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

HW1: Diffusion Limited Capture and Fractal Dimension of a Random Surface

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In Lectures 1-6, we discussed several general topics related to nanobiosensors and the importance of the diffusion geometry of the sensor in defining the settling time.

In week 1, let us solve the following 5 problems as exercises (Problems 1.1, 1.3, 1.6, 1.8, 1.10). **Homework will not be graded**, but once you have worked out a problem, you should look for the answer among the multiple choices. Doing the homework before the solutions are posted will help you understand the material better. We will discuss the solutions at the end of the week in a tutorial.

We will be using two softwares for this class: Octaview and BiosensorLab. Octaview is an open-source, web-enabled version of MATLAB available through nanoHUB.org. See http://nanohub.org/resources/octaview/supportingdocs for a video tutorial. The codes will be provided as a part of the HW set. You will be asked to change parameters to see how the solutions change as a result.

BiosensorLab is a software program used to solve a wide variety of problems related to nanobiosensors – again available through nanoHUB.org. The instructions to solve various problems using BiosensorLab will also be available as a part of the HW set.

Part I: Density and Diffusion of Particles

Tutorial 1.0. For an intuitive understanding of particle diffusion in a fluidic background, visit the website at http://www.falstad.com/gas/. On the right hand side, choose "Brownian Motion" for the setup. You can change the parameters on the slider scale to see how the diffusion is affected by the environment, such as temperature.

Problem 1.1: ***Calculating concentrations.*** **If you take a 1000 mg tablet of headache medicine, what is the increase in the analyte concentration in blood? Assume, the molecular formula of the medicine is $C_8H_9NO_2$ and a typical volume of blood is 5 liters. Choose one of the following answer that best describes your solution.**

A. 1 M.
B. 1 mM.
C. 1 μM.
D. 1 nM.

Problem 1.2: ***Diffusion coefficient of free particles.*** **Calculate the diffusion coefficient of a small protein molecule of radius 2nm. What is the diffusion coefficient for a cell of size ~ 2 um. Assume that the viscosity η=0.01 Poise [g/cm.sec].**

Problem 1.3: ***Diffusion distance of molecules in water.*** **Assume that the diffusion coefficient of a protein is $D_{protein} = 1.1 \times 10^{-6}\ cm^2/s$ and that of a cell is $1.1 \times 10^{-9}\ cm^2/s$. How far would the protein and the cell travel in 10 minutes?**

Once your calculation is done, see which of the following best describes your result:

A. 600 micron for the protein and 20 micron for the cell. .
B. 20 micron for the protein and 600 micron for the cell.
C. 6000 micron for the protein and 200 micron for the cell.
D. 60 micron for the protein and 20 micron for the cell.

Problem 1.4: ***Diffusion Time of free molecules.*** **After influencing receptors in the post-synaptic membrane, the neurotransmitters *not* degraded by enzymes diffuse back to the pre-synaptic membrane, which lies $2x10^{-6}$ cm away, with $D=5x10^{-6}$ cm^2/s. How long does this short journey take? (Taken from R Cotterill, Biophysics: An Introduction, Wiley.)**

Part II: Diffusion flux towards sensors of various geometrical shapes

Problem 1.5: ***Exact solution molecules diffusing across a 1D Membrane.***

During the lectures in the class, we have discussed approximate analytical solution to a variety of diffusion problems. Sometimes it may be important to solve the diffusion equation exactly to compare the analytical results.

A membrane of thickness L separates two chambers kept at different concentrations, namely, 0 and ρ_0. The exact solution of the diffusion equation (by separation of variables) is given by the following equation.

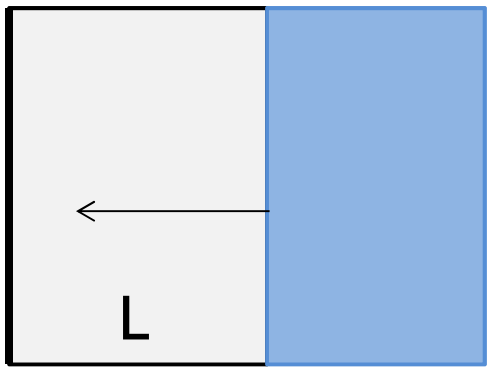
$$\frac{d\rho}{dt} = D\nabla^2\rho$$

$$\frac{dN}{dt} = k_F(N_0 - N)\rho_s$$

$$k_F \to \infty, \rho_s = 0$$

$$\rho(x,t)=\rho_0\left[\frac{x}{L}+\sum_{n=1}^{\infty}\frac{2(-1)^n}{n\pi}\sin\frac{n\pi x}{L}\exp\left(-\frac{(n\pi)^2 Dt}{L^2}\right)\right]$$

$$J(t)=\left(\frac{D\rho_0}{L}\right)\times\left[1+\sum_{n=1}^{\infty}2(-1)^n\exp\left(-\frac{(n\pi)^2 Dt}{L^2}\right)\right]$$



(a) Plot $\rho(x,t)$ for several different times.
(b) What is the steady-state concentration gradient? Interpret this result in terms of the steady-state fluxes we have discussed in the class.
(c) Can you use the diffusion equivalent capacitance approach for this problem? Why or why not?

(Ref: Sze, Semiconductor sensors, p. 432)

Problem 1.6: *Steady state flux towards a disk sensor.*

From the Wikipedia (http://en.wikipedia.org/wiki/Capacitance), find the capacitance of a small disk embedded in an infinite media.

(a) Using the diffusion equivalent capacitance approach, calculate the steady-state diffusion flux.
(b) Compare the flux towards a spherical sensor vs. a disk sensor. Which flux is larger? Can you explain physically the ratio of the fluxes?
(c) Regarding the ratio of fluxes calculated in part (b), which of the following statements is correct:

A. The ratio is 1
B. The ratio is 2
C. The ratio is e
D. The ratio is π.
E. The ratio is $\pi/2$.

Problem 1.7: ***Diffusion-controlled rate for spherical Sensors***

Compute the diffusion-controlled capture of a small molecules of density 1nM by a spherical sensor of radius a=1nm and D= 10^{-5} cm^2/sec.

Problem 1.8: ***Approximate and Exact Solutions*****.**

Show that the exact and approximate solutions (given below) for time-dependent flux and total integrated captured biomolecules by a spherical sensor are in good agreement with each other.

Exact:

$$J(t) = \frac{D\rho_0}{a_0}\left(1 + \frac{a_0}{\sqrt{6Dt}}\right)$$

$$N_{total}(t) = 4\pi a_0^2 \int_0^t J(t')dt' = 4\pi\rho_0 D a_0 \left[t + \left(a_0/\sqrt{6D}\right)\sqrt{t}\right]$$

Approximate:

$$N_{total}(t) = C_t \rho_0 t$$

$$C_t = \frac{4\pi D}{a_0^{-1} - \left(\sqrt{6Dt} + a_0\right)^{-1}}$$

$$A = 4\pi a_0^2$$

(a) Derive the final expression for the approximate solution in the form given above.
(b) Compare the exact vs. approximate solutions by using the Octave code. How would the results differ if 6 was replaced by 2, for example? What does it say about the importance of the diffusion pre-factor?

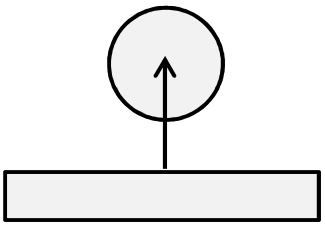
(c) Given N_{total}, how would you calculate the flux toward the sensor?
(d) What is the time-exponent for the asymptotic response to the sensor surface?

For part (d), choose one of the following options to summarize your answer.

A. The time exponent is close to 0.
B. The time exponent is approximately 0.5
C. The time exponent is approximately 1.
D. The time exponent is approximately 2.

Problem 1.9: ***Steady State Diffusion Flux for system with complex geometry.***

Consider a spherical source (radius a, surface density ρ_0) of biomolecules, which are being captured by a planar sensor placed underneath at a distance d>a. Find the Maxwell's formula regarding electrical capacitance for this situation, make appropriate substitutions, and calculate the steady-state flux from the spherical source to the planar sensor surface.



Problem 1.10: ***nanoHUB Exercise using BiosensorLab.***

Assume that you want to design a cylindrical nanowire (NW) sensor of 50 nm radius for the purpose of capturing 20-bp (base pair) DNA molecules. The stability time of the device is limited to 10,000 seconds (about 3 hours). The surface conjugation parameters are not known exactly, but assume for the time being typical values of $k_F = 3\times10^6\ M^{-1}s^{-1}$ and $k_R = 1\ s^{-1}$. The test fluid of 6 cc is injected to the sensor via pipette drop rather than continuous external flow. What is the limit of detection (approximate) for this biosensor?

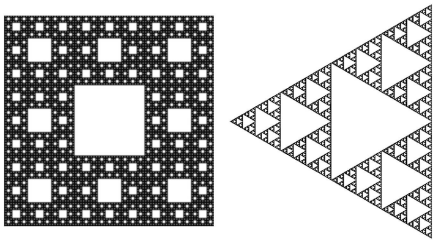
(Note. You will find the detailed instruction regarding how to run the software on nanohub.org in the document 'BiosensorLab-HW1-1p10.pdf').

Choose one of the four answers based on your calculation.

A. 10 mM.
B. 10 pM.
C. 10 fM.

D. 10 aM.

Problems 1.11: ***Fractal Biosensors.***
Consider two sensors with capture surfaces approximated by a Sierpinski carpet (DF=1.89) and Sierpinski triangle (DF=1.58), respectively. Determine the number of molecules captured by these sensors based on the diffusion limited transport theory discussed in the class. Which of the following statement best describes your analysis?



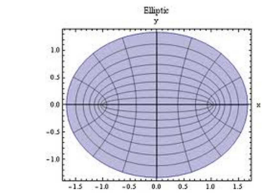
a) The response of Sierpinski carpet will be very similar to that of an isolated cylindrical sensor.
b) The response of Sierpinski triangle will be very similar to that of an isolated cylindrical sensor.
c) Both sensors will behave like isolated cylindrical sensors.
d) The response of Sierpinski carpet will be close to a planar sensor.

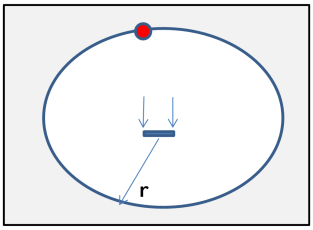
Problem 1.12: ***Diffusion flux with ellipsoidal electrodes.***

Calculate steady state flux between strip of size 2c and an ellipsoid defined by semi-major axis a and semi-minor axis b. Recall that one can define an ellipse in elliptical coordinate as follows

$$\frac{x^2}{c^2\cosh^2(\mu)}+\frac{y^2}{c^2\sinh^2(\mu)}=1 \qquad \text{(Eq. 1)}$$

where μ (tortuosity) is defined by either $c\times\cosh(\mu)\equiv a$ or $c\times\sinh(\mu)\equiv b$. In other words, no sooner are $a, b, and\ c$ defined, the μ is defined as well.





If the steady state capacitance between the flat plate and the ellipsoidal surface characterized by μ, is given by $C_{D,SS}= \mu D/\pi \sim \pi D/\ln(r/a)$, and if the outer ellipsoidal cylinder is kept at concentration ρ_0,

(a) Find the steady-state flux to the sensor surface.
(b) Use the approximate relationship to define a time-dependent solution of the problem.
(c) How does the result compare to those related to concentric hemispherical surfaces?

(Ref: O. Benichou and R. Voituriez, PRL, 100, 168105, 2008.)

End of HW set 1.