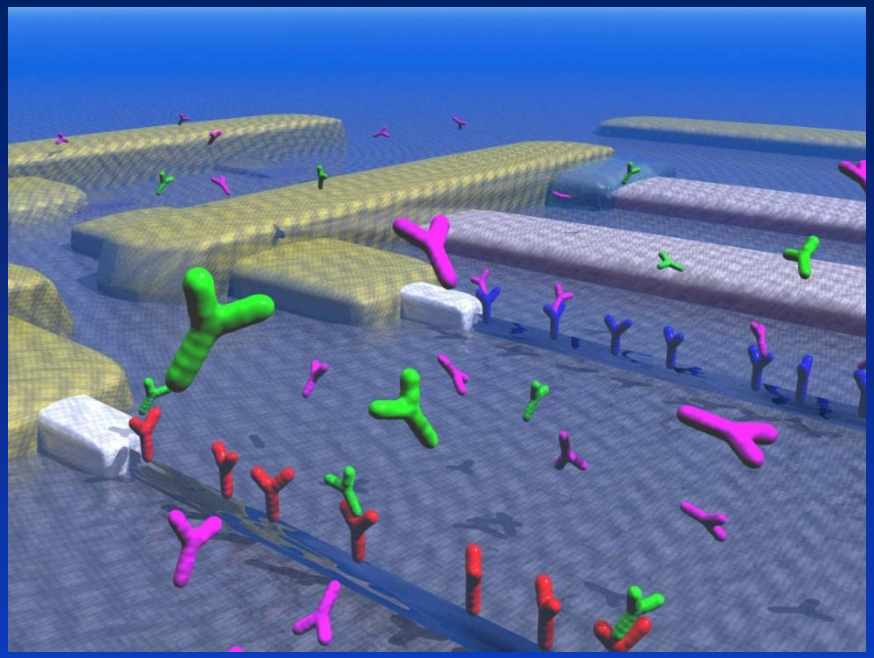
Nanowire FET Biomolecular Sensors



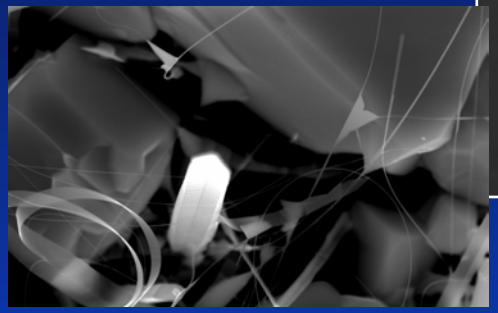
Mark Reed
Yale University

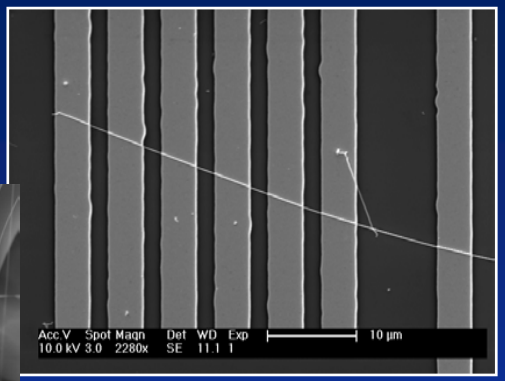
Departments of Applied Physics and Electrical Engineering
Yale Institute for Nanoscience and Quantum Engineering

with: Eric Stern, David Routenberg, Erin Steenblock, Alek Vacic, Nitin Rajan, Prof. Tarek Fahmy

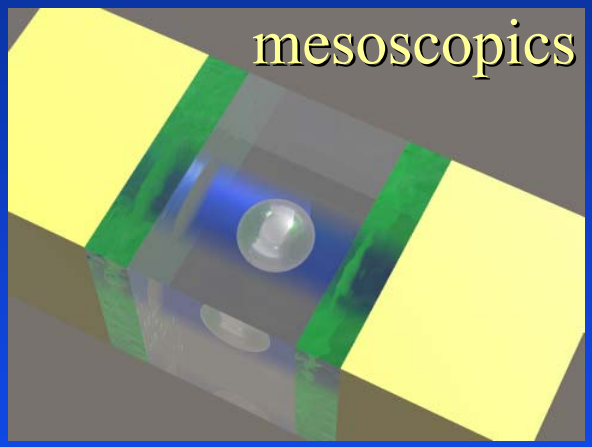
Thanks to: Jin Chen, James Klemic, Daniel Turner-Evans, Pauline Wyrembak , Cathy Jan
Labs of Profs. Ronald Breaker, Andrew Hamilton, Tarek Fahmy

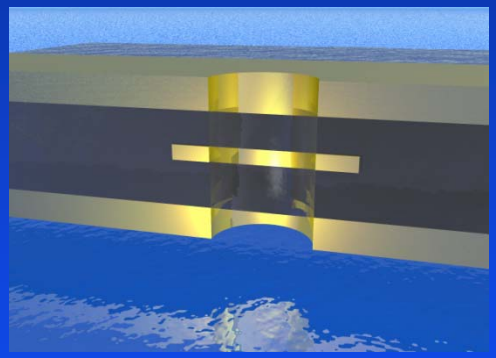
What I won't talk about today



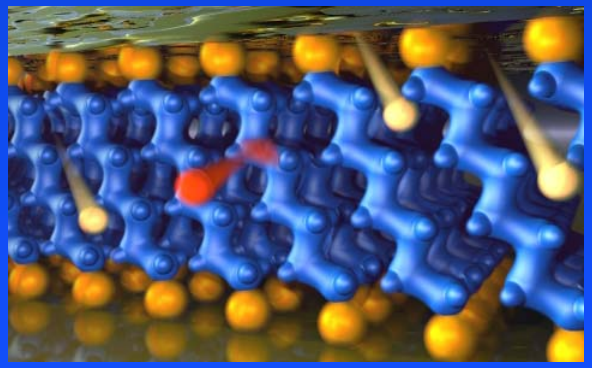


nanowire materials & devices

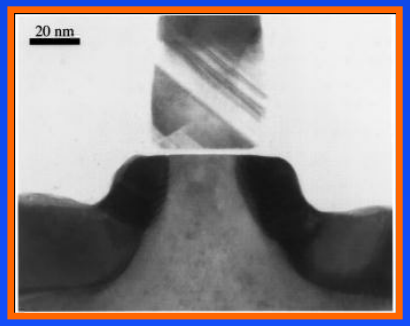




DNA sequencing devices



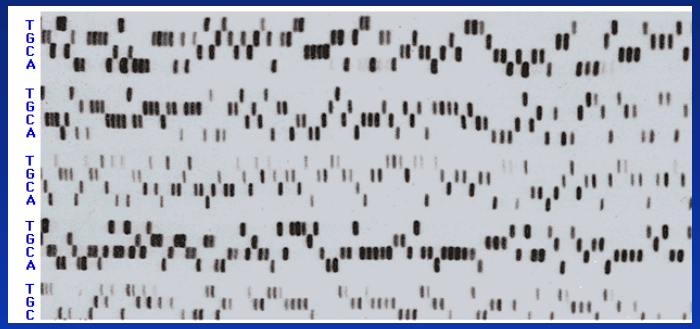
molecular electronic transport, IETS



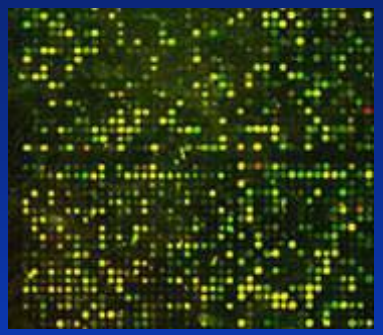
physics of scaled devices

Current Macromolecular Sensing

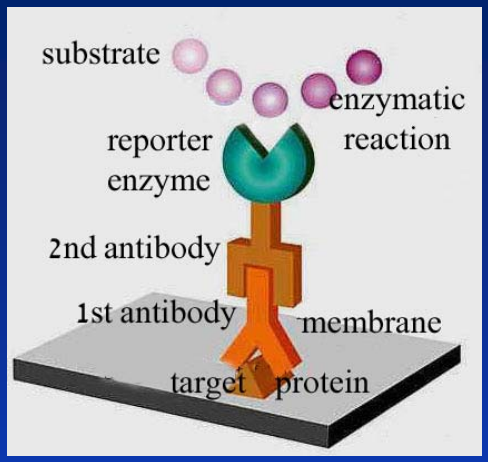
Labeled sensing



DNA sequencing, radiotag

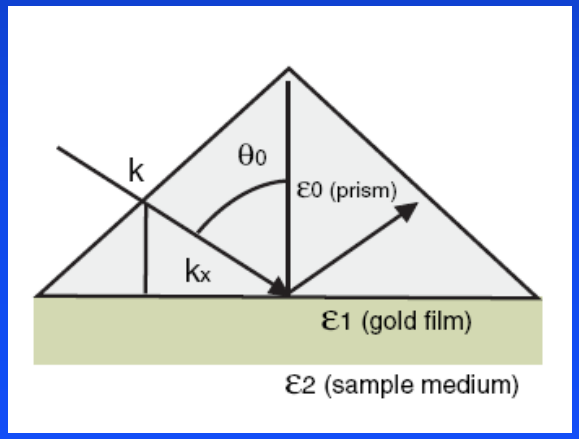


DNA array, fluor

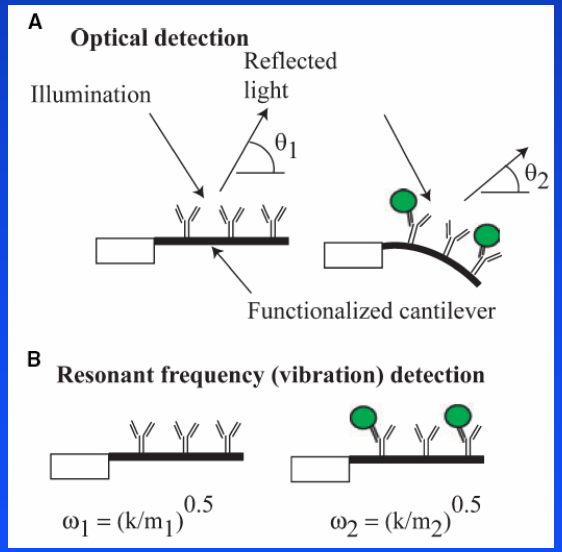


ELISA: Indirect fluor

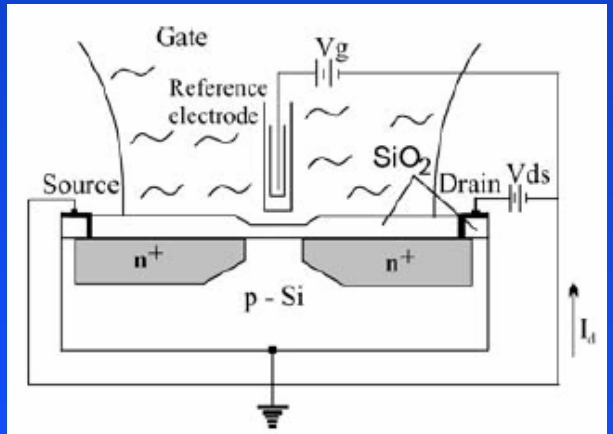
Unlabeled sensing



Surface plasmon resonance

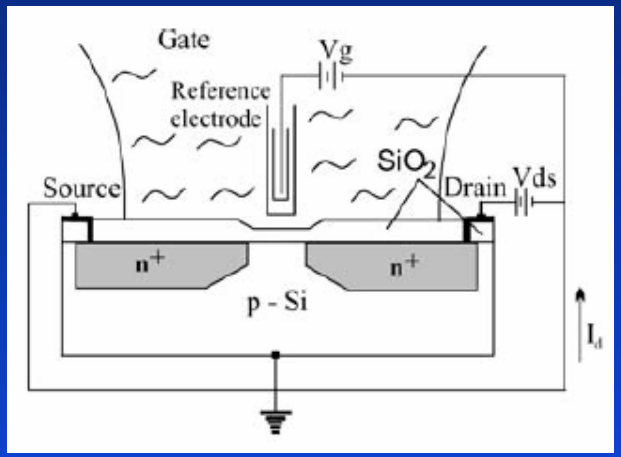


Suspended cantilever



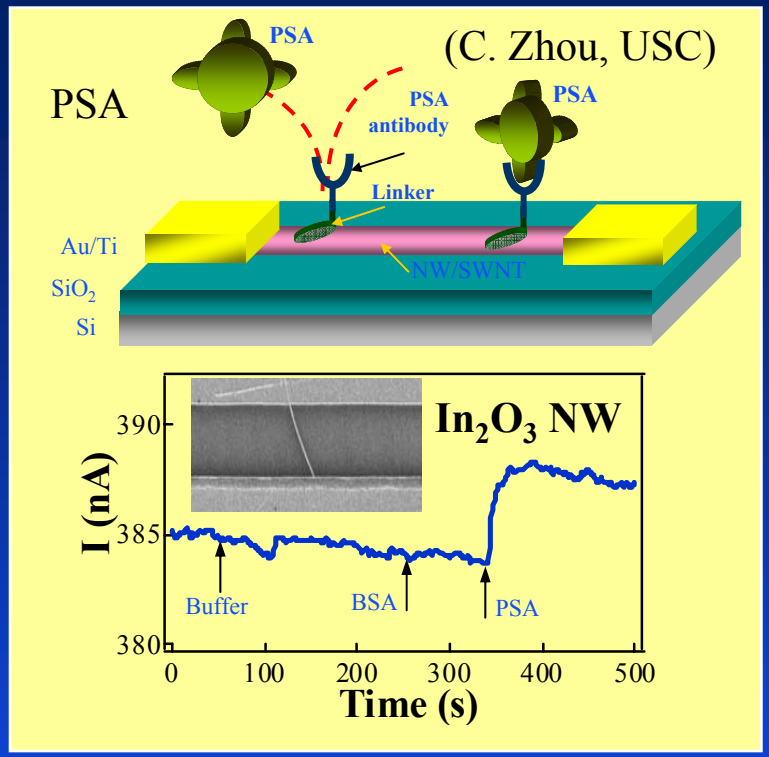
Electrical : ISFET

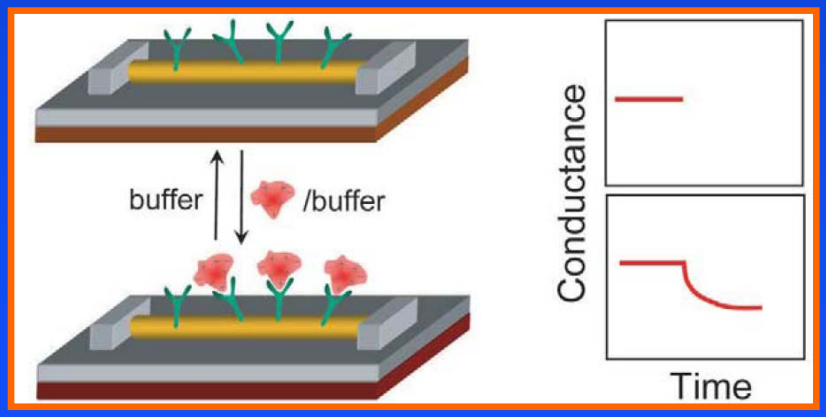
Nanowire biosensors (unlabeled detection)

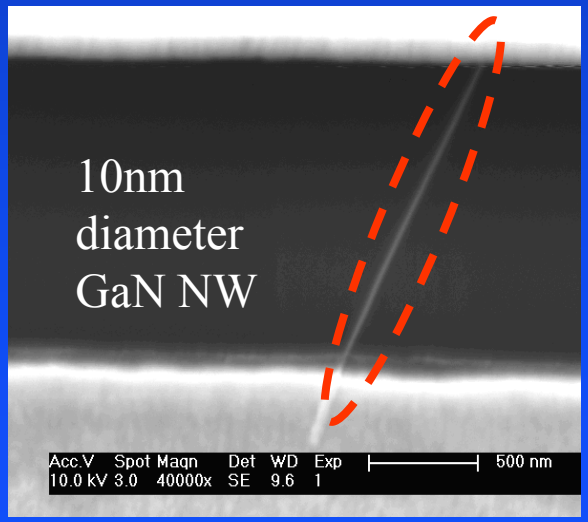


ISFETs detection limits typically ~ μM

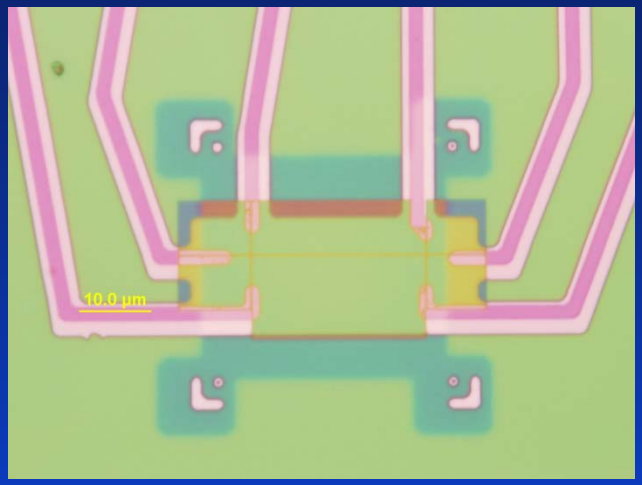
$$\frac{1}{I}\frac{dI}{dQ} \sim \frac{1}{r}$$

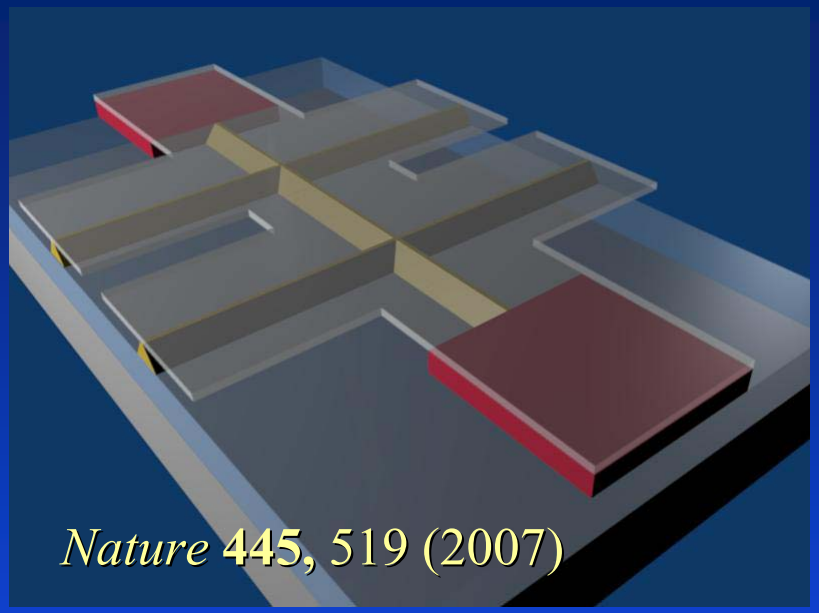


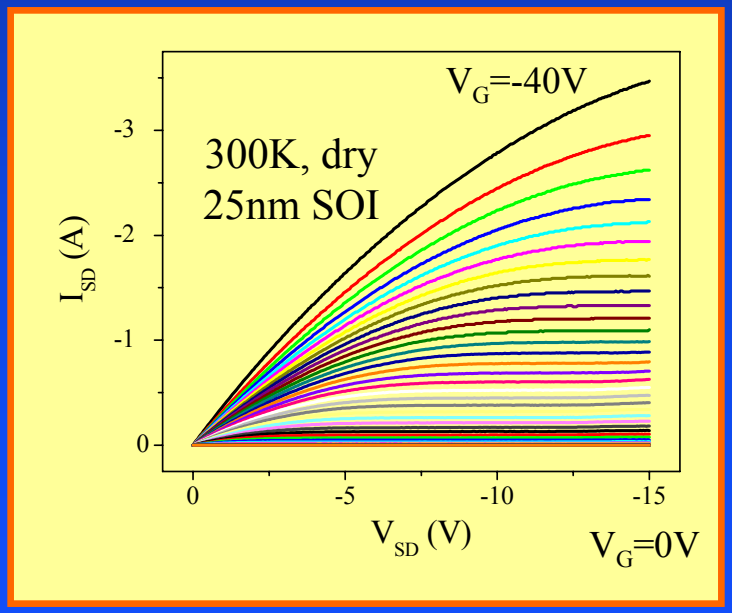


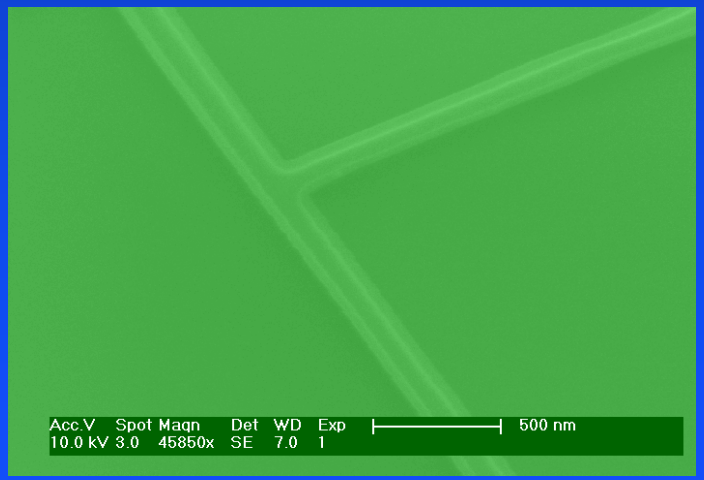


Silicon-on-insulator (SOI) CMOS Nanowires

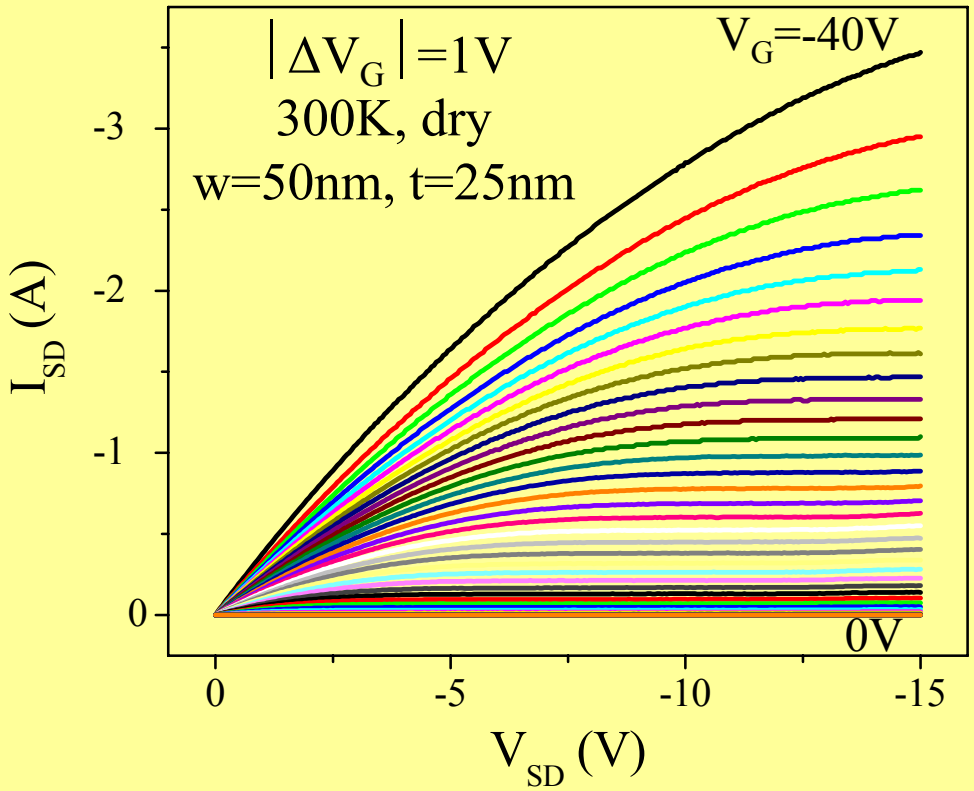




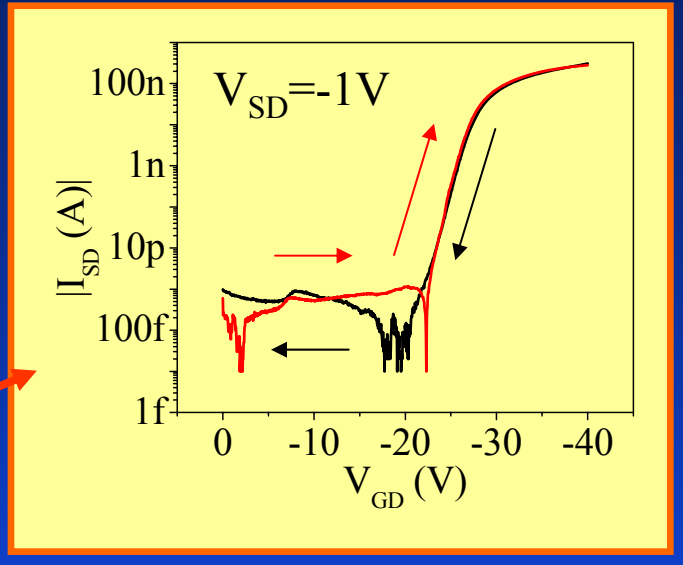


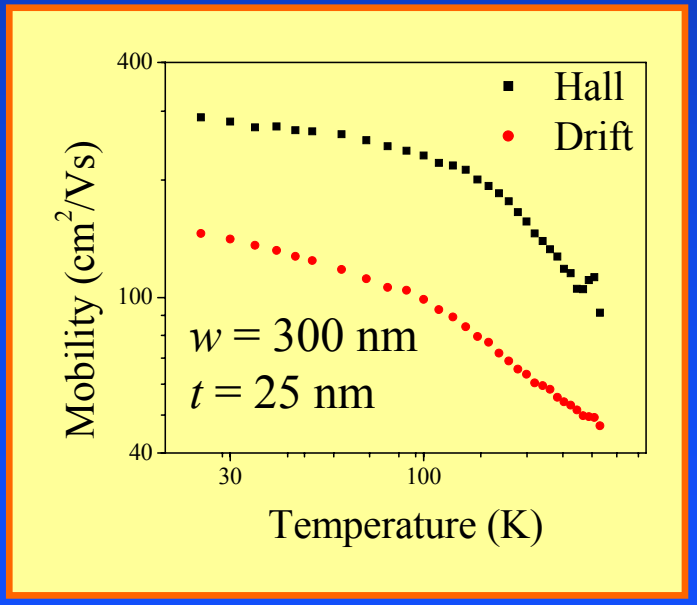


p-type accumulation mode (backgate)



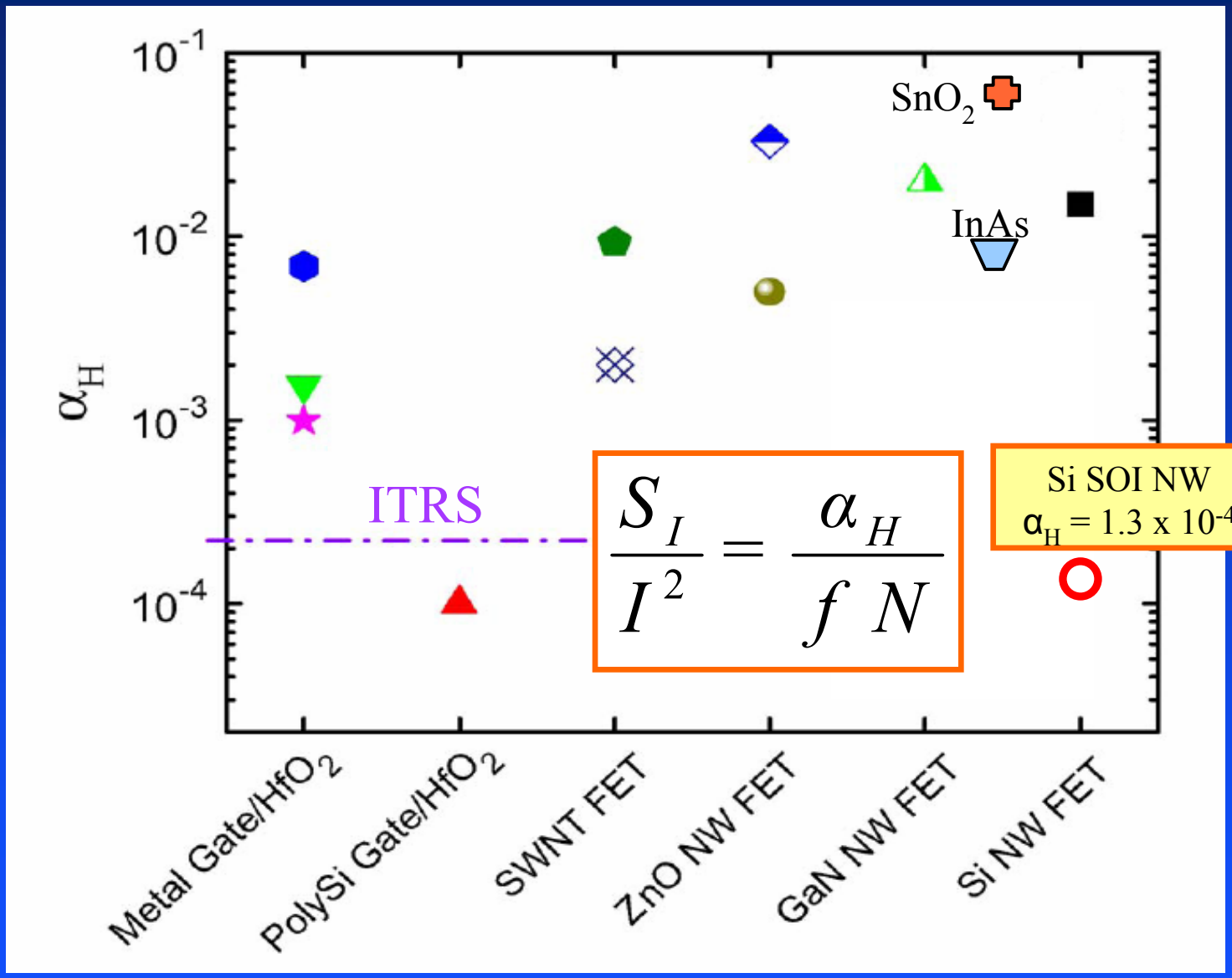
Fully depleted; $n_0 \sim 1 \times 10^{15}$ cm^{-3}



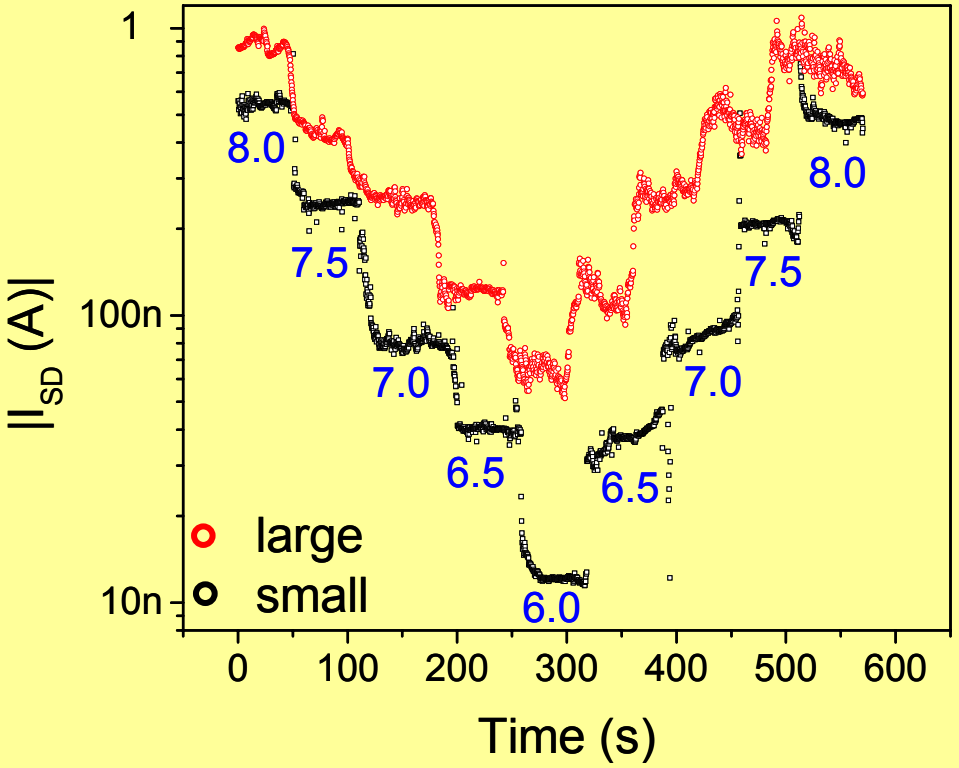


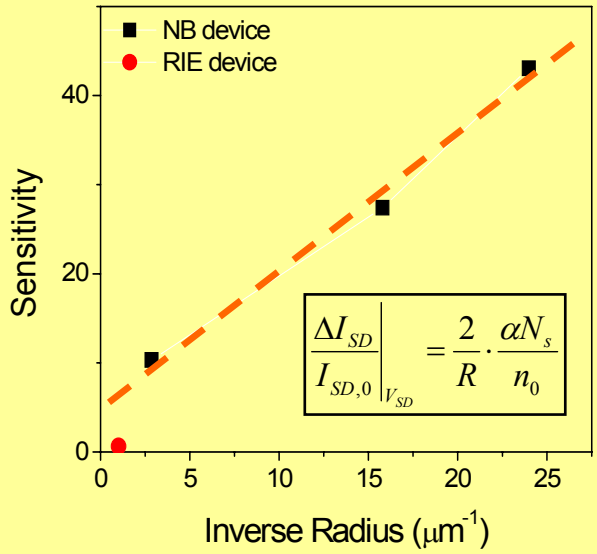
$\bar{\mu}$ = 54 cm^2/V-s μ_{max} = 139 cm^2/V-s

1/*f* noise of nanowires



NW Sensitivity Scaling with Size : pH Sensing



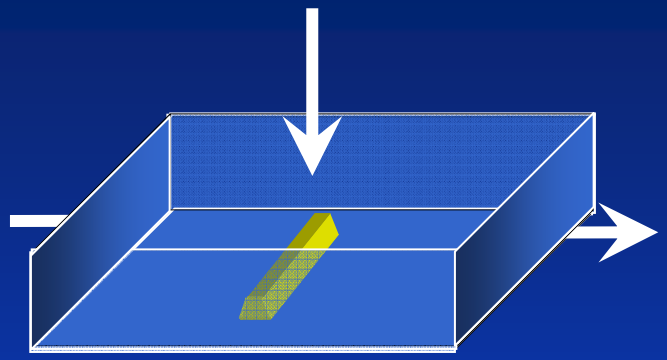


large: w = 1000 nm; t = 80 nm
small: w = 100 nm; t = 25 nm

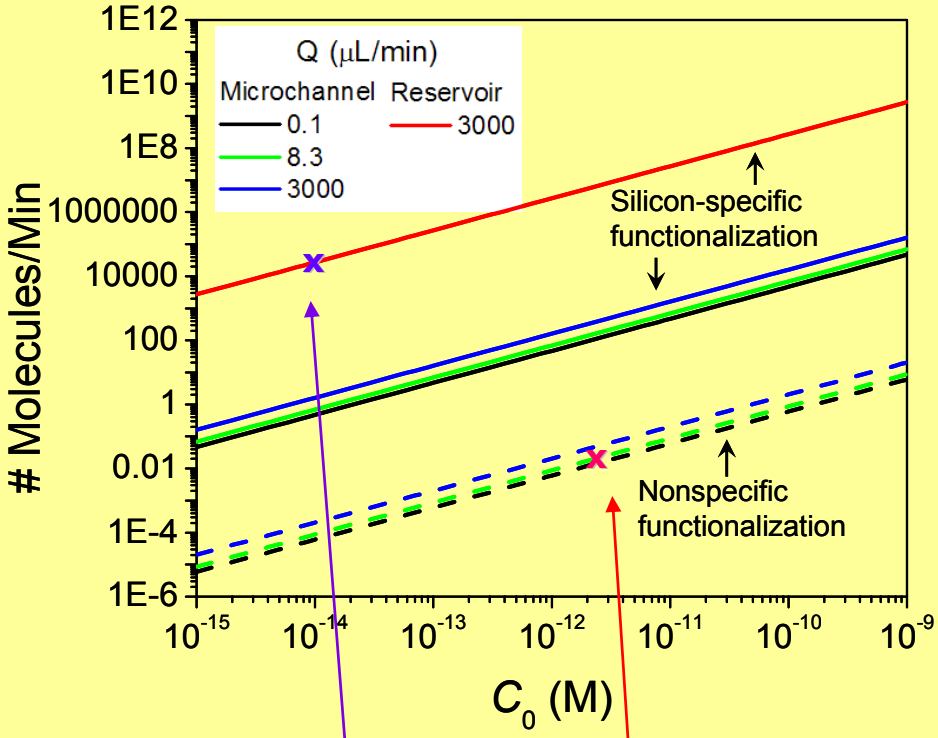
Nernst potential = 60 mV/pH
Subthreshold slope = 60 mV/decade
$\therefore$ max. response is 1 decade/pH

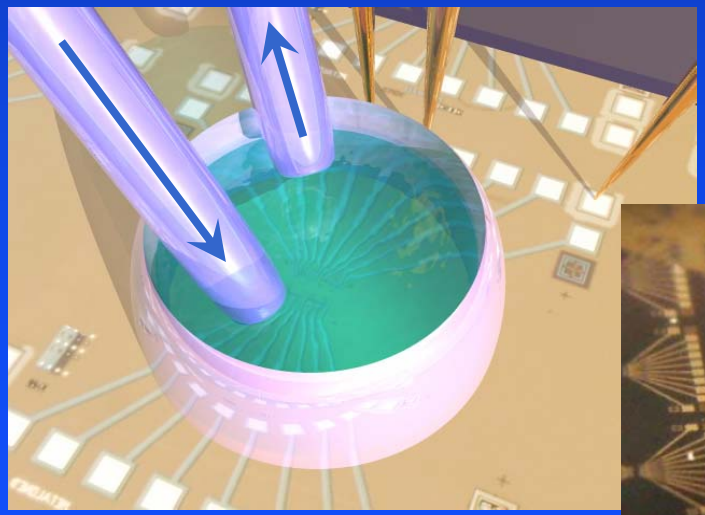
Fluid Considerations

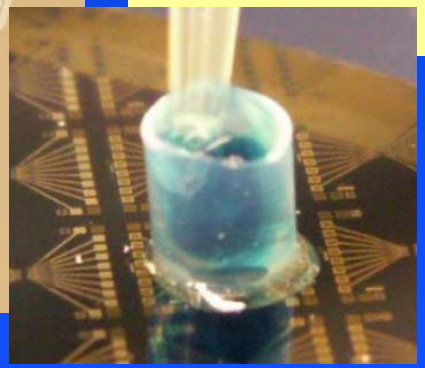
Nano Lett **5**, 803 (2005)



$$J_z = -D\frac{d^2C_0}{dz^2} + u_z C_0$$



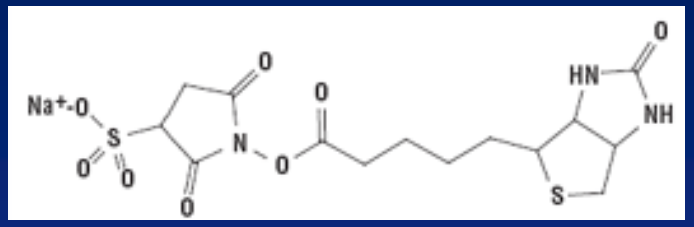


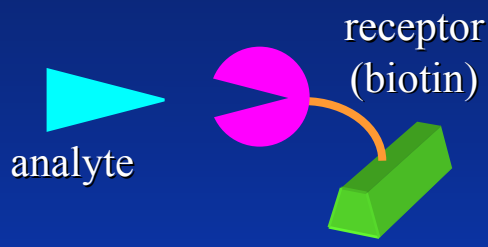


x = microfluidics
Science **293**, 1289 (2001)

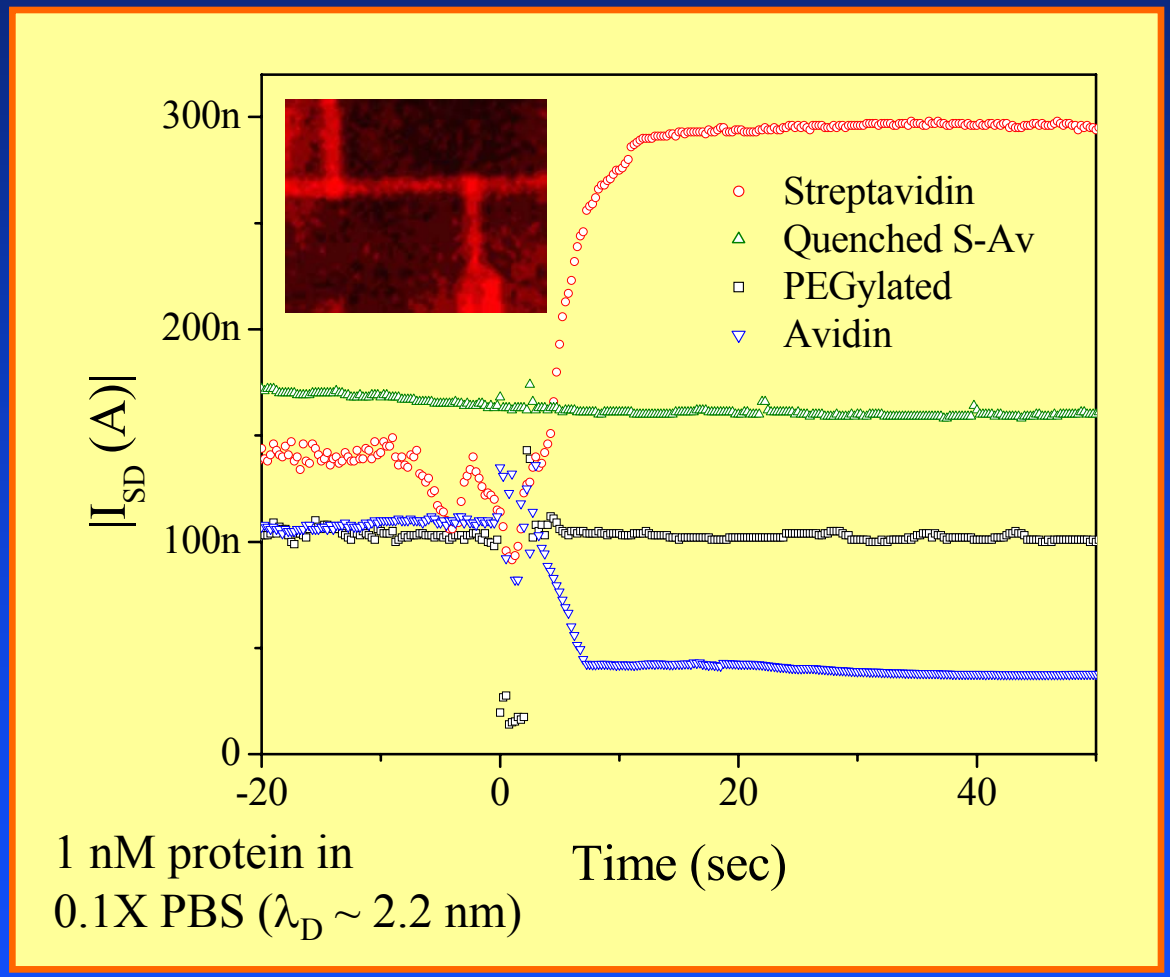
x = mixer (resorvoir)
Nature **445**, 519 (2007)

Biotin-Avidin & Streptavidin Sensing



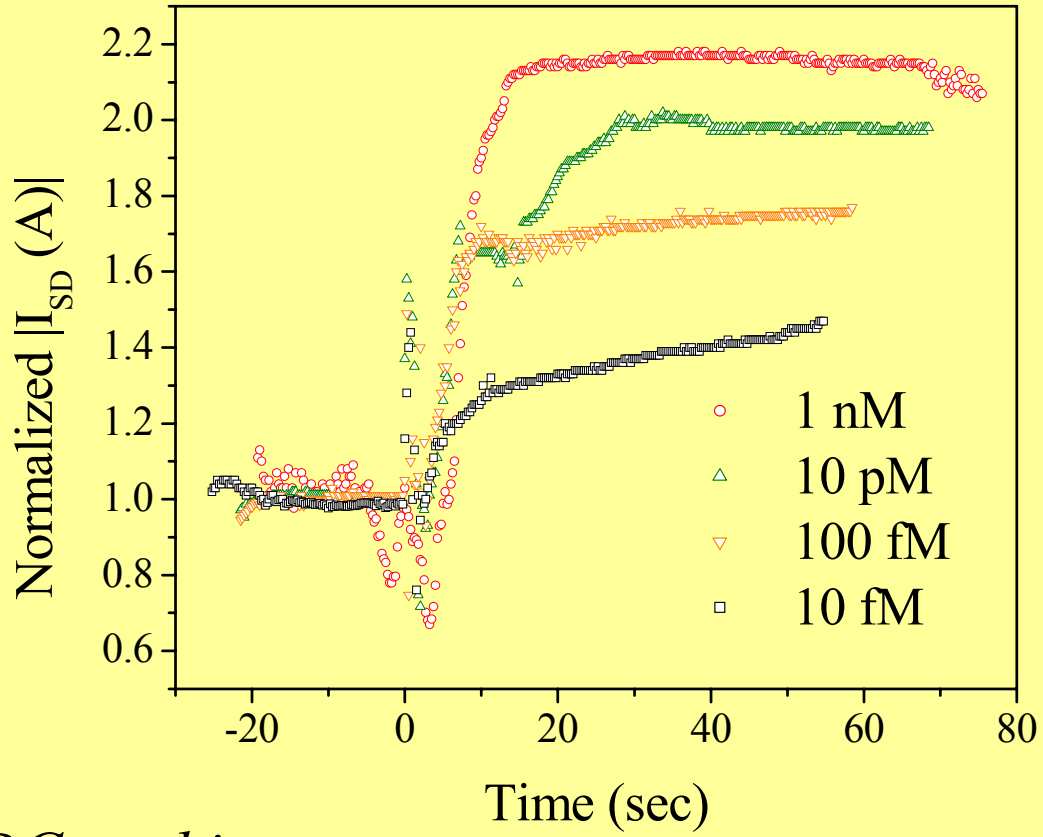


- p-type accumulation mode, biotinylated NW device
- avidin
  - positive charge
  - ⇒ current decrease
- streptavidin
  - negative charge
  - ⇒ current increase
- poly(ethylene glycol) (PEG)-ylated device, quenched avidin controls



Nature, **445**, 519 (2007)

Sensitivity: Concentration Dependence



DC, ambient

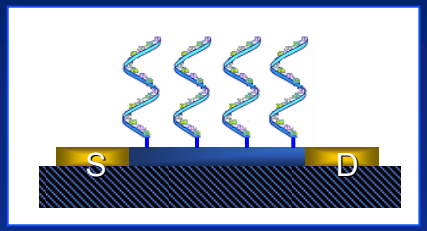
- initial S/N
  ~ 140 (@10fM)

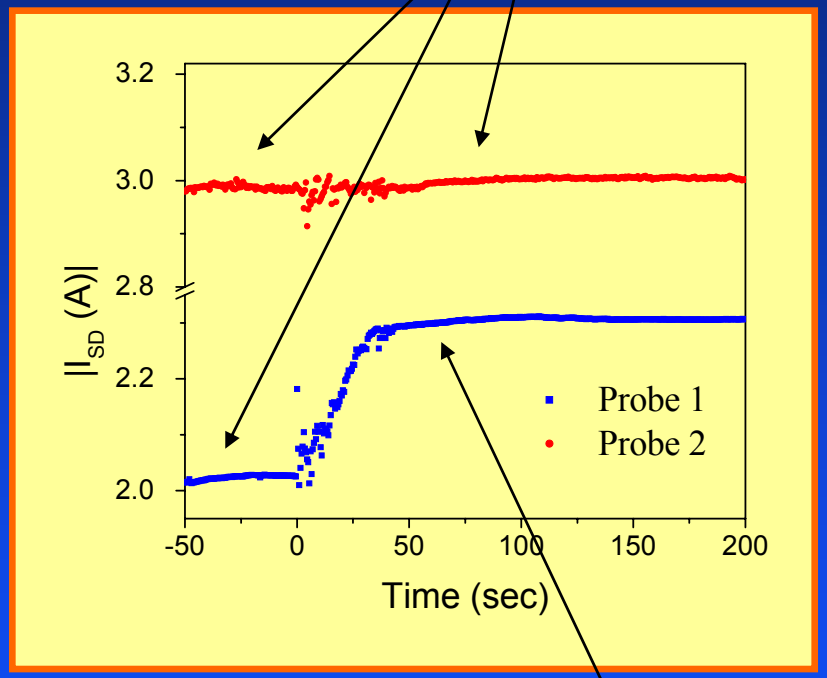
⇒ <100 aM limit
(< 3 fg/ml)

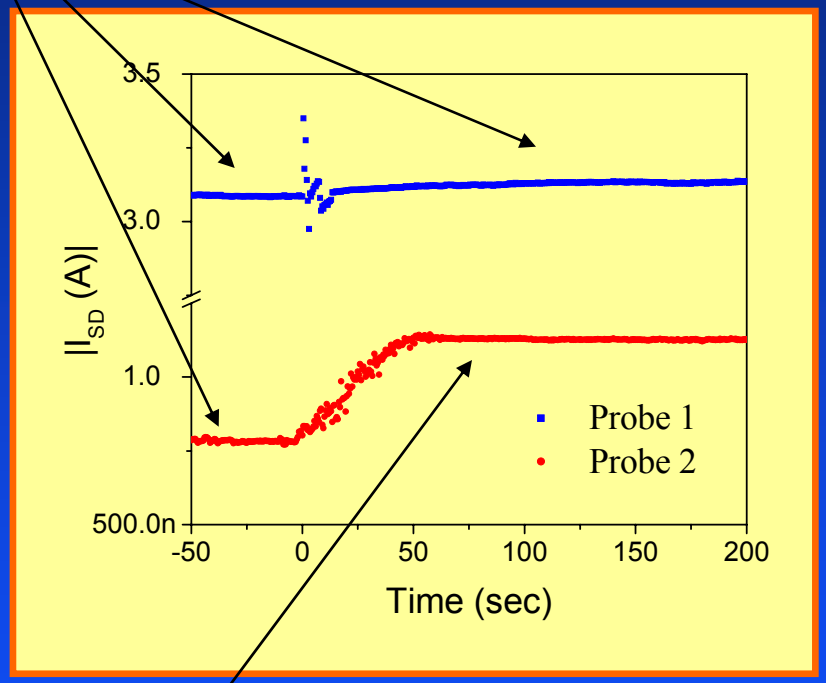
(1 aM = 30 molecule per mm^3)

DNA sensing: criss-cross

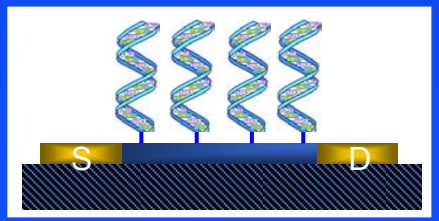
- Capture1 is the complementary strand of Probe1;
- Capture2 is the complementary strand of Probe2





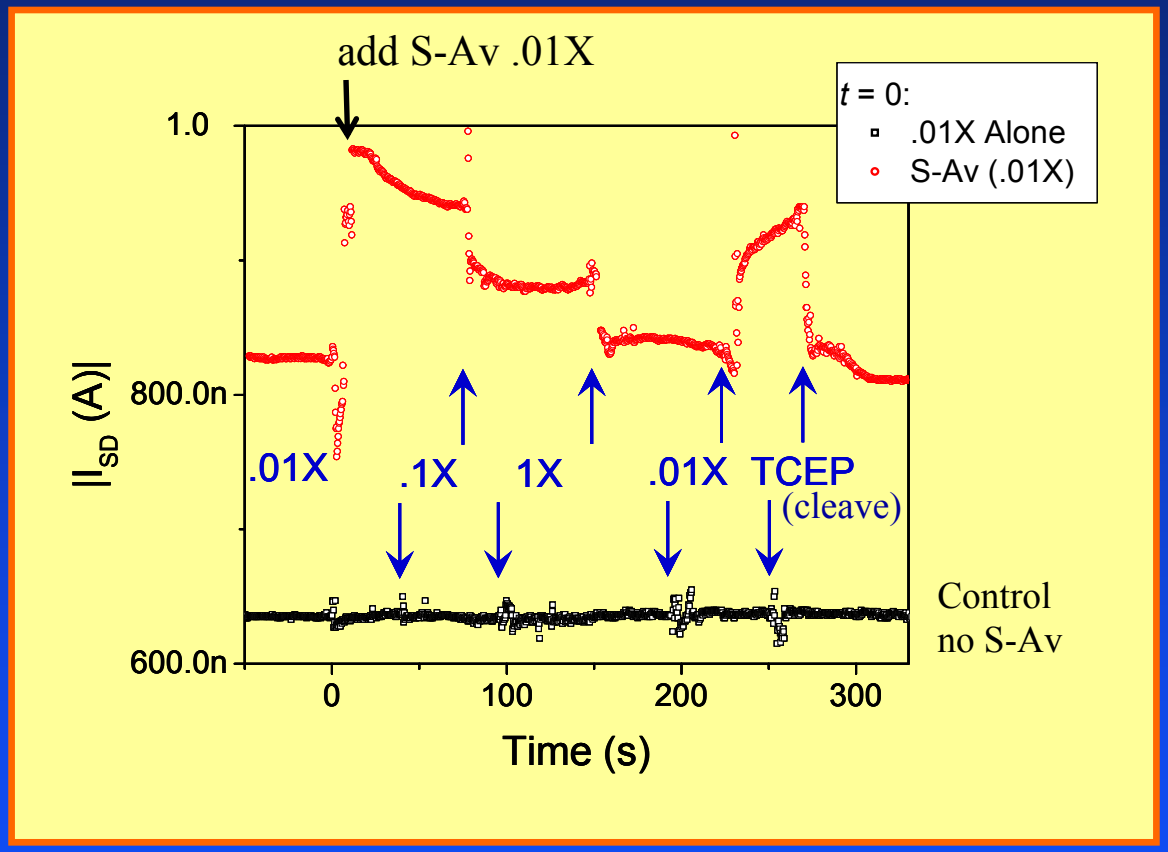


Surface: Capture1



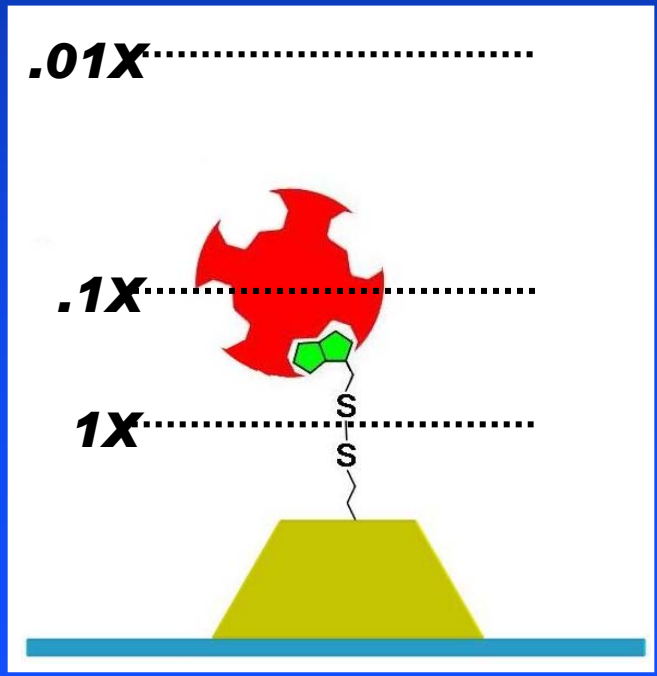
Surface: Capture2

Debye Screening Considerations



$$\lambda_D = \frac{1}{\left(4\pi l_B \sum_i z_i^2 \rho_i\right)^{1/2}}$$

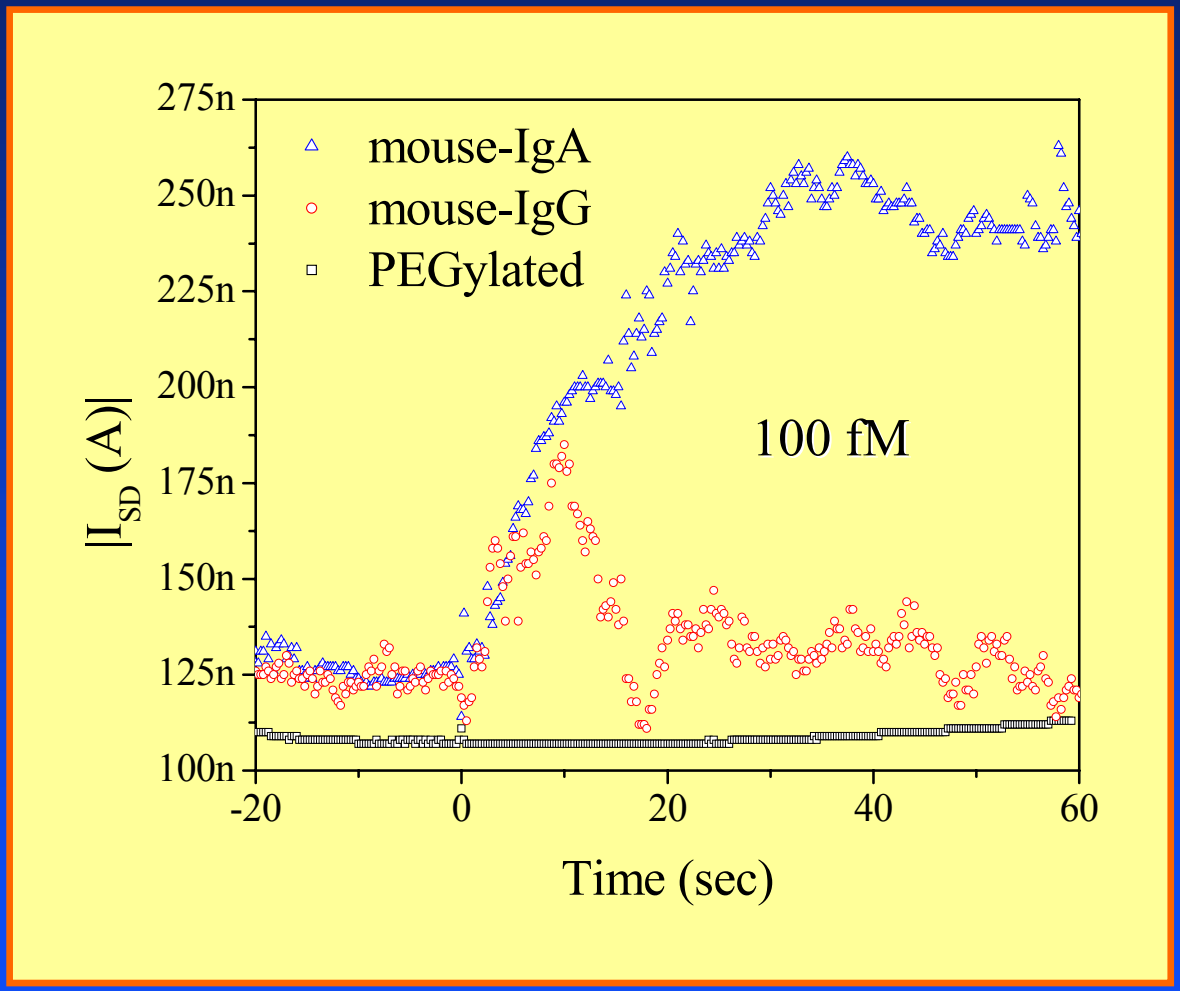
for 0.1 mM PBS,
$\lambda_D \sim 2.2$nm



Stern *et al, Nano Lett.* **7**, 3405 (2007)

Protein Assay: Antibody-Antigen Specificity

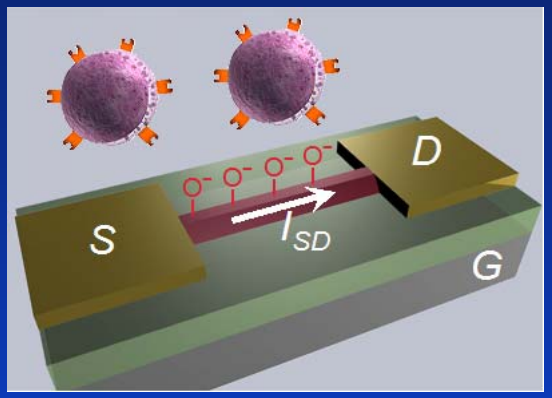
Surface: α-mouse-IgA

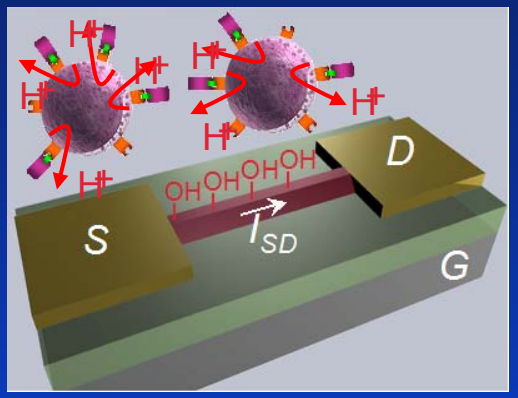


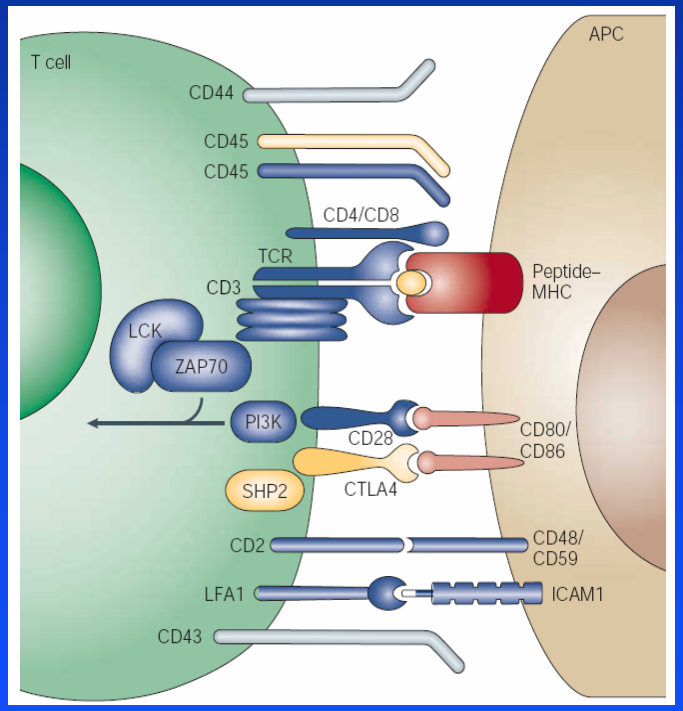
100 fM mouse-IgG/IgA in 1.5 mM bicarbonate ($\lambda_D \sim 6.8$ nm)

Unlabeled Cellular Detection

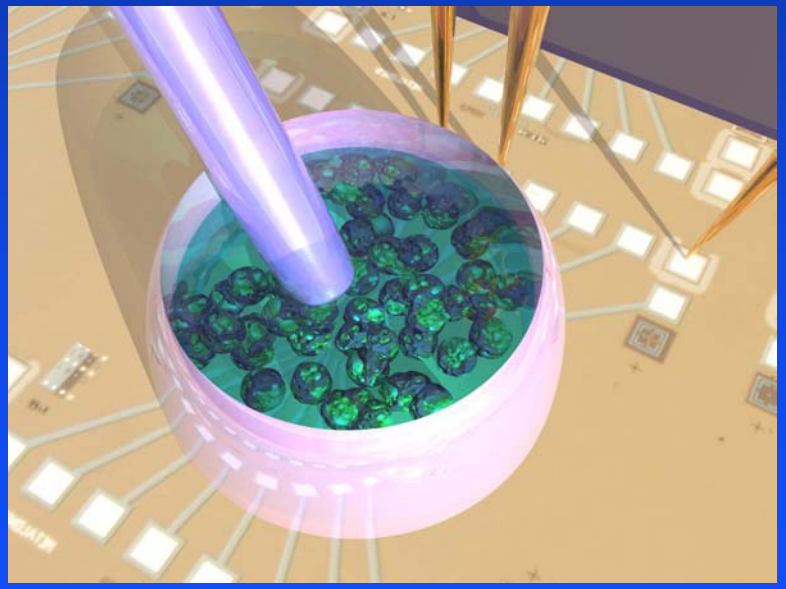
- Most cells (including pathogenic) release H^+ in response to specific stimulation



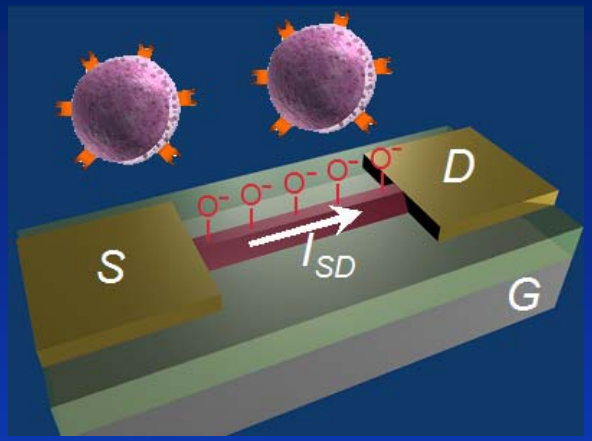


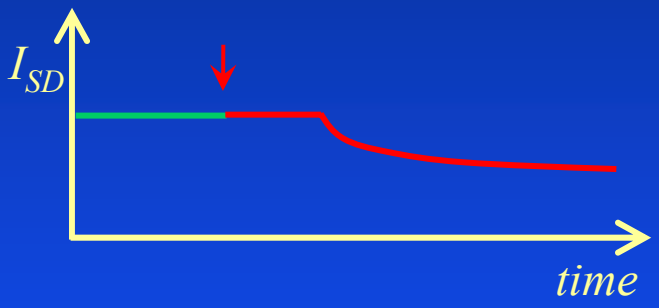


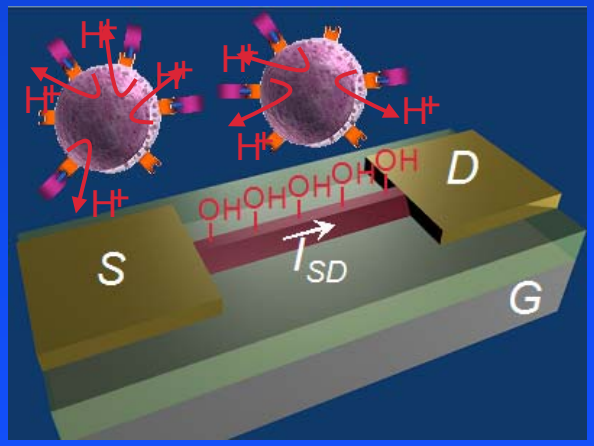
Nat Rev Immunol **3** (2003) 973

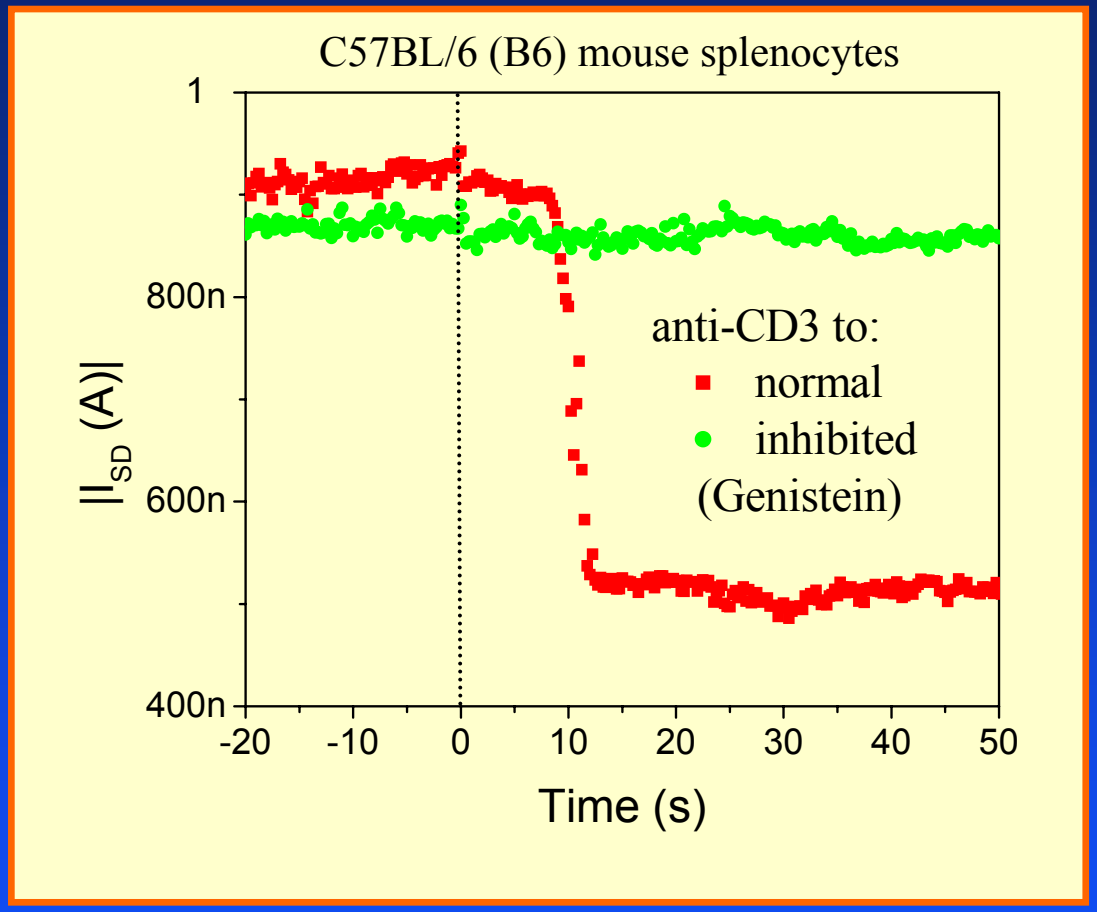


Real-time live cellular response – T-lymphocyte activation







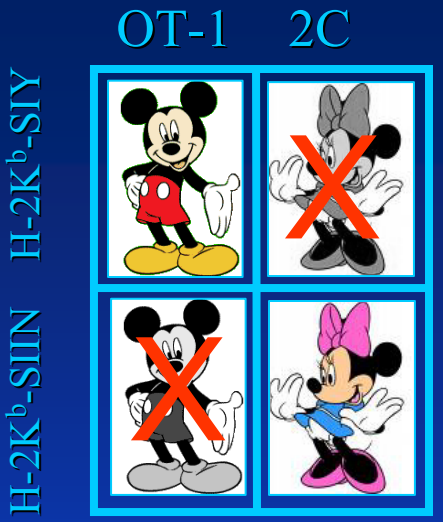


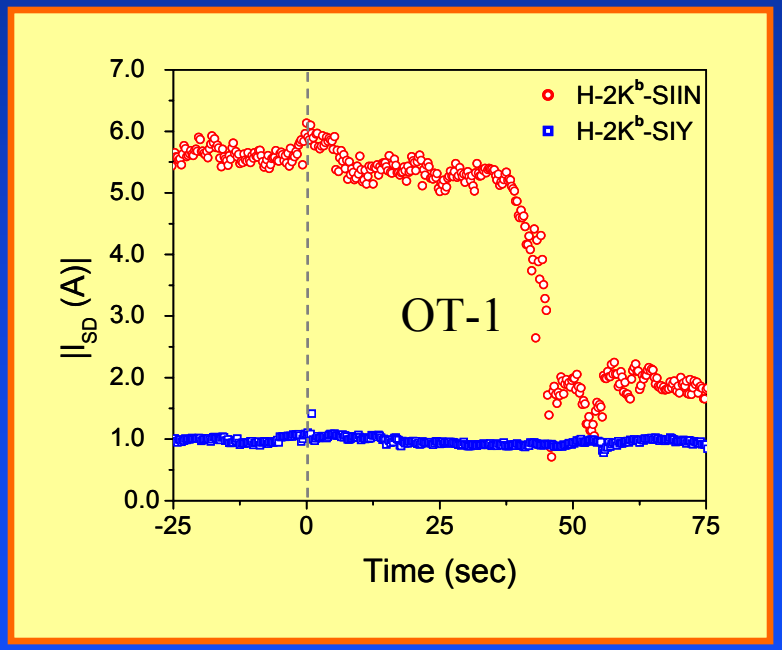
Real-time measurement of cell immune response dynamics

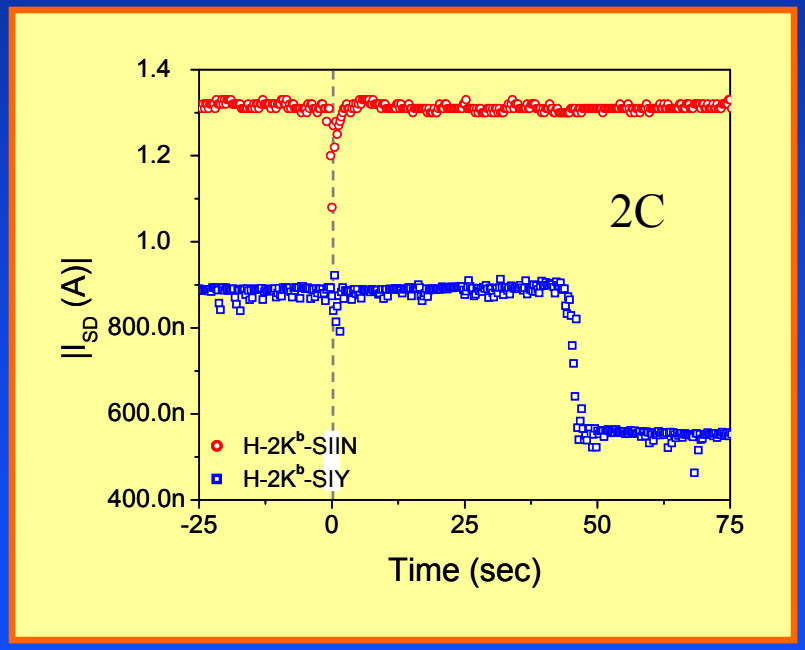
Transgenic peptide-specific MHC T-cell response

OT-1/2C transgenic murine $CD8^+$ T-cells

- OT-1 reacts to H-2K^b-SIIN, not H-2K^b-SIY
- 2C reacts to H-2K^b-SIY, not H-2K^b-SIIN



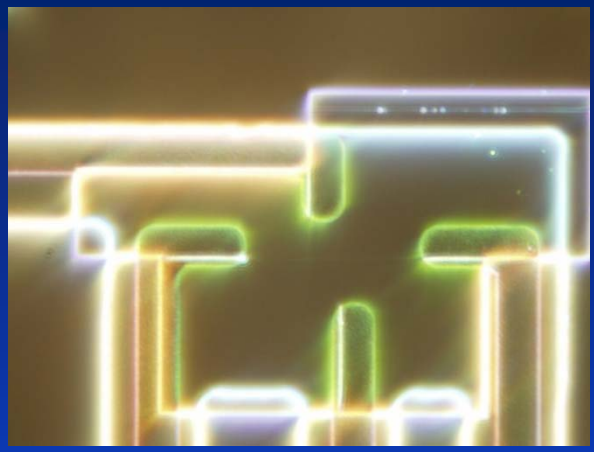




Model system for detecting autoimmune diseases and cancer

Stern *et al*, *Nano Lett.* **8**, 3310 (2008).

Summary



- CMOS-integrable "NWs"
  - Label-free sensing to aM resolution
    - Enables system-level integration
  - Macromolecular assays
- Real-time cellular immune response
  - Applicable to simple, point-of-care diagnostics (all simple DC, ambient)
  - Immune response dynamics
- Rich area for novel device designs, applications

Altura Diagnostics

- <u>The challenge:</u> sensing with physiologic solutions (blood)