What I won’t talk about today

- plasmonics
- mesoscopics
- 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

\[ \frac{1}{I} \frac{dI}{dQ} \sim \frac{1}{r} \]

(C. Zhou, USC)

10nm diameter GaN NW

Buffer

BSA

PSA

PSA antibody

Linker

PSA

In$_2$O$_3$ NW

Au/Ti

SiO$_2$

Si
Silicon-on-insulator (SOI) CMOS Nanowires

Nature 445, 519 (2007)
p-type accumulation mode (backgate)

\[ |\Delta V_G| = 1 \text{V} \]

300K, dry
w=50nm, t=25nm

\[ V_G = -40 \text{V} \]

\[ V_{SD} = -1 \text{V} \]

\[ I_{SD} (\text{A}) \]

\[ V_{SD} (\text{V}) \]

Fully depleted; \( n_0 \approx 1 \times 10^{15} \text{ cm}^{-3} \)

\[ \mu = 54 \text{ cm}^2/\text{V-s} \]

\[ \mu_{\text{max}} = 139 \text{ cm}^2/\text{V-s} \]

\[ w = 300 \text{ nm} \]

\[ t = 25 \text{ nm} \]

\[ \text{Hall} \]

\[ \text{Drift} \]

\[ \text{Temperature (K)} \]

\[ \text{Mobility (cm}^2/\text{V-s)} \]
$1/f$ noise of nanowires

\[
\frac{S_I}{I^2} = \frac{\alpha_H}{f N}
\]

\[
\alpha_H = 1.3 \times 10^{-4}
\]

ITRS
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
∴ max. response is 1 decade/pH
Fluid Considerations

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

Nano Lett 5, 803 (2005)

\[ C_0 (M) \]

\[ \# \text{ Molecules/Min} \]

\[ Q (\mu L/min) \]

Microchannel Reservoir
- 0.1
- 8.3
- 3000

Silicon-specific functionalization

Nonspecific functionalization

\( x = \text{microfluidics} \)

Science 293, 1289 (2001)

\( x = \text{mixer (reservoir)} \)

Nature 445, 519 (2007)
Biotin-Avidin & Streptavidin Sensing

- **p-type accumulation mode, biotinylated NW device**
  - Analyte
  - Receptor (biotin)

- **avidin**
  - Positive charge
  - \( \Rightarrow \) current decrease

- **streptavidin**
  - Negative charge
  - \( \Rightarrow \) current increase

- **poly(ethylene glycol) (PEG)-ylated device, quenched avidin controls**

![Graph showing current change with time for different proteins](image)

<table>
<thead>
<tr>
<th>Analyte</th>
<th>Time (sec)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Streptavidin</td>
<td></td>
</tr>
<tr>
<td>Quenched S-Av</td>
<td></td>
</tr>
<tr>
<td>PEGylated</td>
<td></td>
</tr>
<tr>
<td>Avidin</td>
<td></td>
</tr>
</tbody>
</table>

1 nM protein in 0.1X PBS (\( \lambda_D \sim 2.2 \text{ nm} \))

*Nature, 445, 519 (2007)*
**Sensitivity: Concentration Dependence**

Initial S/N

\[ \sim 140 \text{ (@10fM)} \]

⇒ <100 aM limit

\[ (< 3 \text{ fg/ml}) \]

(1 aM = 30 molecule per mm\(^3\))

**DC, ambient**
DNA sensing: criss-cross

- Capture1 is the complementary strand of Probe1;
- Capture2 is the complementary strand of Probe2.
Debye Screening Considerations

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

for 0.1 mM PBS, \( \lambda_D \sim 2.2\text{nm} \)

Protein Assay: Antibody-Antigen Specificity

Surface: α-mouse-IgA

100 fM mouse-IgA

100 fM mouse-IgG

PEGylated

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

C57BL/6 (B6) mouse splenocytes

anti-CD3 to:
- normal
- inhibited (Genistein)

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

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**

- **The challenge:** sensing with physiologic solutions (blood)