2013 nanoHUB-U Course on
"Principles of Electronic Nanobiosensors"

Homework 5: Selectivity and Integrated Sensor Systems

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Problem 5.1: *Binding energies of matched and mismatched DNA- Energy Selectivity*

In this problem, you will determine the energy-selectivity of DNA sequences. We will consider a 22-mer DNA receptor (e.g. 5'/ TCA ACA TCA GTC TGA TAA GCT A/3') with complementary and mismatched target sequences. Our goal is to determine bond strength in the respective cases.

Using the "Hetero-Dimer" tool in the following analyzer,
https://www.idtdna.com/analyzer/Applications/OligoAnalyzer/ answer the questions:

a) What is the binding energy for the complementary sequences of 5'/ TCA ACA TCA GTC TGA TAA GCT A/3' and TAGCTTATCAGACTGATGTTGA -3' ?
b) What is the binding energy for the complementary sequences of 5'/ TCA ACA TCA GTC TGA TAA GCT A/3' and 5'- TCC TAC ATT GGA CGC ATG TTT T /3'
c) How many mismatches do you have in the 2nd sequence?

In each part, run the tool and check different free energies (ΔG) of forming the DNA duplexes from the given individual strands. Free energy is defined as: $\Delta G_T(total) = \Delta H_{total} - T\Delta S_{total}$

With ΔH and ΔS being the enthalpic and entropic parameters, respectively.

Problem 5.2 *Diffusion limited competitive absorption on biosensor surface*

In this problem, we will explore the spatial selectivity of biosensors and see how the signal to noise ratio degrades rapidly as the ratio of the parasitic molecules to the target molecule is increased. The analysis is based on Nair and Alam, JAP, 107, 064701, 2010. Sec. C 'Limits of SNR for label-free electrical detection'.

A biosensor surface is in contact with a solution containing parasitic and the target molecules. We wish to find the signal to noise ratio (SNR) of the sensor for various ratios of parasitic vs. target molecule densities. Assuming a **parasitic molecule** density (ρ_p) of 10 μM, let us calculate the receptor density (N_0) necessary to achieve a signal to noise ratio of 100 for three **analyte** concentrations (ρ_T), namely, 1nM, 1pM, and 1fM. Explain the trend intuitively. Other

parameters associated with the parasitic molecule and the target molecules are listed in the following table.

SNR	100
σ_T / σ_p	10
k_T / k_p	3×10^7
r_0	$2\times10^{-7}\,cm$
r_p	$10^{-7}\,cm$
θ^∞	0.54

(a) Use the following formula to calculate to solve for the receptor densities for a specific SNR.

$$SNR = \frac{\sigma_T k_T \rho_T}{\sigma_p k_p \rho_p}\frac{N_0}{N_p}$$

$$N_0 = \frac{\theta}{\pi r_0^2}\ , \qquad N_p = \frac{\theta^\infty - \theta}{\pi r_p^2}$$

(b) Verify the results by using BiosensorLab.

- Log on using your nanoHUB id.
- Launch the online tool BiosensorLab (https://nanohub.org/tools/senstran/) and select version II
- In the sensor structure, choose "cylindrical NW sensors" and keep the NW dimensions and other material parameters as the default values.
- In the panel "Types of Simulation", choose 'Selectivity'. Change the corresponding parameters based on the problem statement.

(c) Use BiosensorLab to recalculate SNRs with parasitic molecules sizes from 3×10^{-7}cm to 1×10^{-7}cm and explain how SNR changes with as a function of size of parasitic molecules.

Problem 5.3 ***Applications of sensors in Genome Sequencing***

We will determine the time required to sequence an entire genome containing 4 billion base pairs. One chip has 100 million wells (connected to 100 million transistors), and assume a loading efficiency of 20%. Also assume each read cycle takes 10s. Determine:

(a) How long should the read-length be, so that one chip can sequence the entire genome?
(b) How long will it take to determine the entire sequence?
(c) What is the total time for sequencing, if one needs five reads instead of one?

Problem 5.4: ***Ion-torrent example of genome sequencing by capture of H molecules.***

Consider a semi-infinite system extending from $0 \leq x \leq \infty$. Locate a proton source at $x = R$ and the pH-sensor at $x = 0$. A pulse of N protons are injected at time $t = 0$. The evolution of the proton density as a function of time and position, $p(x,t)$, can be obtained by solving the diffusion equation

$$\frac{dp}{dt} = D\frac{d^2p}{dx^2},$$

(a) For simplicity, assume that the pH-sensor does not absorb any proton ($k_F = 0$), but simply reflects them. The solution of the proton diffusion equation subject to the aforementioned boundary condition is given by

$$p(x,t) = \frac{N}{\sqrt{4\pi Dt}}\exp\left(-\frac{(x-R)^2}{4Dt}\right) + \frac{N}{\sqrt{4\pi Dt}}\exp\left(-\frac{(x+R)^2}{4Dt}\right).$$

Use the Octaview code provided (**Problem5_4_a_1.m**) and plot the proton density $\rho(0,t)$ and $\rho(R,t)$ at various times. Explain the shape of the profiles as a function of time.

(b) Now consider the other extreme, where k_F of the surface is infinite and the sensor surface viewed as a sink, or as fully absorbing. The solution of the diffusion equation with this modified boundary condition is given by

$$p(x,t) = \frac{N}{\sqrt{\pi Dt}}\exp\left(-\frac{x^2+R^2}{4Dt}\right)\sinh\left(\frac{xR}{2Dt}\right).$$

Use the Octaview code provided (**Problem5_4_a_2.m**) to plot the proton densities $\rho(0,t)$ and $\rho(R,t)$ at various times. Explain the shape of the profile as a function of time.

(c) Which of the systems should have faster response and why?