the bare PBS solution and 2pM streptavidin solution have negligible differences, due to small effect of streptavidin to the solution. A histogram of experimental resonance jumps (using the above mentioned 3σ method), accumulated from several experiments is shown in Fig. 6(e). It cuts off at 0.06pm, which is the detection limit of current nanocavity sensor. Furthermore, it can be seen that the most common resonant shift observed in our experiment is 0.07pm, which is within the 0.04-0.08pm range, predicted using theoretical analysis (Fig. 2). The discrepancy between experimental data and theoretical predictions can be attributed to: (i) uncertainties in the size and refractive index of streptavidin, (ii) additional mechanisms that induce additional resonance shift induced by streptavidin (iii) events of pairs or clusters of streptavidins binding on to the nanosensor.

The minimum wavelength shift that can be reliably measured in our system depends on the accuracy in determining the absolute value of the cavity resonance, which in turn depends on the signal-to-noise ration (SNR) of the transmission spectrum measurement. Previous work [14, 26] with similar noise level to ours and SNR$\sim$20dB has demonstrated the ability to extract the cavity resonance (using Lorentzian fitting) with the accuracy of 1/1000th of the resonance linewidth. In our case, this would correspond to an accuracy of $\sim$0.04pm (cavity Q=35,000). Unfortunately, our current measurements fall slightly short off this value, which is attributed to the wavelength fluctuations of the tunable laser source used in our measurements. Using a high resolution wavemeter (Toptica Inc.), we measured the wavelength fluctuation of the laser to be $\sim$70fm, which is on par with the signal from single streptavidin. We found that laser fluctuations are highly dependent on the acoustic noise in the laboratory. For example, we could improve the wavelength stability simply by placing the laser on the sturdy heavy duty table and surrounding it with acoustic foam. This cuts of the wavelength fluctuation in half. Further improvements in the laser stability are still needed in order to reduce the rate of false positive events, and to reach the true potential of our sensor. This will be accomplished by further reducing the acoustic noise in the setup, choosing more stable laser sources or actively stabilizing the laser source with Pound-Drever-Hall technique [27]. Furthermore, an improved cavity design with greater resonance shift to single molecules will also improve the detection of single molecules.

6. Conclusion

In conclusion, we have demonstrated label-free nanoparticle detection and protein detection with single particle sensitivity and single molecule visibility. While single protein detection has been observed recently with hybrid plasmonic-photonic systems [13] and plasmonic nanorods [14, 15], our SOI based platform offers unique advantages, including inexpensive and scalable fabrication using established CMOS processes. The top down fabrication approach also enables highly multiplexed detection with multiple sensors and further integration with electronics and instrumentation. Additionally, the ultra-small mode volume of our cavity makes single molecule detection possible in water, which has proven to be a major limitation of other silicon-based optical cavity sensors. Our device will enable study of biomolecular interactions where fluorescent labeling is not feasible or where sensitivity of current available label-free sensor platforms is inadequate.

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