Semiconductor Nano-Pores Tunability for DNA Sequencing*

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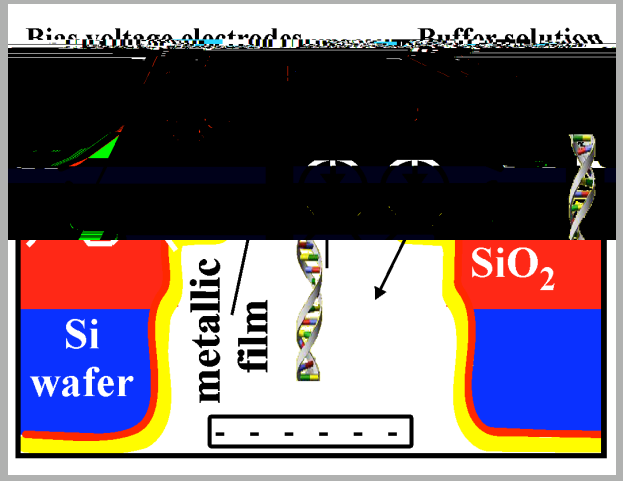
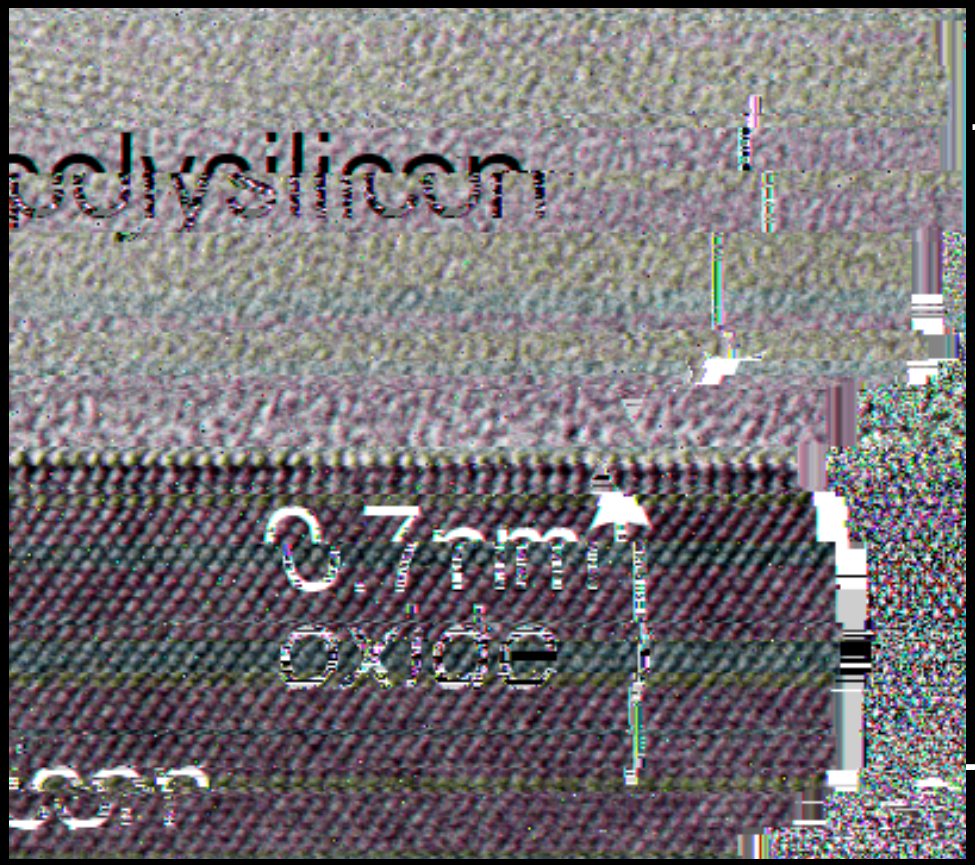


*Work done in collaboration with M Gracheva, A. Aksimentev and G. Timp and supported by NIRT-NSF and NIH

T - O -

- - T - EOB

•ultra-thin membranes



TEM X-section through a gate

Deamer, Branton, Kasianowicz
Golovchenko
Martin

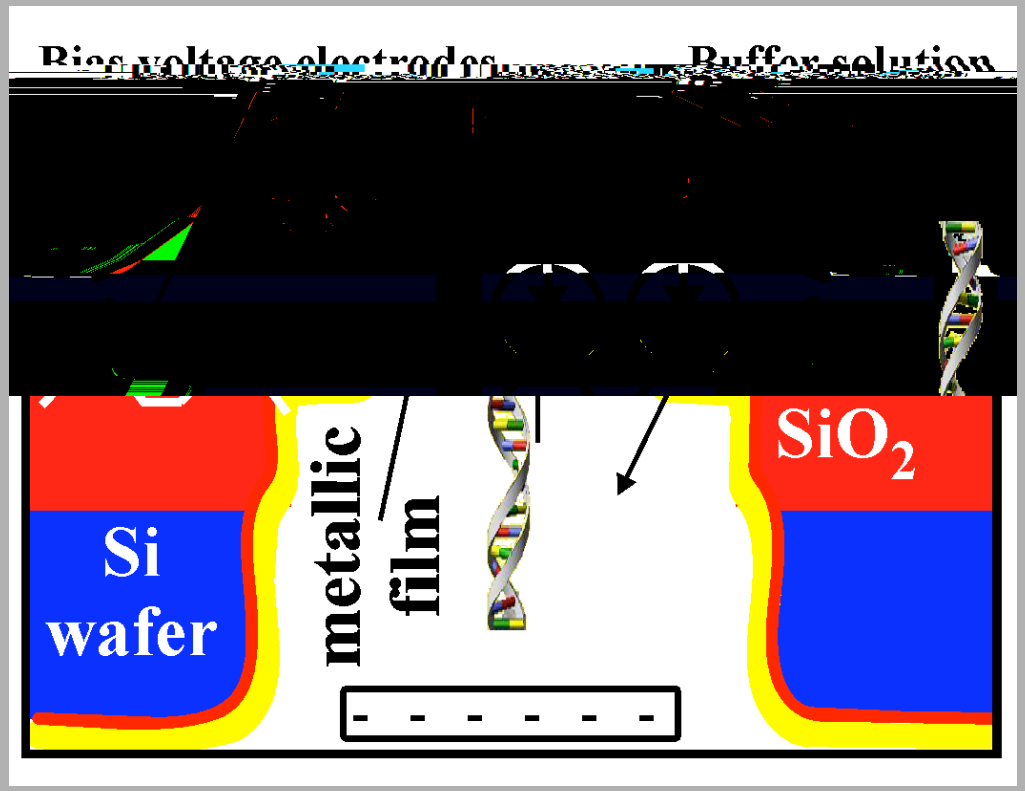
•sub-nm(sub Å Batson) bright e-beam for lithography

EOB

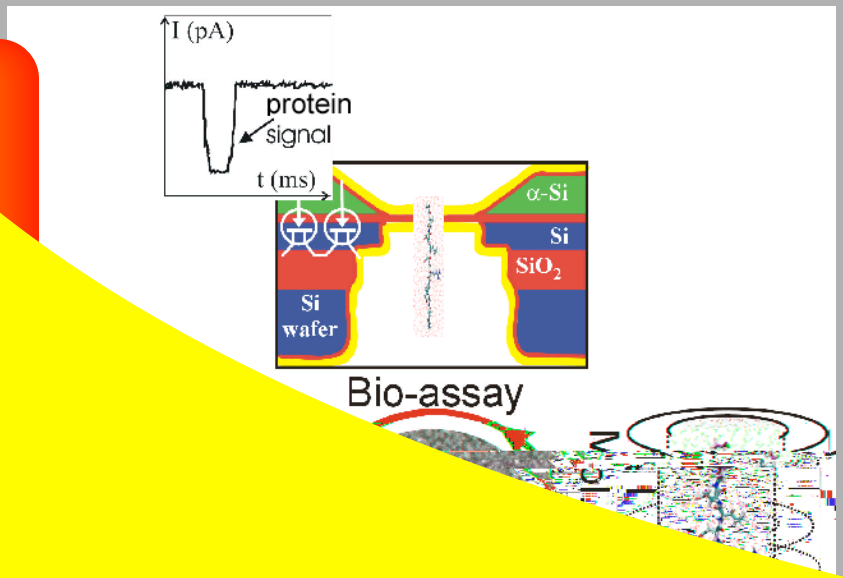
TEM (top-down projection)

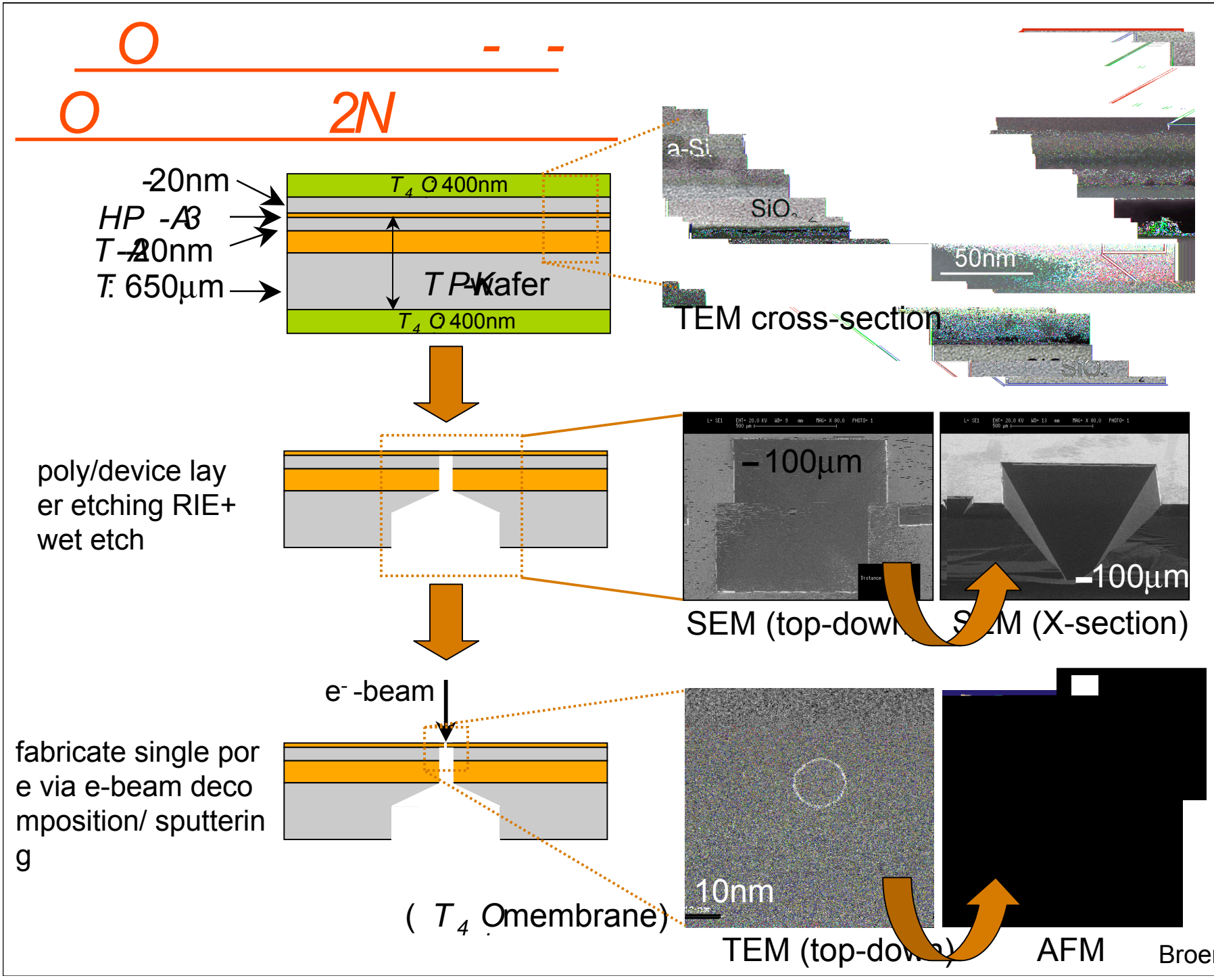
A Challenge:

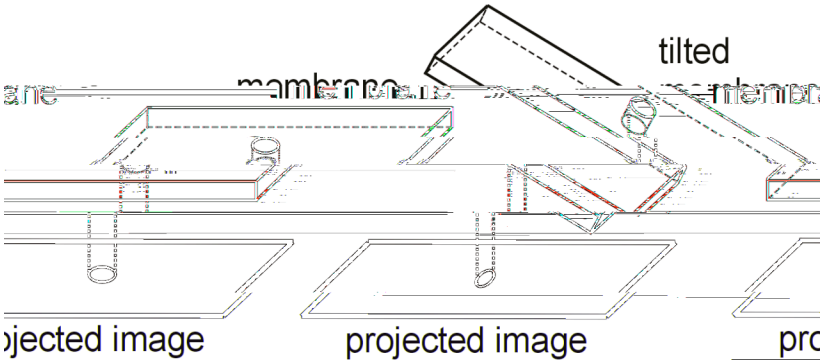
Electronic Detection of DNA Molecular Sequences



Merging Biology and Nano-Electronics: An Integrated Approach.




O
- -
O
2N
-20nm
HP -A3
T-A20nm
T: 650µm
T 4 O 400nm
T PAKafer
T 4 O 400nm
a-Si
SiO2
50nm
TEM cross-section
poly/device lay
er etching RIE+
wet etch
-100µm
-100µm
SEM (top-down)
SEM (X-section)
e- -beam
fabricate single por
e via e-beam deco
mposition/ sputterin
g
(T 4 Omembrane)
10nm
TEM (top-down)
AFM
Broers et al



O -

O - -TEM

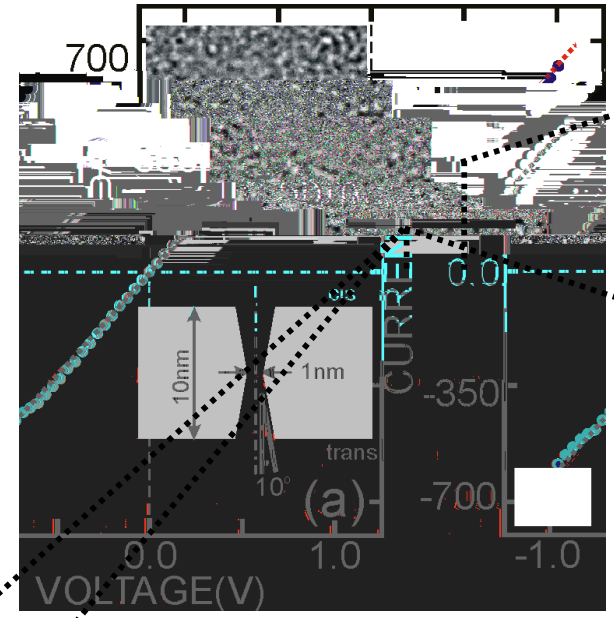
(artificial nanopore in T_4 O membrane)

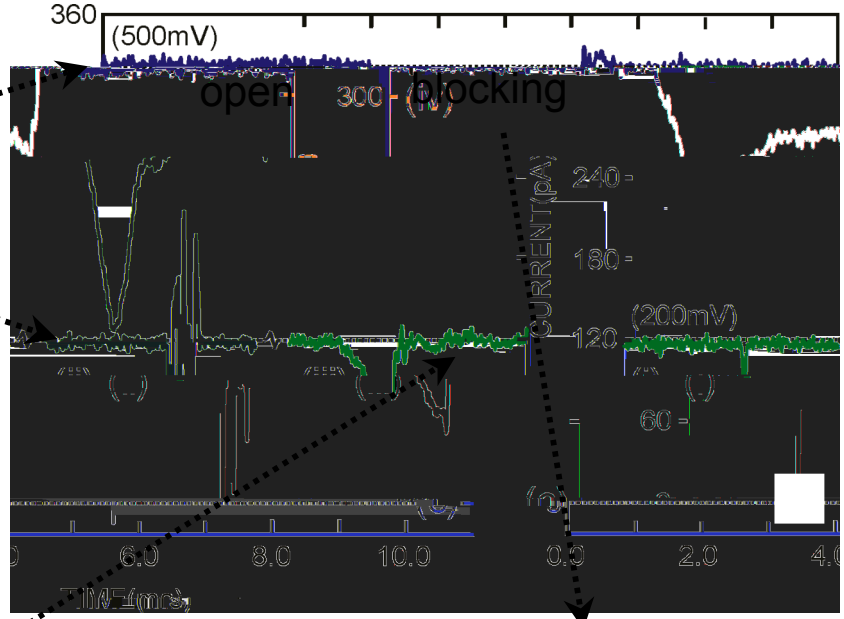
schematic

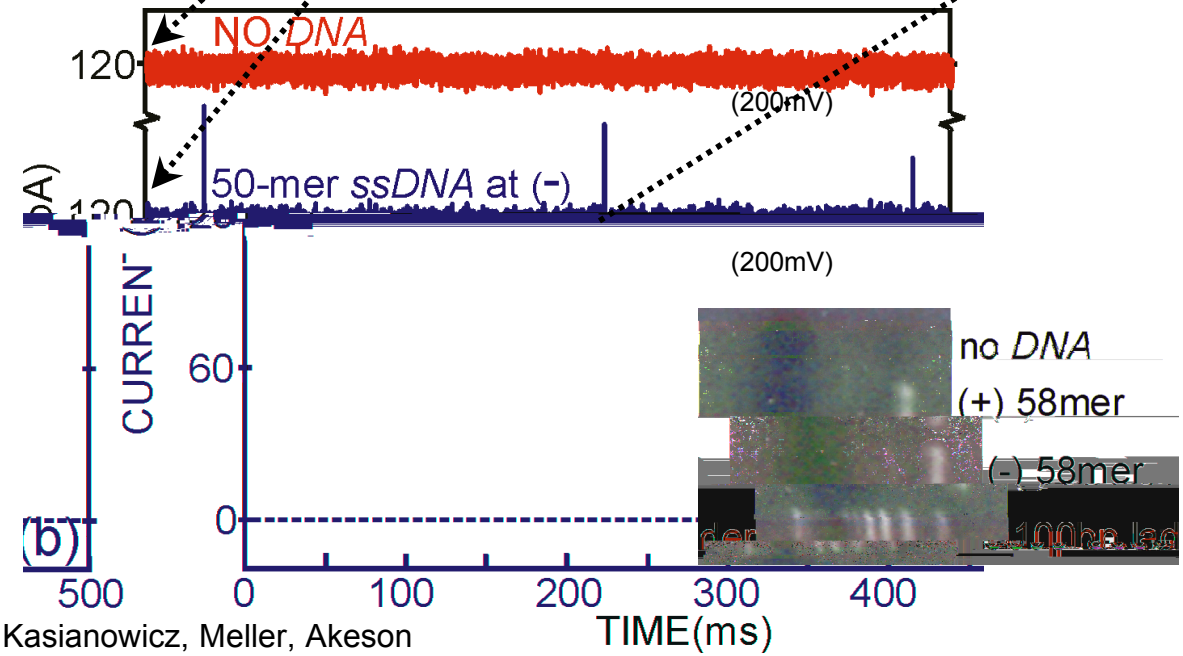
• artificial nanopores have a non-uniform cross-section

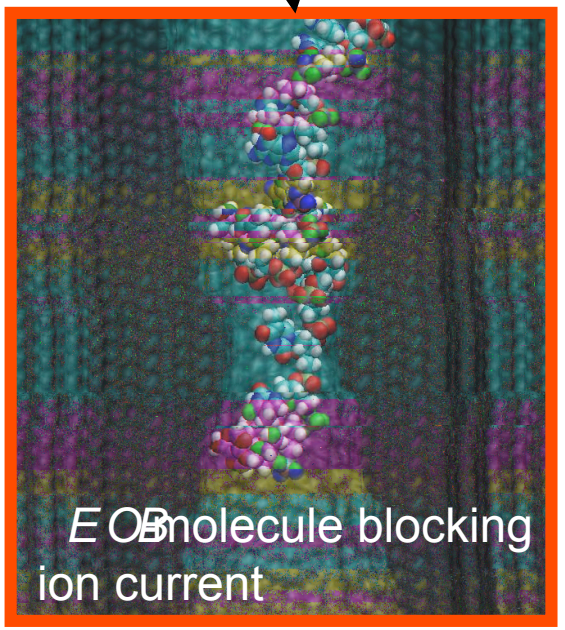
EOBV - - - O

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









Kasianowicz, Meller, Akeson

T - EOB

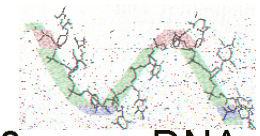
(measurements using a ~1nm diameter nanopore as a stochastic sensor)

50mer- EOB poly(dT) 0.34nm/nucleotide

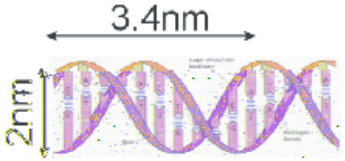
50mer=17nm p~4nm(persistence)

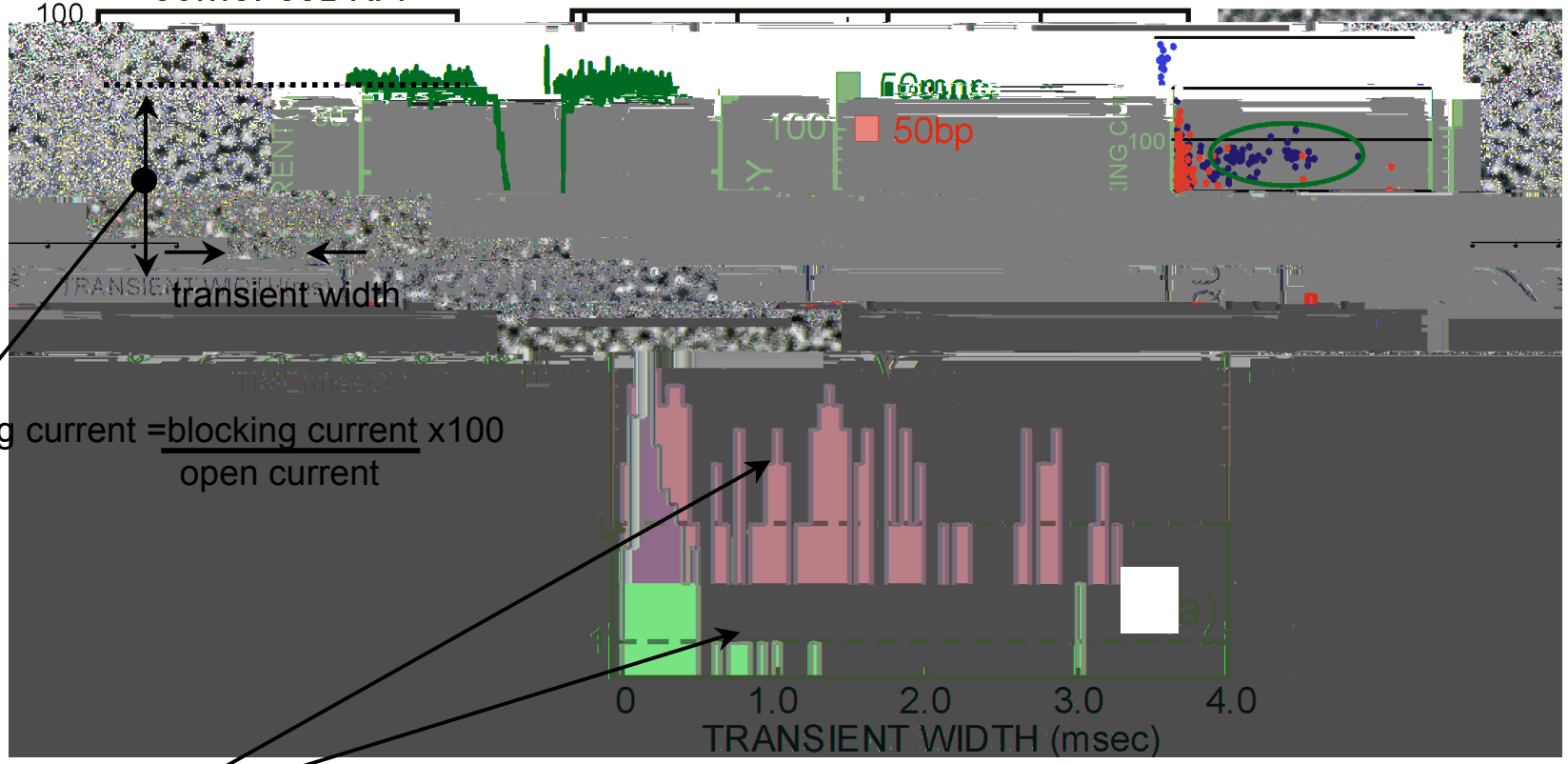
50bp ds EOB 0.34nm/bp

50bp-17nm p~50nm

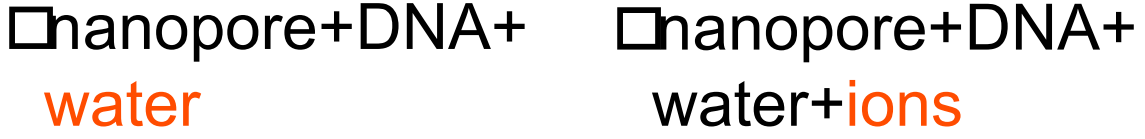


50mer ssDNA

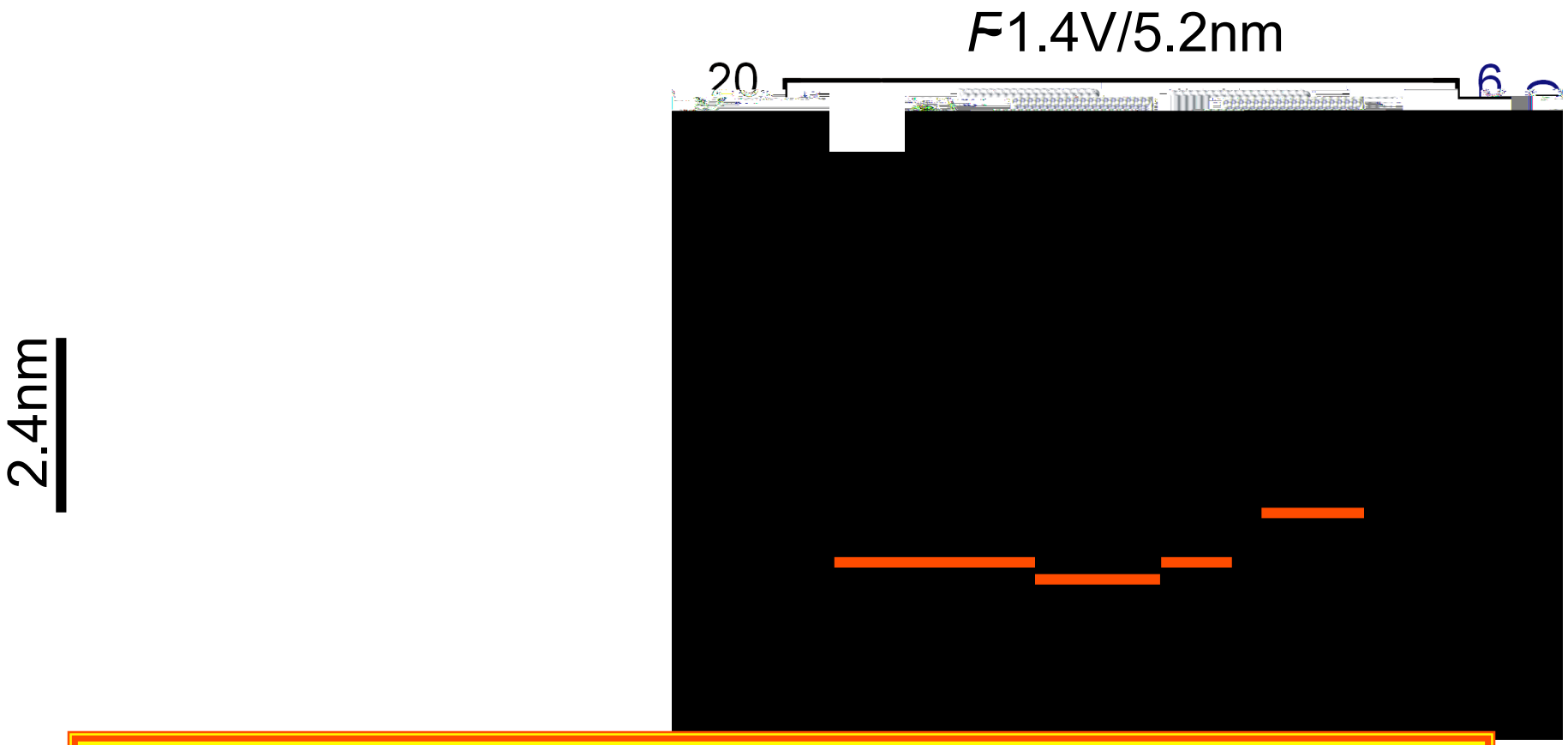




- distribution of transient widths may be used to discriminate between EOB2 EOB


nanopore+DNA+
water
nanopore+DNA+
water+ions

N - E - - EOB - - Si_3N_4 O



• translocation time: 10nsec-3µsec depending on field and pore interactions
• % blocking current correlated with molecular velocity
(• large fields cause the EOB to denature)

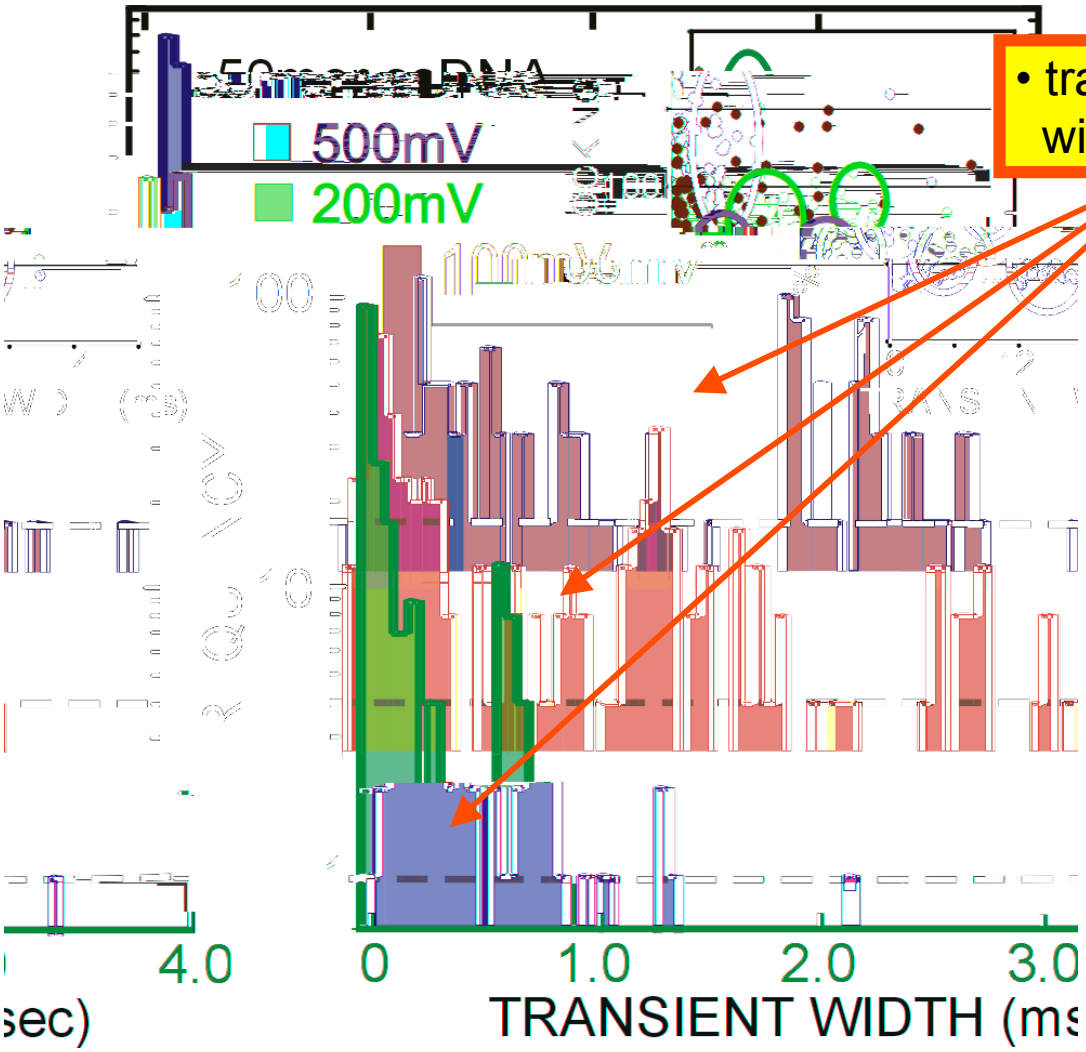
•Simulations: 1.4V/5.2nm → ~400pN
•DNA sequence is CCCCCCCCCCCCCCCCCCCC
•Only those ions that are within 1nm of either DNA or pore are shown; some ions may appear or disappear.

MIT - - BB

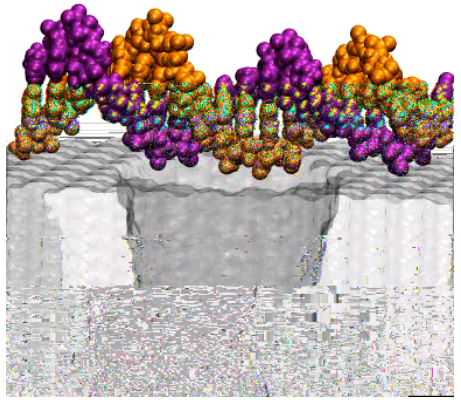
. - - C - D

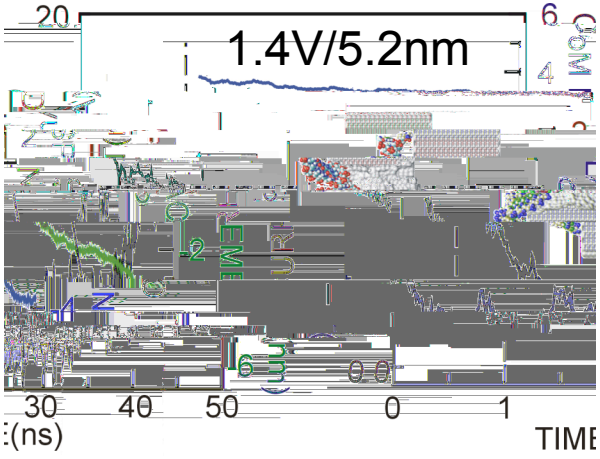
(measurements using a 1.5nm diameter pore in a 10nm thick T_4 O membrane)

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



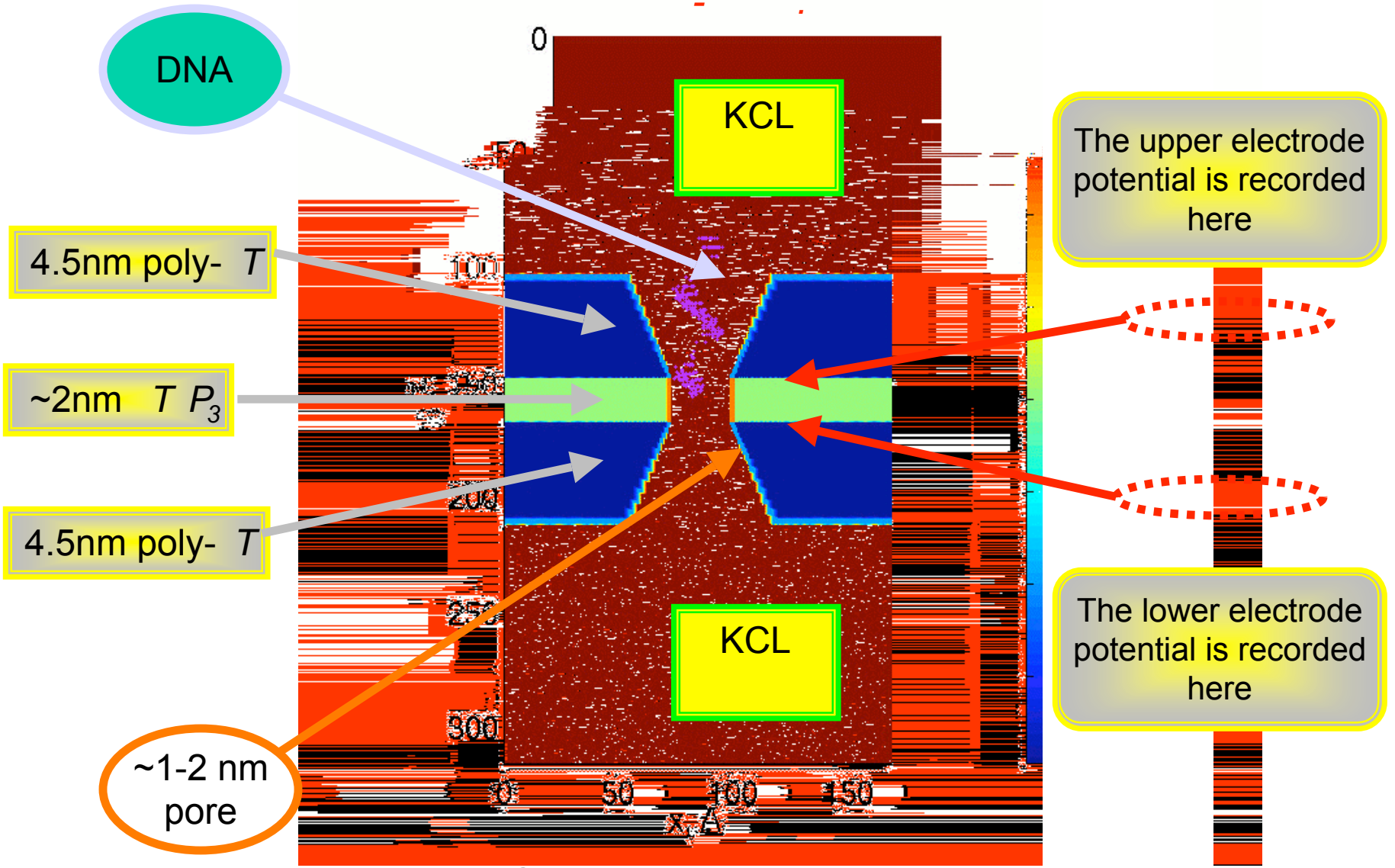
• transient width distribution broadens with increasing voltage





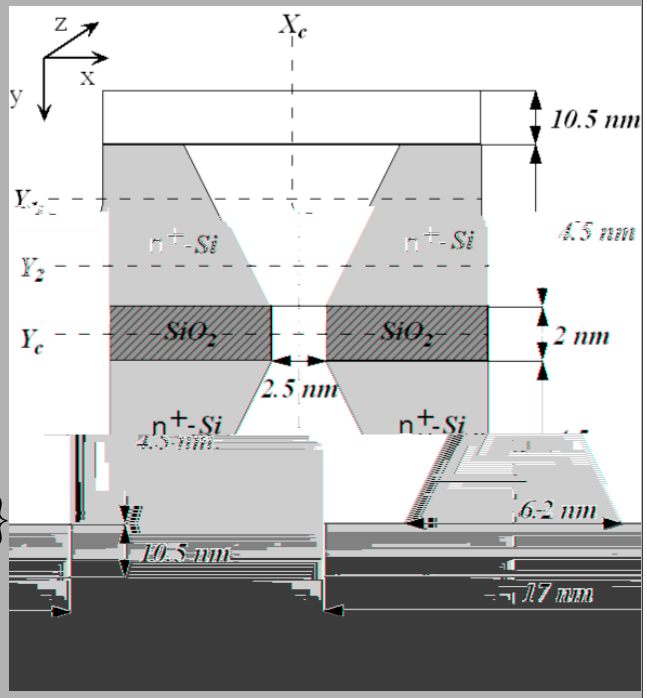
B B

The Electronic Device Aspect



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

Nanopore-Membrane Electrostatic Modeling



Poisson Equation:

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

Charge density:

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

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

$$n(\vec{\ })=N\ \frac{2}{\sqrt{\pi}}\ _{1/2}(\eta\ (\vec{\ }))$$

$$_c(\vec{r})=\frac{E_f\ !\ E_c(\vec{r})}{kT}$$

$$p(\vec{\ })=N\ \frac{2}{\sqrt{\pi}}\ _{1/2}(\eta\ (\vec{\ }))$$

$$_v(\vec{r})=\frac{E_v(\vec{r})\ !\ E_f}{kT}$$

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

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

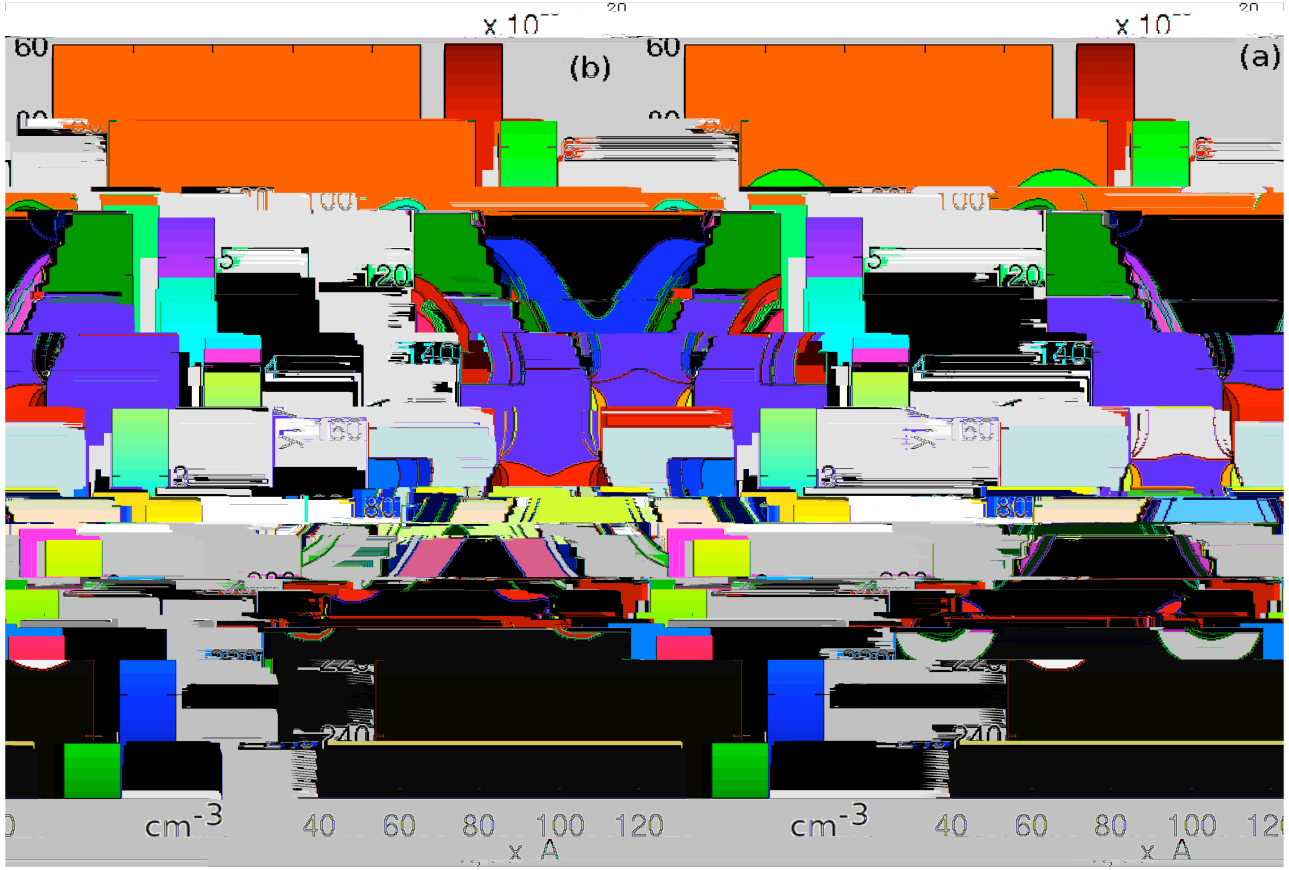
$$[K^+]_0=[Cl^-]_0=c$$

$$(\vec{\ })=-\ \phi(\vec{\ })-$$

$$(\vec{\ })=-\ \phi(\vec{\ })$$

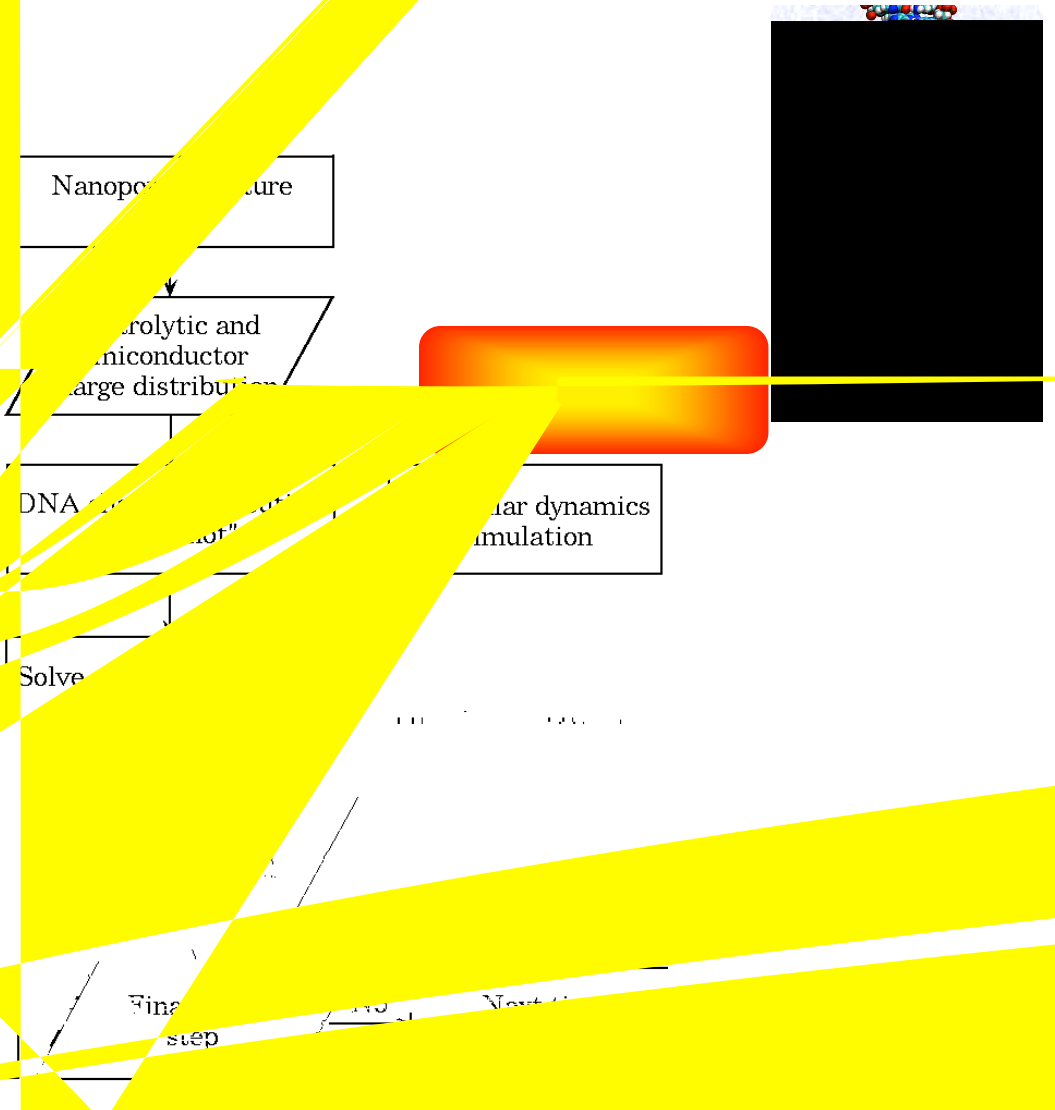
Gracheva et al., Nanotechnology 17, 622-633 (2006)

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

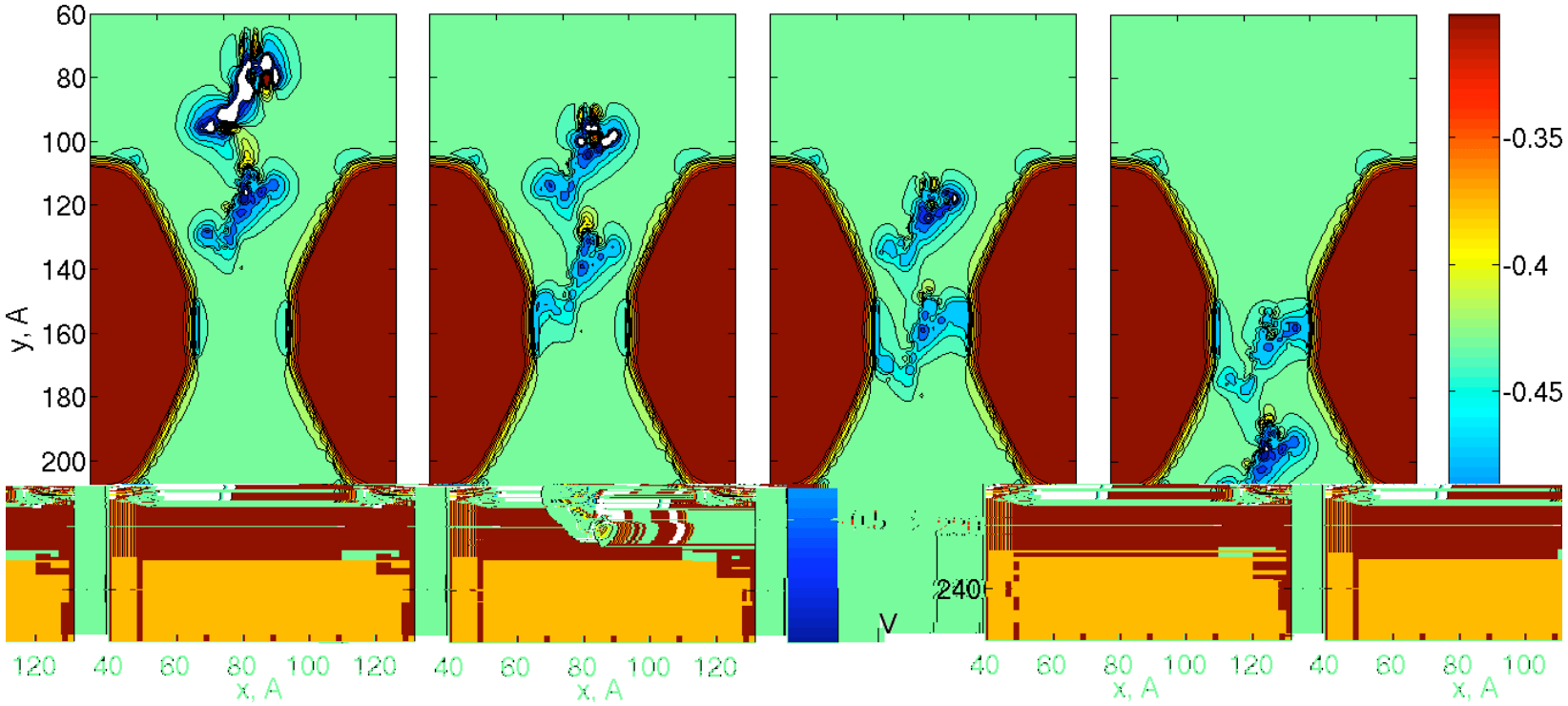


Multi-Scale “Consistent” Poisson Solver

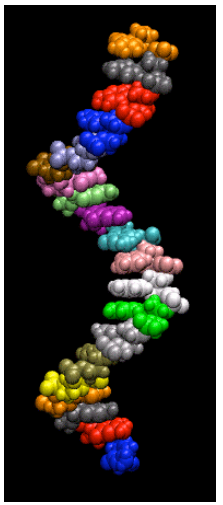
(using interaction with “snapshots” provided by MD)



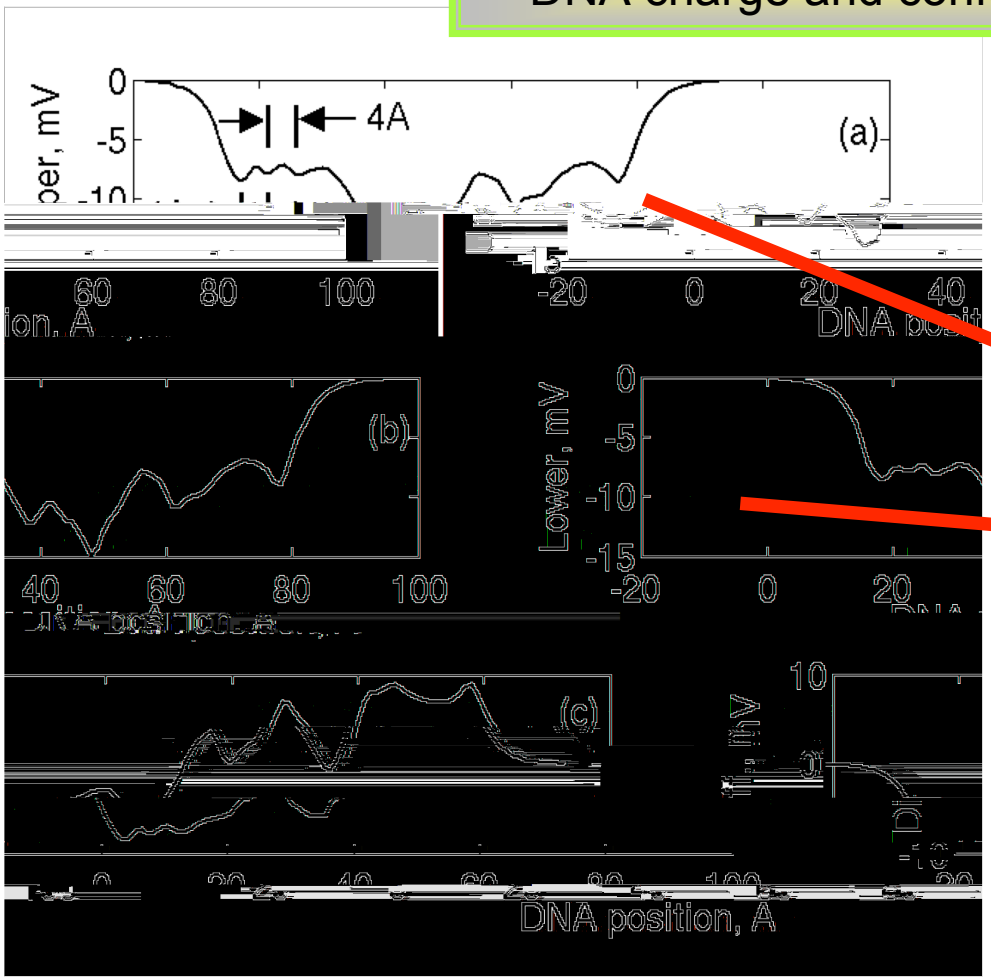
Simulation of ssDNA Translocation Through a 2.5nm Nanopore



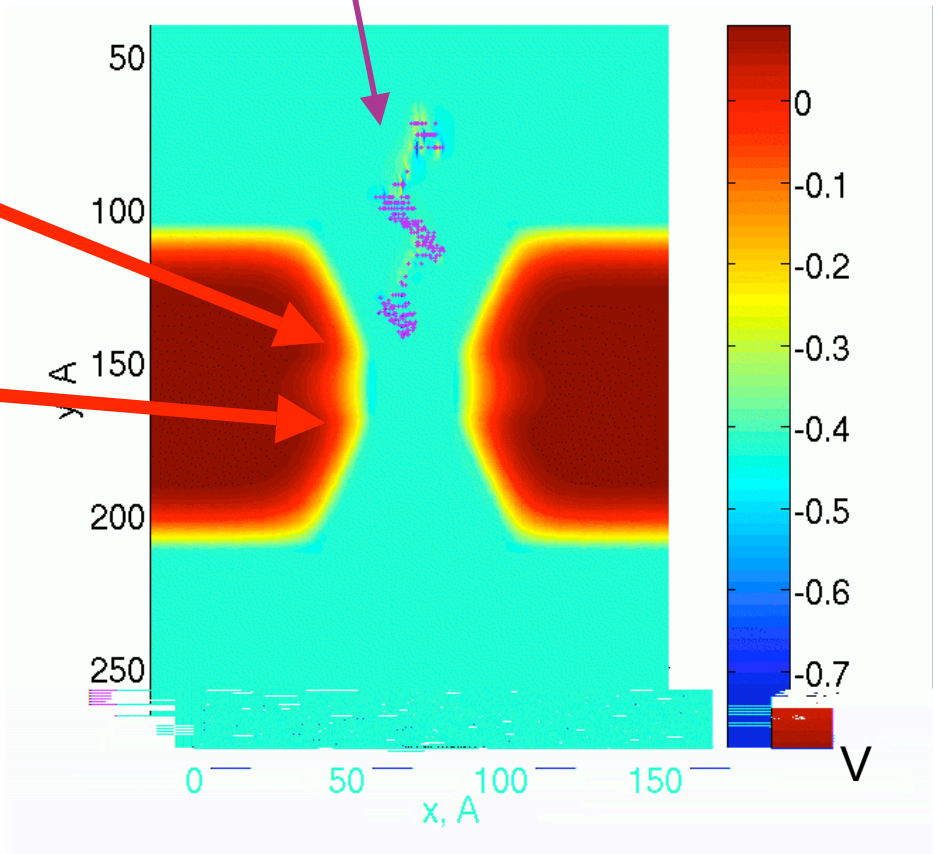
Simulation of unstretched ssDNA Translocation Through a 2.5 nm Nanopore



Electrode Voltage is sensitive to DNA charge and conformation

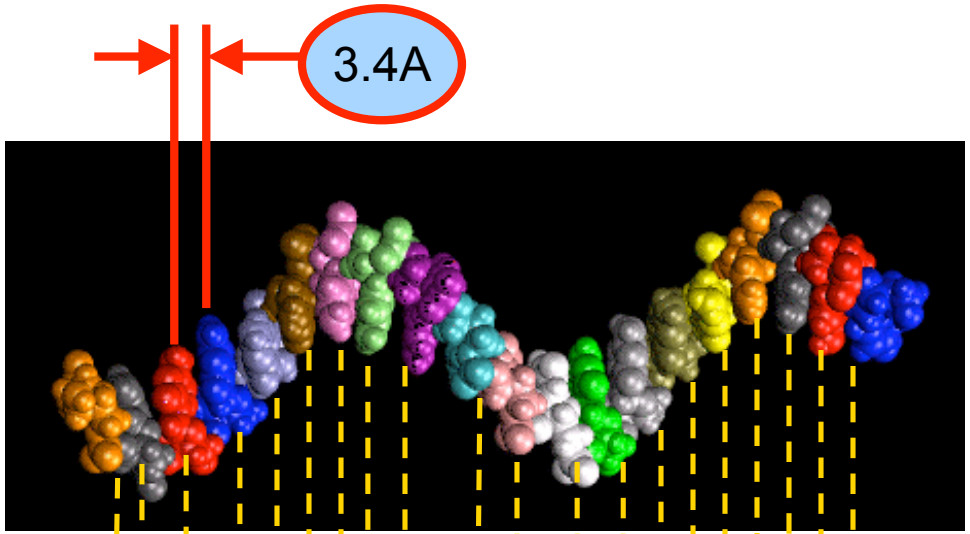


Poly-C20



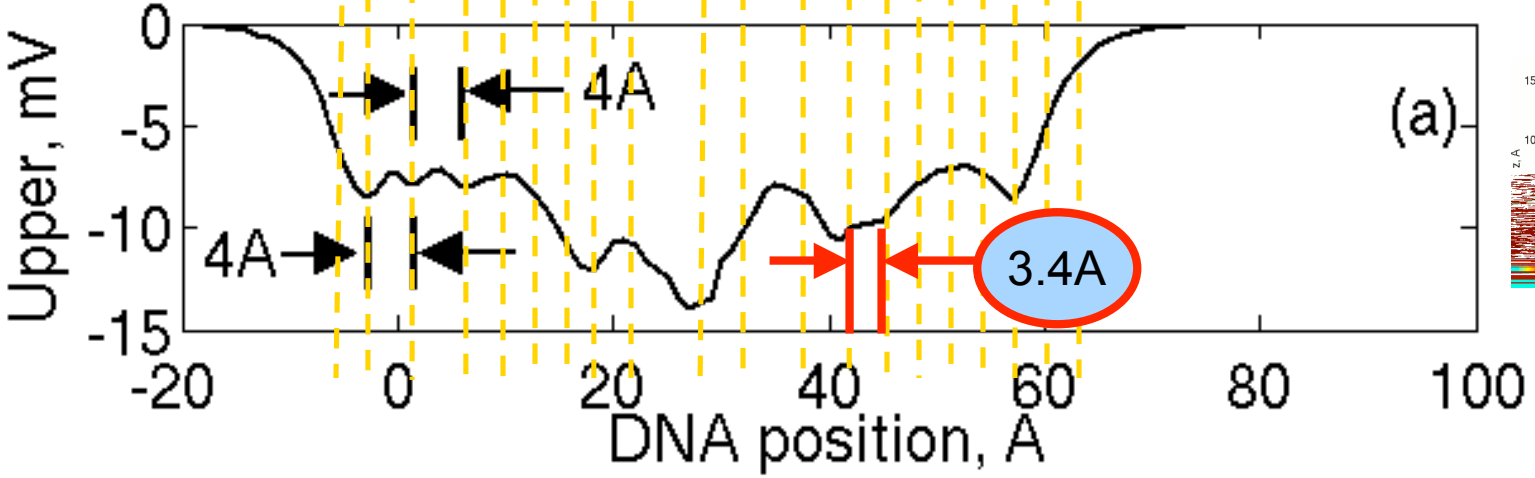
Decoding DNA sequence and configuration

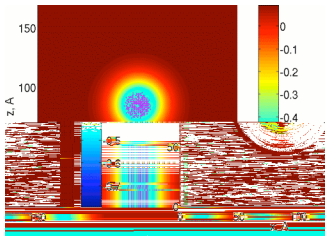
DNA sequence: C-C-C-C-C-C-C-C-C-C-C-C-C-C-C-C-C-C-C-C (ssDNA polyC20)



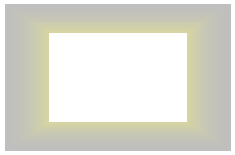
Voltage trace:
- length of the DNA
- features ~3.4 A apart

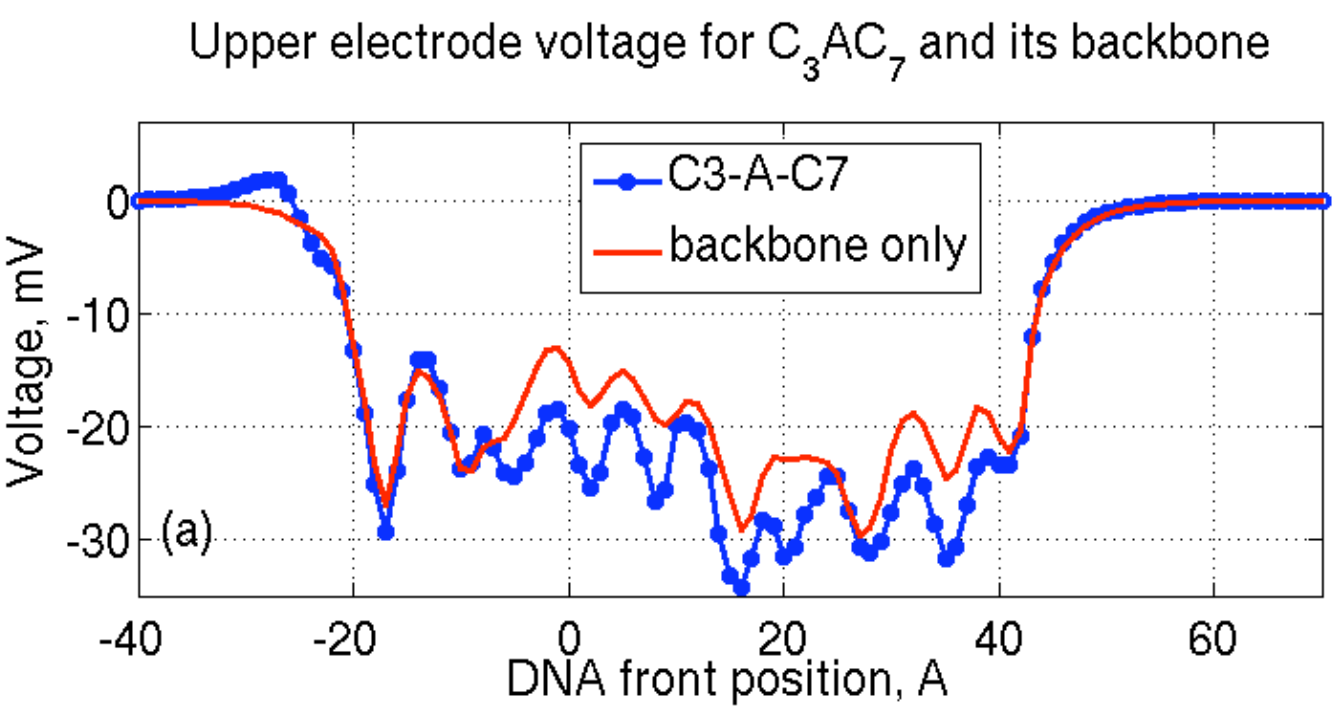
- base composition (ACGT)
- DNA conformation

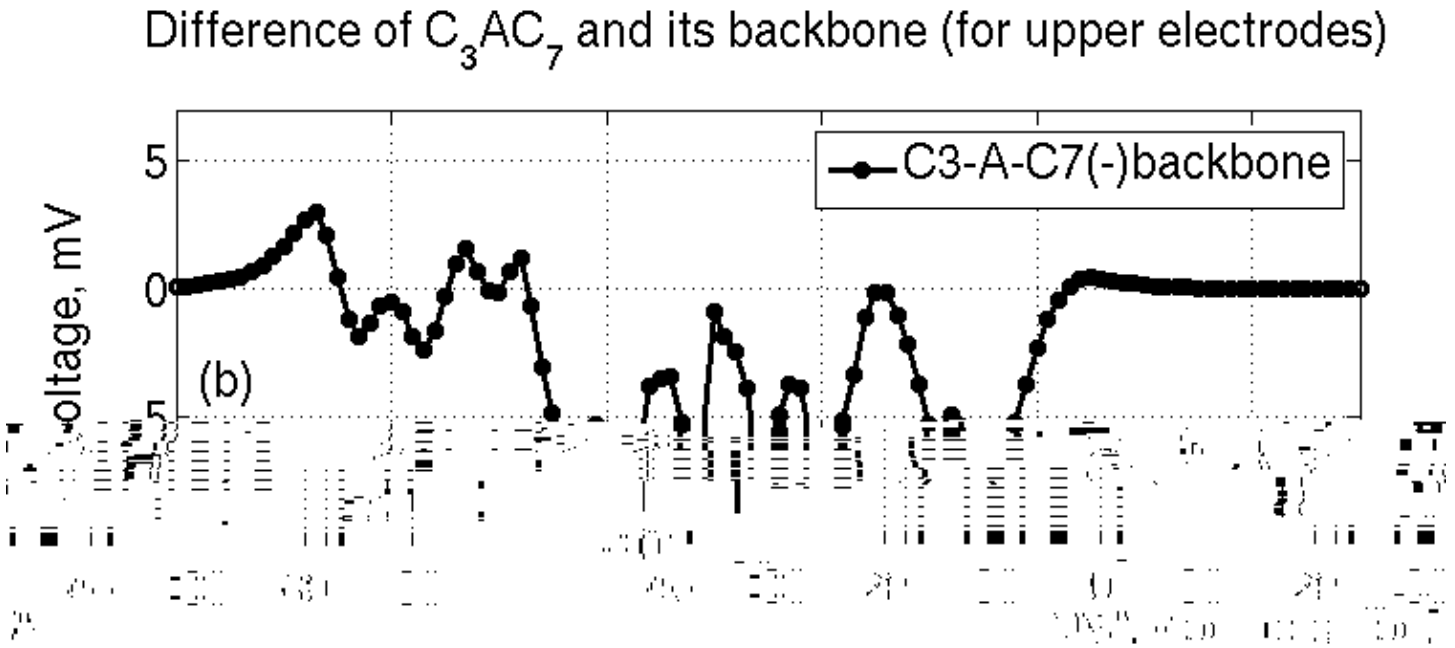




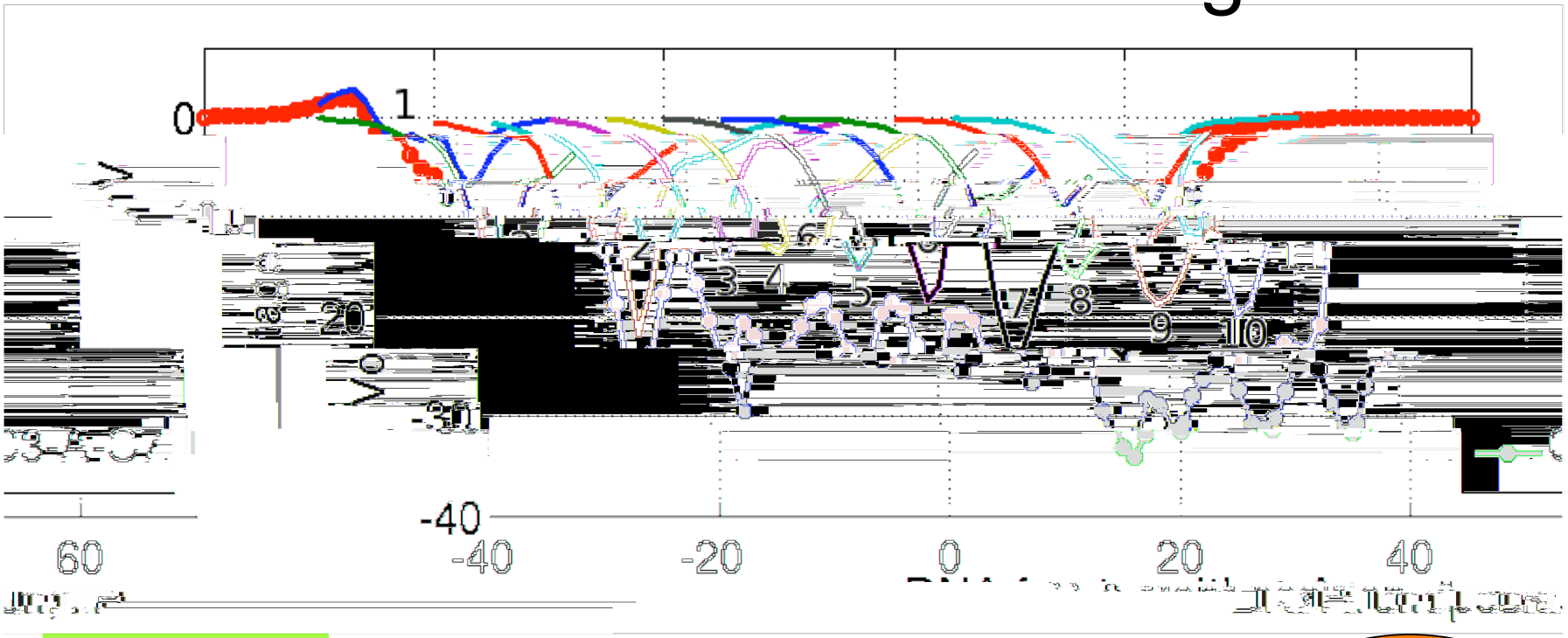
Simulation of Stretched ssDNA Translocation Through a 1.0nm Nanopore



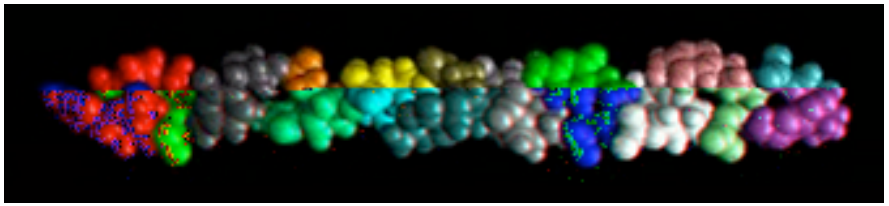

Upper electrode voltage for C_3AC_7 and its backbone
C3-A-C7
backbone only
Voltage, mV
0
-10
-20
-30
(a)
-40
-20
0
20
40
60
DNA front position, A


Difference of C_3AC_7 and its backbone (for upper electrodes)
C3-A-C7(-)backbone
oltage, mV
5
0
(b)

The whole DNA translocation and translocation of the eleven fragments

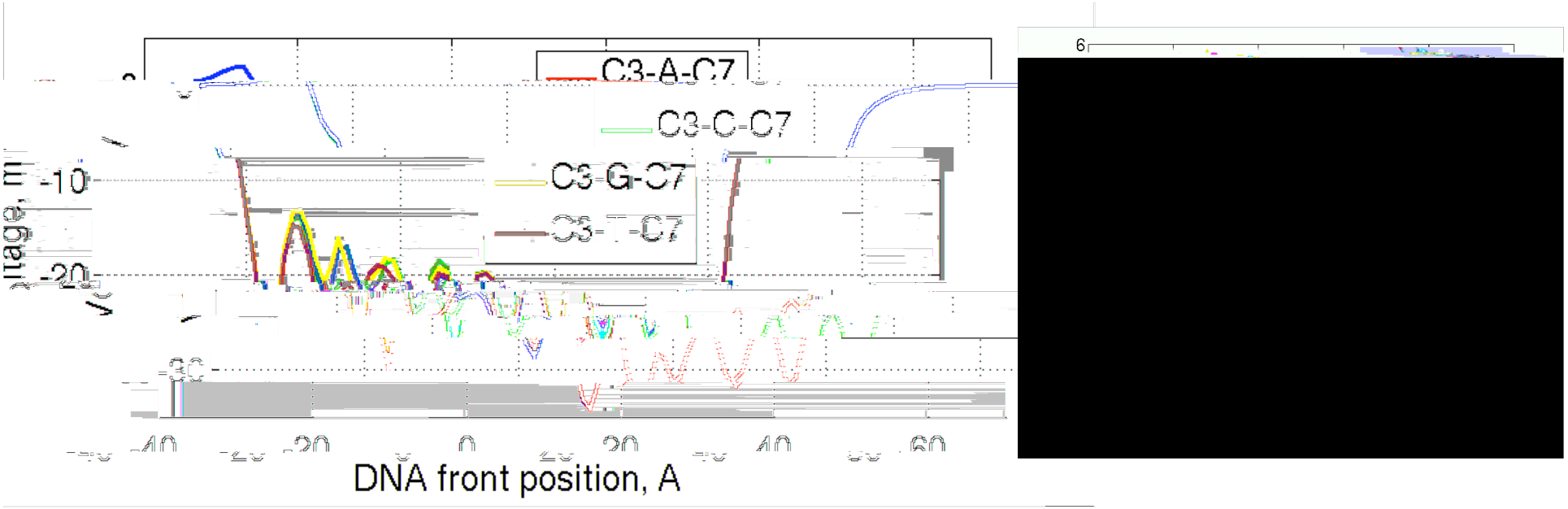


C3-A-C7 and 11 backbone segments with bases



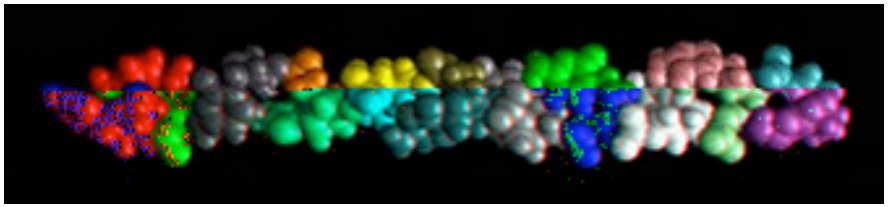
Look how wide the signal of one base can be!!!

The whole DNA translocation with one base mutation



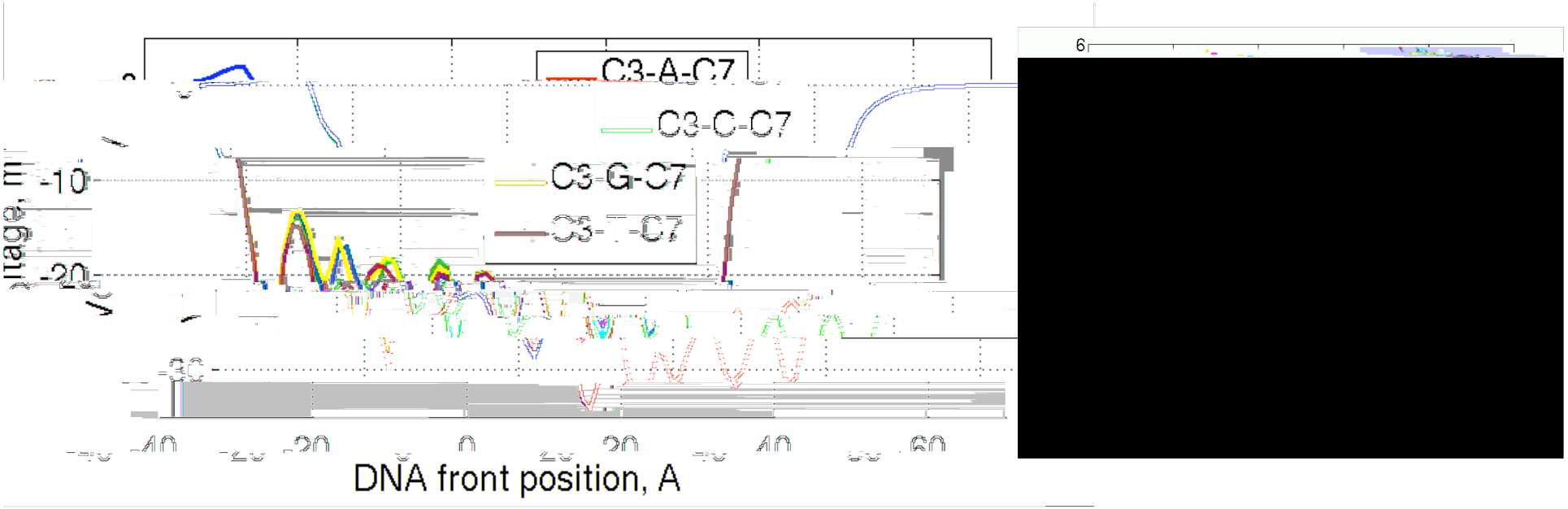
Mutated base #4

In the same conformation!!!



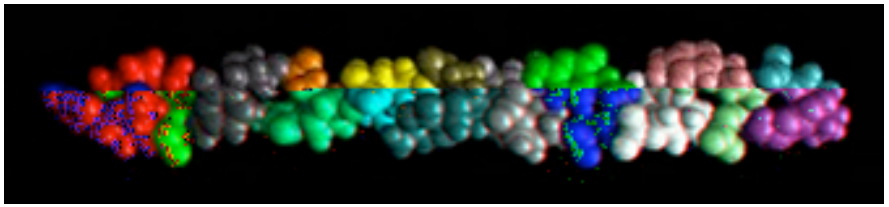
The signal difference is localized in the vicinity of base #4

The whole DNA translocation with one base mutation



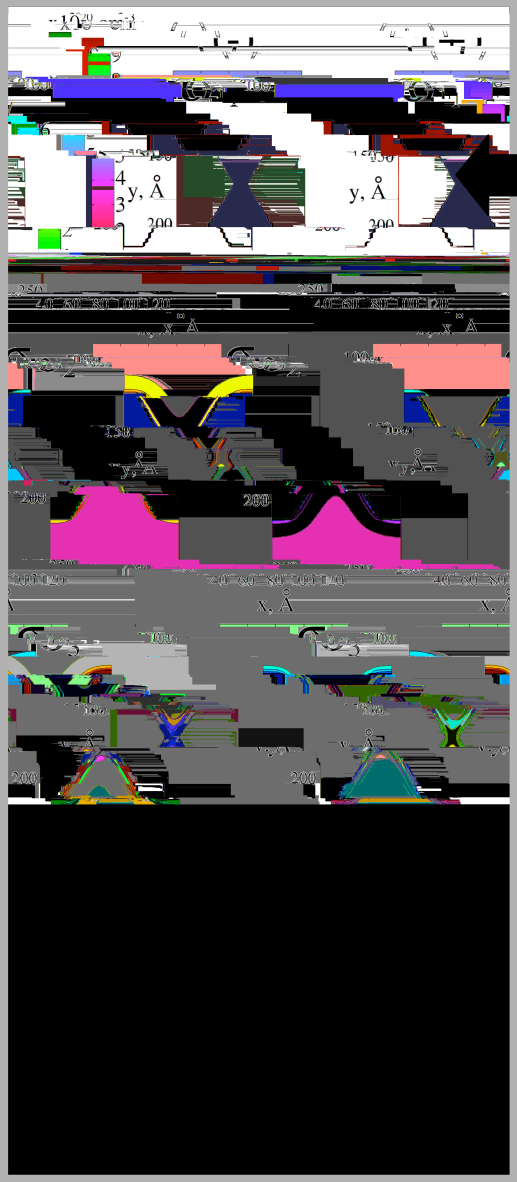
Mutated base #4

In the same conformation!!!



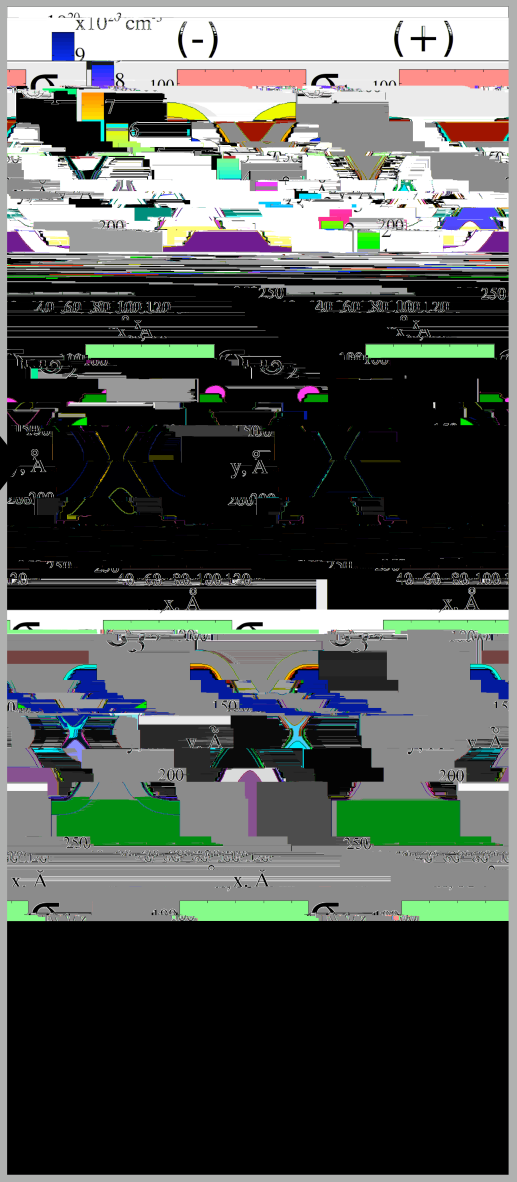
The signal difference is localized in the vicinity of base #4

Semiconductor Membrane: Double Layer Engineering



SiO_2: dielectric material
no carriers of either sign

n+-Si: heavily doped Si semiconductor material
Fixed positive charge
$N_d^+ = 2 \times 10^{20}$ cm^{-3},
electrons, some holes

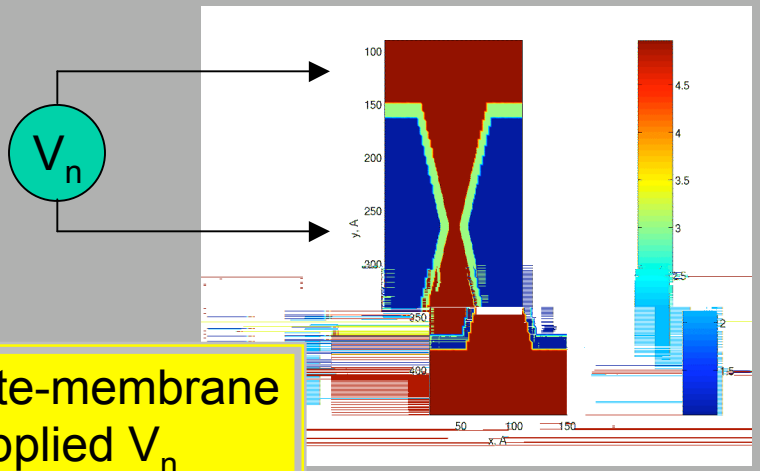


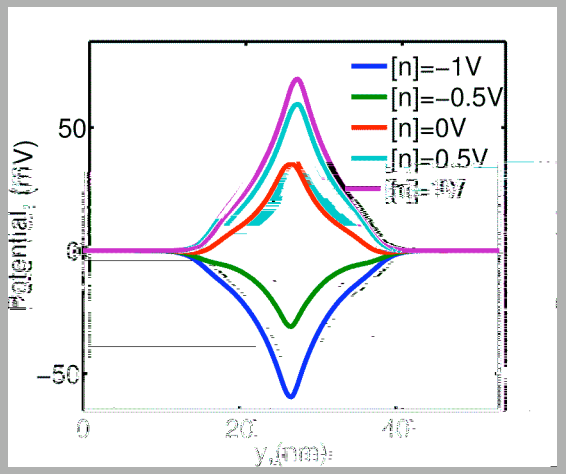
Surface charge:
$\sigma_1 = 0$
$\sigma_2 = -0.0064$ Cm^{-2}
$\sigma_3 = -0.019$ Cm^{-2}
$\sigma_4 = -0.032$ Cm^{-2}

[KCl]=1M

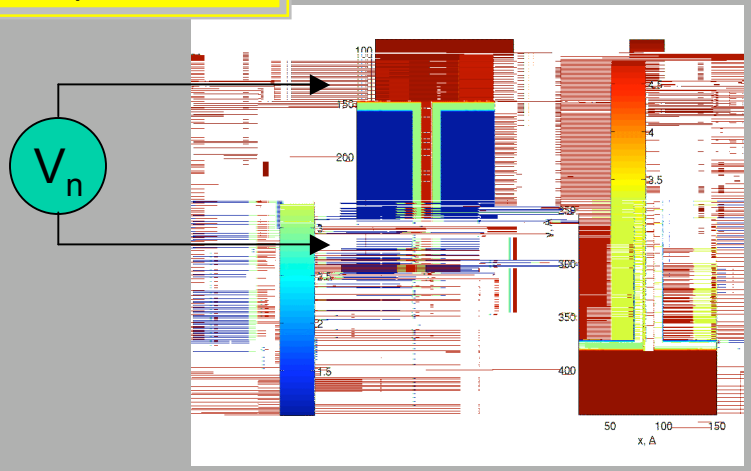
Gracheva & Leburton
Nanotechnology 18, p.145704 (2007)

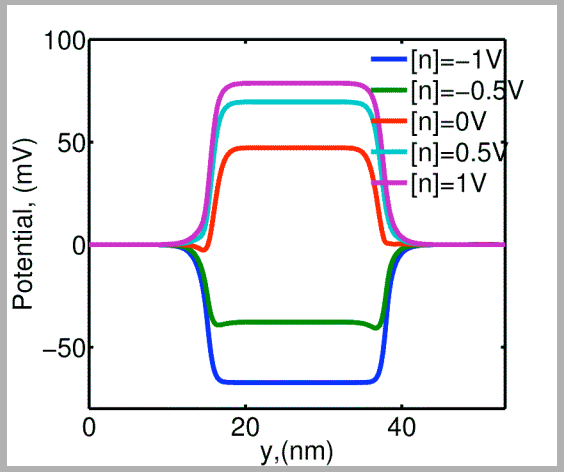
Semiconductor Membrane: Electrical Tunability





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

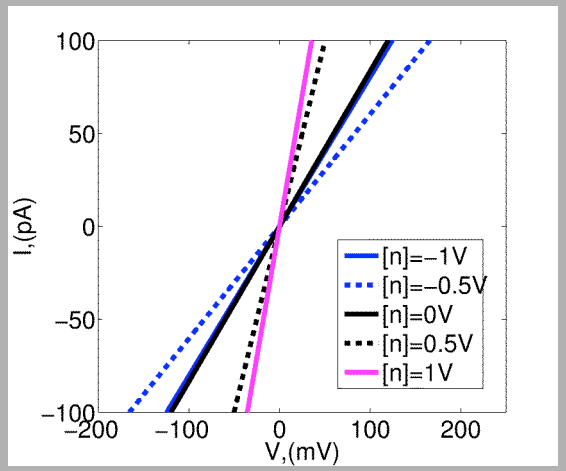


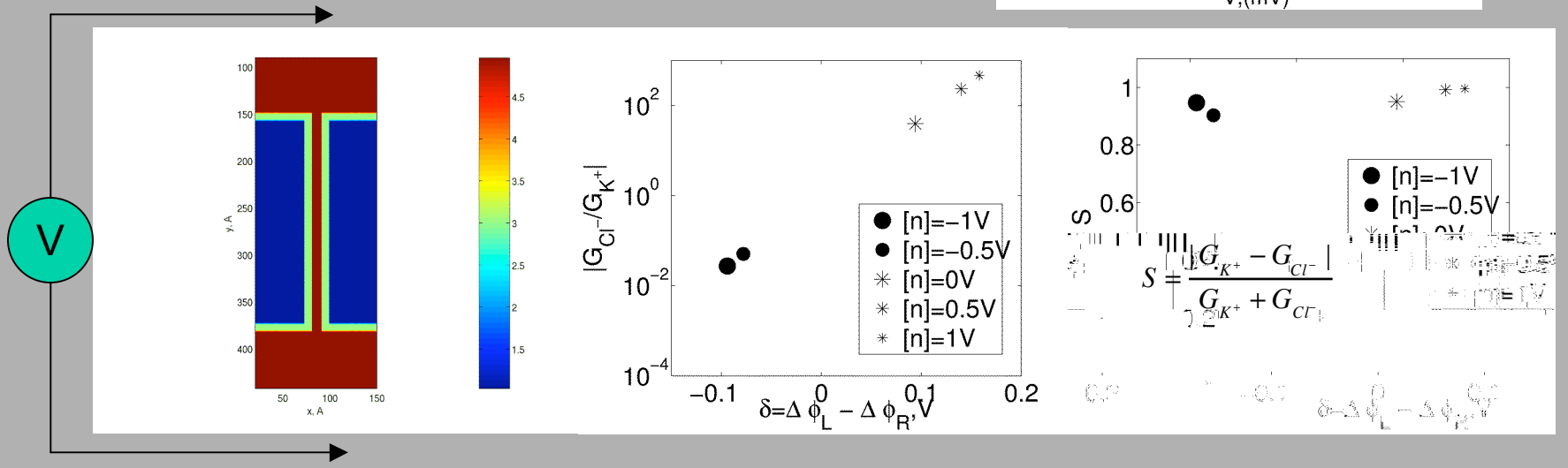


[KCl]=0.1M

Controlled Ionic Conductance & Filtering (Linear Response)

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

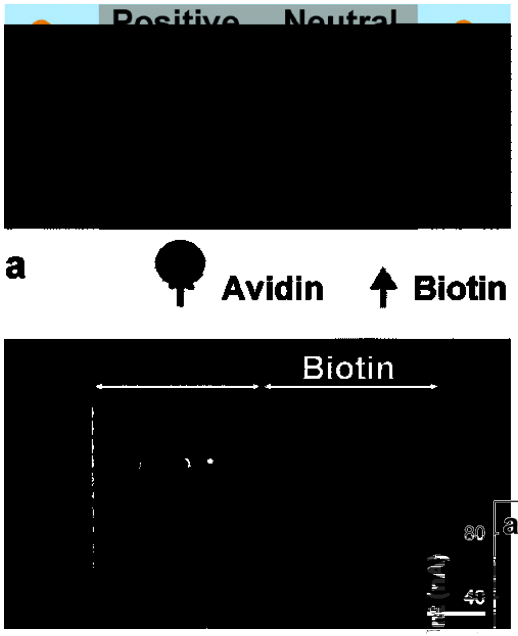


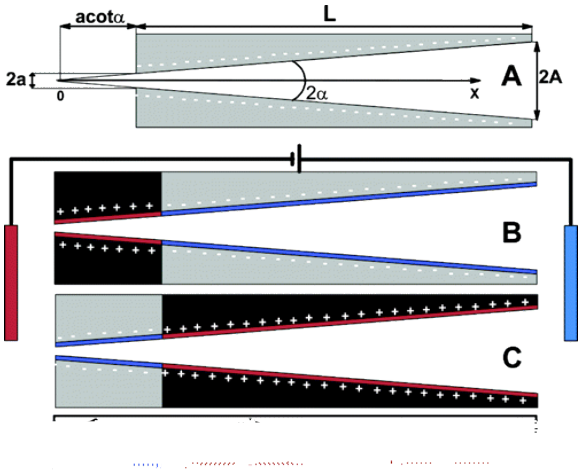


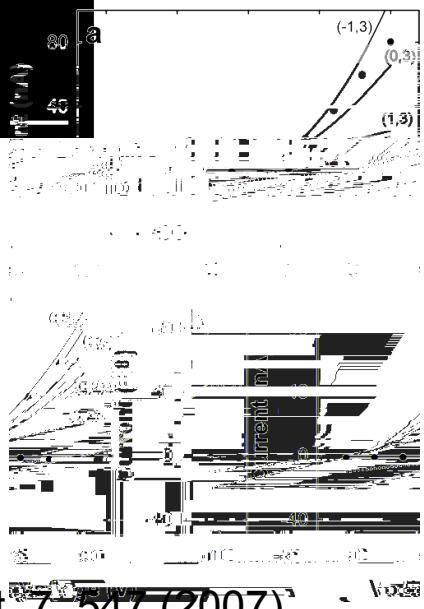
[KCl]=0.1M

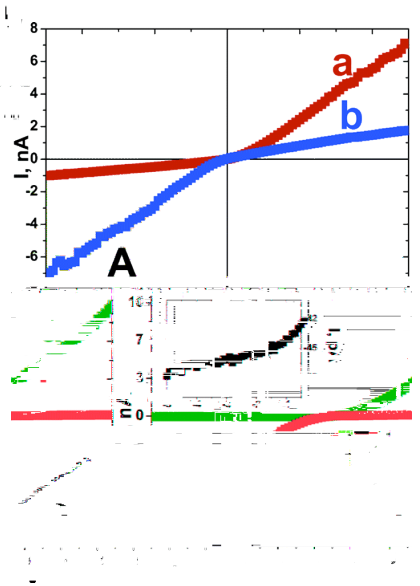
Vidal, Gracheva & Leburton,
Nanoscale Res. Lett. 2, p. 61 (2007)

Toward Ionic Rectification: Static Dipolar Surface Charges





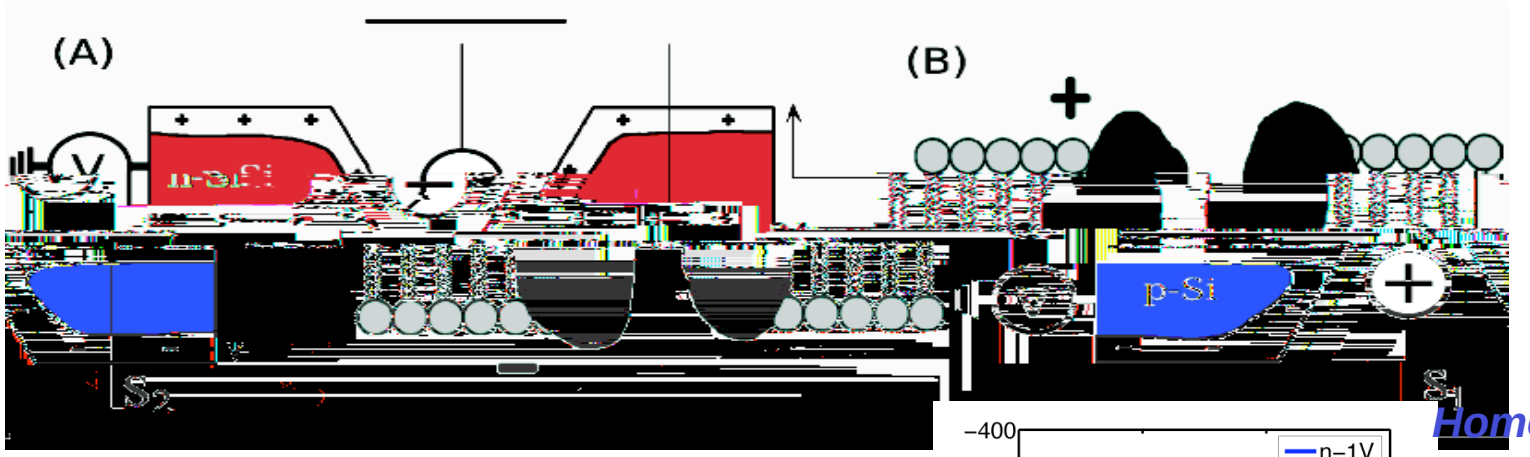




R. Karnik et al. Nanolett, 7, 547 (2007)

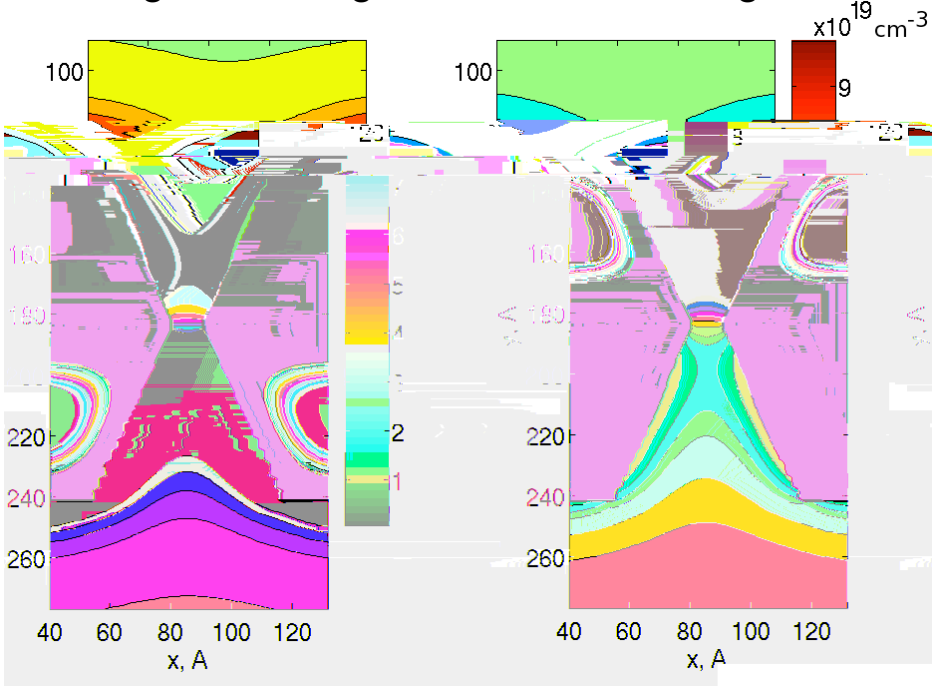
I. Vlassiouk et al. Nanolett, 7, 552 (2007)

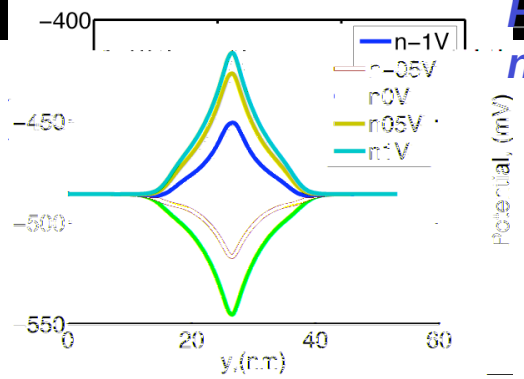
P-N Semiconductor Membrane



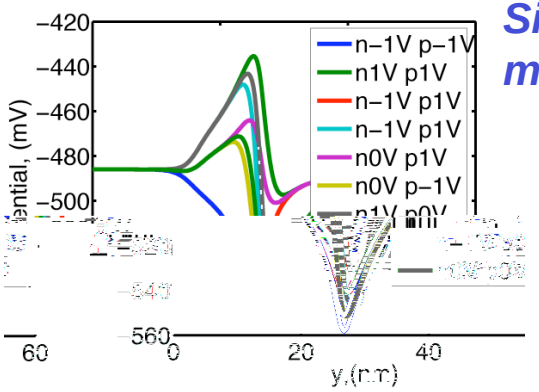
Negative charge

Positive charge





Homogeneous n-Si membrane



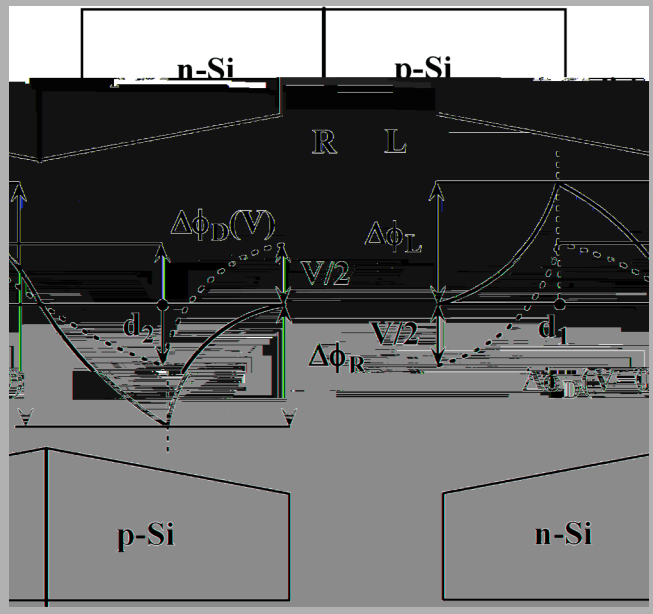
Si PN membrane

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):

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

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

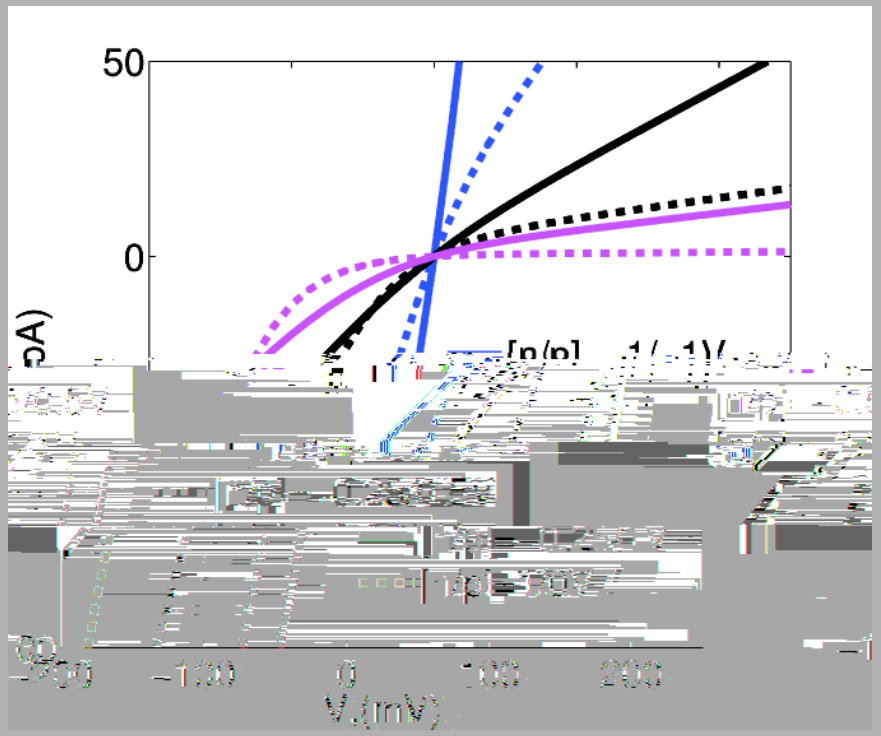
$$V = -(\Delta\phi_L(V) + \Delta\phi_D(V) + \Delta\phi_R(V))$$

$$\Delta\phi_D(V) = \Delta\phi_D(V=0) - V \quad \leftarrow \text{assume}$$

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

Tunable Rectification and Ion Filtering

Rectification



Ion selectivity