idic channel for 10 minutes, followed by a removal of residual siloxane by flushing with 95% ethanol. The resonance shift during this process was monitored in real time (Fig. 3(b)), indicating the APTES had sufficiently reacted with the activated silicon surface. Next, 10mM of glutaraldehyde (Sigma) and 10mM of sodium cyanoborohydride (Sigma) pre-mixed solution were injected for 2 hours, followed by a wash with phosphate buffered saline (PBS). This created aldehyde termination on the sensor surface. Anti-CEA (1ug/mL) was subsequently injected for 1 hour and washed by PBS for 5 minutes. Figure 3(c) shows that anti-CEA was successfully captured on the sensor surface. Finally, different concentrations of CEA (0.1, 1, 10, 100pg/mL; 1, 10, 100ng/mL and 1, 10μg/mL in PBS) were consecutively injected to the microfluidic channel. The fluid rate was kept at 2μL/min, delivered by a syringe pump (Harvard Apparatus). Figure 3(d) shows the representative resonance curve before and after the CEA sensing experiment. Figure 3(e) shows the real time resonance shift during the sensing process, extracted by Lorentzian fitting. The red dotted line indicates different steps for different concentrations of CEA. A clear binding signal was observed starting from 10pg/mL. At concentrations above 1μg/mL, PBS wash brought the sensor resonance back to the baseline. This indicates that the sensor surface was saturated by antigen-antibody binding, and all excess shifts were due to physical absorption, which was washed off by PBS. In Fig. 3(f), we plotted resonance shift v.s. concentration of CEA, and fitted the curve with Langmuir equation [30]. From fitting, we obtained the dissociation constant of 14ng/mL, consistent with the results obtained by commercial label-free instruments [31].

5. Conclusion

In summary, we demonstrated the detection of CEA biomarker from 0.1pg/mL to 10μg/mL, over 8 orders of magnitude and achieving a detection limit of sub-pg/mL. The dissociation constant of CEA protein was also obtained from the concentration measurement. The sensor chips in our experiment were fabricated by scalable deep UV lithography and have shown high yield and high dose tolerance, with a mean Q factor of 9,000. The top-down fabrication approach also enables high density integration and interfacing between photonics and electronics. This shows great promise in achieving low-cost, high-sensitivity, and high-throughput automated biomedical point-of-care testing tools.

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