A microfluidics-integrated photonic nanosensor for rapid and sensitive detection Ebola virus antigens

Faheng Zang[1], Zhijuan Su[1], Gerardo Kaplan[2], and Stephen Y. Chou[1,*]

[1]Department of Electrical Engineering, Princeton University, Princeton, NJ 08544
[2] Laboratory of Emerging Pathogens, Center for Biologics Evaluation and Research, Food and Drug Administration, Silver Spring, MD 20993
chou@princeton.edu

We present a multi-scale photonic nanoantenna-array-based lateral-flow biosensor platform for rapid detection of Ebola virus (EBOV) antigens. The nanostructured sensor utilizes plasmonic-enhanced fluorescence and successfully detects EBOV soluble glycoprotein (sGP) at the concentration of 1pg/mL. It is a 1000-fold lower detection limit compared to conventional enzyme-linked immunosorbent assay (ELISA). This sensor only requires 25 μL of antigen solution thanks to the integration of open-channel capillary microfluidics. The assay duration has been reduced by 4-fold compared to the bulk setup. These results demonstrated this multi-scale biosensor as a promising lab-on-chip for ultrasensitive and fast detection of pathogens.

Lateral-flow immunoassay-sensors provide efficient point-on-care solution for antigen detection. However, attributed to the low sensitivity and reliability, these devices are not commonly used for EBOV disease diagnosis. Our sensor solves these challenges through integration of nanophotonic sensors and autonomous microfluidics. This multi-scale EBOV sensor simultaneously enables antigen detection with high sensitivity, minimal sample volume, and rapid response.

The biosensor was composed of a nanostructured antenna array and a microstructured capillary pump layers (Figure 1a). The 3D nanostructured antenna array was first fabricated through nanoimprint lithography and thin-film processes. Its optical absorption peak matched the excitation laser wavelength at 785 nm (Figure 1c,d). Then, a 50μm-thick capillary microfluidic layer was fabricated using KMPR negative resist on the nanosensor surfaces and activated using O_2 plasma to render surface hydrophilicity (Figure 1b). Figure 2a shows the assay format on the nanosensor. In each assay step, the capillary microfluidic pump took in 25 μL reagents and incubated for 25 minutes. Figure 2b showcased the digital detection of individual fluorescence "hotspot" on the sensor surfaces. Fluorescence intensity on the sensor has demonstrated strong dependency to sGP dilutions from 1:100000 to 1:10 in sodium phosphate buffer (Figure 2c). In comparison, the ELISA can only detect 1:128 sGP dilution (data not shown).

This rapid Ebola virus antigen sensor with multi-scale nanostructured photonic transducers and capillary microfluidics demonstrates a proof-of-concept as a rapid and sensitive immunoassay test platform for a wide range of on-site applications.

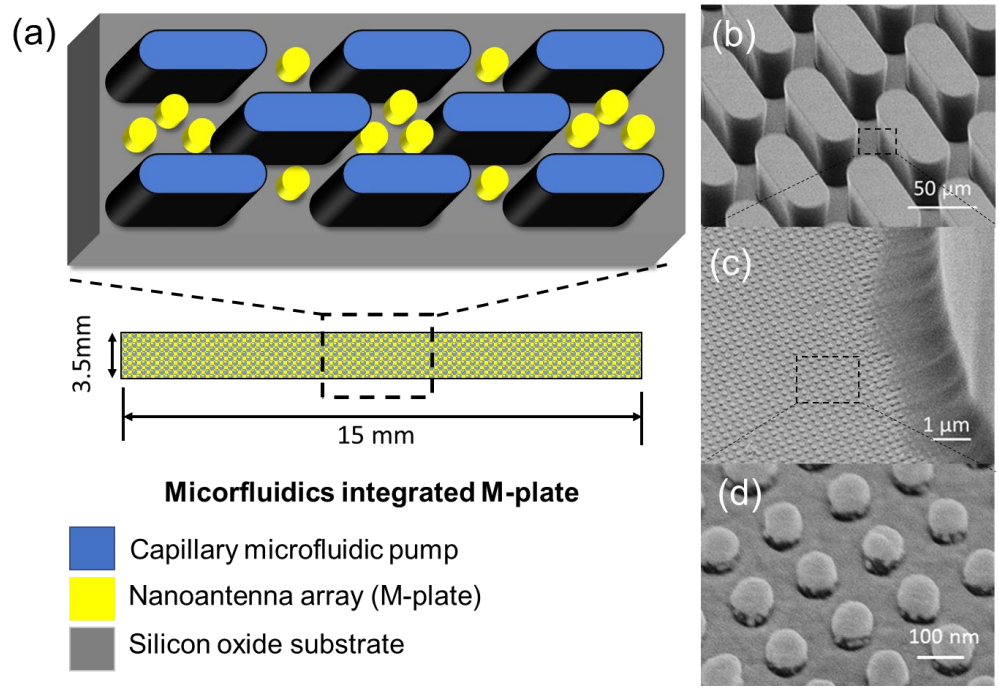

Figure 1: Schematic and scanning electron microscopy (SEM) images showing the microfluidics-integrated nanostructured EBOV sensor. (a) A schematic showing the overall dimension of a single microfluidics-integrated EBOV nanosensor test strip. (b) SEM image of the high aspect ratio capillary microfluidic pump made by KMPR resist. (c) An exploded view of the nanoantenna array beside the edge of a microfluidic bar structure. (d) The zoom-in view of 3D nanoantenna structures.

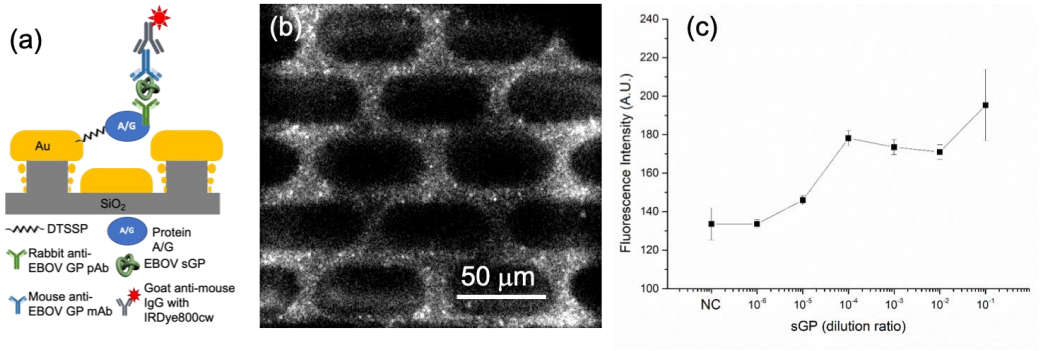

Figure 2: (a) EBOV sandwich assay format, (b) fluorescence image of microfluidics-integrated nanosensor surface after EBOV assay, and (c) fluorescence intensity changes with increasing EBOV sGP concentrations on the rapid EBOV sensor.