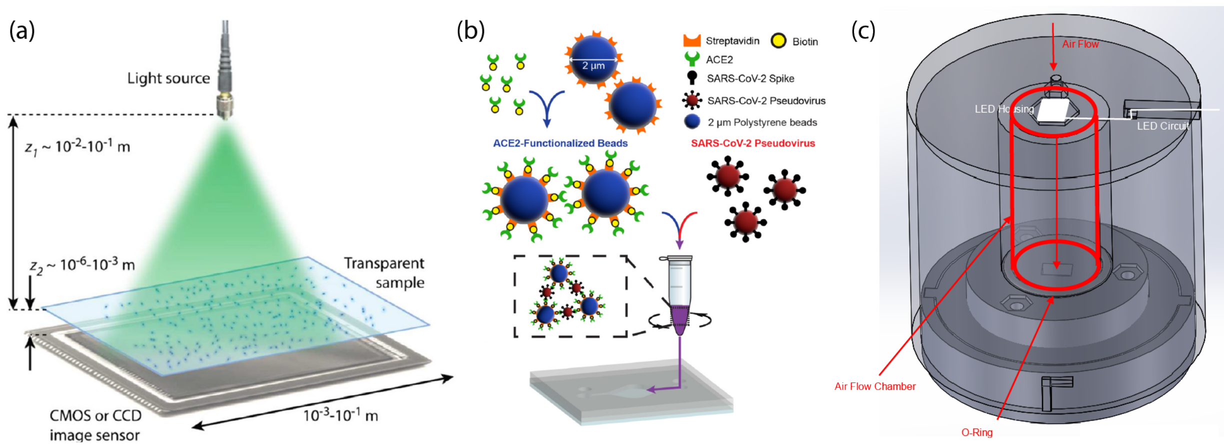

Fig. 1. Lensfree sensing setups. (a) Basic lensfree imaging setup. We use LEDs combined with band-pass filters and ∼100 µm diameter pinholes as light sources. Adapted from [2]. (b) Agglutination assay procedure for sensing SARS-CoV-2. (c) Airborne ultrafine particulate matter sensor.

We sense airborne particulate matter by pumping air into a lensfree microscope (Fig. 1c). The sample collection slide is coated with a viscous liquid polyethylene glycol, which serves the dual purpose of capturing particles as well as creating a deformable liquid nanofilm that enhances the holographic scattering signal generated by the nansocale particulate matter by forming a nanolens. Unlike previous nanolens-based sensing [4], here the nanofilm is deposited in advance of the particles, making it possible to track particle deposition in real-time. This is a key feature in air-quality sensing, where hour-by-hour tracking of air quality is important.

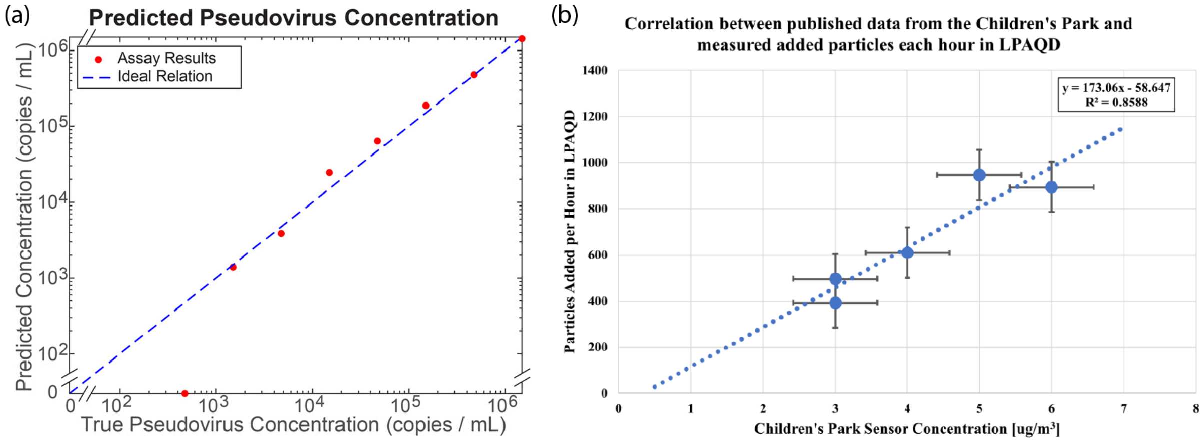

Fig. 2. Lensfree sensing results. (a) Our sensor signal versus known viral concentration. Adapted from [2]. (b) Our sensor signal versus co-located independently published airborne $PM_{2.5}$ levels.

3. Results and Discussion

Our imaging system is able to resolve the individual 2μm beads in the COVID-19 sensing agglutination assay. Our machine learning algorithm achieves 88.6% accuracy in classifying each cluster according bead count. We perform a pair of measurements on two different sample dilutions to disambiguate whether a low level of binding corresponds to a low analyte concentration or an extremely high analyte concentration that saturates all the ACE2 receptors before beads have a chance to aggregate. With this approach, our results closely track the known viral concentrations of our test samples (Fig. 2a), and we achieve a limit of detection of 1.27×10^3 copies/mL, which is of the same order of magnitude as polymerase chain reaction (PCR) tests. The advantage of our approach over PCR tests is its speed, taking less than 3 hours. Rapid antigen tests for COVID-19 are faster, but approximately 3 orders of magnitude less sensitive, resulting in later diagnoses, after individuals are already infectious.

In our airborne particulate matter sensing device, we are able to sense, count, and size individual particles as small as 100 nm (ultrafine particulate matter, $PM_{0.1}$). Conventional particulate matter sensors only report the total mass of particulates smaller than 2.5 μm, $PM_{2.5}$, without being able to count individual particles or distinguish ultrafine particulate matter from fine particulate matter. Recent research has shown that a given mass of ultrafine particulate matter is significantly more hazardous than the equivalent mass of micro-scale particulate matter [5]. To confirm the sensing capability of our device, we have verified the sizes of individual sensed particles using electron microscopy. We have also correlated our measured particulate matter levels, measured on-site, with those measured by our local government at a children's park (Fig. 2b).

Acknowledgements

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