

**2013 Nanohub-U Course on  
“Principles of Electronic Nanobiosensors”  
Sensitivity of Potentiometric Sensors**

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In this 3<sup>rd</sup> HW set, we will discuss screening of spherical charges, the origin of charges of a biomolecule such as DNA or protein, and beating the screening limit by super-Nernst sensors.

**Problem 3.1: Screening of charge on a spherical sensor surface**

- (a) Recall from Lecture 14 that the Poisson equation for weak salt concentration can be written in form  $\nabla^2\psi = -\psi/L_D^2$ , where  $L_D^2 \equiv \kappa_w \epsilon_0 k_B T_L / (2z^2 I_0 N_{av} q^2)$

Show that the solution of the Poisson equation for 3D spherical sensor is given by

$$\psi = \frac{Q}{4\pi\epsilon_r \epsilon_0 r} \left( \frac{L_D}{L_D + a} \right) \exp\left( \frac{-(r-a)}{L_D} \right)$$

Here  $L_D$  is the Debye screening distance,  $a$  is the radius of the sensor, and  $Q$  is the charge of the sensor surface.

- (b) Find an approximate formula for a point source sensor with  $a \rightarrow 0$ . Does this formula remind you of potential of spherical charges you know? What are the similarities, what are the differences?

**Problem 3.2: Biomolecules and Screening at low salt concentration.**

Consider a spherical protein of radius  $a=2\text{nm}$ , with a total charge of  $20q$ . The protein is immersed in a NaCl solution of  $0.05\text{M}$ .

- a) Calculate the screening length by using the formula  $L_D^2 = \epsilon_r \epsilon_0 k_B T_L / 2z^2 I_0 N_{av} q^2$  .  
b) Use the formula derived in Problem 3.2 to find the potential 3 nm from the center of the protein molecule (i.e. 1 nm away from the surface).

**Problem 3.3: Debye length vs. Bjerrum lengths.**

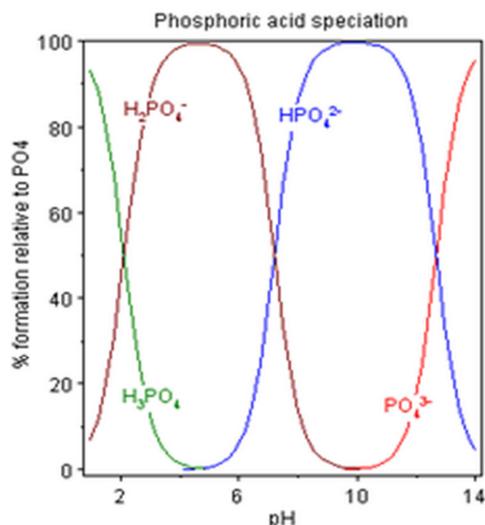
Bjerrum length is defined as the distance at which the potential due to charge is reduced to  $k_B T / q$ . Recall that the potential profile around a spherical charge is given by

$$\psi = \frac{Q}{4\pi\epsilon_r \epsilon_0 r} \left( \frac{L_D}{L_D + a} \right) \exp\left( \frac{-(r-a)}{L_D} \right)$$

- Assuming  $L_D$  is very large, derive an expression for the Bjerrum length.
- Show that the Bjerrum length in air is 56 nm, but in water it is 0.713 nm.
- How does Bjerrum length compare with that of the center-to-center distance of a DNA molecule?

**Problem 3.4: Charge of a biomolecule as a function of pH.**

A researcher is using a pH range from 2 to 8 to demonstrate a particular effect associated with DNA molecules. He claims that the charge of the DNA molecules is independent of pH. Based on the figure below, do you think that this claim is justified?



**Problem 3.5: Calculating charge of a protein molecule as a function of pH.**

- Calculate the electric charge of Prostate Specific Antigen (PSA) molecule (2ZCH:H) -- which has 229 amino acids connected by peptide bonds -- as a function of pH and show that point of zero charge occurs at  $pH \sim 7.1$ .

Use the total charge formula

$$Q = q \left( \sum_i^{Positive\ AA} i \frac{1}{1 + m_i} + \sum_j^{Negative\ AA} j \frac{-1}{1 + m_j} + \frac{1}{1 + m_{NH_2}} + \frac{-1}{1 + m_{COOH}} \right)$$

where  $i$  corresponds to K, R, and H, and  $j$  corresponds to D, E, C, and Y. The table below summarizes the number of the charged amino acids as well as their reaction constants ( $\alpha$ ,  $\beta$ , ... in the protein charge equation in lecture 14) in the PSA sequence.

Amino Acid	K	R	H	D	E	C	Y
Count (i or j)	11	5	2	11	5	8	11

<b>pK</b>	10	12	6.5	4.4	4.4	8.5	10
<b>m</b>	$10^{\text{pH}-10}$	$10^{\text{pH}-12}$	$10^{\text{pH}-6.5}$	$10^{4.4-\text{pH}}$	$10^{4.4-\text{pH}}$	$10^{8.5-\text{pH}}$	$10^{10-\text{pH}}$

Terminal group	NH <sub>2</sub> (+ve)	COOH (-ve)
Count	1	1
pK	8	3.1
<b>m</b>	$10^{\text{pH}-8}$	$10^{3.1-\text{pH}}$

(b) Follow the instructions below to calculate the protein charge using a more sophisticated calculator and compare the results obtained from the simple calculation above. How do the results compare.

Step 1. Go to the Protein Data Bank website: <http://www.rcsb.org/pdb/home/home.do>

Step 2. Search the protein that we are looking for by typing names like 'Prostate Specific Antigen' in the search box.

Step 3. When the results are displayed, scroll down the page, where you will see variants of protein specific antigen displayed. For now, choose one such as 2ZCH:H. It will take you to a page like <http://www.rcsb.org/pdb/explore/explore.do?structureId=2ZCH>. Note that if you had searched for a different protein, such as breast cancer marker HER2 and clicked 1N8Z variant from search results, you will be directed to <http://www.rcsb.org/pdb/explore/explore.do?structureId=1N8Z>

Step 4. Click the Display Files at the upper right corner of the webpage associated with the protein.

Step 5. Click FASTA sequence and then the sequence will be displayed on the webpage. FASTA is name of the format used by a program to align DNA and protein database searches. Here we use FASTA just to get the sequence of DNA or Amino acid -- we will not be using the FASTA program.

Step 6. For running protein calculator, copy the sequence it and paste to the designated place in the calculator. For example, you can use <http://www.scripps.edu/~cdputnam/protcalc.html>.

**Problem 3.6: Beating the Nernst response by NP-NW sensors.**

Consider an accumulation-mode NP-NW transistor pair. What is the maximum pH sensitivity for such a device with AlGa<sub>N</sub> serving as the channel of the planar FET (T1), and Si-NW as the NW-FET (T2) with the following properties?

- AlGa<sub>N</sub> has mobility of 2000 cm<sup>2</sup>/V.s, Tox=45nm, W=1um (T1)
- Si-NW has mobility of 100 cm<sup>2</sup>/V.s, Tox=15nm, W=50nm (T2)
- L<sub>1</sub>=L<sub>2</sub> , V<sub>DS1</sub>=V<sub>DS2</sub>.

In the following problem set, we will explore the sensitivity of three different types of sensors, namely, pH-sensitivity of a NW sensor, Double-gate biosensor, and extended-gate biosensors.

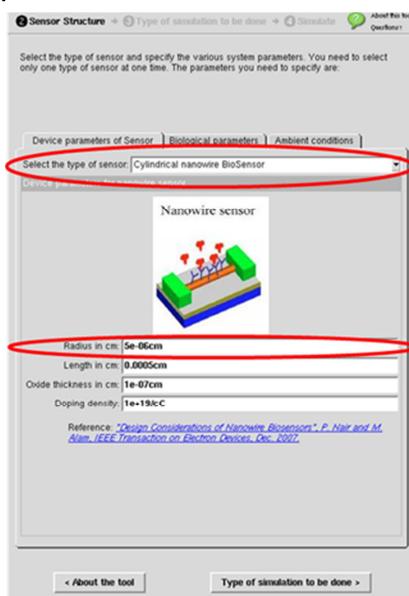
### Problem 3.7: Calculating pH response of a NW sensor using BiosensorLab

In this problem, we examine the sensitivity of the biosensor to change of pH in the fluid. This illustrative example is based on lectures on Sensitivity of potentiometric sensors.

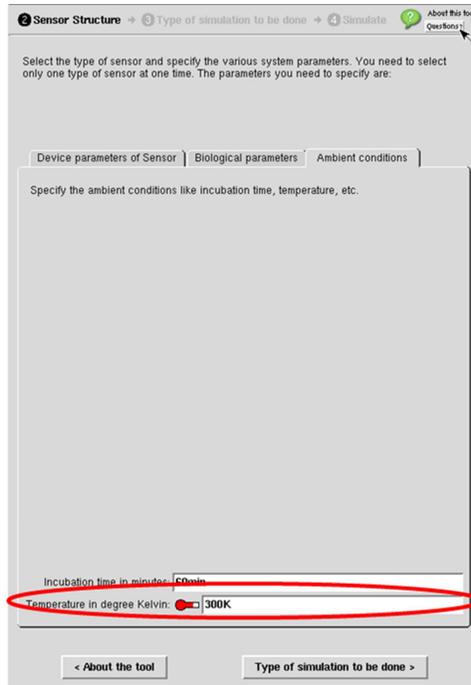
Use Biosensor Lab (v2.0) to determine the following: If pH of the test fluid changes from 3 to 7, how much does the surface potential change?

#### Preparing the simulator

- In the “Device parameter of Sensor” tab, select the option “Cylindrical nanowire Biosensor”. Keep oxide thickness, doping density, width and length the same as default values. Note these values so that you can refer to them later.



- This problem is only related to pH aspects of the NW sensor. So we can skip all the parameters under “Biological Parameter” tab.
- The measurements are done at room temperature, so set the Temperature in degree Kelvin to be 300 K in the “Ambient Condition” tab.



- Move on to the “Type of simulation” phase. This question is related to Sensitivity of biosensors, therefore turn on the “Sensitivity” switch in the “Type of simulation to be done” phase.



- Click on simulate.