Rapid, Electronic, and Accessible Detection of COVID-19

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The emergence of COVID-19 and other epidemics in the past has caused significant losses to society and economy[1]. Conventional diagnosis of infectious diseases relies on Polymerase Chain Reaction (PCR), Enzyme-Linked Immunosorbent Assay (ELISA), and Rapid Antigen Test (RAT). However, PCR and ELISA are time-consuming, instrument- and personnel-demanding, and not always accessible to all. RATs are faster but can present false negative results due to low sensitivity[2]. Here, we demonstrate a prototyped inexpensive, miniaturized sensing system to detect SARS-CoV-2 antibodies and antigens directly from body fluids with a high sensitivity (atto molar), a fast turn-around time (15 to 30 min) and low cost (a few dollars per test).

Our digital, in-solution sensing platform is based on an innovative biomolecular signaling process that uses gold nanoparticles (AuNPs). AuNPs were functionalized as ligands with strong affinity targeting antibodies or antigens of SARS-CoV-2. For antigen detection, to produce AuNP dimers and clusters, AuNPs were functionalized with two sets of monoclonal antibodies (mAbs) targeting non-overlapping epitopes of N-proteins. For antibody detection, we tested the efficacy of target antibodies that bind and neutralize viruses using S-proteins or RBD proteins. The detection was carried out in a single microcentrifuge tube by mixing samples to be tested with AuNP sensor solution, followed by accelerated antibody-antigen binding via centrifugation, a brief incubation, and finally a vortex agitation. The centrifugation strongly localizes the reagents to the tube bottom to greatly improve the Limit of Detection (LoD), while the vortex step resuspended non-reactive AuNPs free-floating, thus retaining high selectivity. After tests, the amount of free-floating AuNPs was measured and digitized using a Portable Electronic Detector (PED) to characterize and quantify the antigens and antibodies. The PED was specifically designed to supply stable power and minimize readout errors.

We evaluated the performance of sensing system by spiking antigens and antibodies in various media using our optimized sensing protocol. The SARS-CoV-2 antibodies were measured with ultra-low LoD (4, 7, 45 aM in PBS, serum, and blood), and the antigen N-proteins were detected in saliva and nasal fluids with 155 and 260 aM LoDs, or ~3 orders of magnitude better than ELISA[3]. These results suggested that our platform can produce high-sensitivity detection comparable to and better than ELSIA, while significantly reducing turnaround time and cost.

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[1] R. E. Baker et al., Nature Reviews Microbiology 20, (2022).

[2] A. Parihar et al., ACS Applied Bio Materials 3, (2020).

[3] A. F. Ogata et al., Clin Chem 66, (2020).

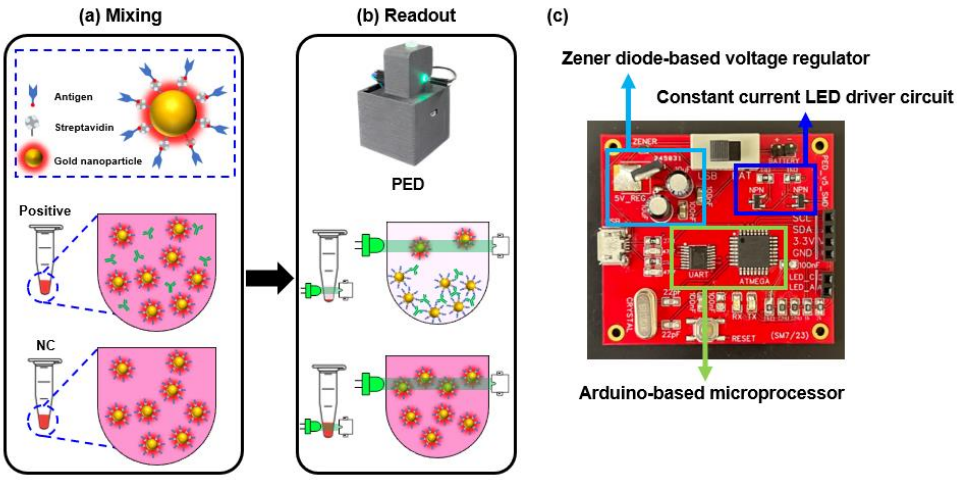

Figure 1: Nanoparticle-supported, rapid electronic detection of infectious diseases. (a) Schematic showing the AuNP sensor solution for antibody detection, where antigens were functionalized on AuNPs by biotin-streptavidin reaction. NC: negative control with no added antibodies or antigens. (b) Schematic showing the readout system. Test samples were mixed with the sensor solution, centrifuged, incubated, and vortex agitated. Samples read from the PED system. The AuNP precipitation amount was related to the number of test molecules, and the NC sample did not contain any precipitation. (c) Optical image showing a PCB board for signal processing, including a built-in voltage regulator circuit, constant current LED driver circuit, and microcontroller for signal processing and communication with laptops via Wi-Fi or Bluetooth.

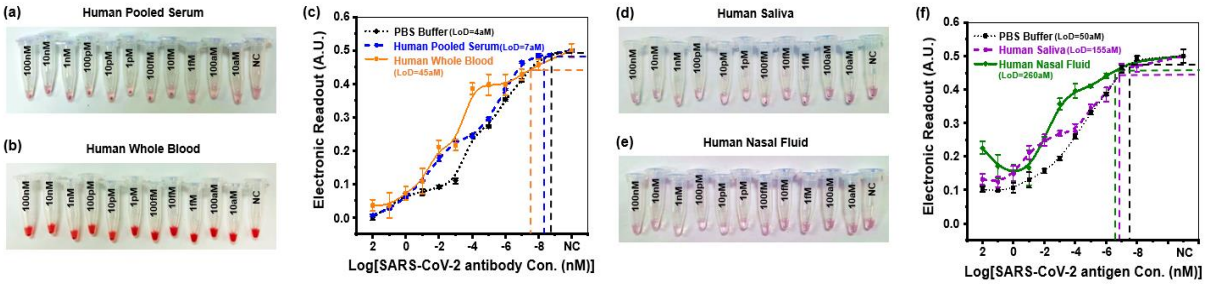

Figure 2. Experimental demonstrations of SARS-CoV-2 antibody and antigen detection. (a-b) Optical images showing antibody samples ready for PED readout: (a) in human pooled serum, and (b) in human whole blood. The testing concentrations range from 100 nM to 10 aM. NC: buffer only. (c) Extracted readout signals plotted against antibody concentration in PBS buffer (black dotted line, LoD=4 aM), serum (blue dashed line, LoD=7 aM), and whole blood (orange solid line, LoD=45 aM). (d-e) Optical images showing antigen samples ready for readout. Similarly, the testing concentrations range from 100 nM to 10 aM. (d) in human saliva, (e) in human nasal fluid. (f) Extracted readout signals plotted against antigen concentration in PBS buffer (black dotted line, LoD=50 aM), saliva (purple dashed line, LoD=155 aM) and nasal fluid (green solid line, LoD=260 aM).