

Supporting Information

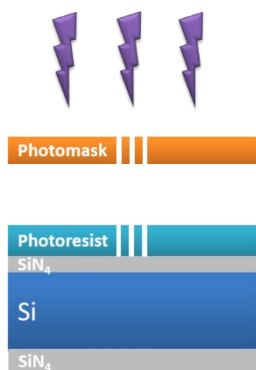
Plasmonic nanohole array biosensor for label-free and real-time analysis of live cell secretion

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a. UV Radiation

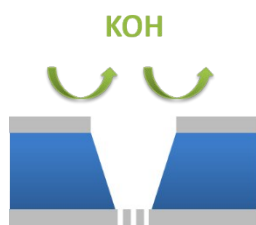


I. Deep-UV lithography

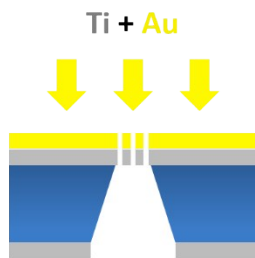
$\text{SF}_6 + \text{Ar}$



II. Dry etching



III. Dry/Wet etching



IV. Metal Deposition

b.

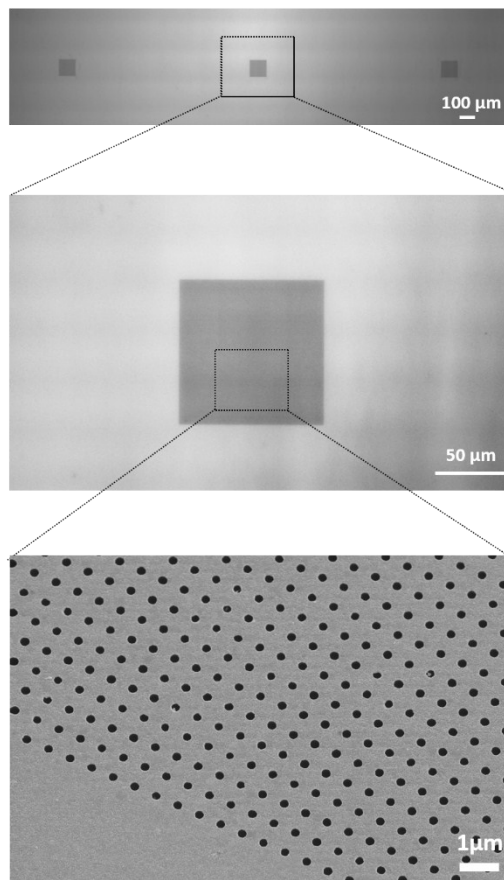


Figure S1. (a) The fabrication process of the gold NHAs on free-standing silicon nitride membrane. (b) The optical image on the top panel showed the layout of the three in-line NHAs, with each array measuring 100×100 μm as shown in the middle panel. The nanohole structures on the membrane were shown in the zoomed SEM image.

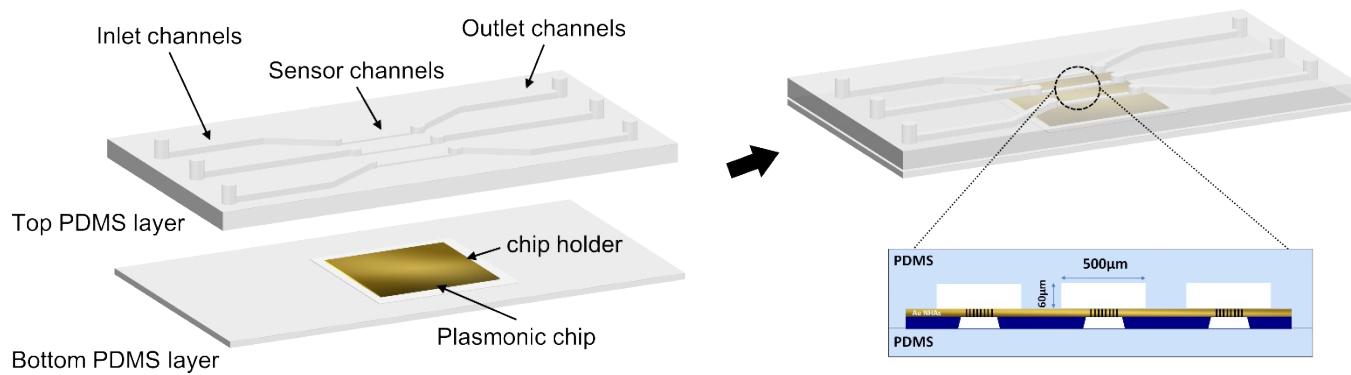


Figure S2. Assembly of the microfluidic detection module. The sensor arrays on the plasmonic chip were aligned with the corresponding sensor channels embedded in PDMS. Each line of the sensor arrays was sealed in a PDMS microchannel measuring 500 μm wide and 60 μm high.

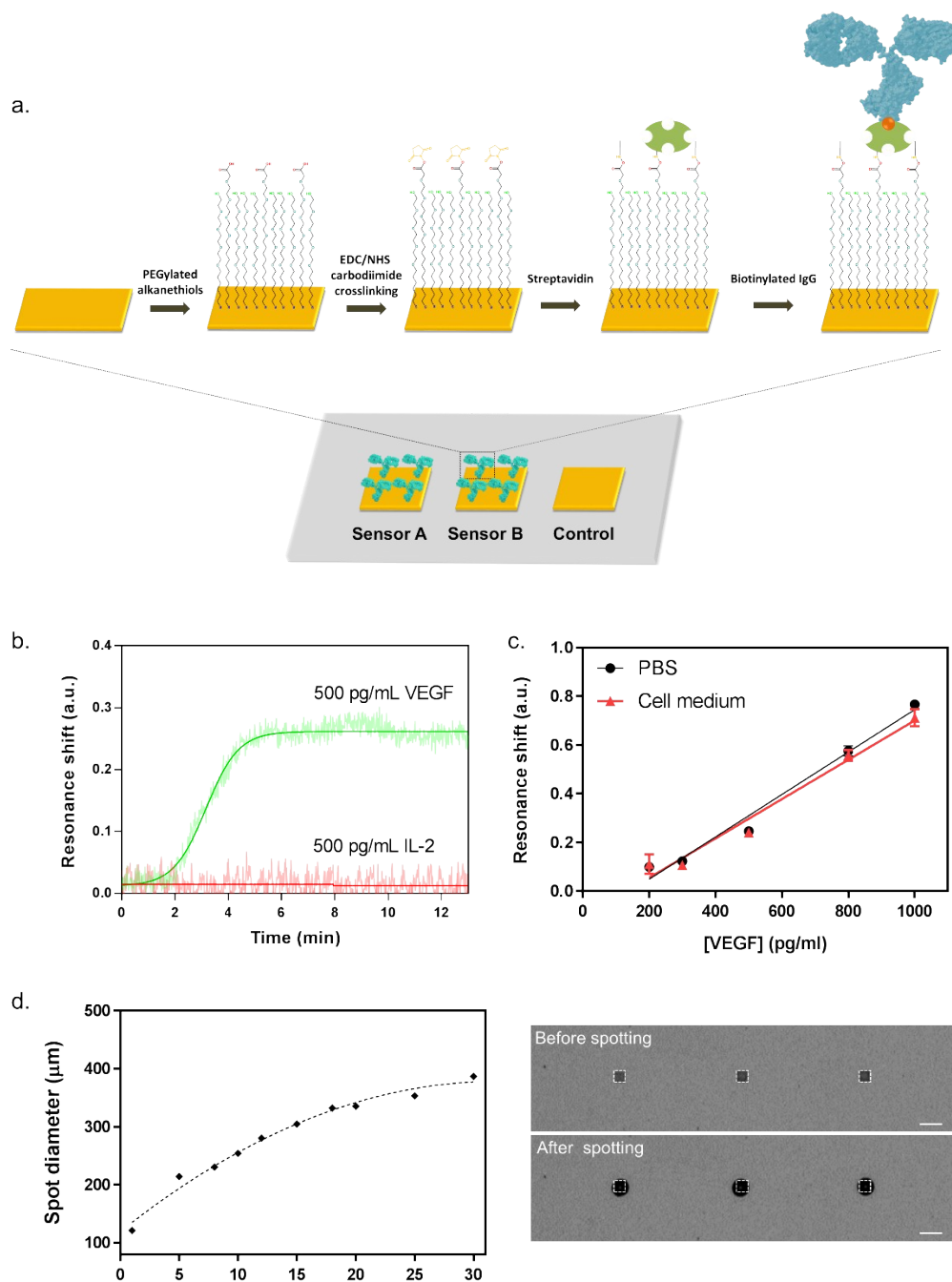


Figure S3. Stepwise illustration of the surface functionalization process was shown in (a). The selectivity and specificity of the plasmonic biosensor were confirmed by comparing the plasmonic response of 500 pg/mL VEGF and IL-2 (b) and calibration of VEGF spiked in PBS solution versus complete cell culture media (c). (d) The correlation between droplet number and resulting spot size was shown on the left. On the right, the NHAs were highlighted by the white dashed boxes, and they were entirely covered by antibody droplets after the spotting. (Scale bar: 200 μ m)

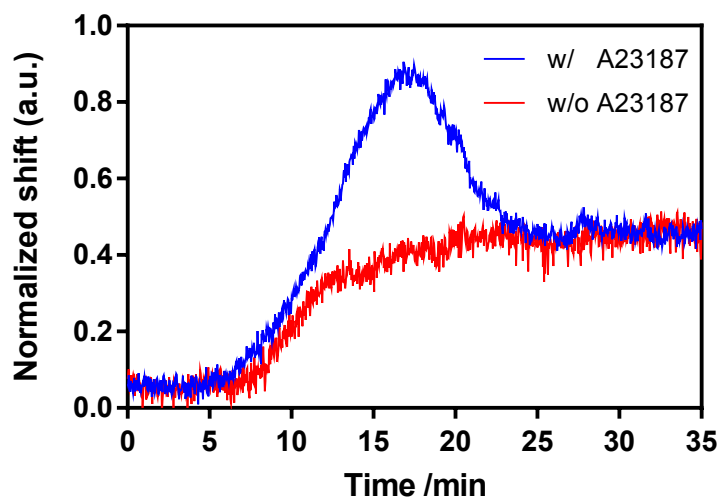


Figure S4. Influence of the VEGF stimuli, A23187, on the optical signal. The VEGF samples ($1\mu\text{g/ml}$) prepared with A23187 (blue curve) or without A23187 (red curve) were injected into the bisosensor functionalized with anti-VEGF antibodies. Despite the bulky refractive index change induced by the stimuli, there is no significant spectral shift between these two samples, indicating that A23187 does not interfere with VEGF detection.