Semiconductor Nano-Pores Tunability for DNA Sequencing*

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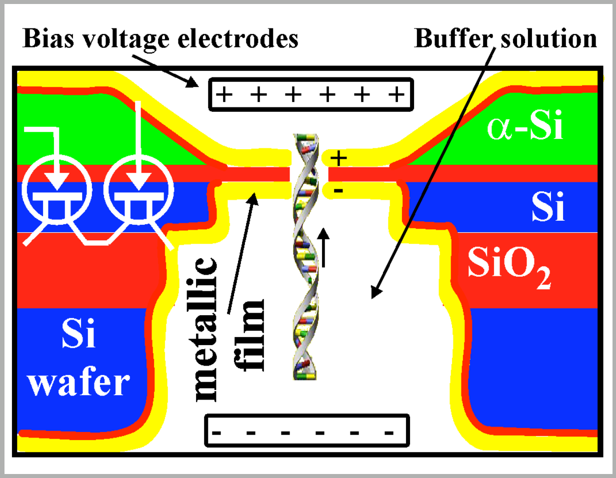
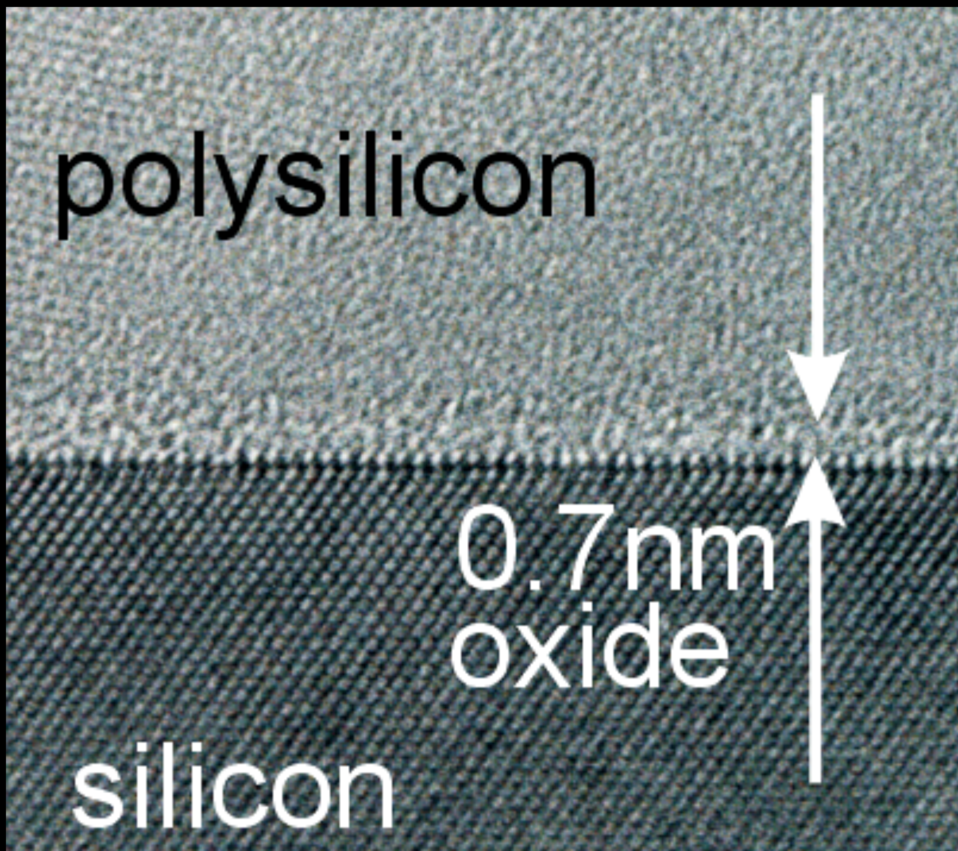


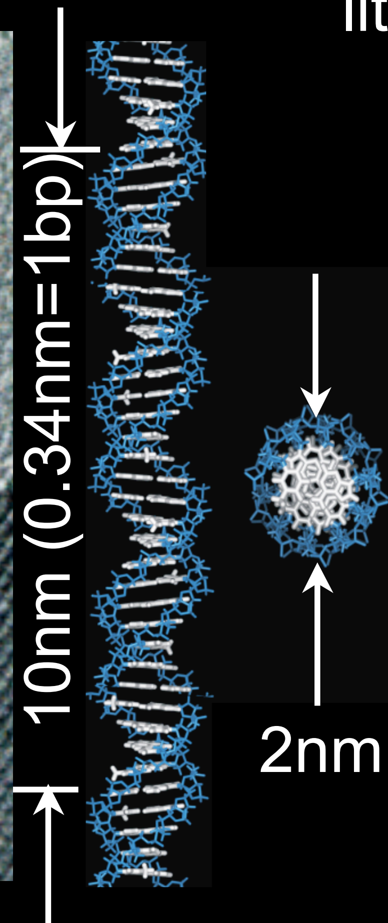
*Work done in collaboration with M. Gracheva, A. Aksimentiev and G. Timp and supported by NIRT-NSF and NIH

Silicon Nanotechnology for Sequencing DNA

•ultra-thin membranes

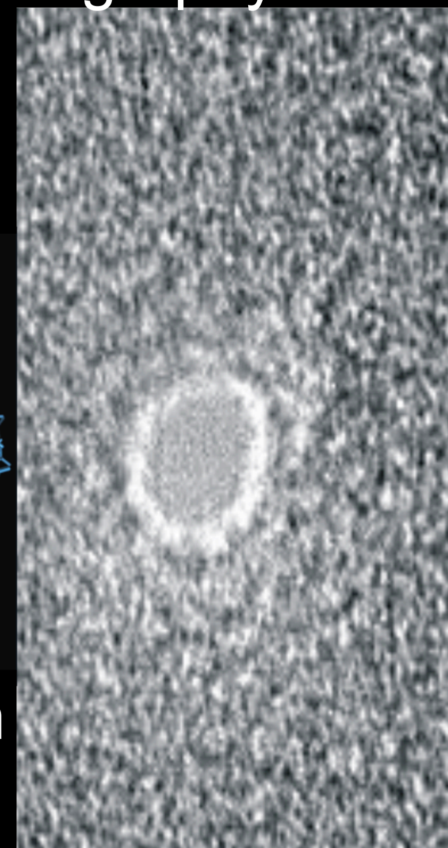


TEM X-section through a gate



DNA

•sub-nm(sub Å Batson) bright e-beam for lithography

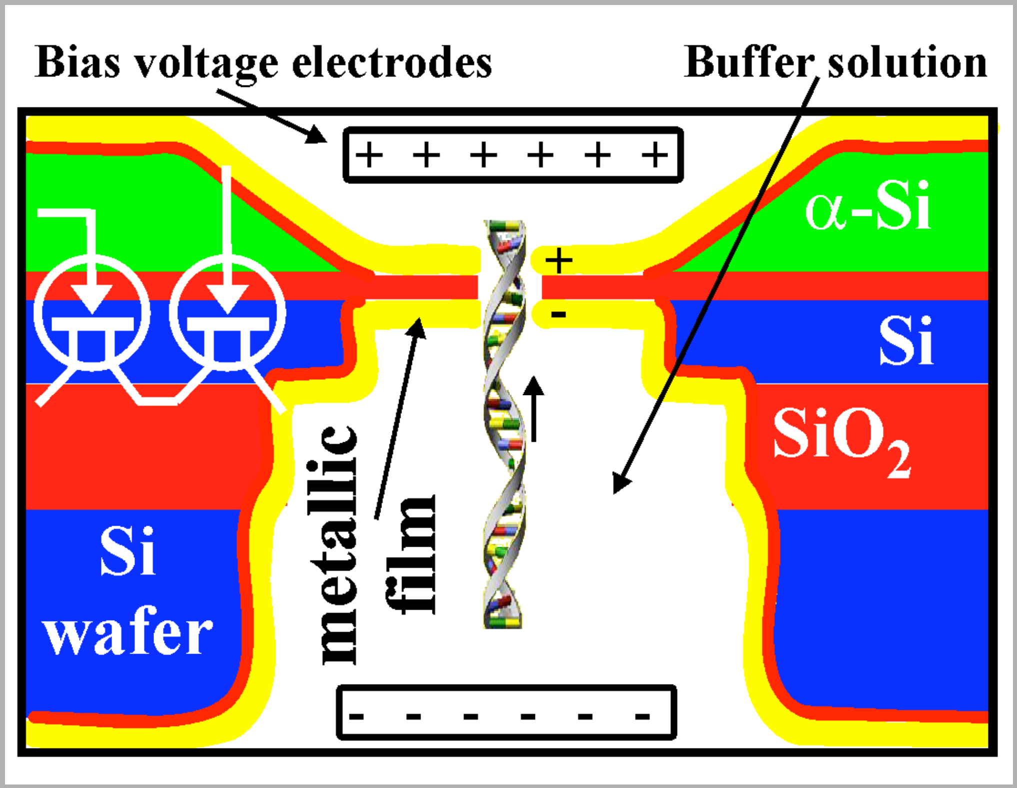


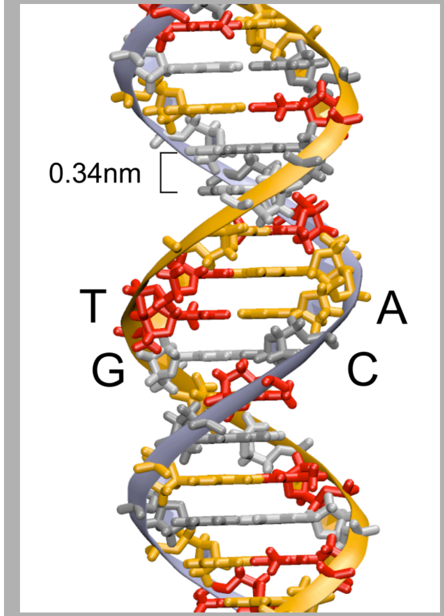
TEM (top-down projection)

Deamer, Branton, Kasianowicz
Golovchenko
Martin

A Challenge:

Electronic Detection of DNA Molecular Sequences

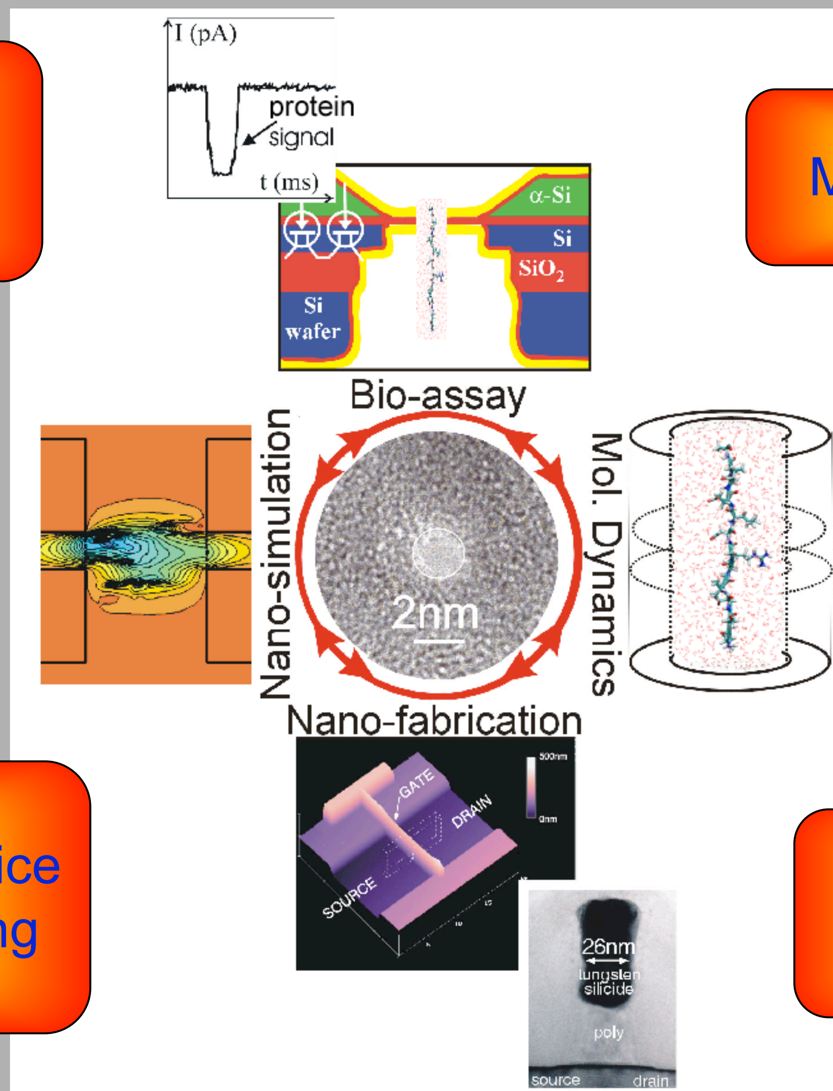




Merging Biology and Nano-Electronics: An Integrated Approach.

DNA translocation experiments

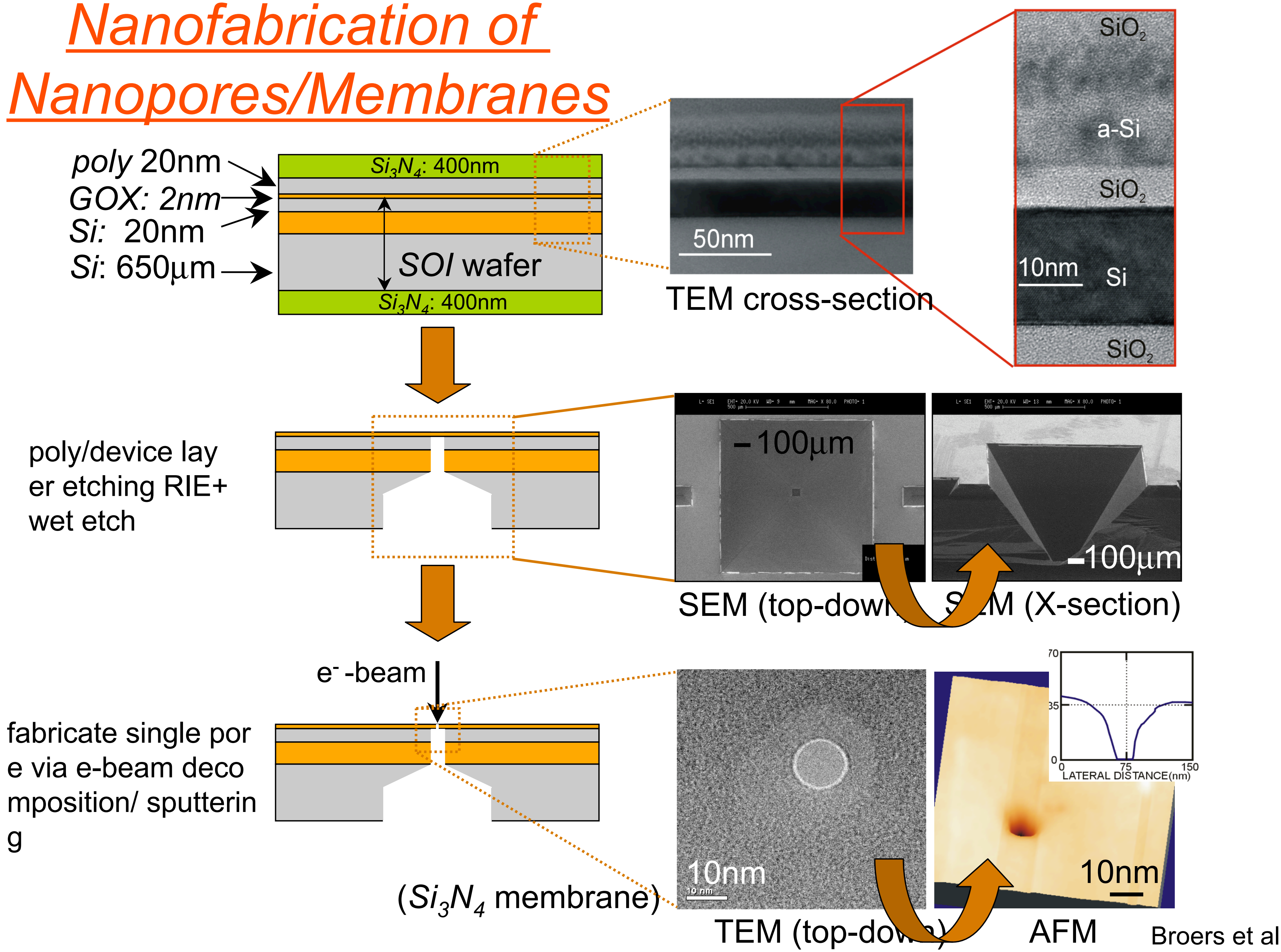
MD simulation



Self-consistent device and circuit modeling

Nano-pore fabrication

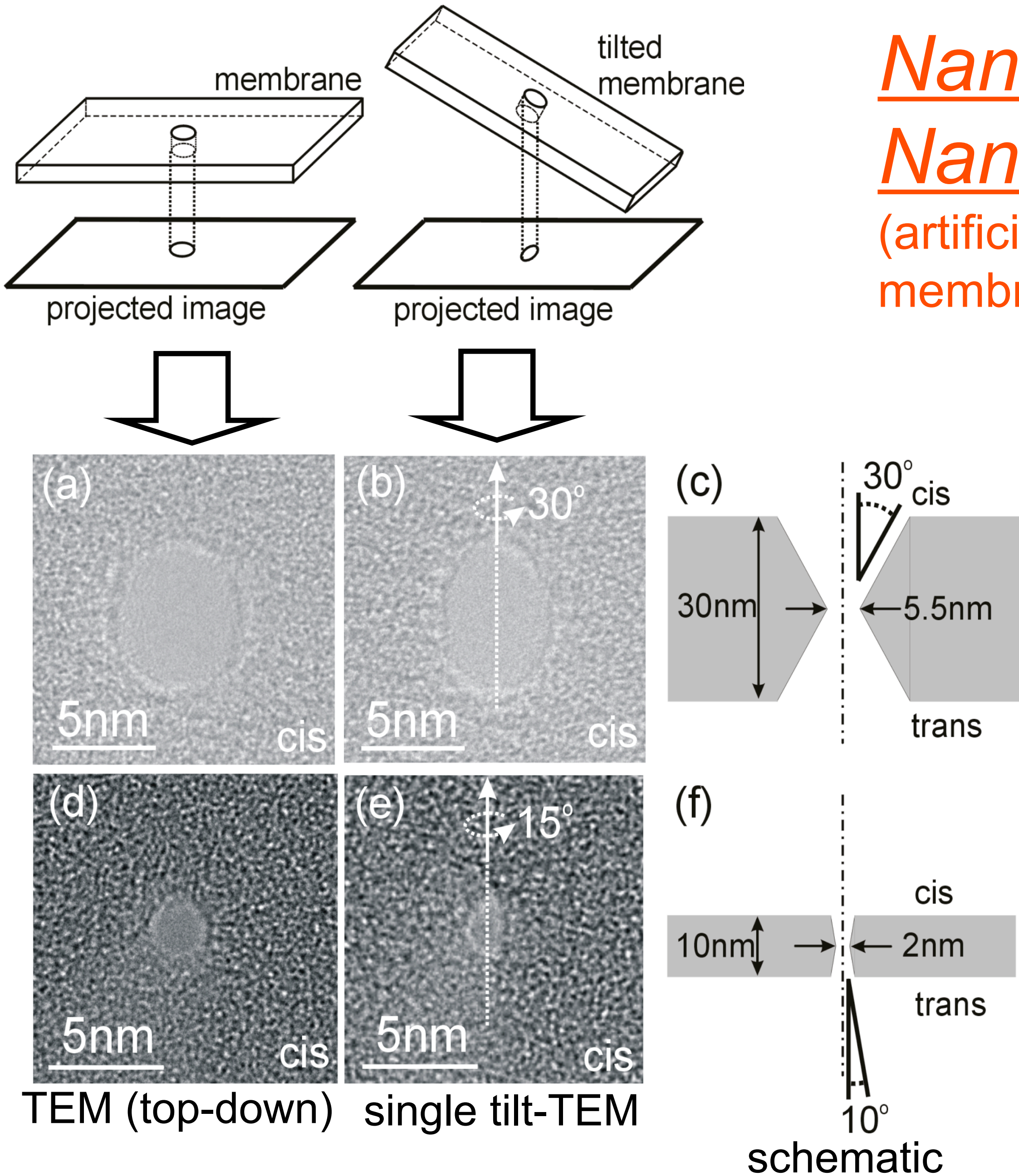
Nanofabrication of Nanopores/Membranes



Broers et al

Nanometrology of Nanopores using ***TEM***

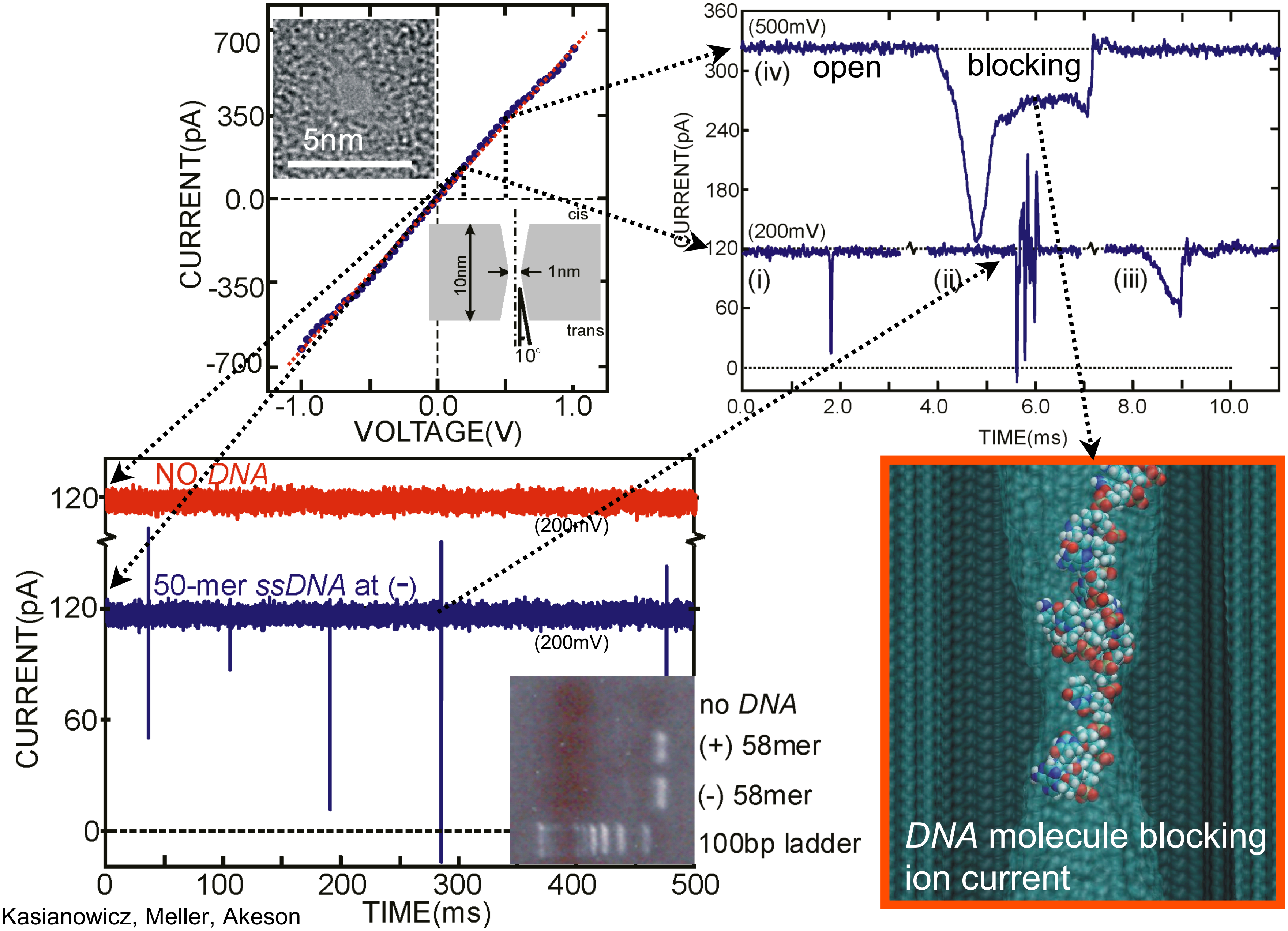
(artificial nanopore in Si_3N_4 membrane)



- artificial nanopores have a non-uniform cross-section

DNA Translocations through a Nanopore

(measurements using a 1nm diameter nanopore like a molecular Coulter counter)



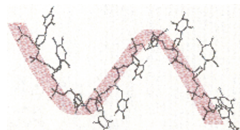
Kasianowicz, Meller, Akeson

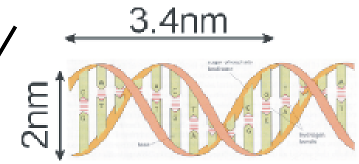
Sorting DNA polymers

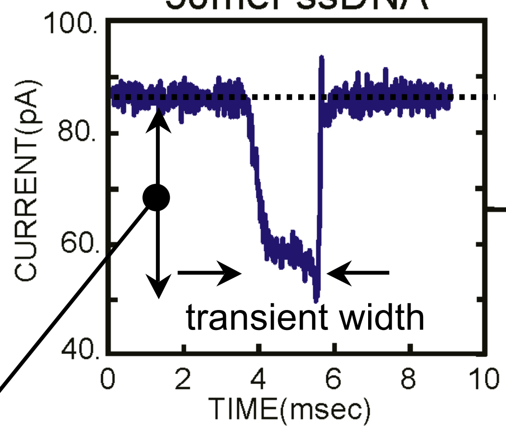
(measurements using a ~1nm diameter nanopore as a stochastic sensor)

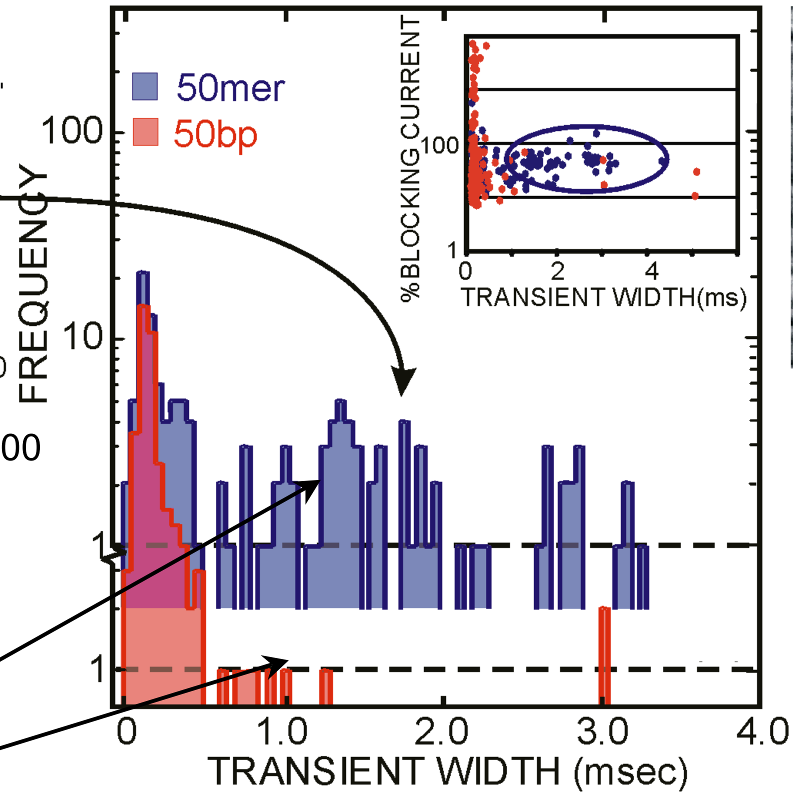
50mer *ssDNA*: poly(dT) 0.34nm/nucleotide
50mer=17nm p~4nm(persistence)

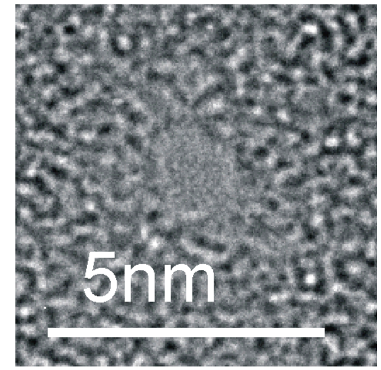
50bp ds*DNA*: 0.34nm/bp
50bp-17nm p~50nm











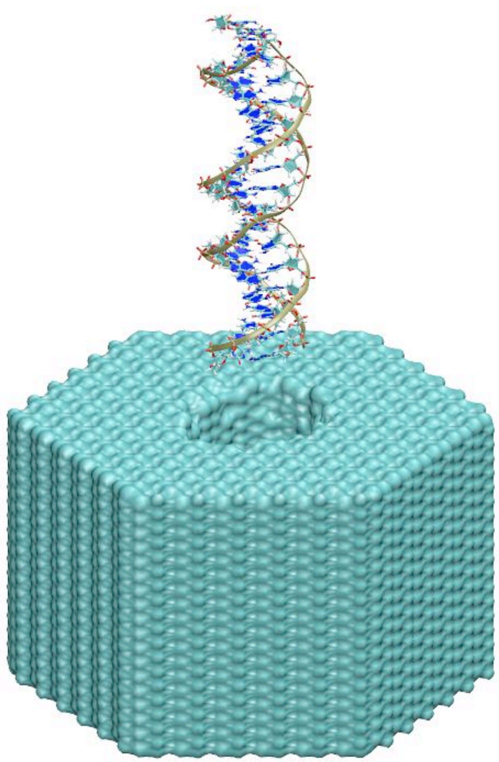
% blocking current = $\frac{\text{blocking current}}{\text{open current}}$ x100

- distribution of transient widths may be used to discriminate between *ssDNA/dsDNA*

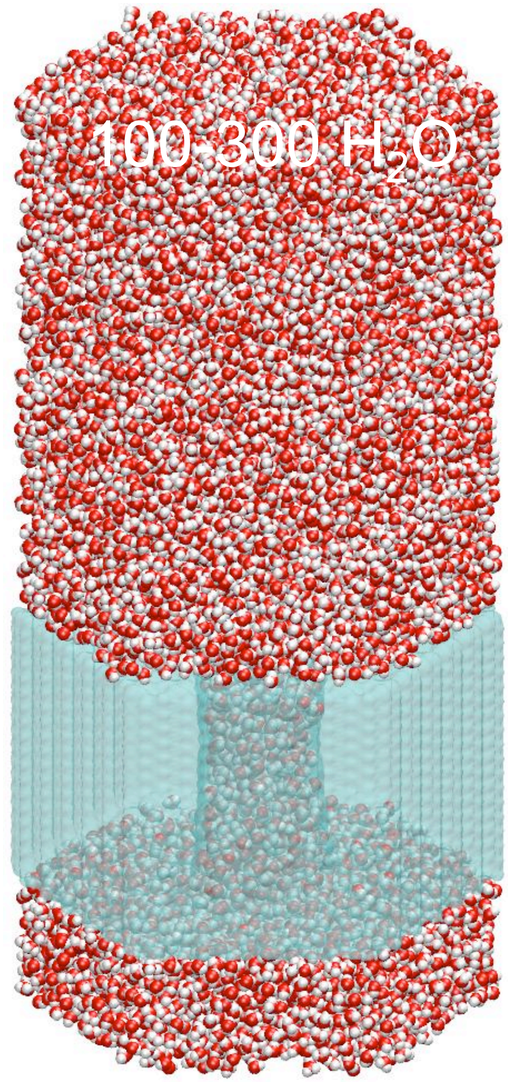
Molecular Dynamics of DNA in a Nanopore

(force fields: CHARM27: DNA, *Si_3N_4*, *TIP3 H_2O*, ions; AMBER95: DNA)

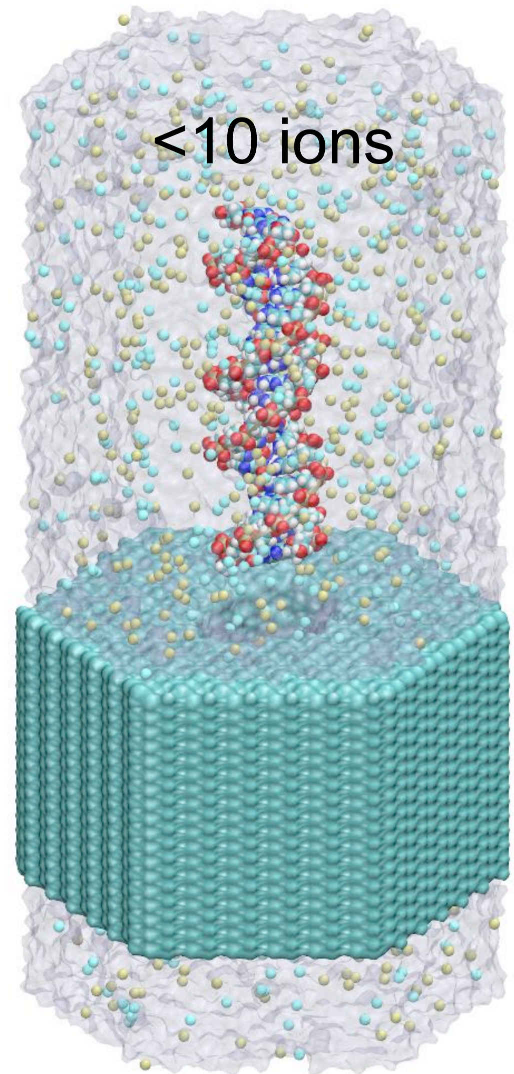
1 DNA molecule



• nanopore+DNA



• nanopore+DNA+ water



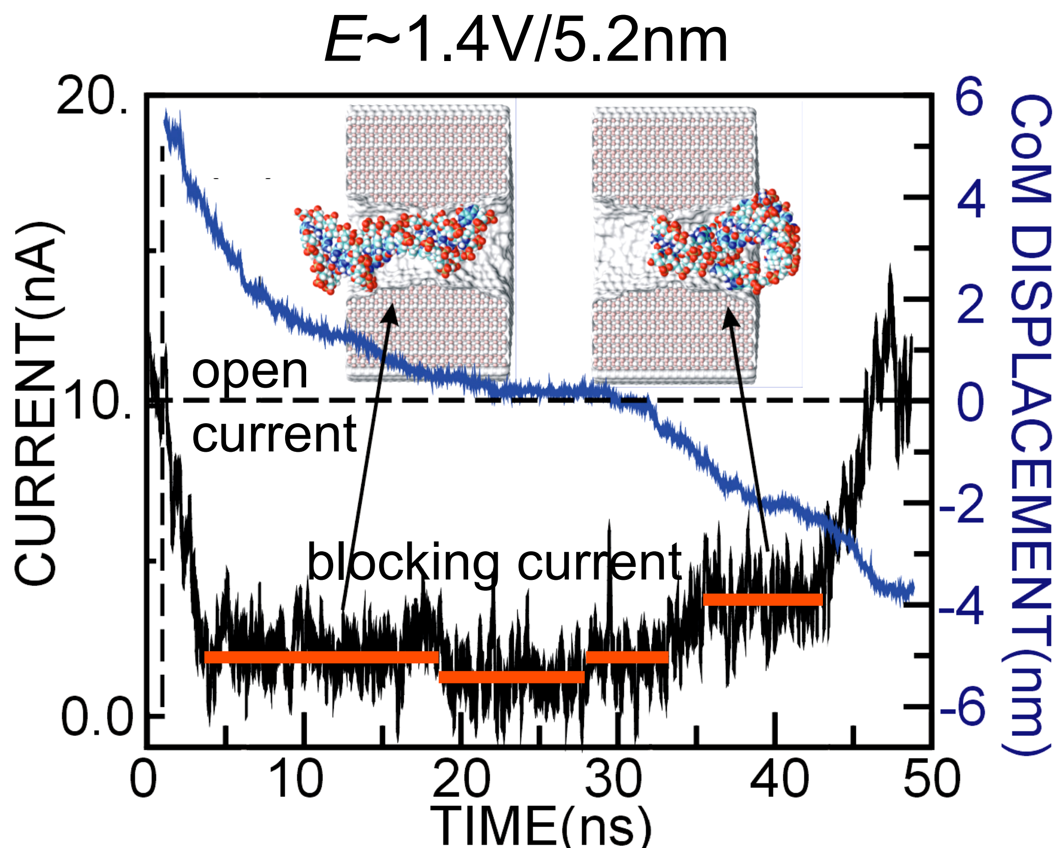
• nanopore+DNA+ water+ions

K. Schulten and A. Aksimentiev

Molecular Dynamics of DNA in a ***Si_3N_4*** *Nanopore*

2.4nm

QuickTime™ and a
decompressor
are needed to see this picture.



- translocation time: 10nsec-3μsec depending on field and pore interactions
- % blocking current correlated with molecular velocity

(• large fields cause the *DNA* to denature)

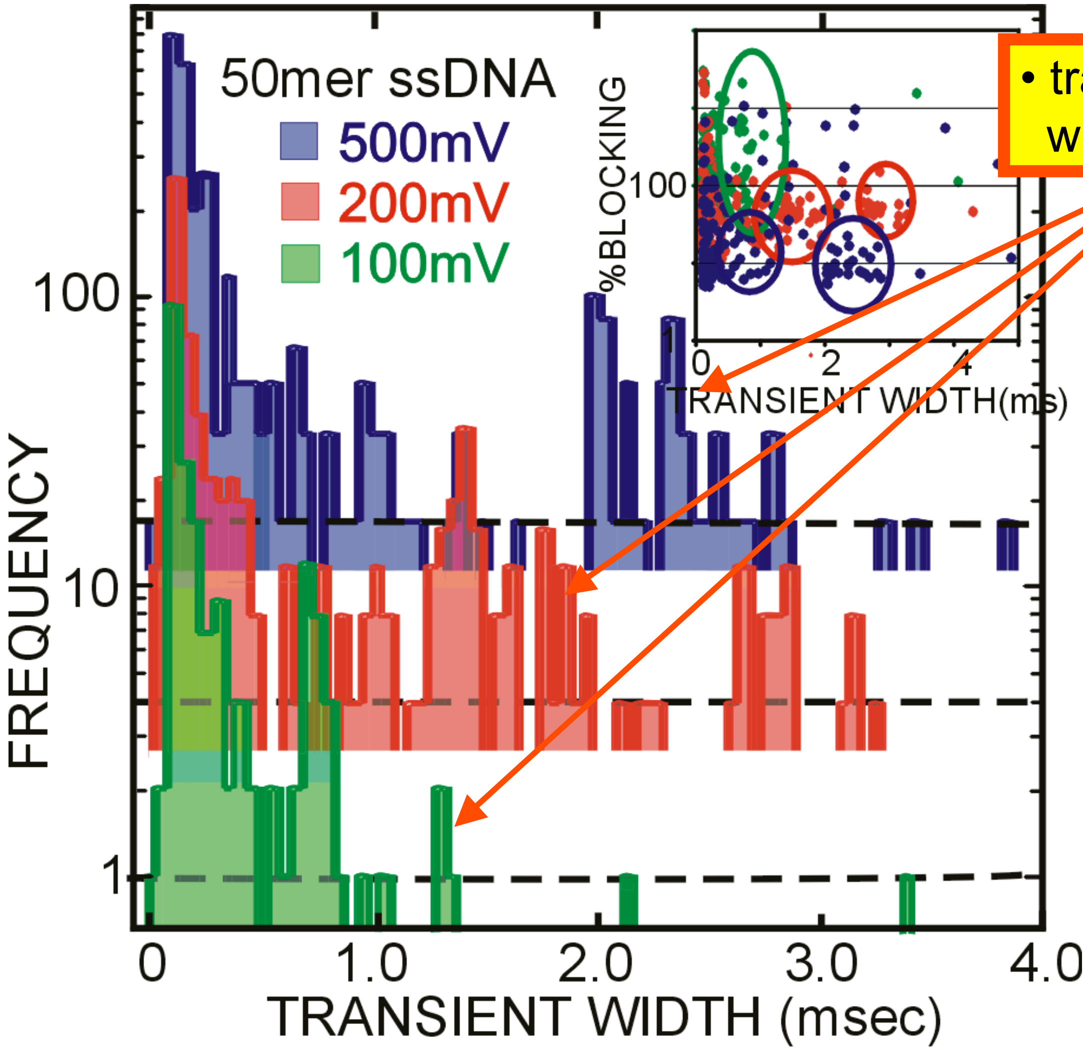
•Simulations: 1.4V/5.2nm → *F~400pN*
•DNA sequence is CCCCCCCCCCCCCCCCCCCC
•Only those ions that are within 1nm of either DNA or pore are shown;
some ions may appear or disappear.

K. Schulten and A. Aksimentiev

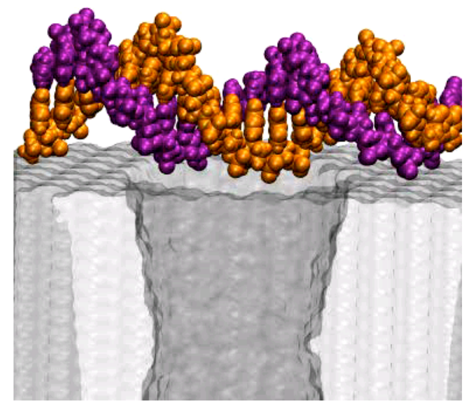
Voltage-dependence of Blocking Current

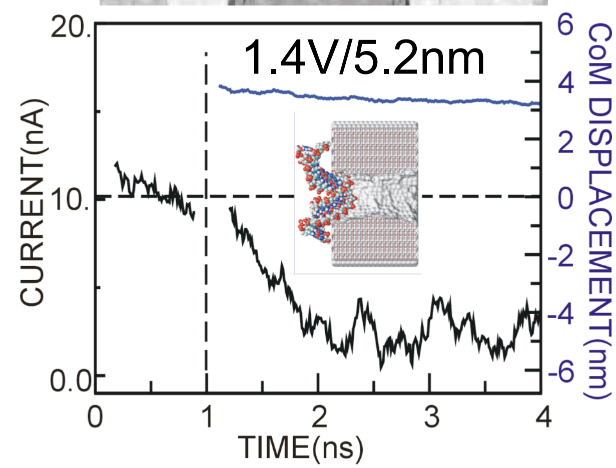
(measurements using a 1.5nm diameter pore in a 10nm thick Si_3N_4 membrane)

(*ssDNA*) poly(dT) 0.34nm/nucleotide
50mer=17nm p~4nm(persistence)



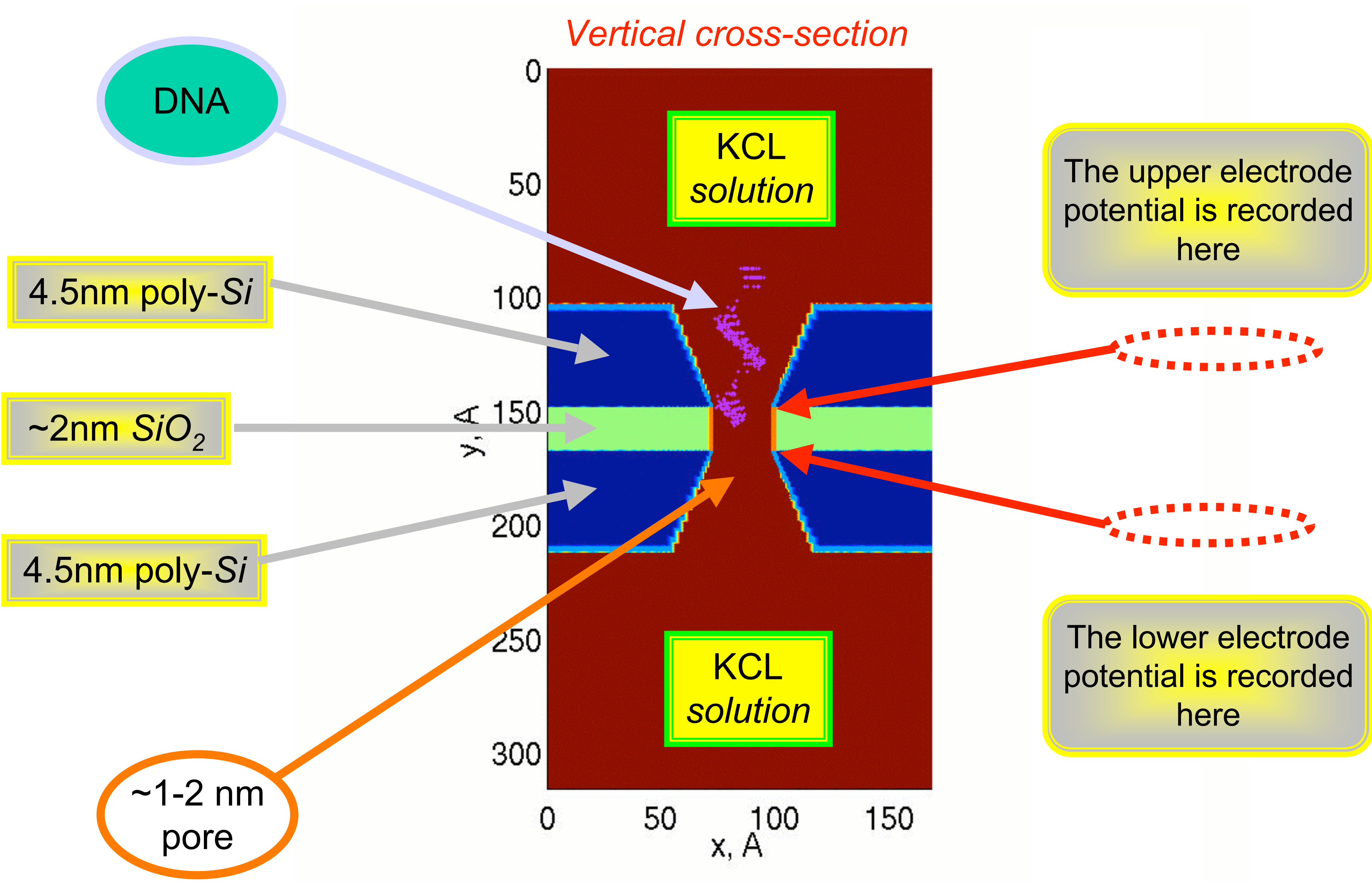
- transient width distribution broadens with increasing voltage





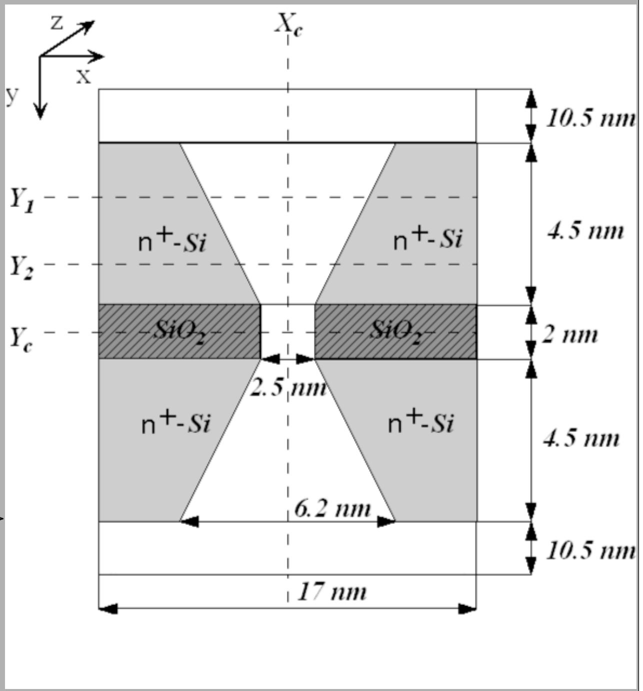
A. Aksimentiev

The Electronic Device Aspect



Gracheva et al. Nanotechnology 17(3), 622-633 (2006)

Nanopore-Membrane Electrostatic Modeling



Poisson Equation:

$$\vec{\nabla}\cdot(\varepsilon(\vec{r})\vec{\nabla}\phi(\vec{r})) = -\rho(\vec{r})$$

Charge density:

$$\rho_{solid-state}(\vec{r}) = q\{N_d^+(\vec{r}) - N_a^-(\vec{r}) + p(\vec{r}) - n(\vec{r})\}$$

$$\rho_{solution}(\vec{r}) = q\{[K^+](\vec{r}) - [Cl^-](\vec{r})\} + \rho_{DNA}(\vec{r})$$

$$n(\vec{r}) = N_c \frac{2}{\sqrt{\pi}} F_{1/2}(\eta_c(\vec{r})) \qquad \eta_c(\vec{r}) = \frac{E_f - E_c(\vec{r})}{kT}$$

$$p(\vec{r}) = N_v \frac{2}{\sqrt{\pi}} F_{1/2}(\eta_v(\vec{r})) \qquad \eta_v(\vec{r}) = \frac{E_v(\vec{r}) - E_f}{kT}$$

$$[K^+](\vec{r}) = [K^+]_0 \exp(q\phi(\vec{r})/kT)$$

$$[Cl^-](\vec{r}) = [Cl^-]_0 \exp(-q\phi(\vec{r})/kT)$$

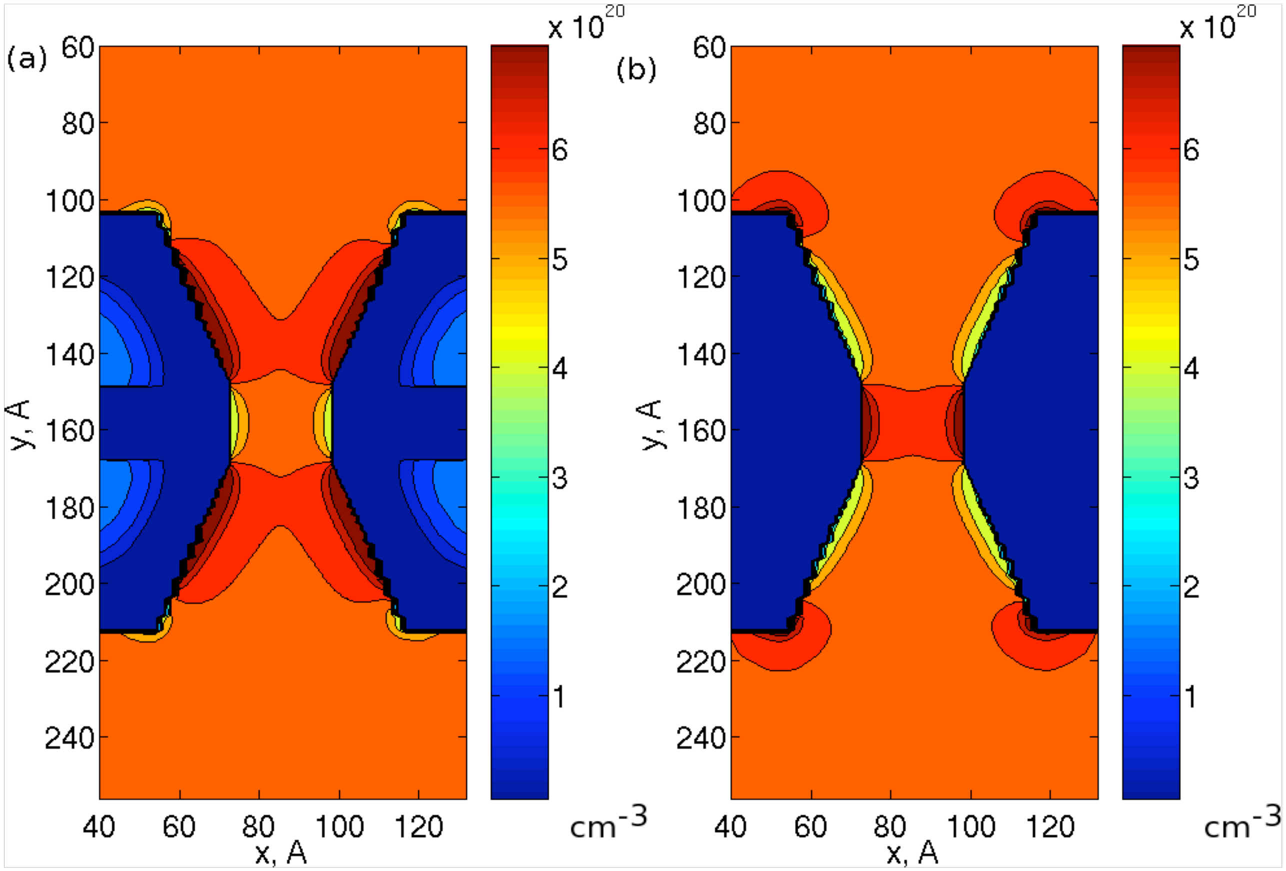
$$[K^+]_0 = [Cl^-]_0 = c$$

$$E_c(\vec{r}) = -q\phi(\vec{r}) - E_g$$

$$E_v(\vec{r}) = -q\phi(\vec{r})$$

Gracheva et al., Nanotechnology 17, 622-633 (2006)

Empty pore negative (left) and positive (right) charge in the structure and solution



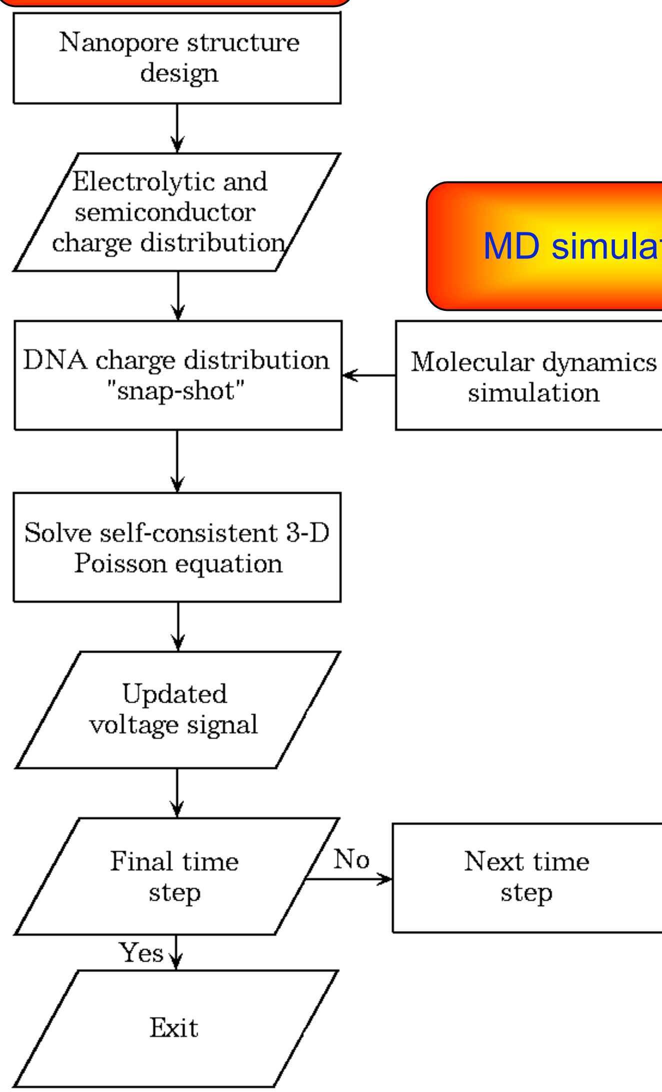
Multi-Scale "Self-consistent" Poisson Solver

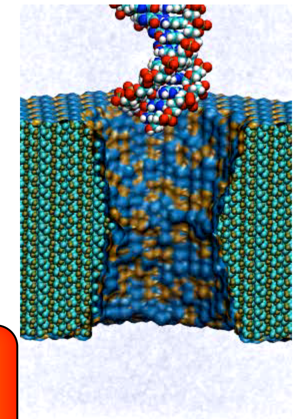
(used in conjunction with "snapshots" provided by MD)

Nanopore structure design

MD simulation

Semiconductor device simulation

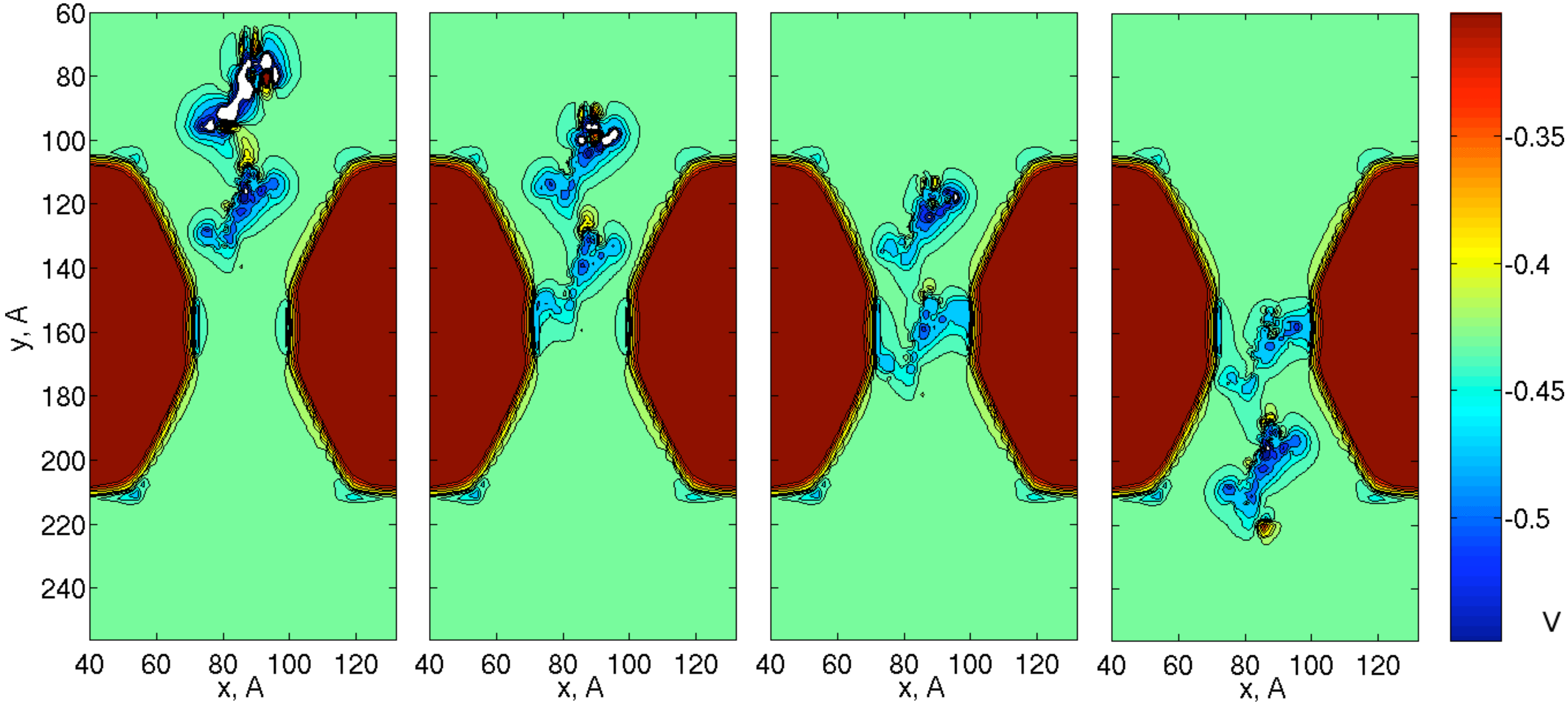




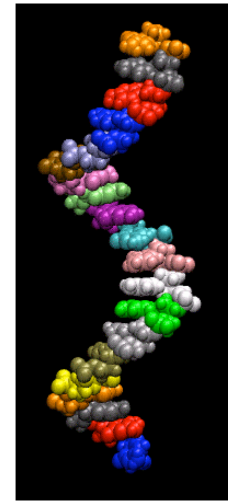
$$\nabla(\varepsilon \nabla \phi) = -\rho$$

$$\rho = \begin{cases} [K^+] - [Cl^-] \ \ in \ \ electrolyte \\ [K^+]_0 \exp(q\phi / kT); \ [Cl^-] = [Cl^-]_0 \exp(-q\phi / kT) \\ q(p - n + N_d^+ - N_a^-) \ \ in \ \ semiconductor \end{cases}$$

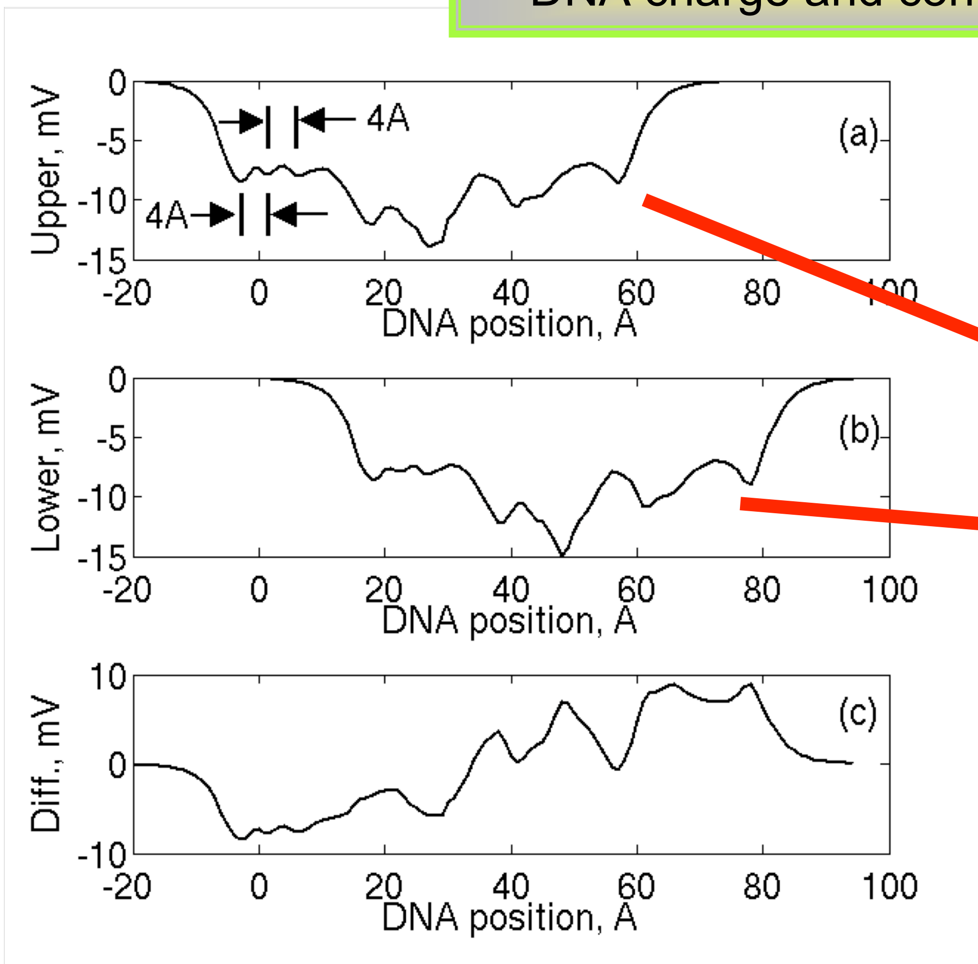
Simulation of ssDNA Translocation Through a 2.5nm Nanopore

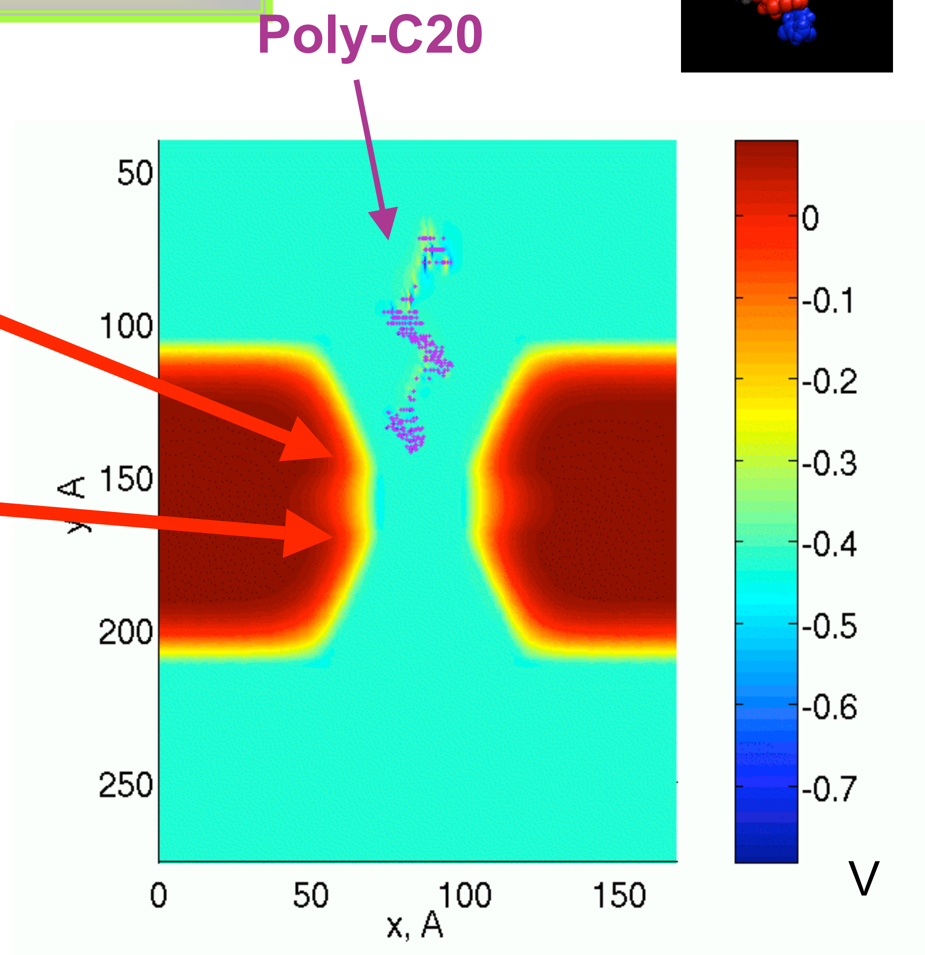


Simulation of unstretched ssDNA Translocation Through a 2.5 nm Nanopore



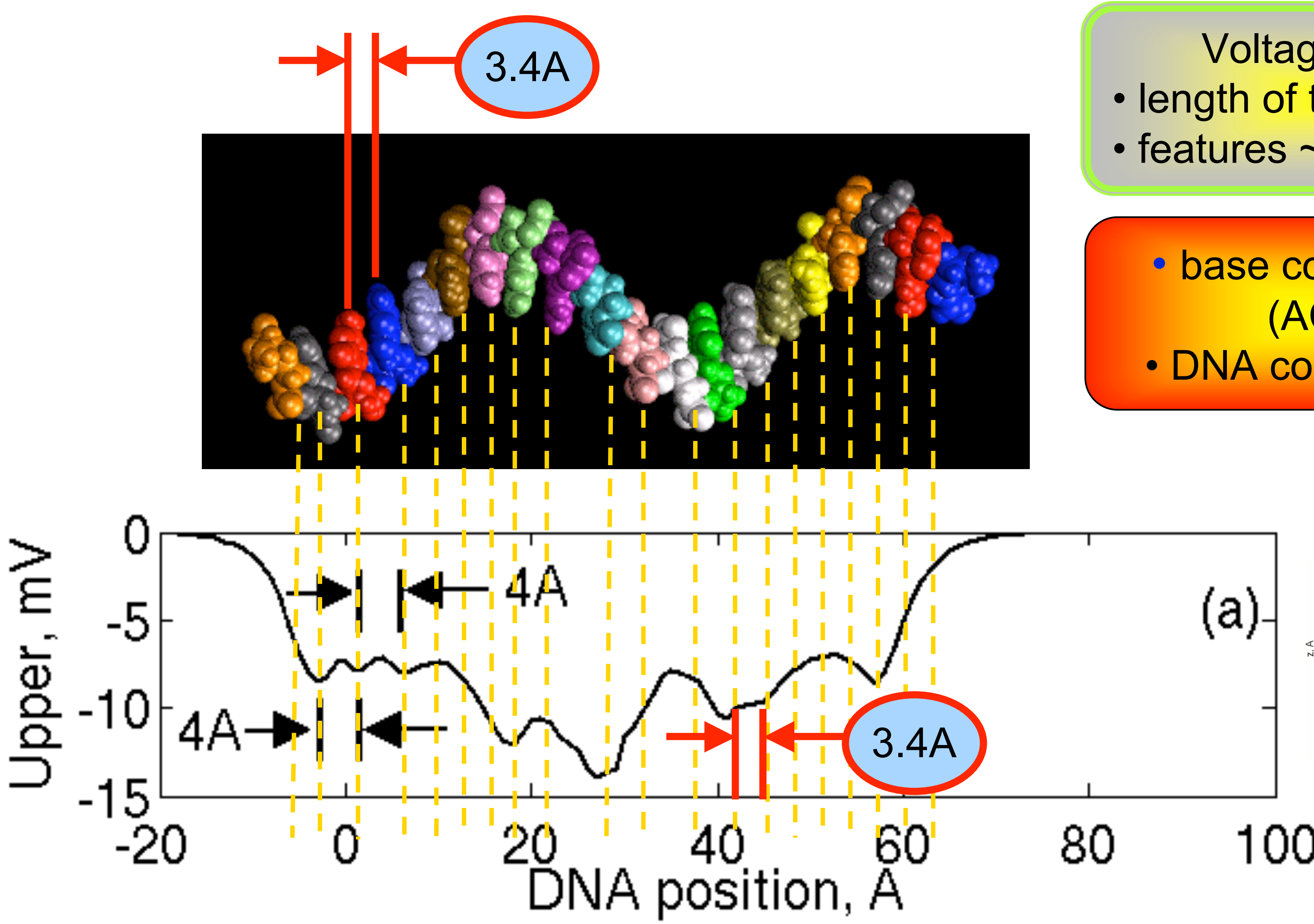
Electrode Voltage is sensitive to DNA charge and conformation





Decoding DNA sequence and configuration

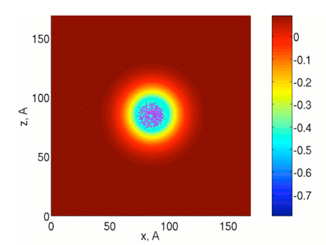
DNA sequence: C-C-C-C-C-C-C-C-C-C-C-C-C-C-C-C-C-C-C-C (ssDNA polyC20)



Voltage trace:

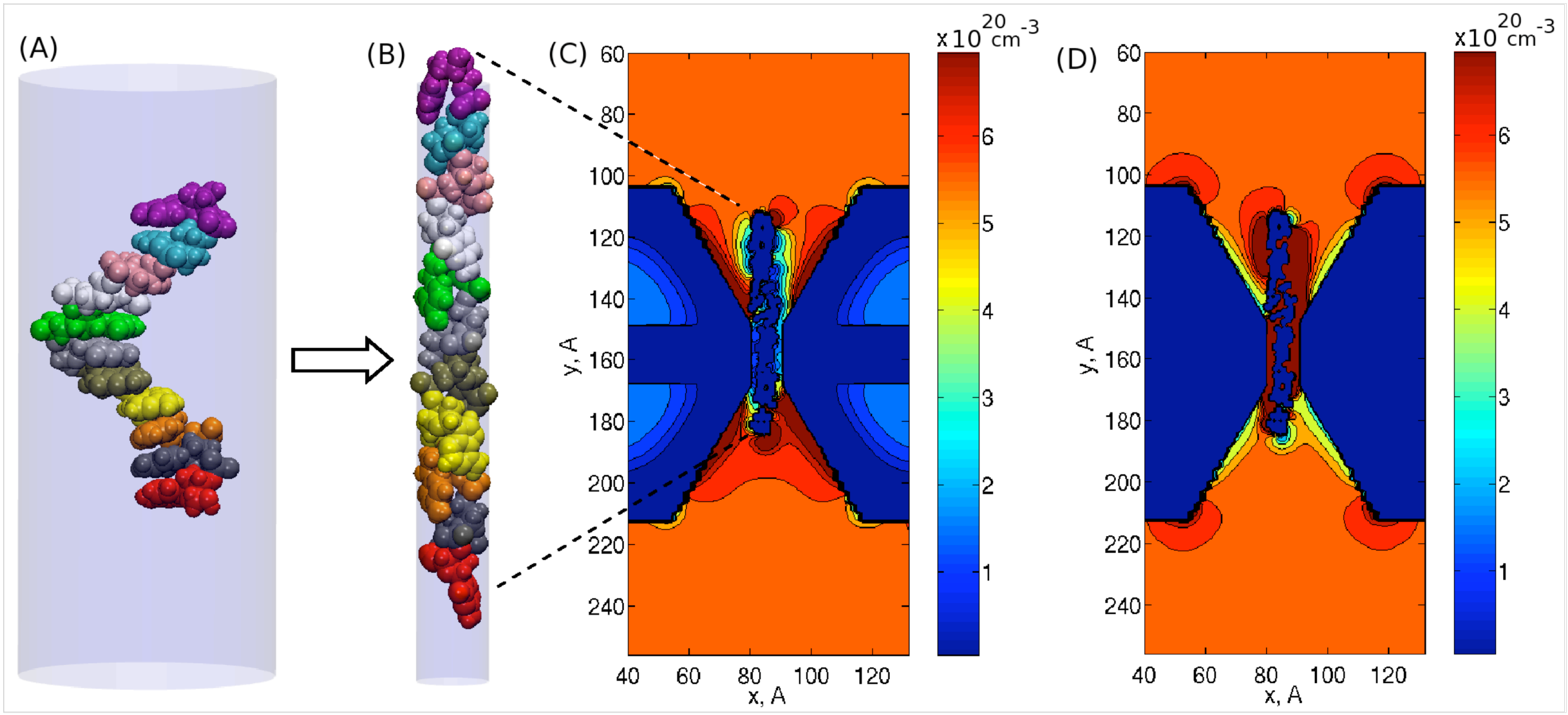
- length of the DNA
- features ~3.4 A apart

- base composition (ACGT)
- DNA conformation



Simulation of Stretched ssDNA Translocation Through a 1.0nm Nanopore

11 bases

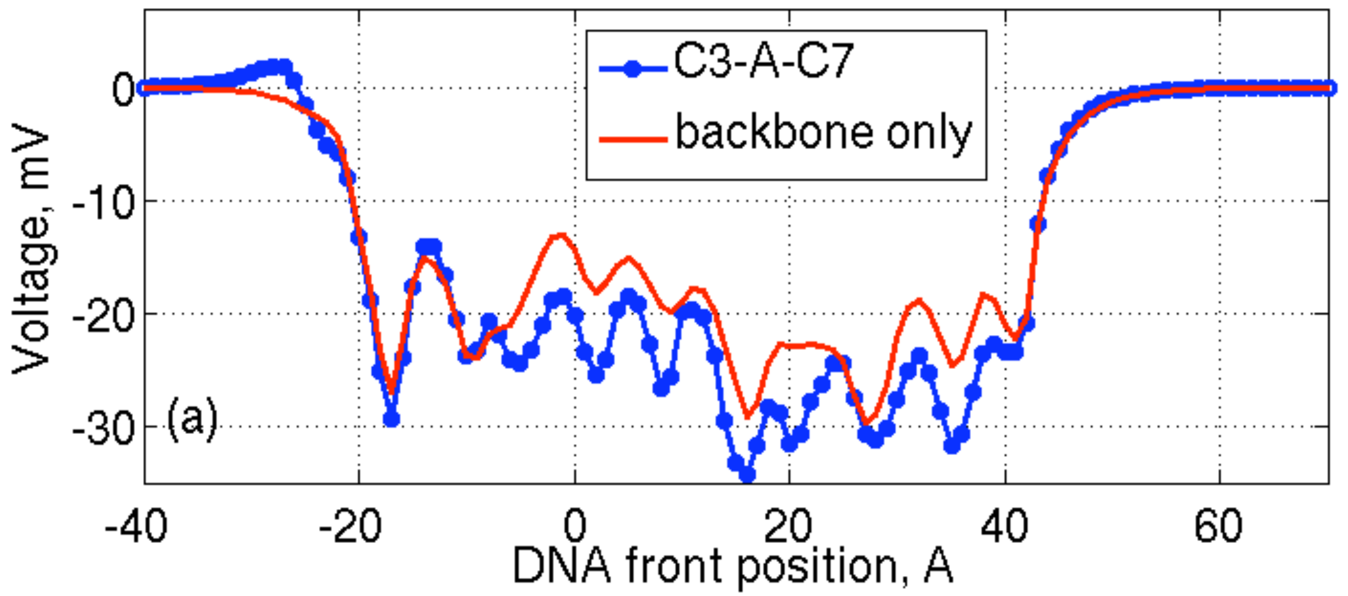


2.5nm pore

1.0nm pore

Gracheva et al Nanotechnology 17(13), p.3160 (2006)

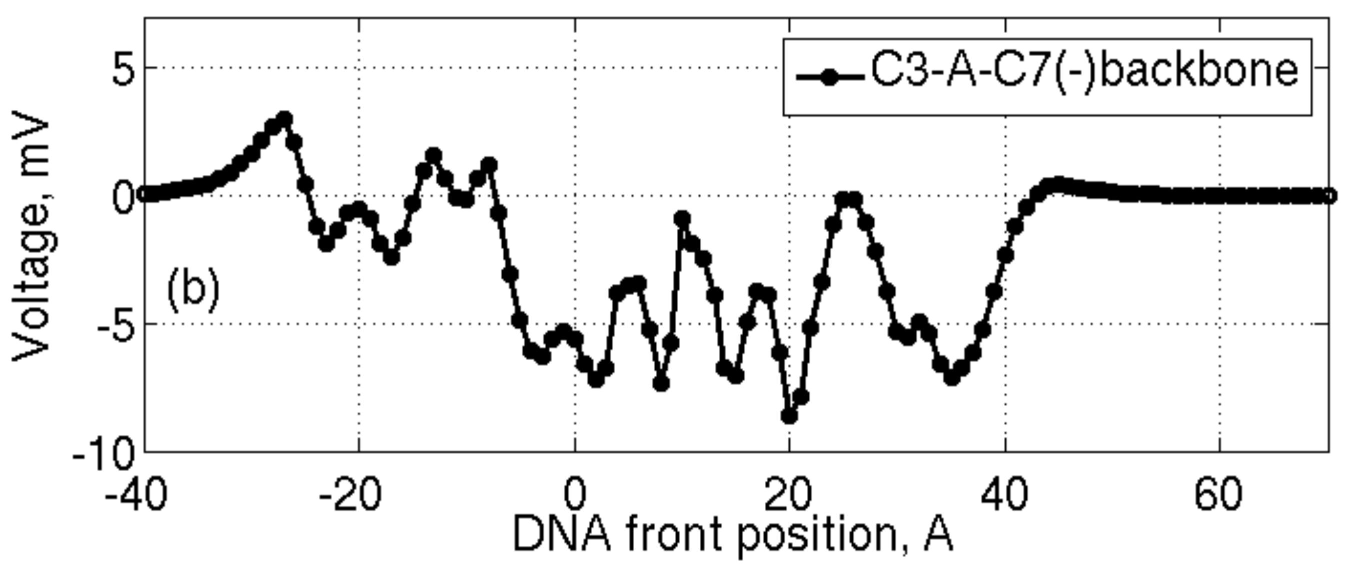
Upper electrode voltage for C_3AC_7 and its backbone



11 bases

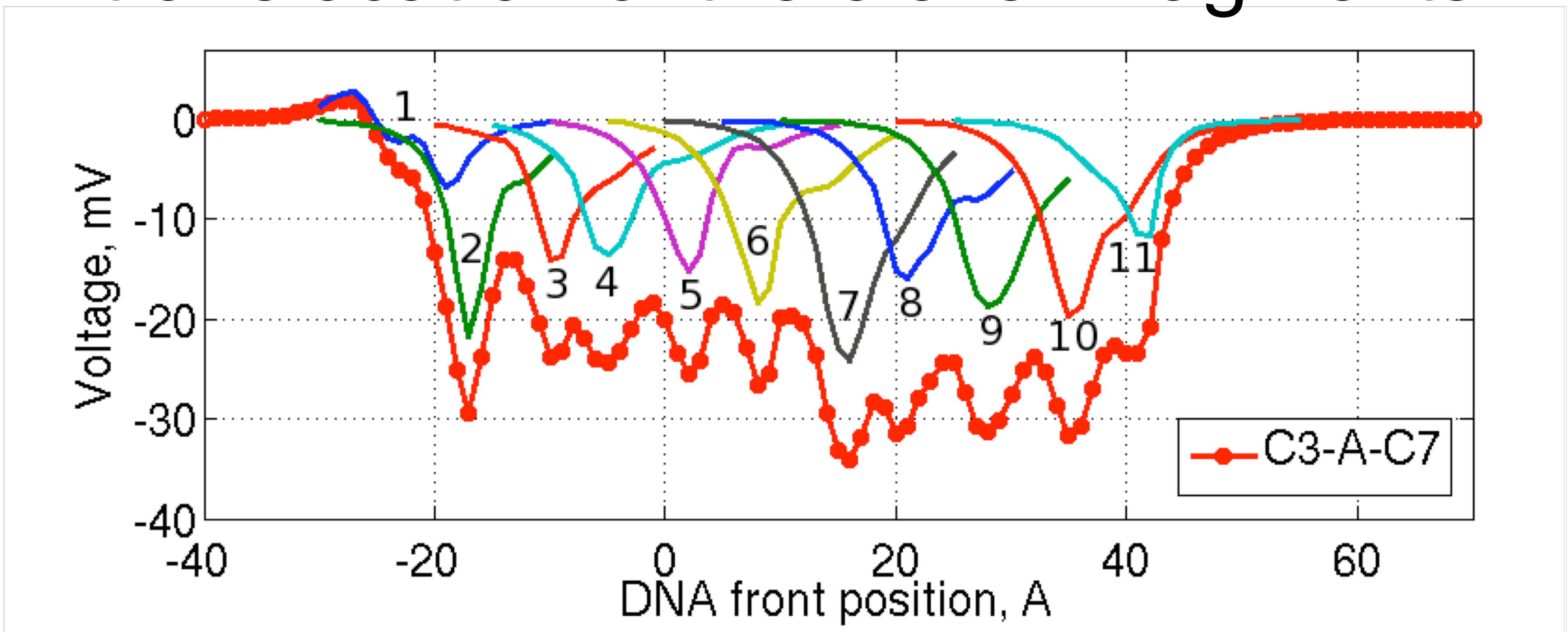
C3-A-C7

Difference of C_3AC_7 and its backbone (for upper electrodes)

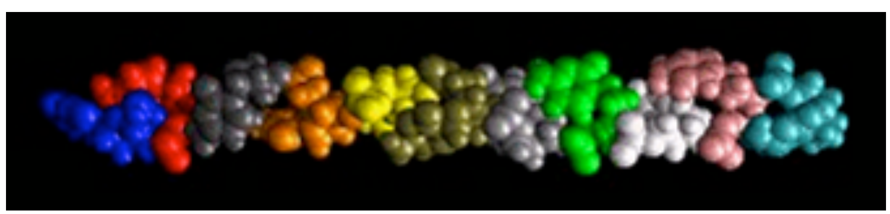


Backbone signal ~30mV
Bases ~10mV

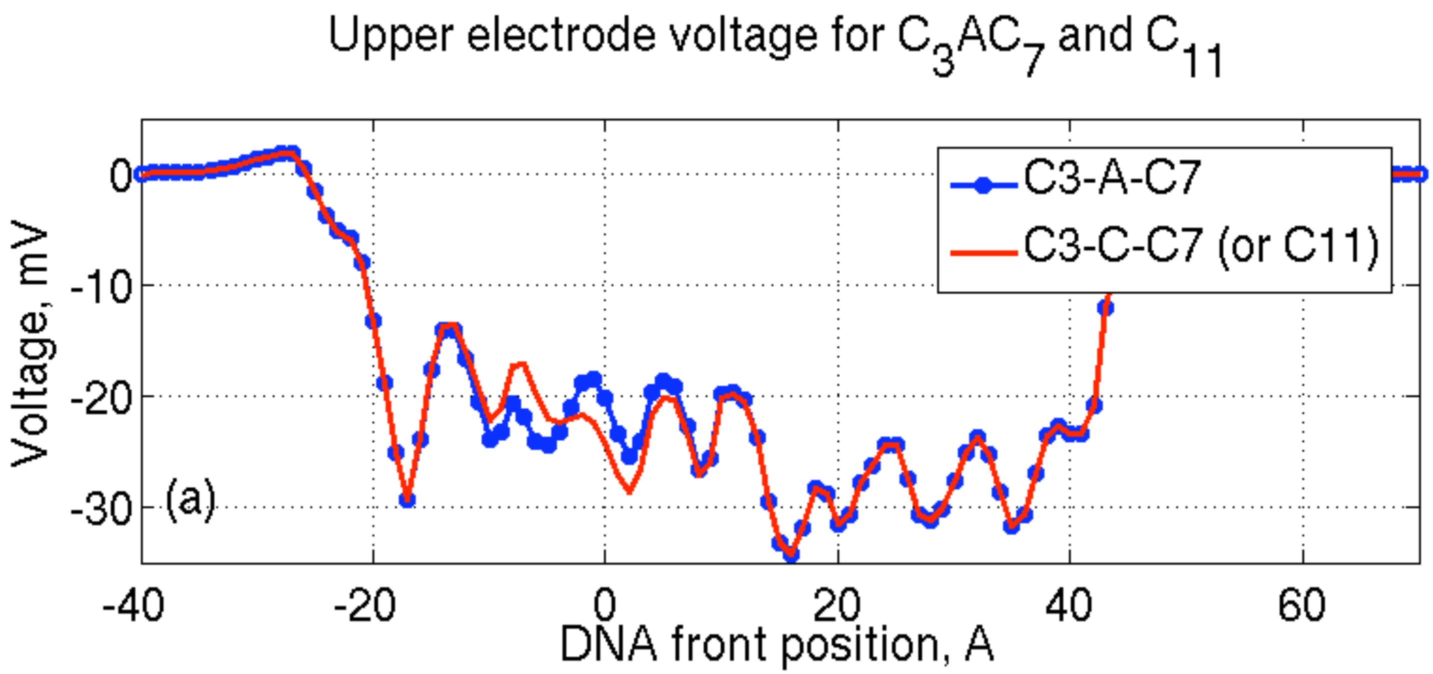
The whole DNA translocation and translocation of the eleven fragments

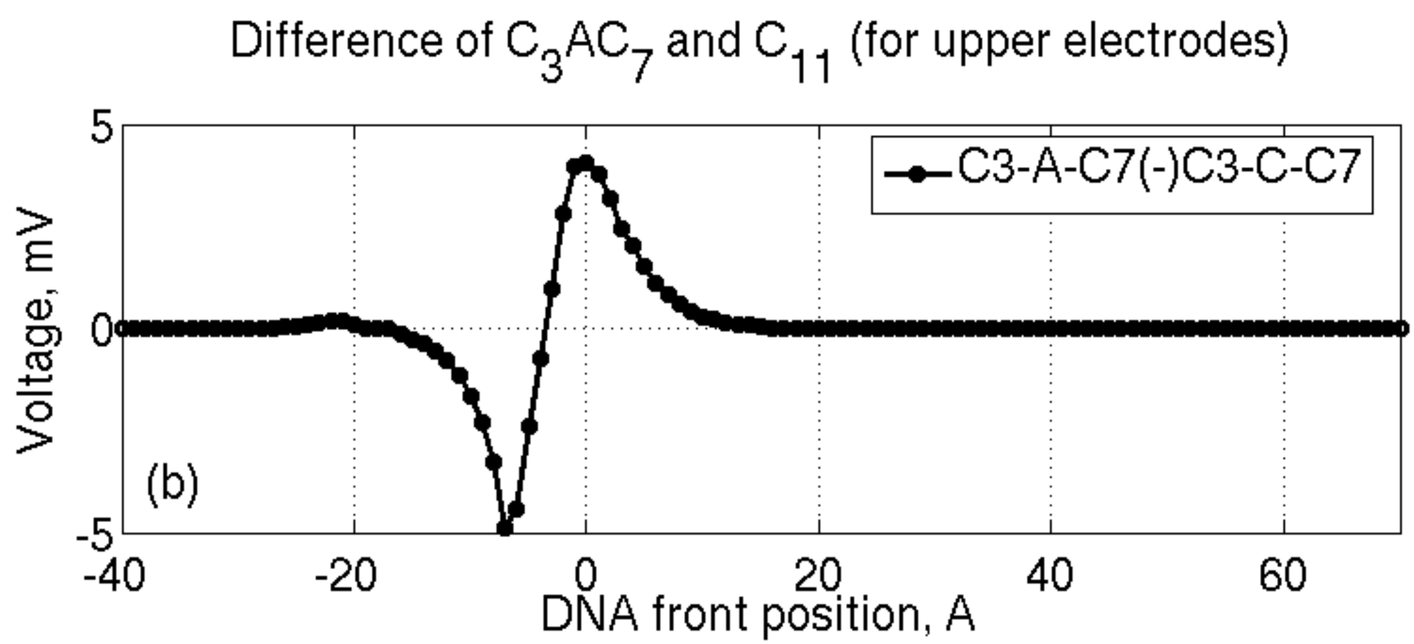


C3-A-C7 and 11 backbone segments with bases



Look how wide the signal of one base can be!!!





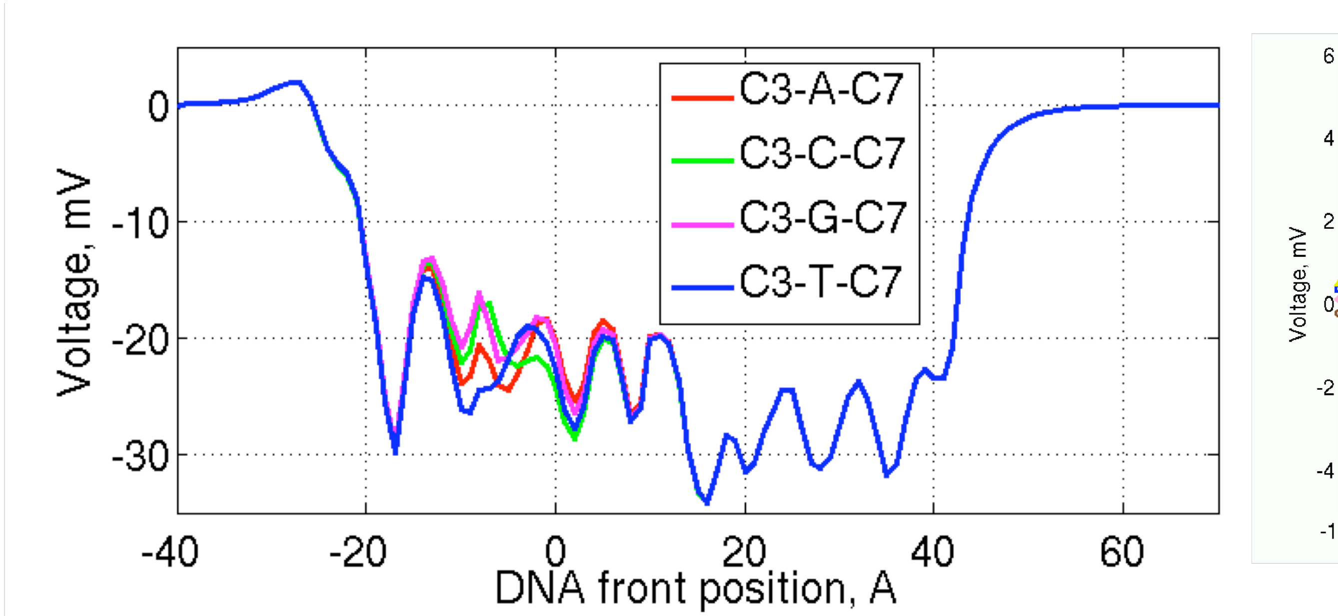
In the same conformation!!!

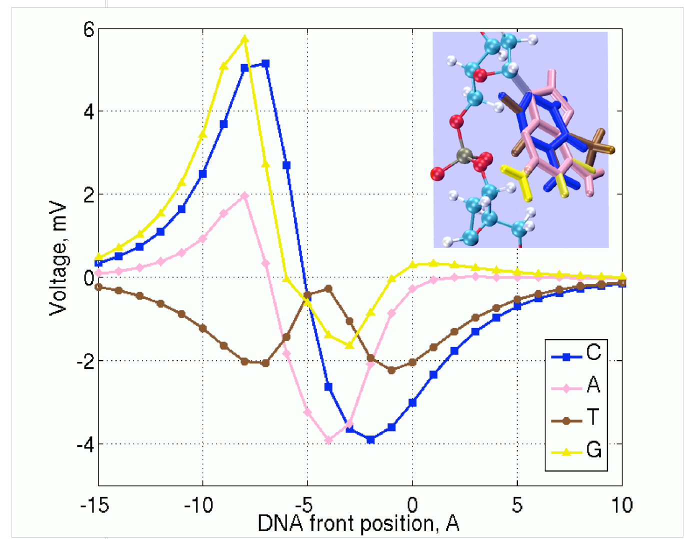
C3-A-C7

C3-C-C7
or
C11-mutant

Difference
between A and C
~5mV

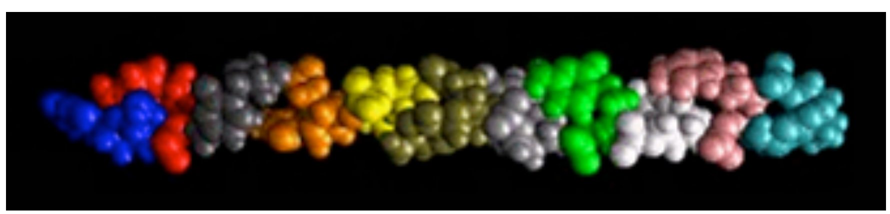
The whole DNA translocation with one base mutation





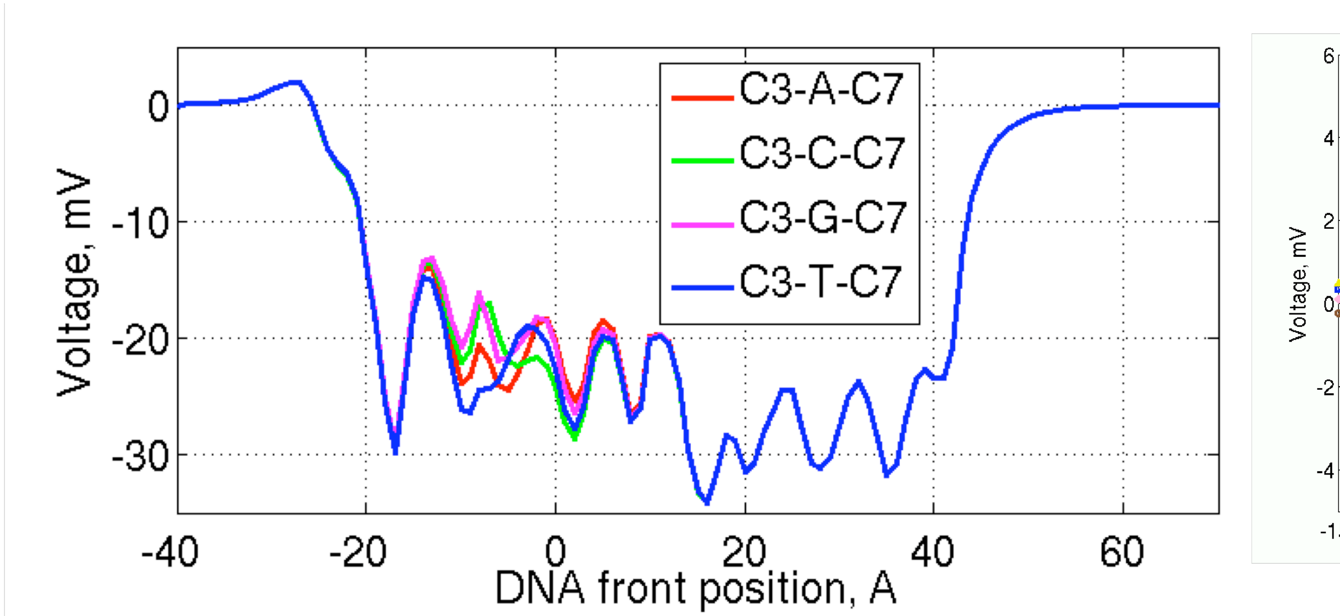
Mutated base #4

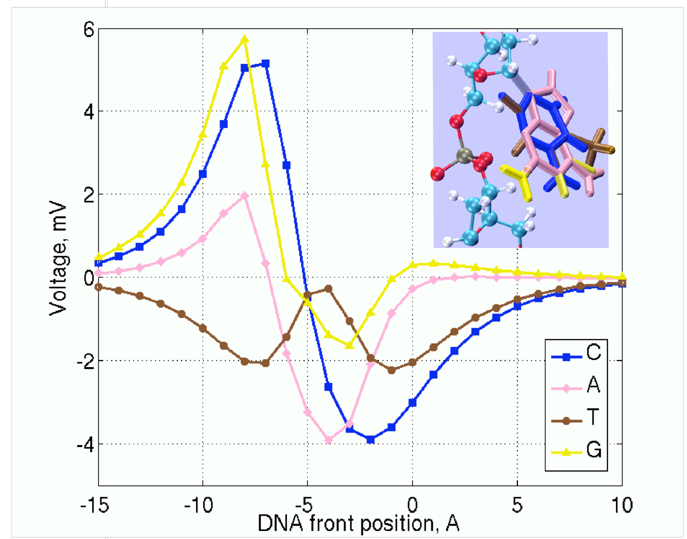
In the same conformation!!!



The signal difference is localized in the vicinity of base #4

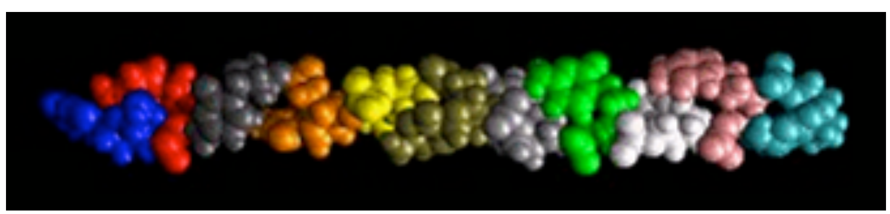
The whole DNA translocation with one base mutation





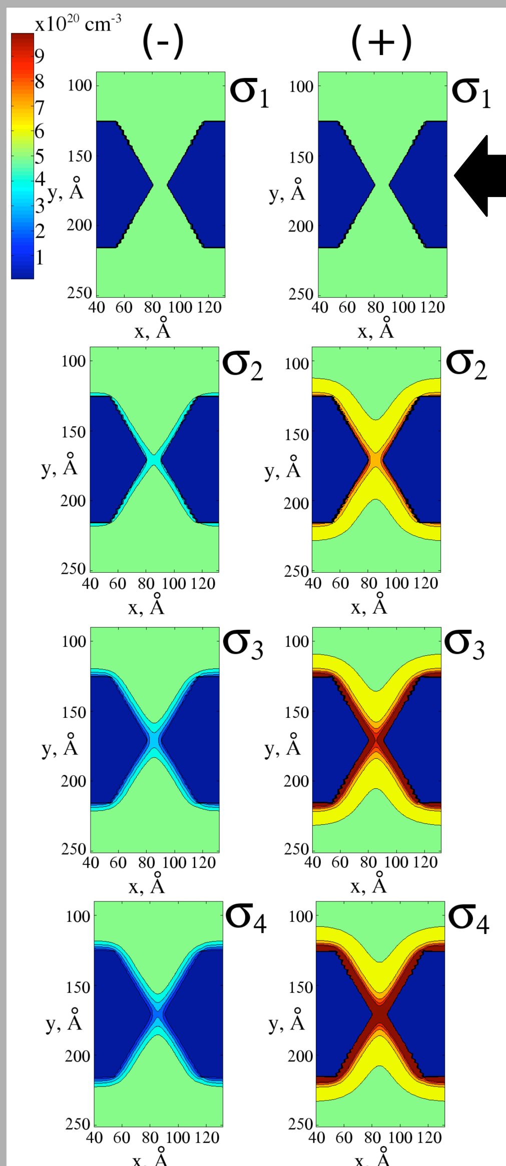
Mutated base #4

In the same conformation!!!



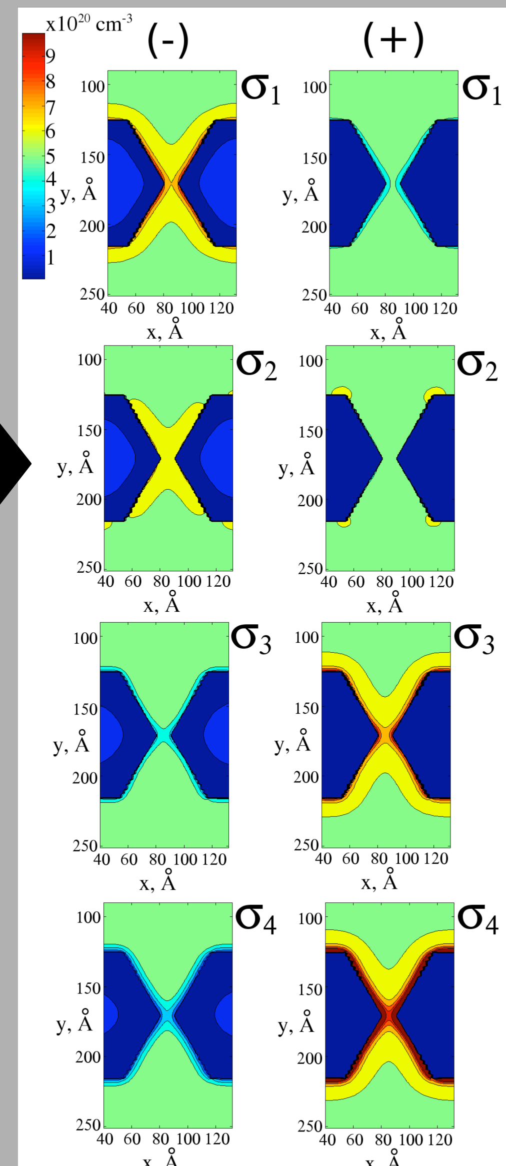
The signal difference is localized in the vicinity of base #4

Semiconductor Membrane: Double Layer Engineering



SiO_2: dielectric material
no carriers of either sign

n+-Si: heavily doped Si semiconductor material
Fixed positive charge
$N_d^+=2x10^{20}$ cm^{-3},
electrons, some holes

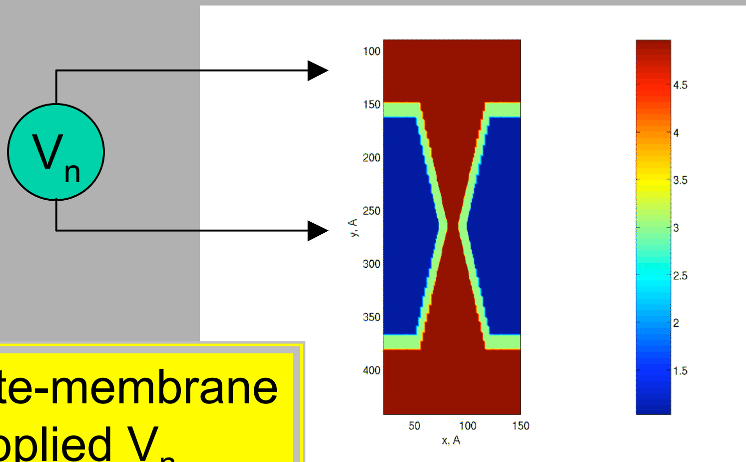


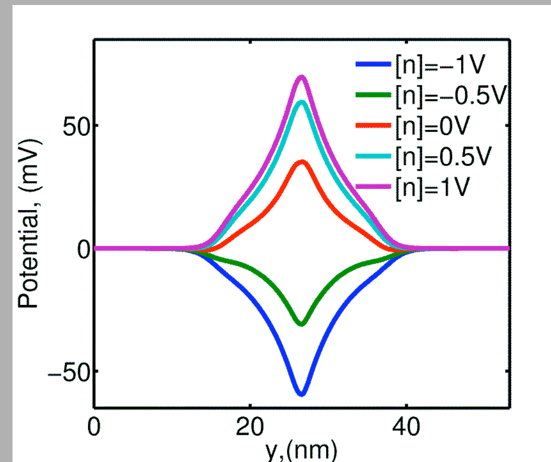
Surface charge:
$\sigma_1=0$
$\sigma_2=-0.0064$ Cm^{-2}
$\sigma_3=-0.019$ Cm^{-2}
$\sigma_4=-0.032$ Cm^{-2}

[KCl]=1M

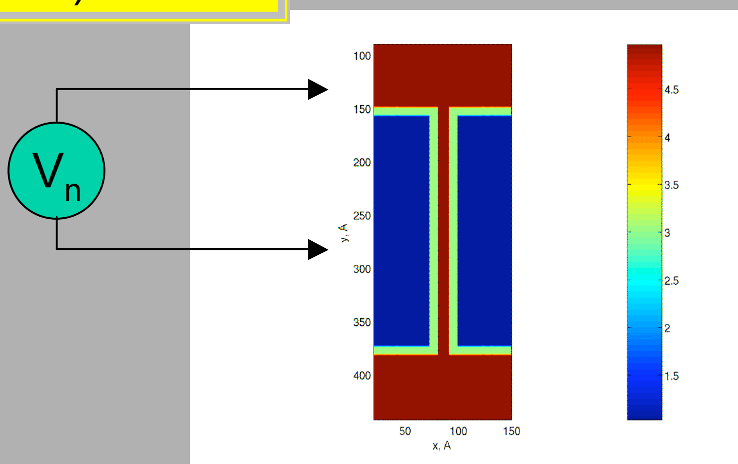
Gracheva & Leburton
Nanotechnology 18, p.145704 (2007)

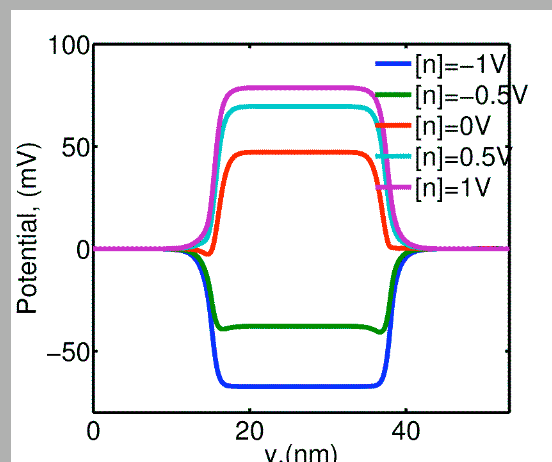
Semiconductor Membrane: Electrical Tunability





Electrolyte-membrane bias is applied V_n ([n] in figures)

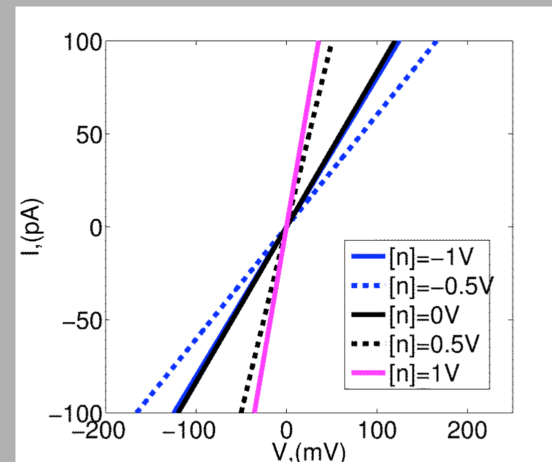


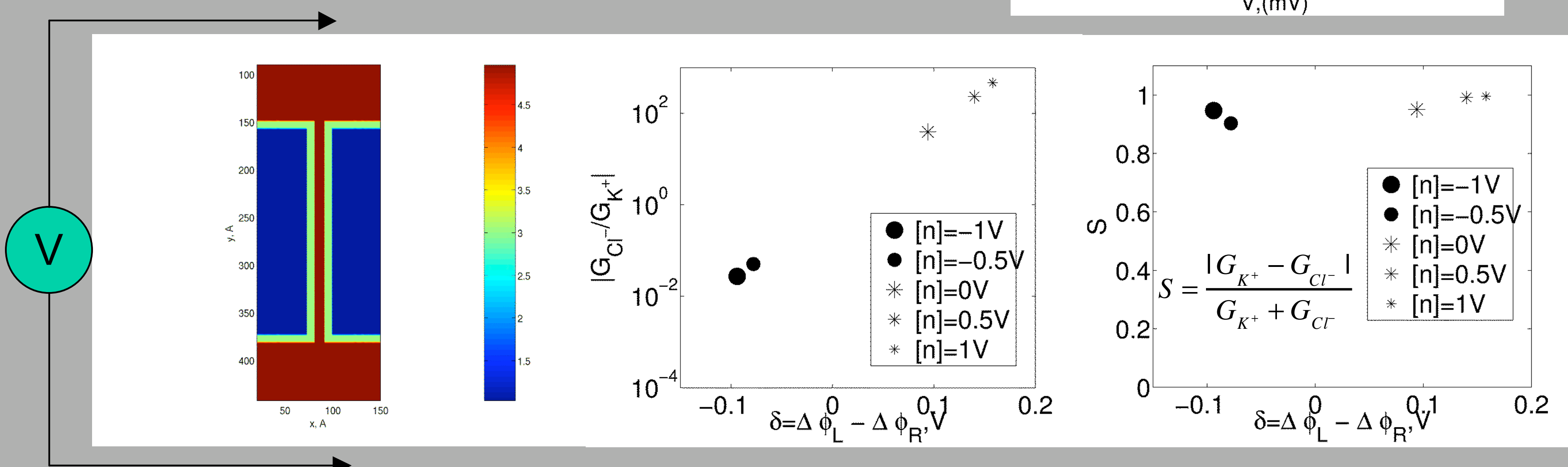


[KCl]=0.1M

Controlled Ionic Conductance & Filtering (Linear Response)

Current-voltage characteristics: assume constant field in the nanopore
Conductance: G=dI/dV
Selectivity: $S=|(G_{Cl}-C_K)/(G_{Cl}+G_K)|$

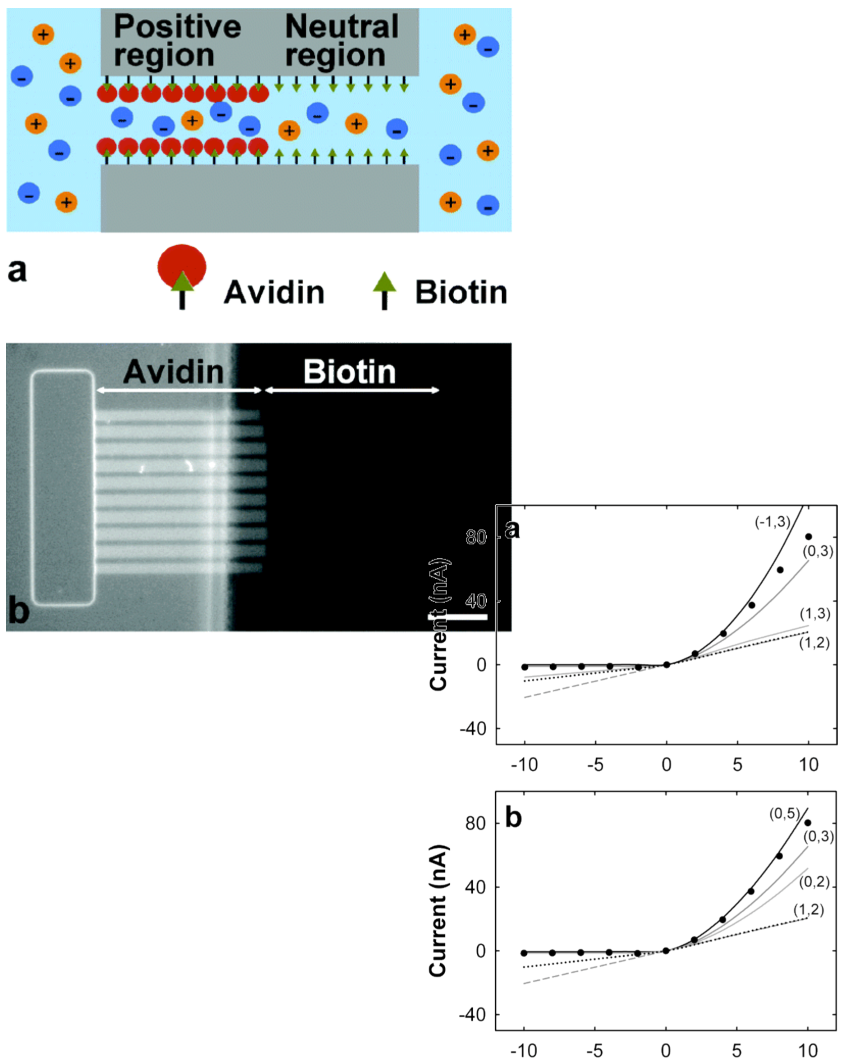




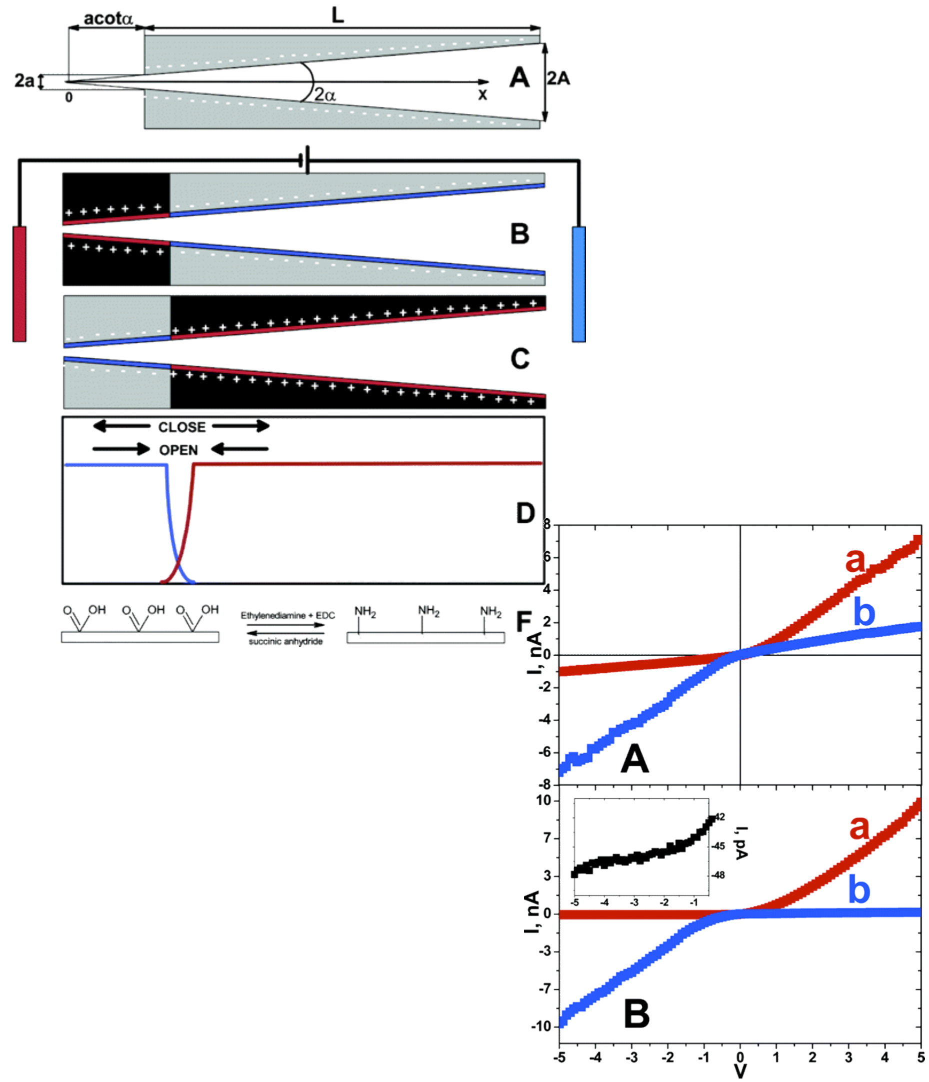
$[KCl]=0.1M$

Vidal, Gracheva & Leburton,
Nanoscale Res. Lett. 2, p. 61 (2007)

Toward Ionic Rectification: Static Dipolar Surface Charges

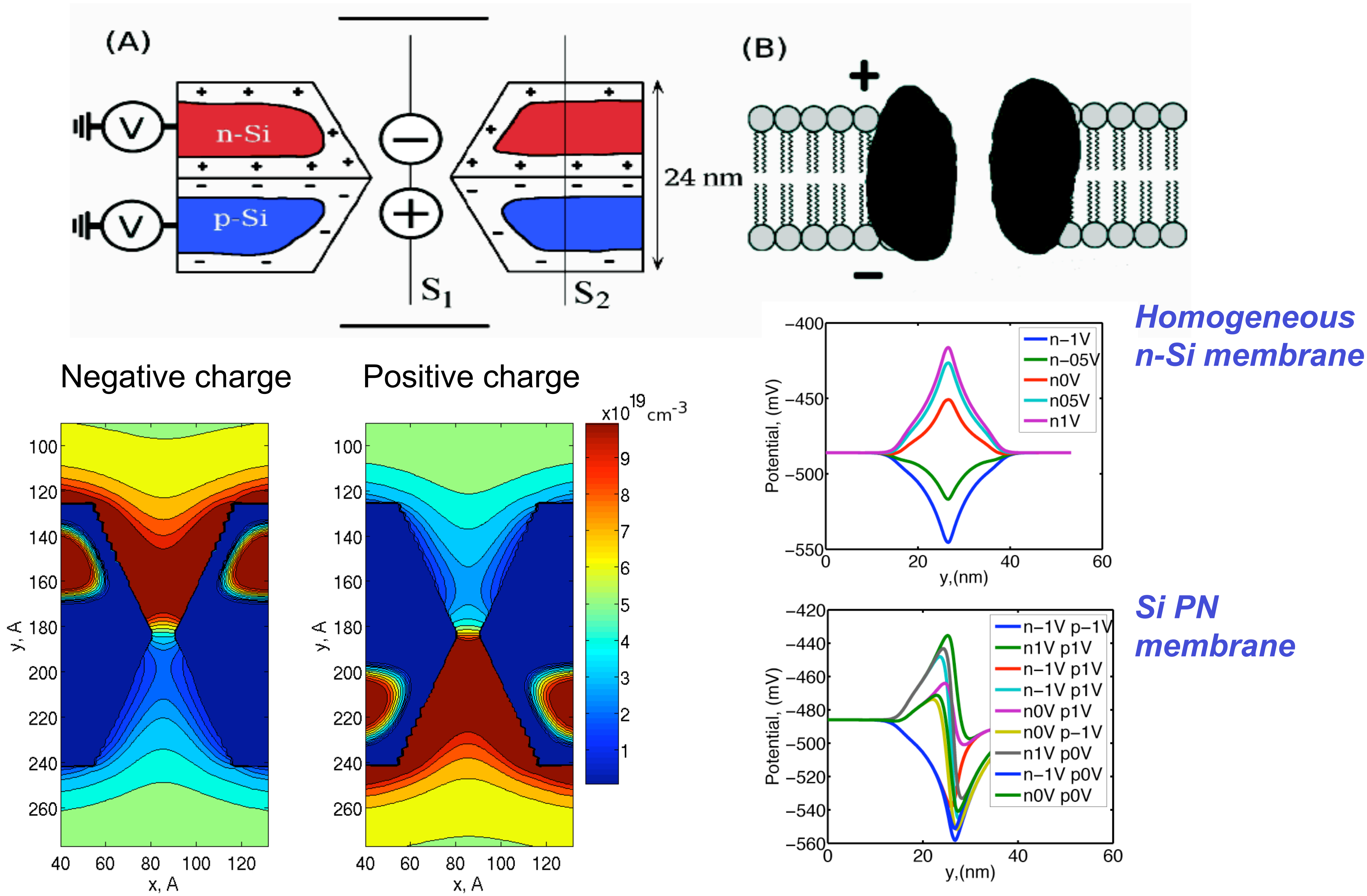


R. Karnik et al. Nanolett, 7, 547 (2007)



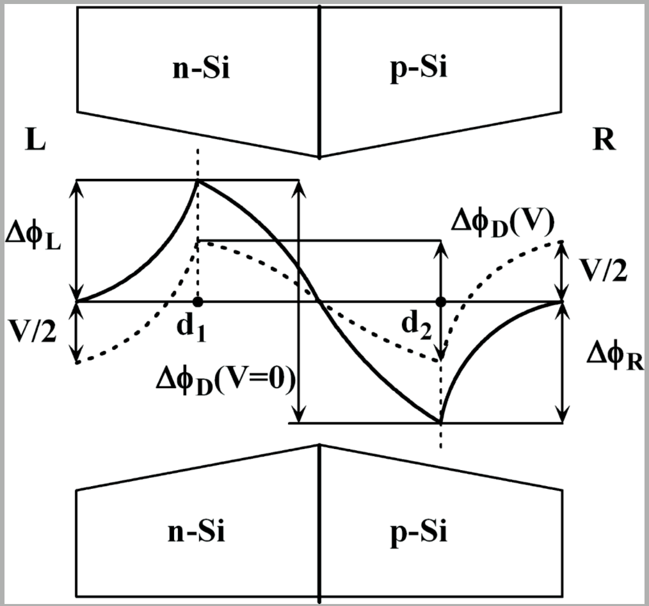
I. Vlassiouk et al. Nanolett, 7, 552 (2007)

P-N Semiconductor Membrane



Gracheva et al., Nano Letters 7, 1717-1722 (2007)

Ionic Transport Model



Total ionic current:

$$I = \pi r^2 \sum_i z_i J_i$$

Ionic fluxes*:

$$J_i = -D_i \frac{dc_i}{dx} - z_i D_i c_i \frac{F}{RT}\frac{d\phi}{dx}$$

$$J_i = \frac{z_i F}{RT}\frac{D_i \Delta\phi_D}{(d_2 - d_1)}\left[\frac{c_i(d_i)\exp(-z_i F\Delta\phi_D / RT) - c_i(d_2)}{1 - \exp(-z_i F\Delta\phi_D / RT)}\right]$$

Constant field approximation on segment (d_1;d_2):

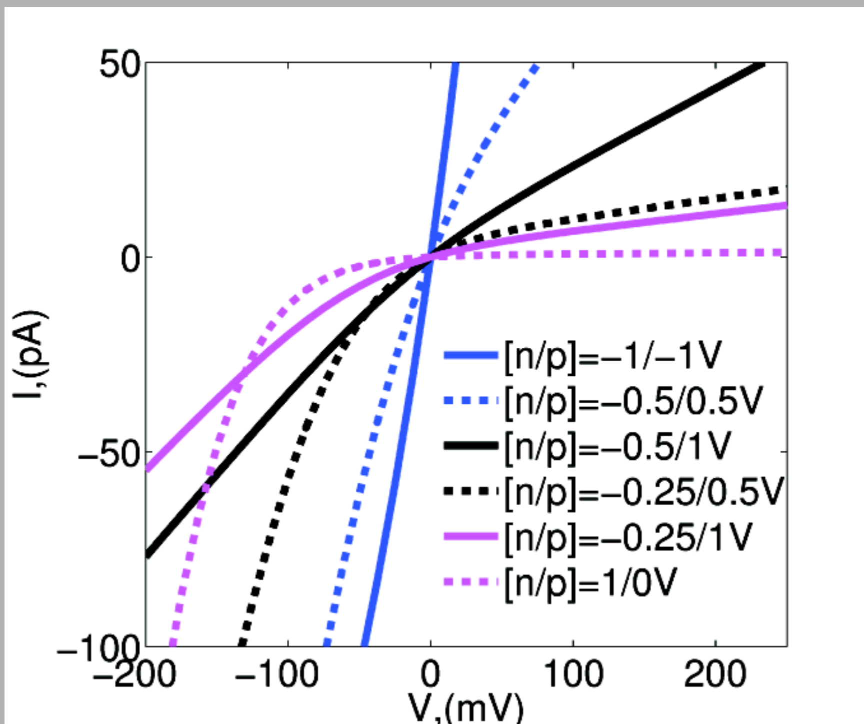
$$c_i(d_1) = c_{i,L}\exp(-z_i F\Delta\phi_L / RT)$$
$$c_i(d_2) = c_{i,R}\exp(-z_i F\Delta\phi_R / RT)$$

$$V = -(\Delta\phi_L(V) + \Delta\phi_D(V) + \Delta\phi_R(V))$$
$$\Delta\phi_D(V) = \Delta\phi_D(V=0) - V$$ ←assume

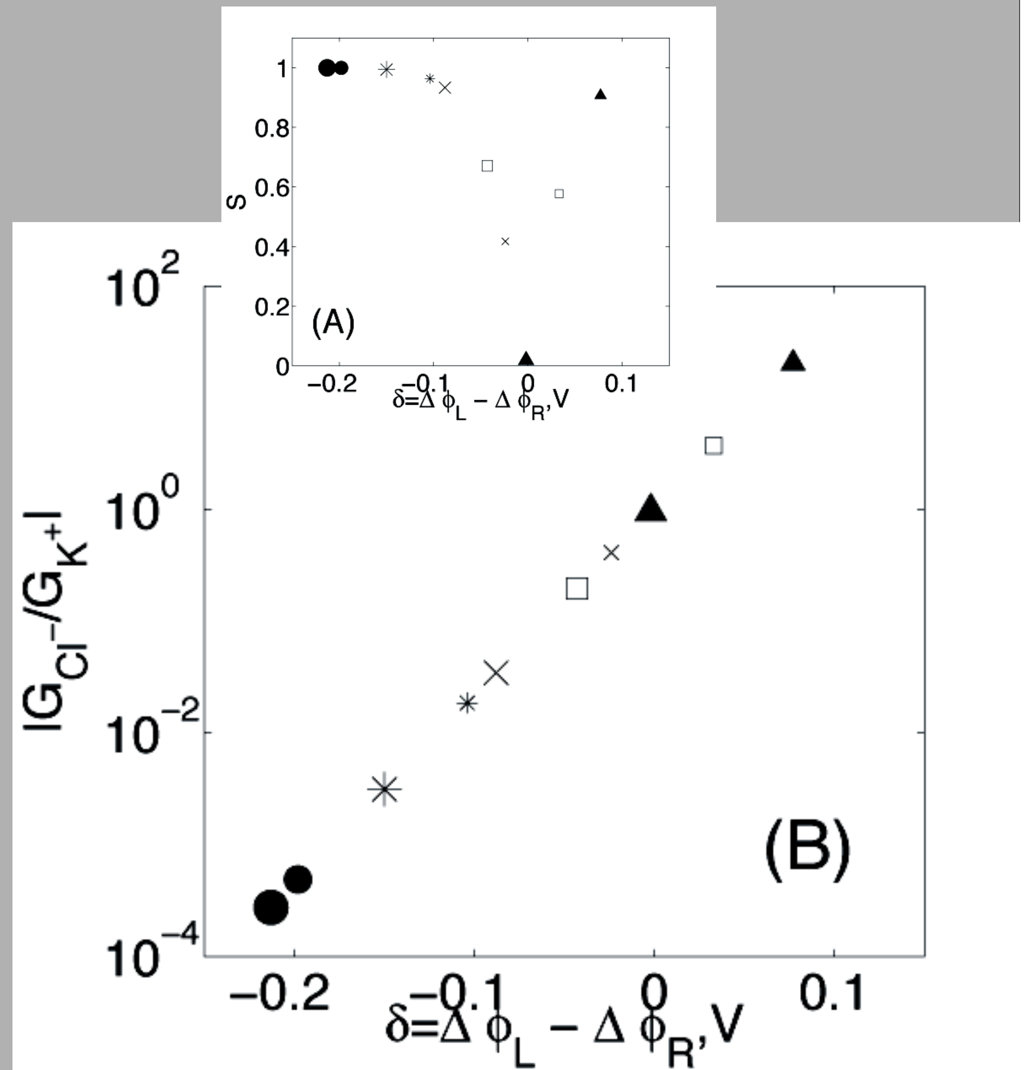
*After Ramírez et al., Phys. Rev. E 68, 011910(1)-011910(8) (2003)

Tunable Rectification and Ion Filtering

Rectification



Ion selectivity



Future: fast DNA sequencing?

- Nano-bio-electronic scheme for DNA sequencing
- Integrated multi-scale MD-Self consistent Poisson approach.
- Individual bases electrically detectable, BUT noise and conformation analysis!!!
- Electrical tunability of semiconductor membranes for double layer control.
- PN membranes for tunable rectification and ionic filtering.