Integrated Angle-insensitive Nano-plasmonic Filters for Ultra-miniaturized Fluorescence Microarray in a 65-nm Digital CMOS Process

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Supporting Information

Throughout the paper, there are several metrics used in characterizing the limit of detection of sensor, including the maximum ratio between excitation and fluorescence power, minimum surface density of fluorophores, and minimum volume concentration of DNA. While the last metric depends on the extinction coefficient and quantum efficiency of fluorophores as well as the assay protocol (for volume concentration), the ratio between excitation and fluorescence power is independent of these factors therefore is one of the most direct metrics in characterizing the sensor performance. The SNR of the sensor can be expressed by the ratio between the fluorescence signal and the combination of various noise sources:

$$SNR = \frac{\frac{P_f R_f T}{e}}{\sqrt{(\frac{V_{Ncir} C_{fb}}{e})^2 + (\frac{V_{Nadc} C_{fb}}{e})^2 + \frac{(P_f + \frac{P_l}{\beta}) R_f T}{e} + \frac{2 I_d T}{e} + (\frac{\eta_{ex}(P_f + \frac{P_l}{\beta}) R_f T}{e})^2 + (\frac{\eta_{bio} P_f R_f T}{e})^2}} \quad (1)$$

where P_f is the fluorescence light power, R_f is the photodiode responsivity (A/W) at the fluorescence wavelength, T is the integration time, e is the electron charge, V_{Ncir} is the photosensing circuits noise, C_{fb} is the feedback capacitance of the CTIA, V_{Nadc} is the readout noise, P_l is the excitation light power, β is the sensor's responsivity ratio between the fluorescence and excitation wavelength (mainly determined by the filter performance), I_d is the dark current, η_{ex} represents the normalized standard deviation of the fluctuation of the LED excitation power, and η_{bio} represents the biological noise (the variation of surface density of fluorophores when the same bio-protocol is repeated).

The terms in the denominator represent the sensing circuits noise, readout noise, photon shot noise, dark current shot noise, excitation power fluctuation noise, and biological noise. It can be seen that the SNR increases monotonically with integration time T, therefore, the optimum SNR is achieved when the integration time is maximized such that the highest voltage swing V_{SW} of the CTIA is reached. This implies

$$T = T_{max} = \frac{V_{SW} C_{fb}}{(P_f + \frac{Pl}{\beta}) R_f} \tag{2}$$

Using the maximum integration time and ignoring the dark current shot noise (which in practice is negligible), the maximum ratio between the excitation and fluorescence power at $SNR = 1$ can be derived as

$$\frac{P_l}{P_f}(SNR=1)=\beta\sqrt{\frac{1-\eta_{bio}^2}{\eta_{ex}^2+\frac{V_{Ncir}^2+V_{Nadc}^2}{V_{SW}}+\frac{e}{V_{SW}C_{fb}}}-1}\approx\beta\sqrt{\frac{1-\eta_{bio}^2}{\eta_{ex}^2+\frac{V_{Ncir}^2+V_{Nadc}^2}{V_{SW}^2}+\frac{e}{V_{SW}C_{fb}}}} \quad (3)$$

In Fig. 9 in the main article, the total noise including excitation light fluctuation, circuits and readout noise and photon shot noise is measured to be

$$V_{Total}=\sqrt{(V_{SW}\eta_{ex})^2+V_{Ncir}^2+V_{Nadc}^2+\frac{eV_{SW}}{C_{fb}}}=3.5mV \quad (4)$$

In our design, V_{SW} is measured to be around 1 V. With the large-dynamic-range (over 90 dB) photon detection circuits, the integration time can be easily adjusted to reach full voltage swing in typical excitation settings (e.g. 0.2 mW/mm^2). Assuming the worst-case $\beta = 45$ dB (Fig. 7b in the main manuscript), practical biological noise estimation $\eta_{bio} = 20\%$, the maximum ratio between excitation and fluorescence signal can be estimated to be to be greater than 70 dB for the implemented system. If multiple signal acquisition (e.g. 100 times) can be performed to each sensing pixel, the total noise can be further reduced by simple averaging, thereby giving another 7 dB sensitivity boost to the system. In practical bio-sensing settings, the quantum dot-based fluorophore[63] we use has the absorption coefficient of $1.06 \times 10^7 cm^{-1}M^{-1}$, corresponding to the molecular absorption cross section of $1.76 \times 10^{-14}cm^2$. Assuming the estimated quantum efficiency of 0.5, fluorescence light collection efficiency of 0.1 (due to around $\approx 100\mu m$ separation between fluo-

rophores and photodetectors), 77 dB fluorescence/excitation power ratio will give a detection limit of 0.23 dot/μm^2. This is in accordance with the measured 1 dot/μm^2 limit of detection as shown in Fig. 10. During the biosensing measurements, we use a LED (< 0.2 mW/mm^2), and typically 100 ms integration time is enough to reach full voltage swing given the excitation light power level.