NANO MICRO small

Supporting Information: A nanoelectronic-enzyme linked immunosorbent assay (ne-ELISA) for detection of proteins in physiological solutions

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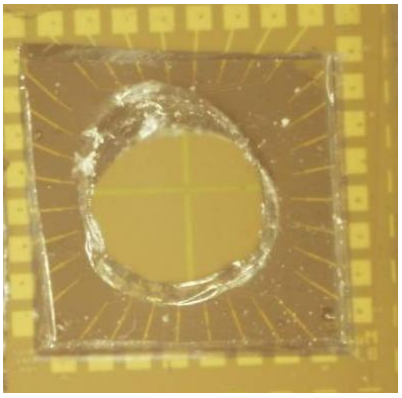
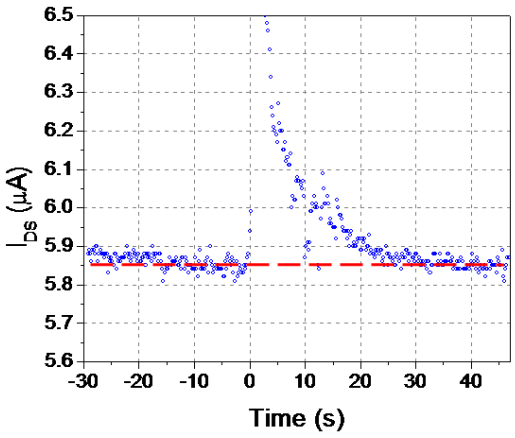
Sensing Calculation. In order to calculate the number of urease molecules present in the sensing reservoir, we began by determining the increase in $[H^+]$. For the 1.6 pg/mL IL-2 sample, the pH increased by 0.05 units, corresponding to ~1.1 × 10^{-9} M, or ~4.3 × 10^{-15} mol in the 4 μL reservoir. This pH change is solely due to the urease (Fig. S2), thus, using the unit definition of urease obtained from the manufacturer, this corresponds to ~6.7 × 10^{-11} mg urease. Converting to mols (480 kDa) yields ~1.4 × 10^{-19} mol or ~8.4 × 10^4 molecules. Accounting for a ~100 nm^2 antibody hydrodynamic footprint, a maximum of ~10^9 IL-2 molecules can bind the (gold) lead surface area (~10^5 μm^2) in the 4 μL reservoir, thus a maximum of ~10^9 IL-2 molecules (or ~1.7 × 10^{-15} mol) can be bound. The reservoir solution volume is 4 μL, but only a small percentage of the IL-2 molecules in the reservoir will be exposed to the surface and, thus, able to bind.

Sensitivity Calculations. The change in pH plotted in Fig. 9 was calculated by first determining the normalized ΔI_{DS}/pH unit $\left(\frac{\Delta I_{DS}}{pH\ unit} = g_m(wet) \cdot m + b \right)$, where m and b are the slope and

intercept, respectively, of the trendline from Fig. 7. The observed change in channel current (I_{DS}) was then divided by this value to obtain the calculated change in pH.

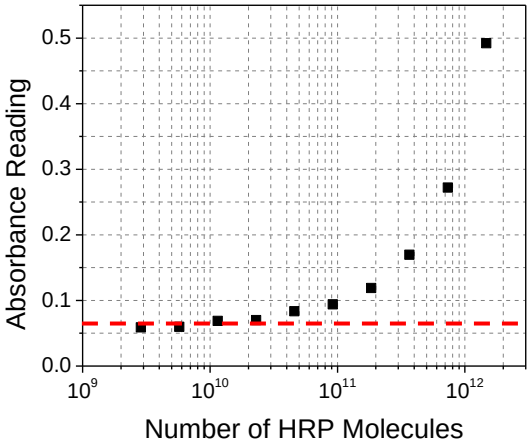


Supplementary Fig. S1. Optical micrograph of a single die with a reservoir defined by a PDMS gasket. Contact pads on the die edges fan into parallel Ni/Au leads, which contain nanowire devices such as that shown in Fig. 2.



Supplementary Fig. S2. Response [I_{DS}(*time*)] of a sensor configured for IL-2 detection with no IL-2 added during the protein-binding step (Fig. 1Biii). At *time* = 0 the 100 mM urea solution

was added to the pH 8.0 buffer. The dashed red line shows the initial current level. For this device, ΔI_{pH} = 1.8 nA.



Supplementary Fig. S3. Plot of the absorbance reading (λ = 450) vs. streptavidin-HRP concentration after a 15 min reaction with TMB as the substrate. The red dashed line shows the average reading for 12 control wells to which no enzyme was added (OD = 0.0611).