Technology CAD for Modeling and Design of Bio-Devices

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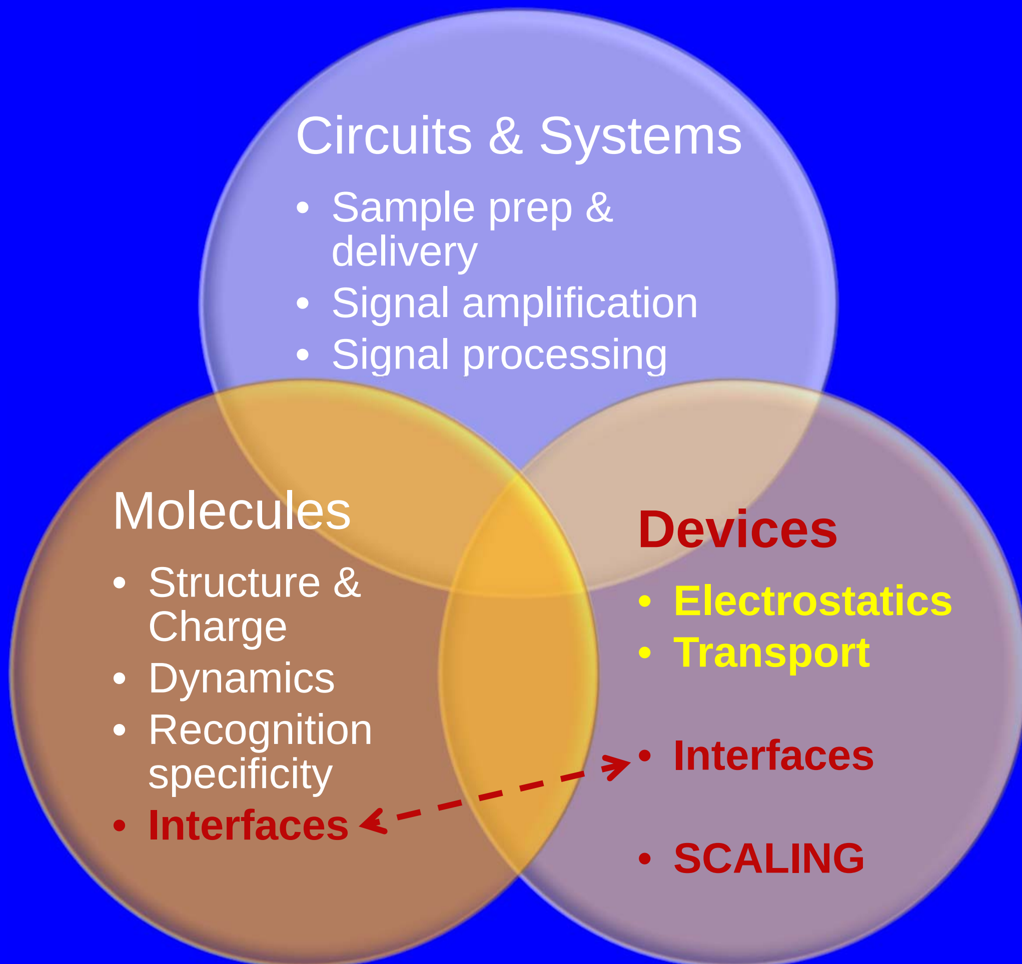
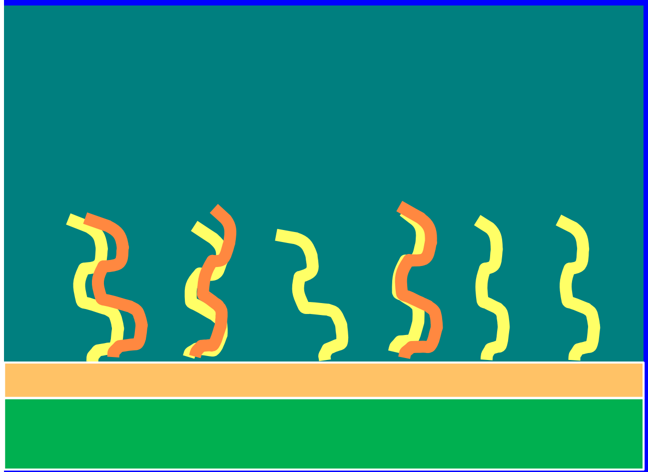
Biosensors: Multi-Scale Systems

Process Modeling Issues

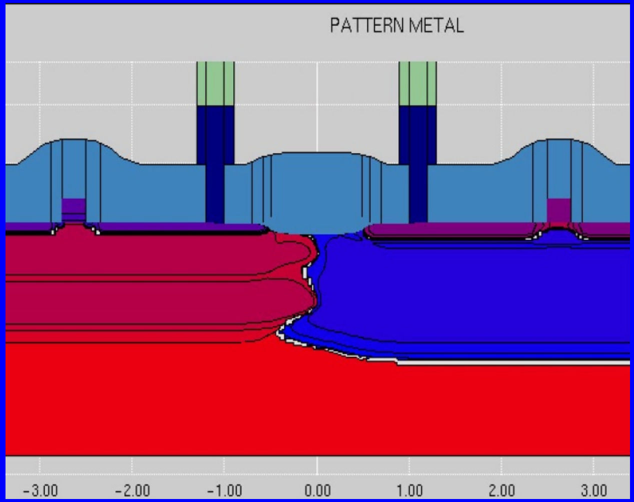


BioTCAD Emphasis on Devices

Need for Process Modeling



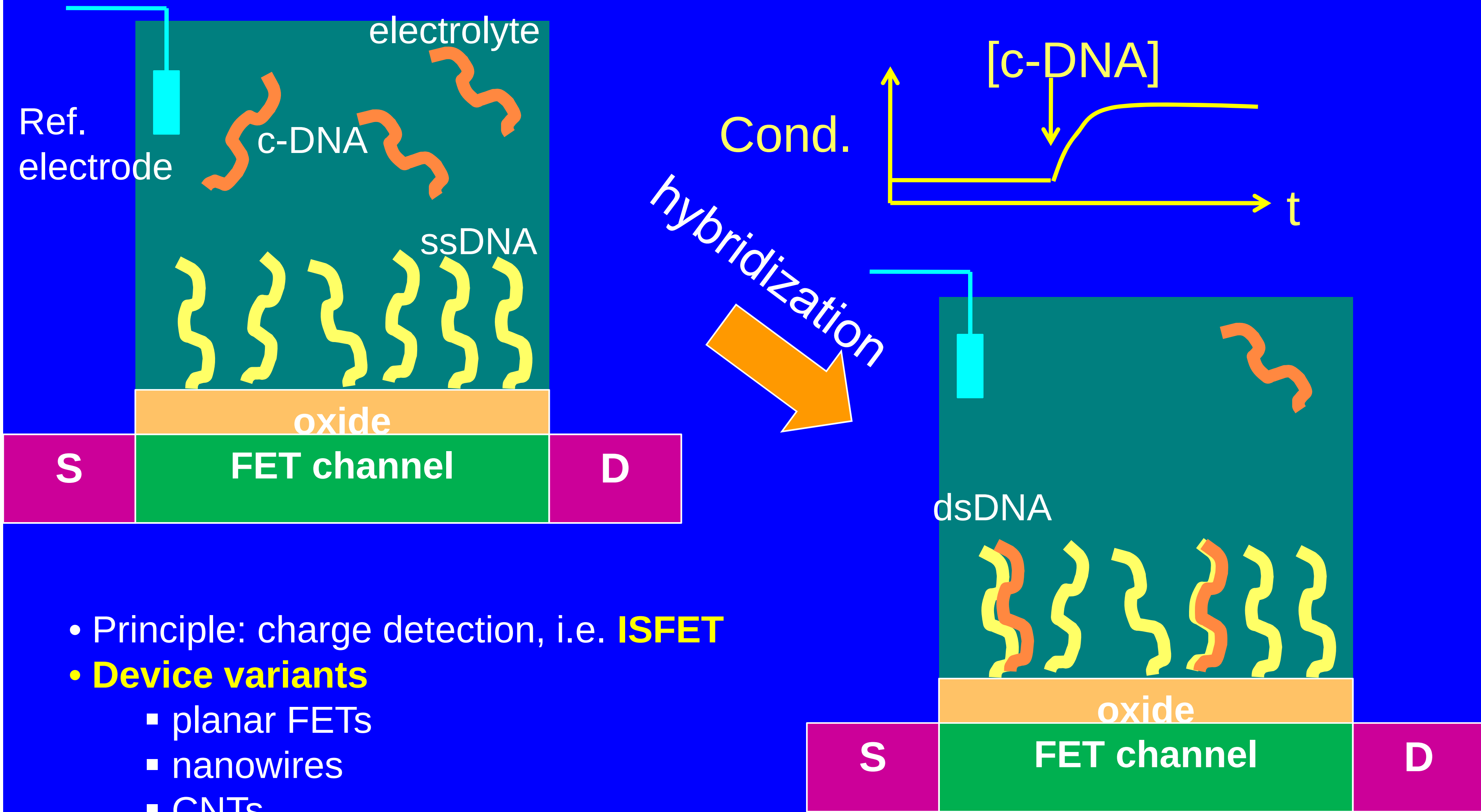
- Surface morphology is critical
- extremely complicated due to large internal degrees of freedom



How to model a plate of spaghetti?

Just like semiconductor TCAD, **process** engineering and modeling are needed for bio-devices to go from lab science to real products

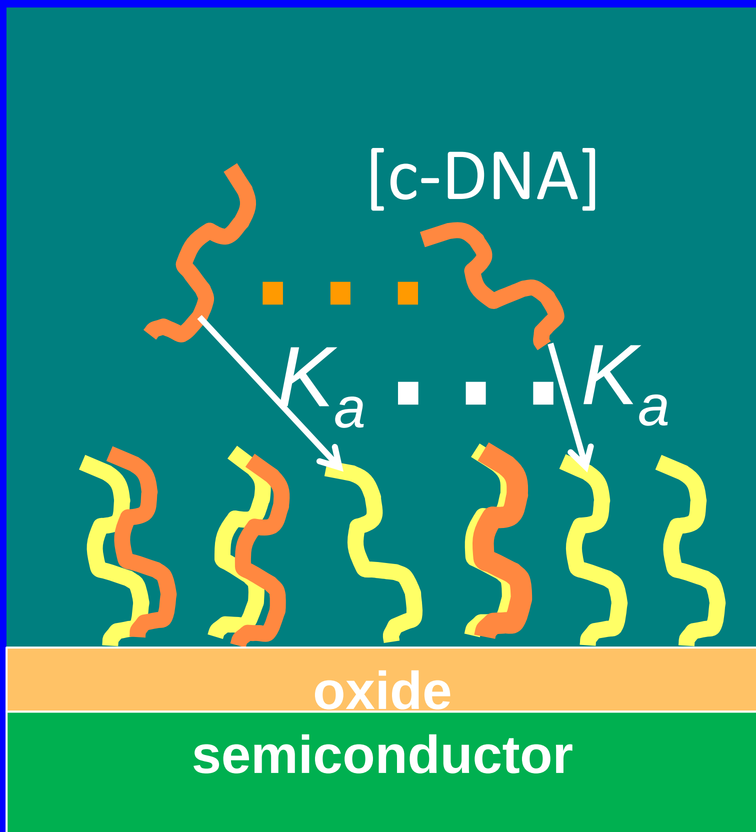
Field Effect Biosensors



- Principle: charge detection, i.e. **ISFET**
- **Device variants**
  - planar FETs
  - nanowires
  - CNTs
  - hybrid, e.g. Au NP+CNT

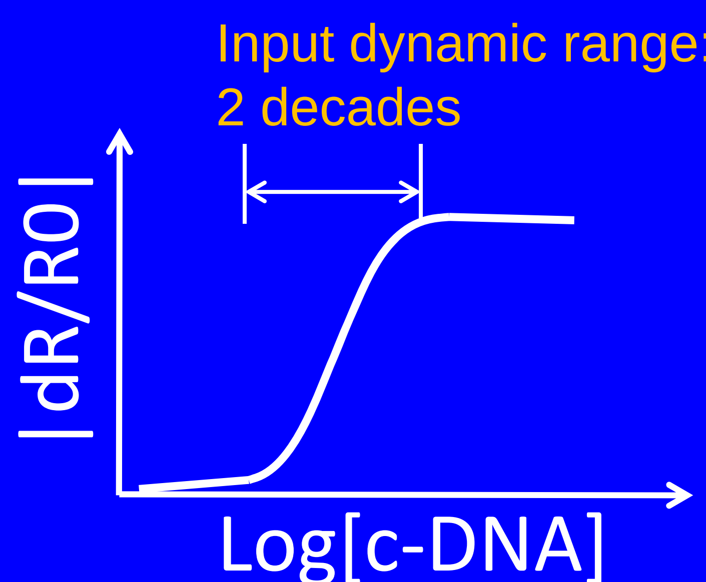
Binding Kinetics: An Ideal Picture

Our target is **[cDNA]** in the bulk solution



- *Langmuir adsorption model*

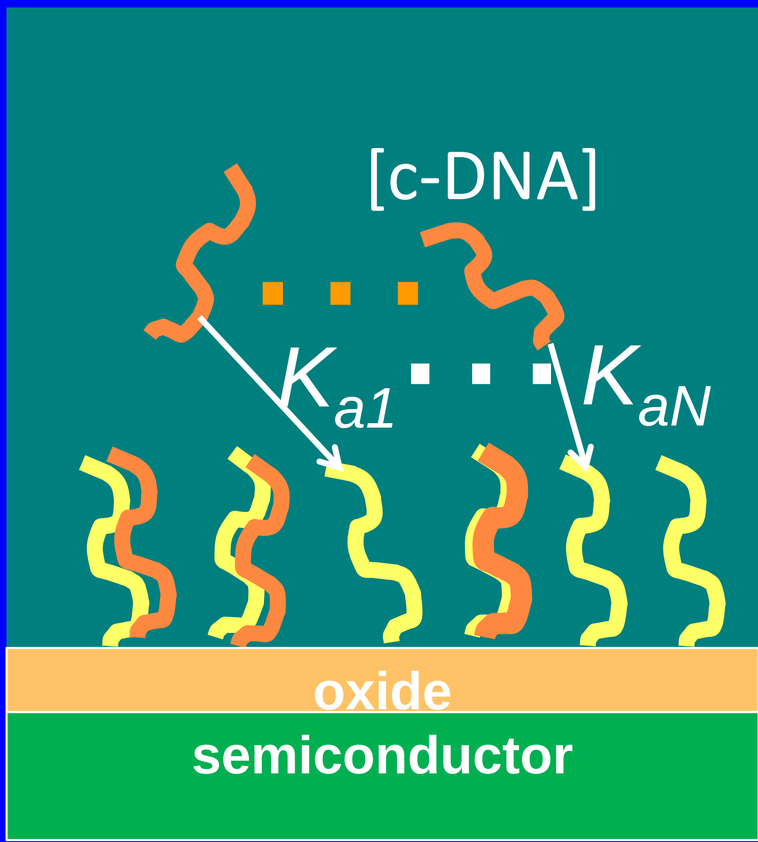
$$N_{ds} = N_p \frac{K_a[cDNA]}{K_a[cDNA]+1}$$



- Binding equilibrium constant:

K_a (*i.e.* ~ $k_{captured} / k_{release}$)

A More Realistic Picture



Heterogeneity of binding kinetics

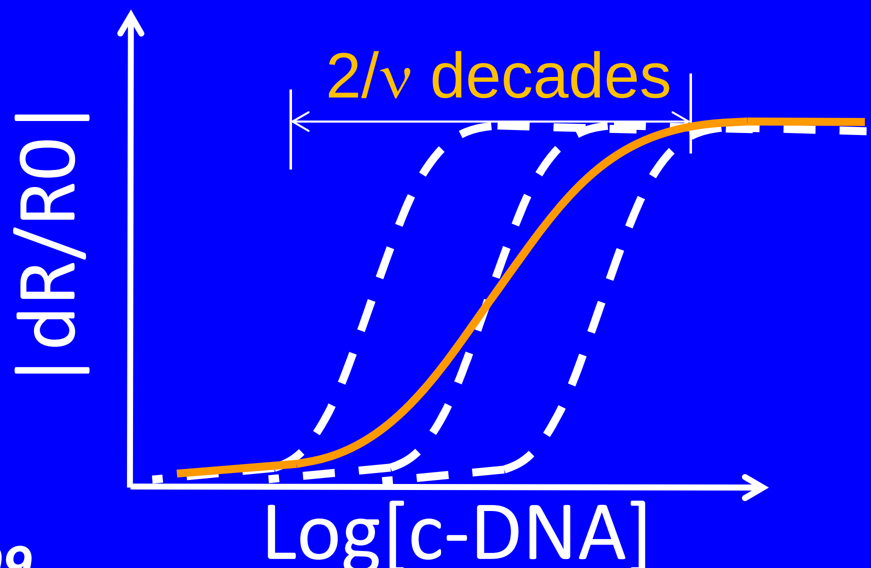
Liu and Dutton, JAP, 014701, 2009

- A distribution of binding constants:

$$K_{a1}, K_{a2} \ldots K_{aN}$$

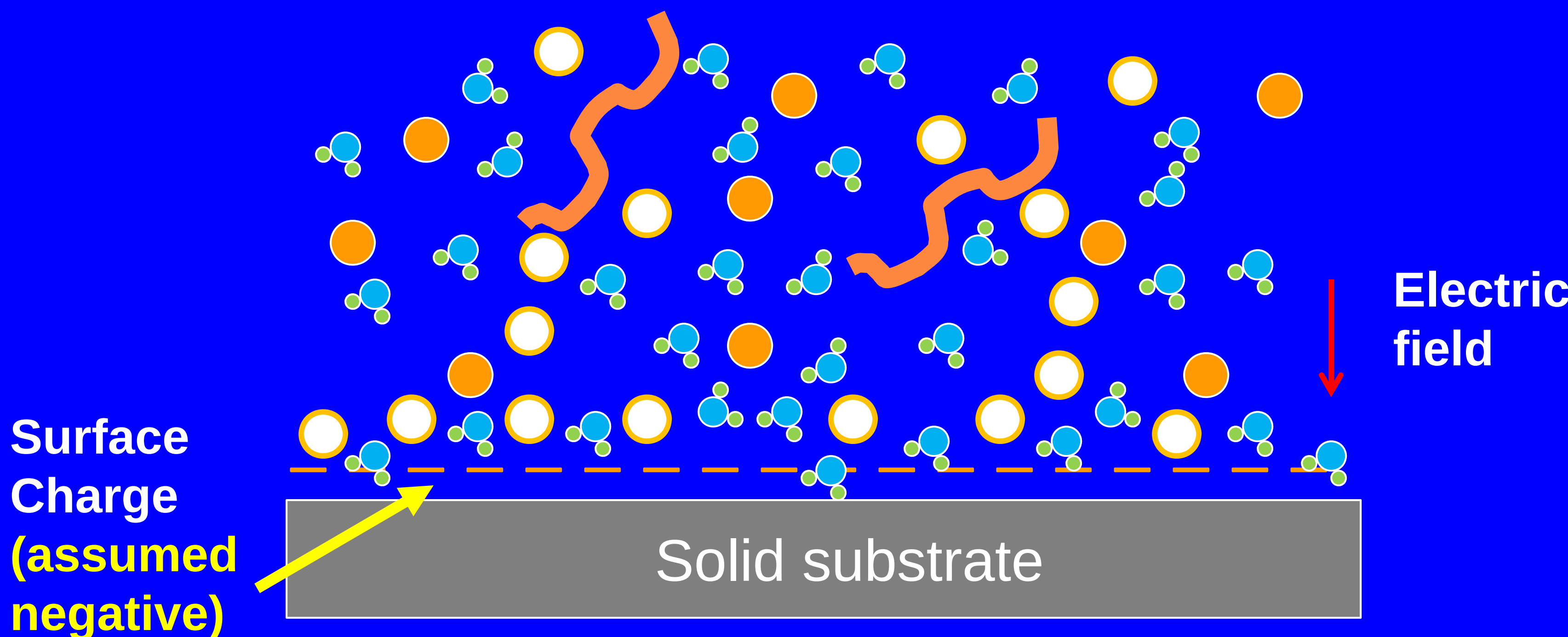
- *Generalized Langmuir model*

$$N_{ds} = N_p \frac{\left(K_a\left[cDNA\right]\right)^{\nu}}{\left(K_a\left[cDNA\right]\right)^{\nu}+1} \qquad 0<\upsilon\leqslant 1$$

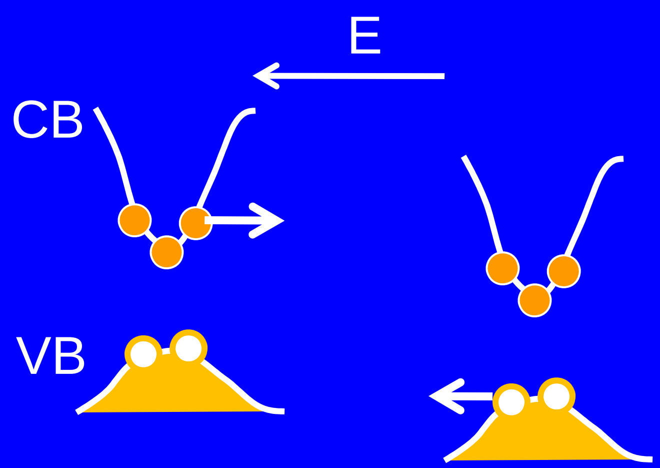


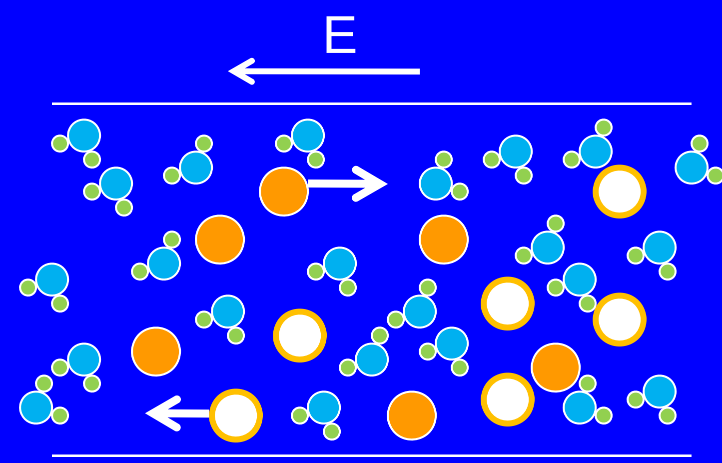
Key Elements of Modeling

- anions, e.g. Cl^-
- cations, e.g. Na^+
- Biomolecules, e.g. DNA
- water molecules



Transport Modeling: Semiconductor vs. Ion Solution

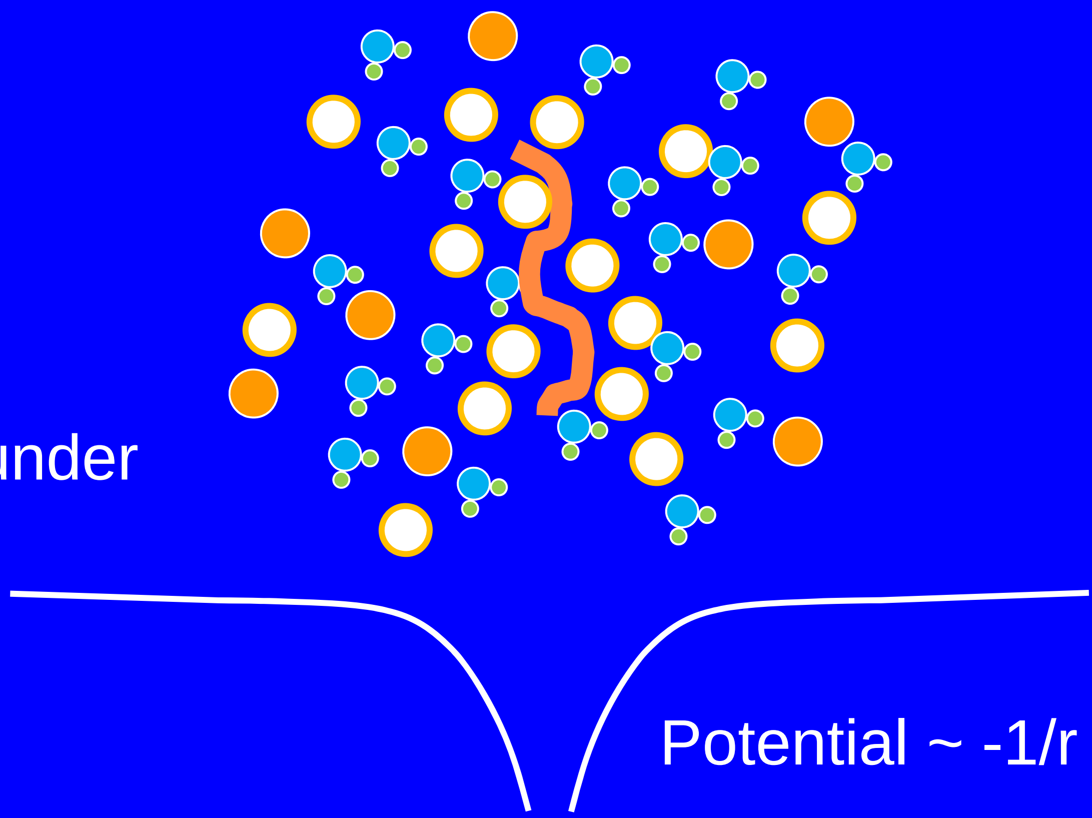




Semiconductor	Ionic Conductor
• Electrostatics: Poisson • Electron/hole: drift-diffusion • crystal lattice: phonon transport	• Electrostatics: Poisson • Cation/anion: Nernst-Planck • water molecules: Stokes for micro/nano flow

Basic Physics: Charge Screening

DNA charge effectively screened by counter ions under <u>equilibrium</u>

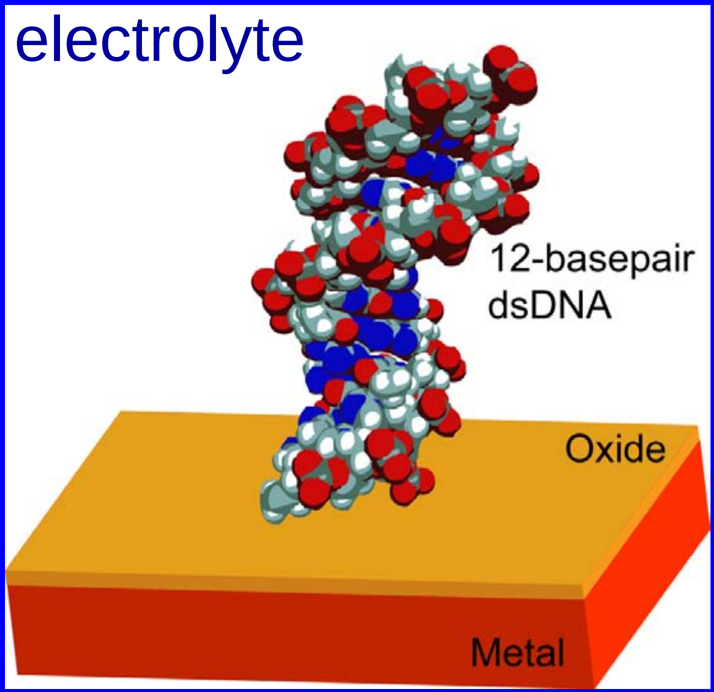


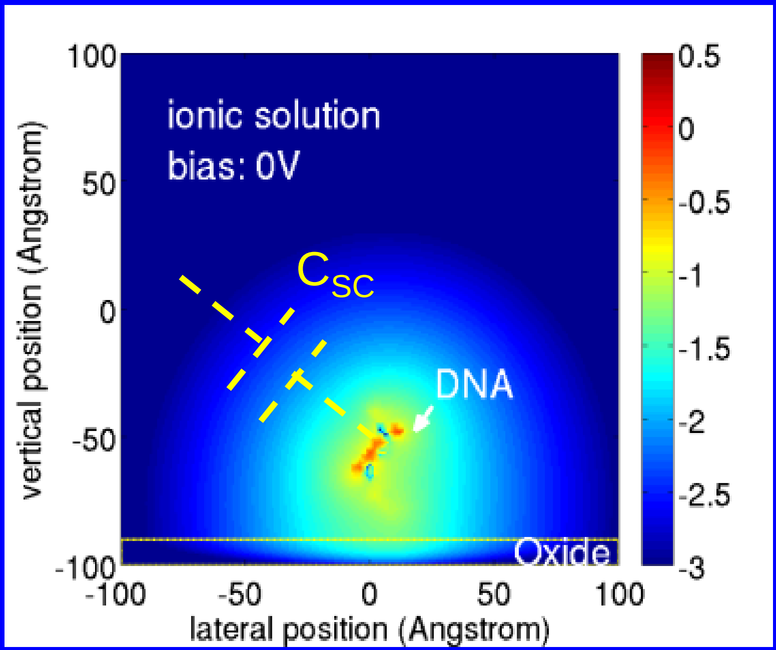
Potential ~ -1/r * exp(-r/Λ_D)

Debye length Λ_D:

- ~ 0.8nm in blood serum (150mM)
- ~ 0.4nm in sea water

Electrostatics and Screening I





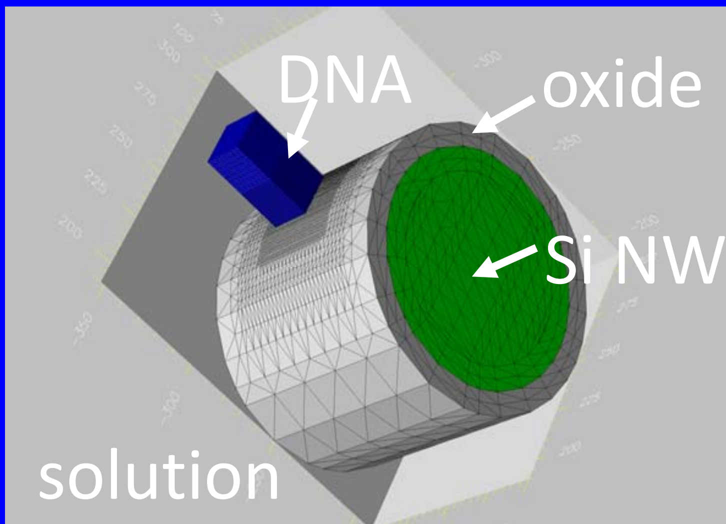
Equilibrium

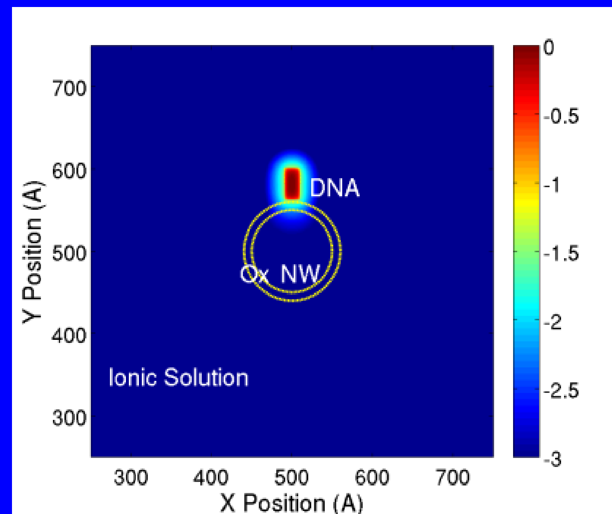
• single DNA on an oxide/metal surface
• 10 mM ionic concentration

Liu et al. IEDM, p.491, 2008

Potential from Poisson-Boltzmann solution:
• completely screened in vicinity of DNA
• *very little penetration* into substrate, i.e. being sensed

Electrostatics and Screening II



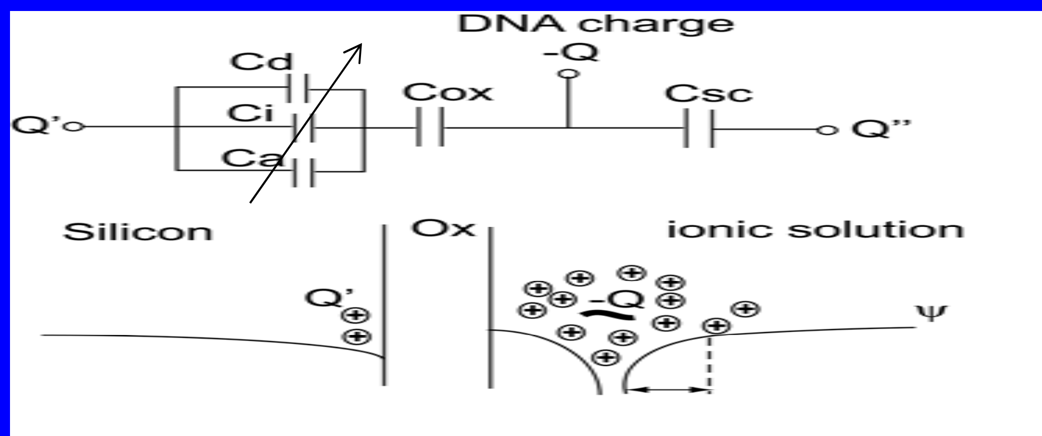


Poisson-Boltzmann solution of potential

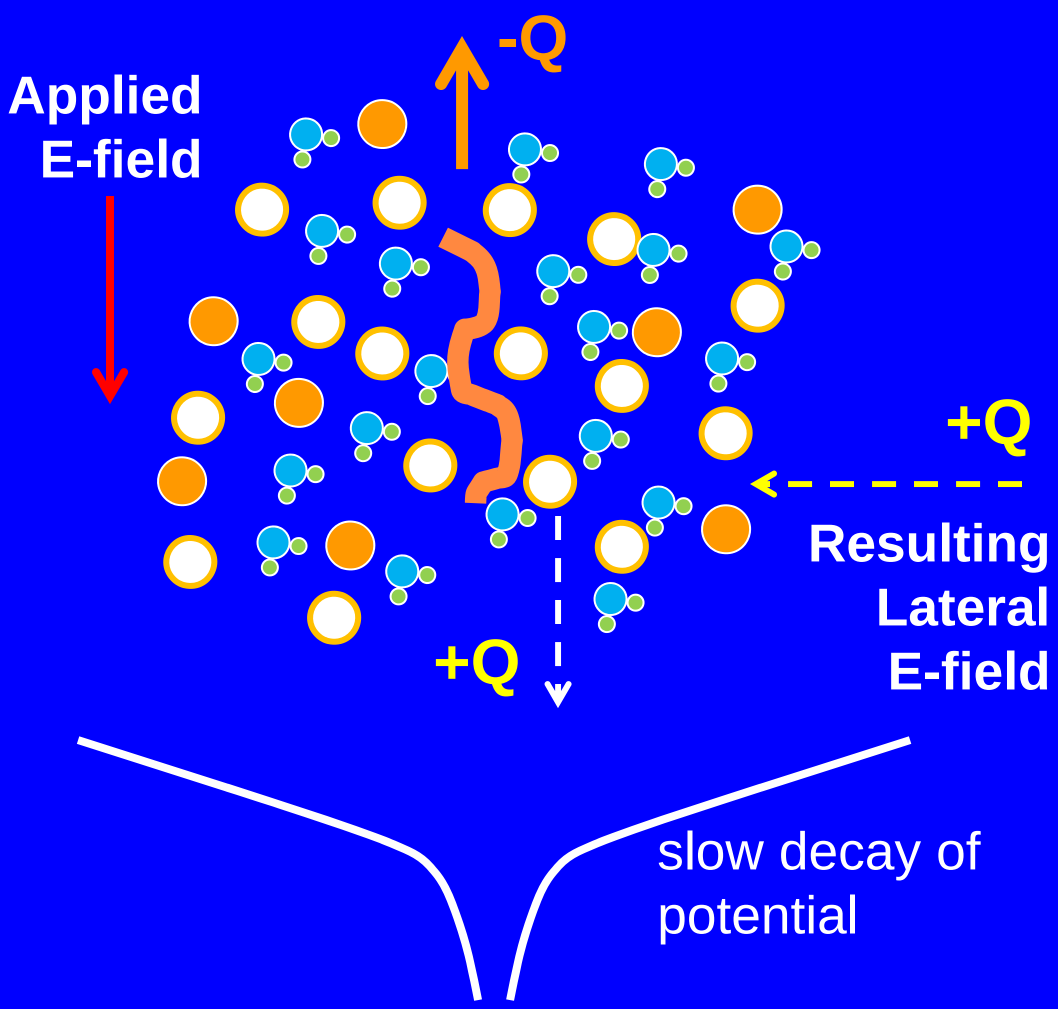
Limit on sensed charge:

$$Q' = \frac{C_{NW}}{C_{NW} + C_{SC}} Q$$

(Charge partitioning)



Basic Physics: Descreening

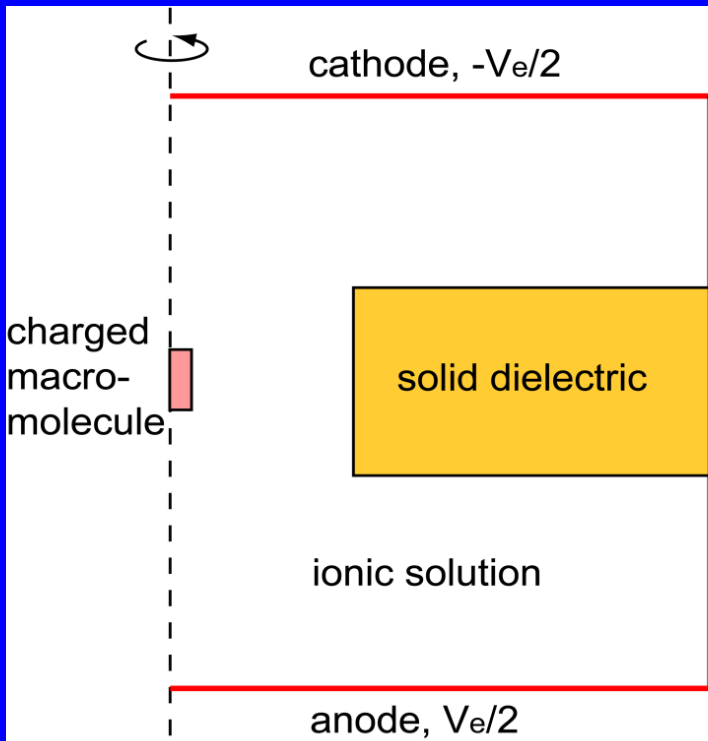


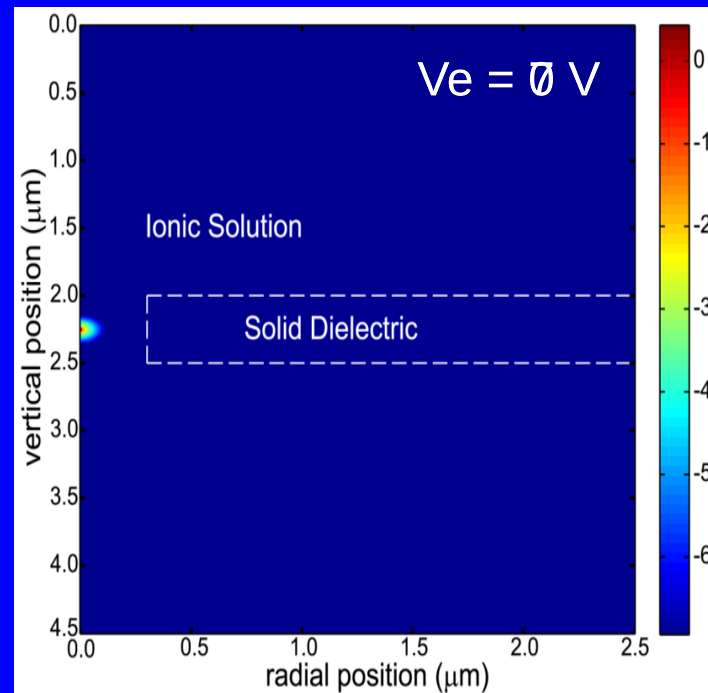
NO longer in equilibrium:

- DNA and counter ions move oppositely

- Strong E-field
  → counter ion cloud cannot fully relax (Onsager, 1957)
  → only partial screening
  → charge sensing beyond the Debye length limit

Descreening of DNA in Nanopore





PNP solution

• (**Left**) Cylindrical symmetric pore where a charged biomolecule is placed at the center; External bias is applied at top/bottom boundaries.
• (**Right**) potential change due to presence of the charged biomolecule

Liu, Sauer and Dutton, JAP, 084701, 2008

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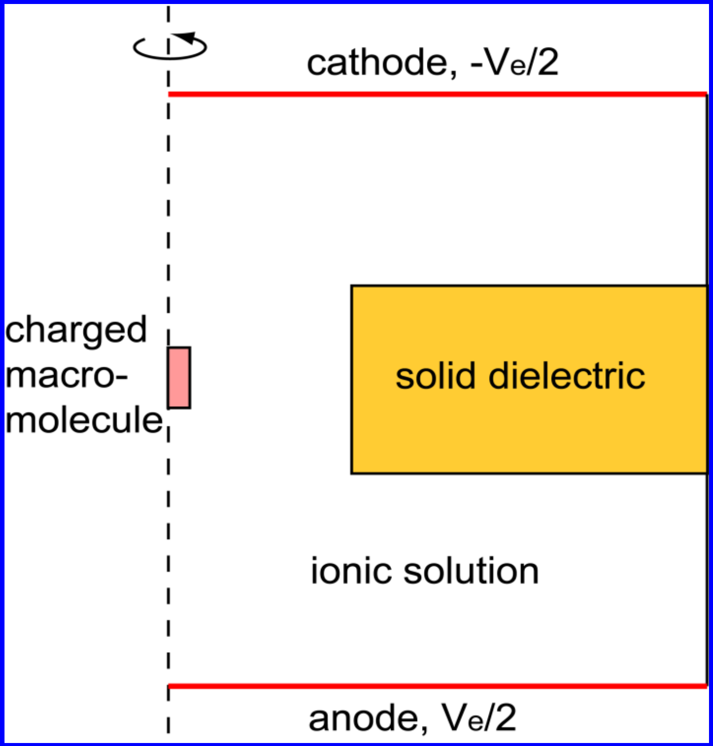

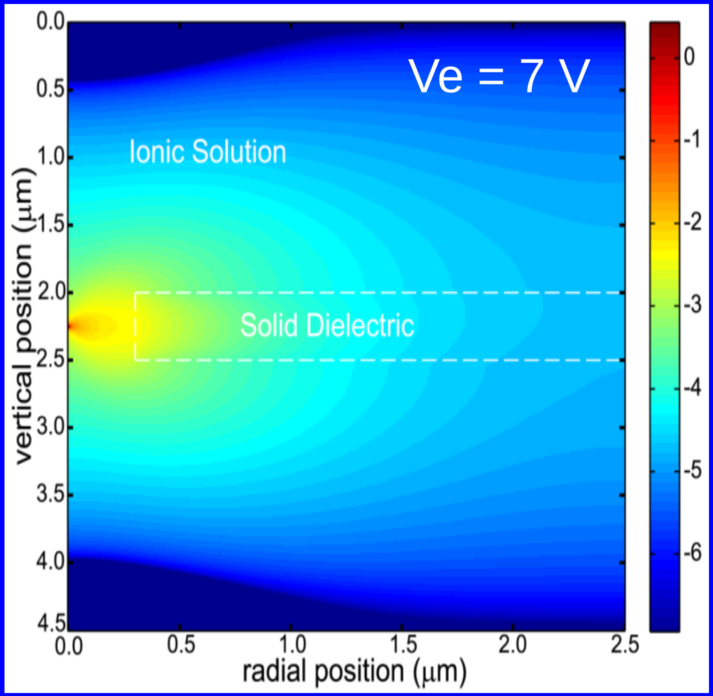

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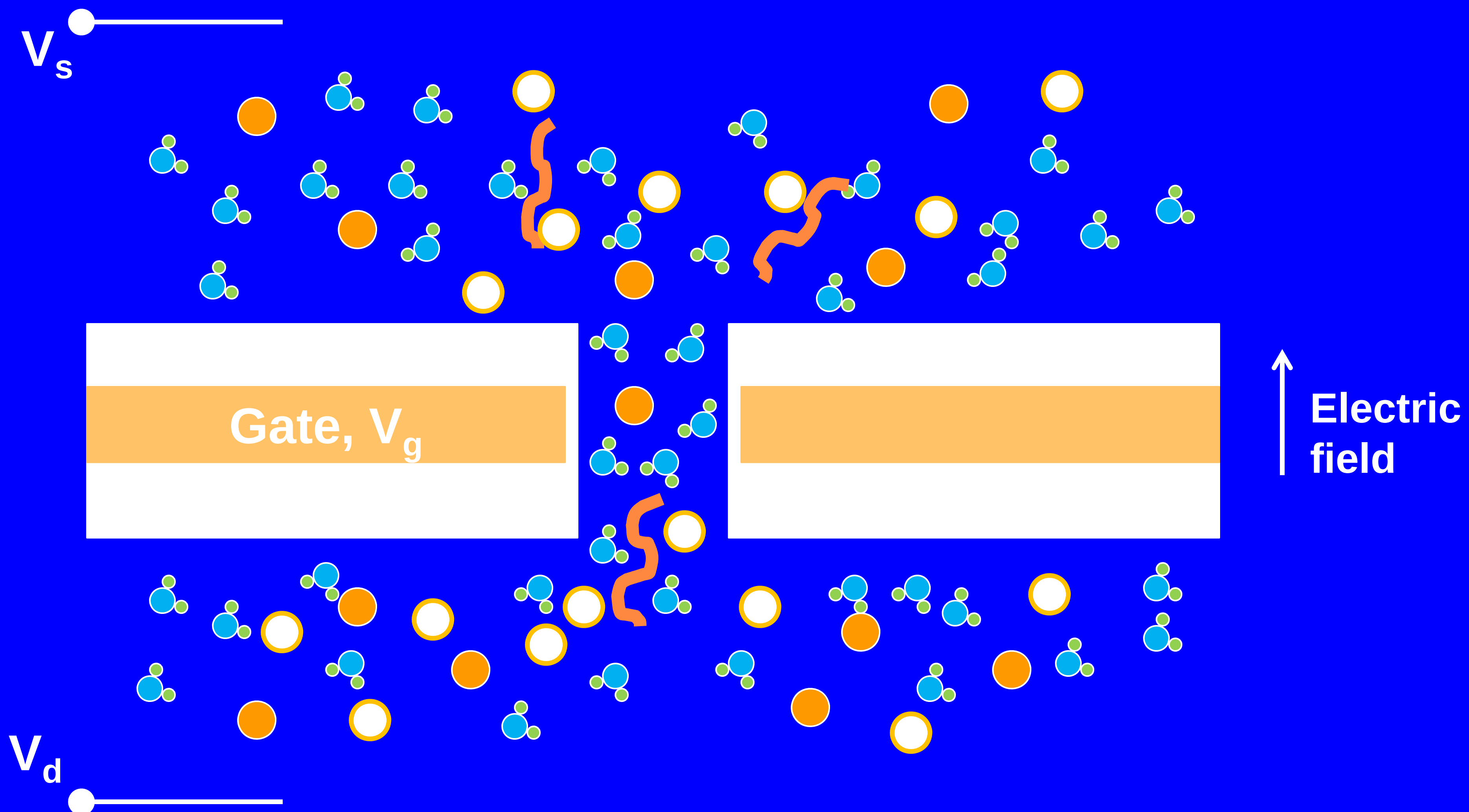
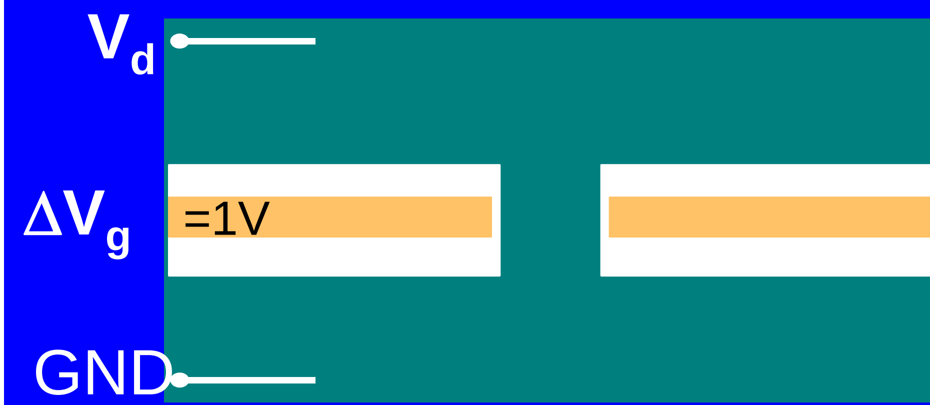
Field Effect Gated Nanopores

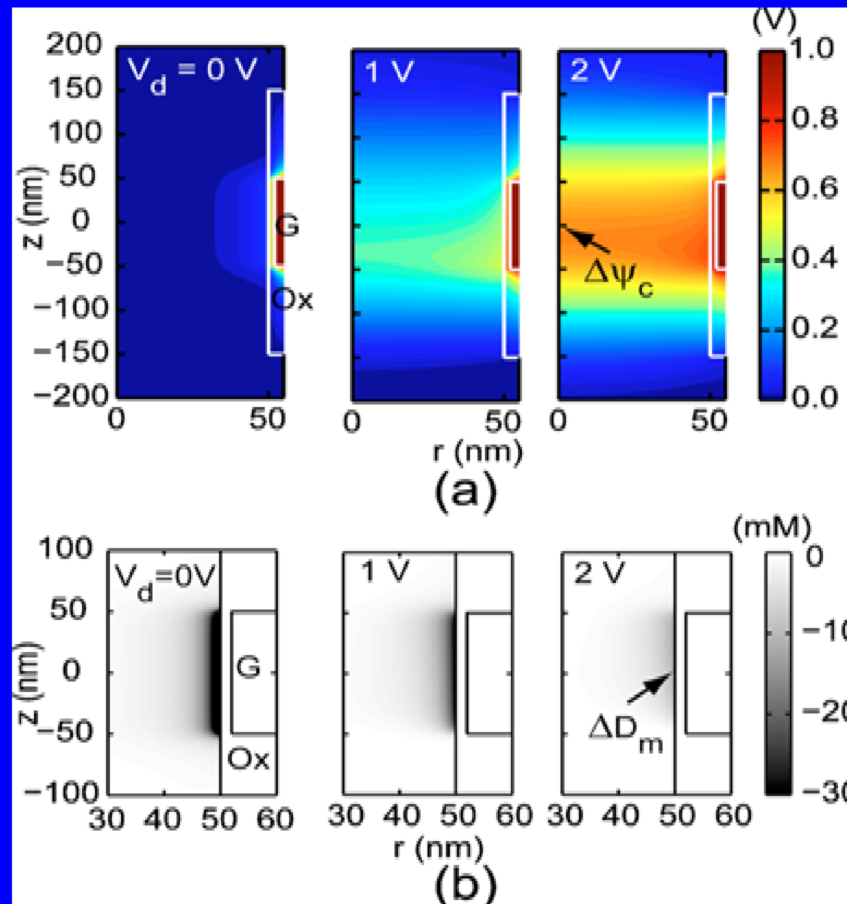


Descreening of Gating Potential



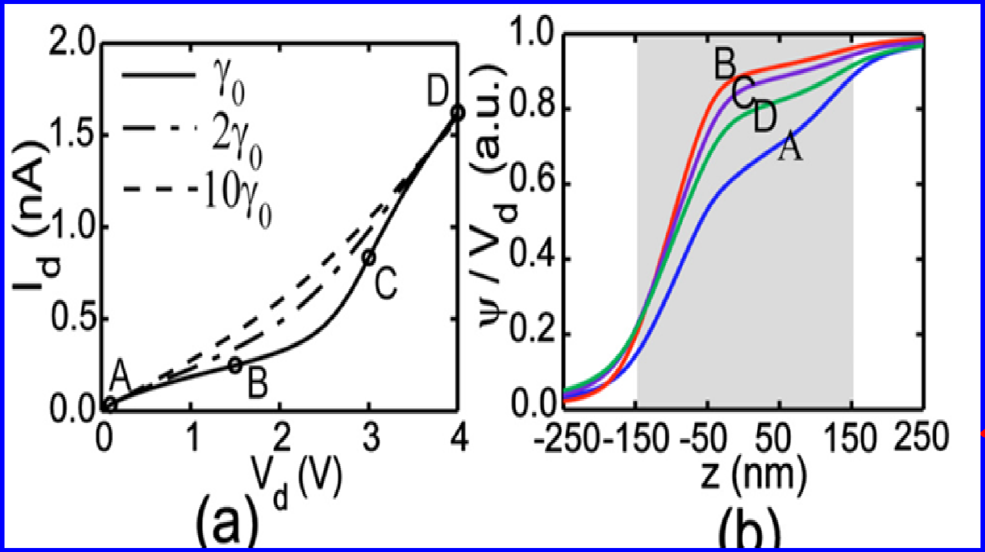
As V_d increases:

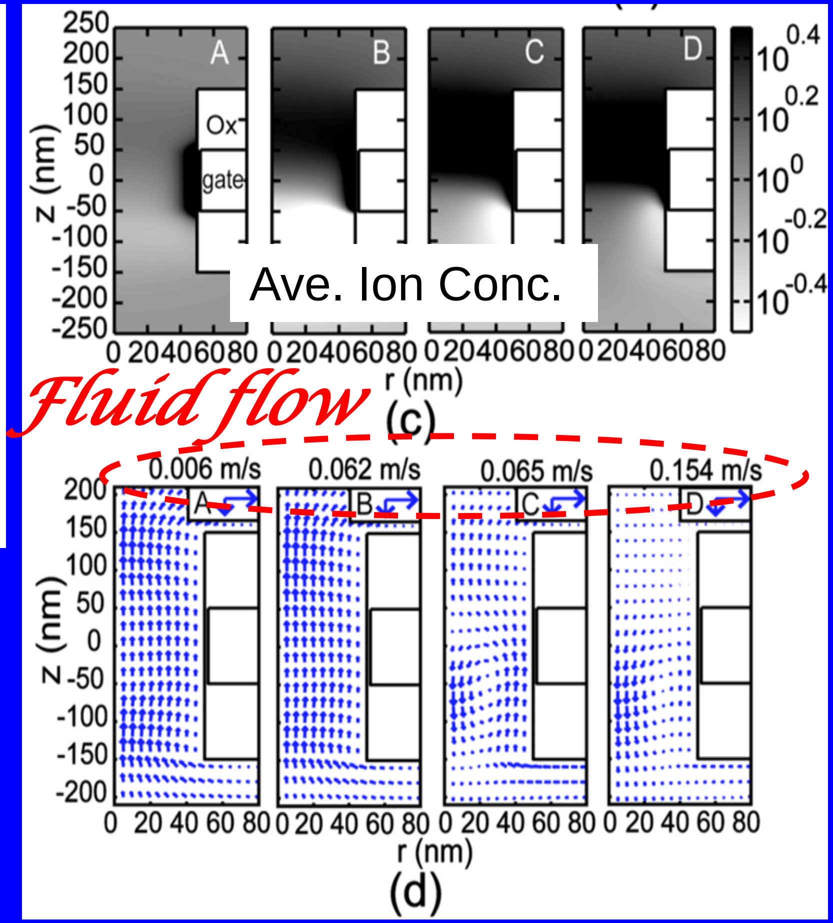
- more penetration of gate potential into the channel
- reduced amount of counter ions in electrical double layer



Liu, Huber, Tabard-Cossa, Dutton, APL, 143109, 2010

Ionic and Fluidic Transport
(Drain Bias Effects on Flow)



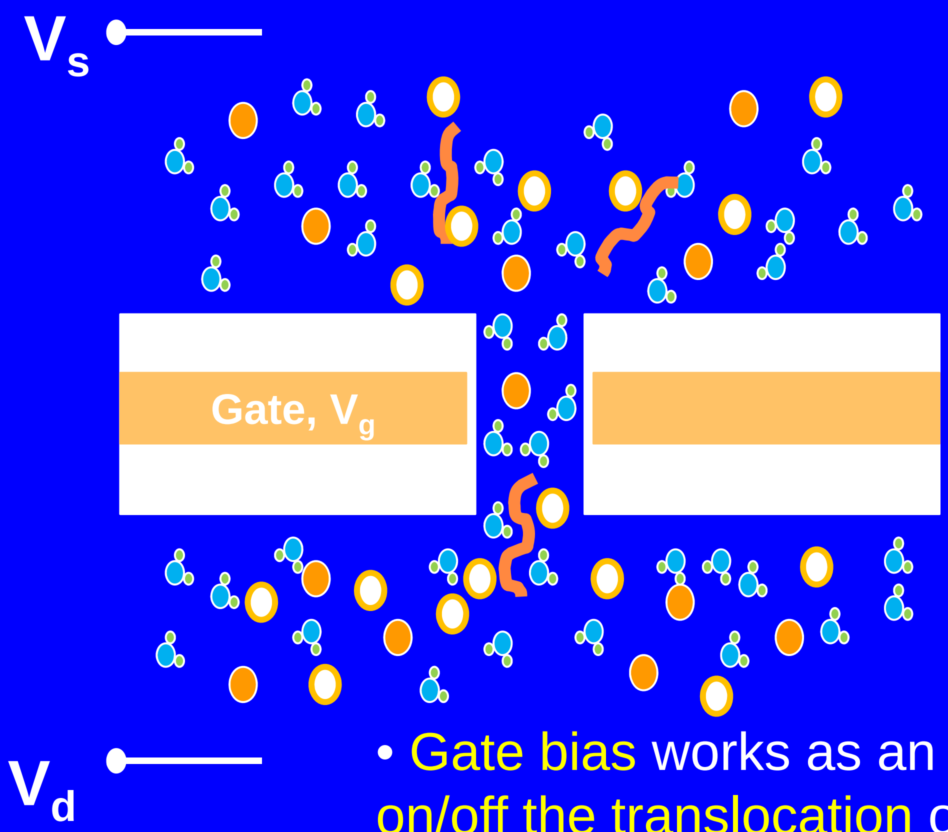


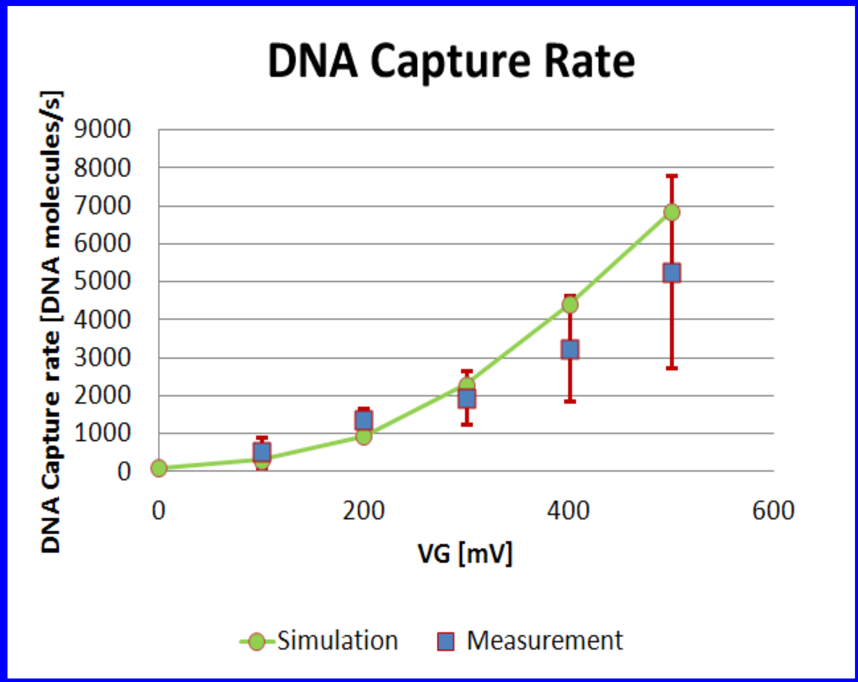
Very rich device physics:
- highly nonlinear Id-Vd
- concentration polarization
- complex of electroosmosis

Extend design space using dual and/or multiple gates:

- ***Liu, Ran, Dutton, IEDM p.371, 2010***
- ***Liu, Huber, Dutton, APL, 253108, 2010***

Gating of DNA Translocation
(Nano-Fluidic "Transistor")





- Gate bias works as an electrical valve that turns on/off the translocation of DNAs from source to drain
- TCAD offers quantitative modeling and design capability ***(Paik, Liu et al. IEDM, p.705, 2011)***