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

Beating the diffusion limit and Senstivity of Potentiometric Biosensors

Muhammad A. Alam
Network of Computational Nanotechnology
Discovery Park, Purdue University.

In this HW problem set, we will discuss approaches to beat the diffusion limit. There are four problems (two Octaview codes are also provided). The basic concepts we discussed in the class are simple, but we must solve a few specific problems to make sure the concepts are fully understood. See HW1 for additional information regarding two software to be use: Octaview and BiosensorLab. We will discuss the solutions at the end of the week.

Problem 2.1: *Beating the diffusion limit.* Let us use the following example to illustrate the efficiency of biobarcode sensor in being able to detect analytes at ultra-low concentration within a very short period of time. Assume the analyte density of 1 pM, diffusion coefficient of the analyte molecule is D=10^{-5} cm^2/Sec and its radius is a_0=10 nm. The density of magnetic particles introduced in the solution is ρ_{MP}=1 mM.

(a) Calculate the number of biomolecules that have escaped capture after t=1 nanosecond, 10 nanosecond, and 100 nanosecond.
(b) How long should we wait before 99% of the target particles are captured.
(c) None of the times calculated above change if the analyte density is reduced to 1 fM? Can you explain why?
(Hint: Be careful about units when calculating τ.)

Solution:

(a) Let us begin by calculating τ, the mean time to capture. To choose the correct formula for τ, note that, $\rho_{MP} \geq \rho_T$, and therefore τ is determined by the density of MP, i.e.,

$$\tau = \frac{1}{4\pi D a_0}\frac{1}{\rho_{MP}}$$
$$= \frac{1}{(4\pi)(10^{-5})(10^{-6})}\frac{1}{10^{-3}(6.02\times10^{23})10^{-3}}$$
$$= 13.2\times10^{-9}\,\text{Sec}$$

Since the fraction that survives is given by $dn_T/dt = -n_T/\tau$, or $n_T(t)/n_T(0) = e^{-\frac{t}{\tau}}$, therefore, 92.7%, 46%, and 5.12x10^-2% survives after 1, 10, and 100 nsec, respectively.

(b) After 99% of the target particles are captured, only 1% survives. Therefore,

$$
\begin{aligned}
t &= -\tau \ln\left[n_T(t)/n_T(0)\right] \\
&= -1.32\times10^{-8} * \ln(0.01) \\
&= 60.8\times10^{-9}\,\text{Sec}
\end{aligned}
$$

In other words, if one suspects that a pM analyte is present, one must wait ~5 times the mean capture time to be 99% sure that the target molecules are capture.

(c) At 1pM target concentration, only a fraction of the MP (1pM out of 1mM) get to catch a target particle. When the analyte density is reduced to 1fM, an even smaller fraction (1 fM out of 1mM) are lucky to catch a particle. Therefore, while the number of MP-analyte conjugates reduces dramatically with analyte concentration, the time to capture them does not, because it is defined by the vitual box surrounding the target (which is dictated by the MP density).

Problem 2.2: ***Beating the diffusion limit by super-hydrophobic surfaces.***

(a) Show that, the contact angle θ^* of a droplet can be designed by the following formula: $\cos\theta^* = \phi\cos\theta_E - (1-\phi)$**,** where, ϕ is the fractional area covered by the pattern (see lecture slides), and θ_E is the contact angle of the water droplet on a flat surface.

(b) What is the value of θ_E for Teflon and SU-8 (google it)? Which one of them is hydrophobic/hydrophilic?

(c) Using the relationship in part (a), plot how θ^* varies with the design parameter ϕ for Teflon and SU-8. Would it be possible to design a super-hydrophobic surface from a hydrophilic material?

Solution:

(a) From lecture notes, recall that $\gamma_{LV}\cos\theta_E = (\gamma_{SV} - \gamma_{SL})$

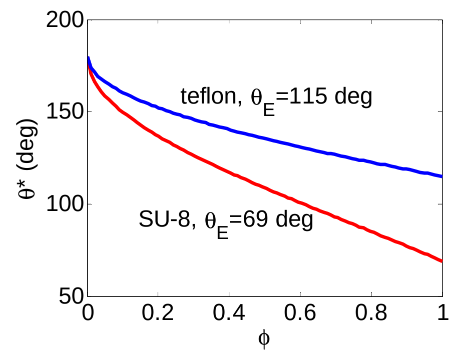
$\therefore \gamma_{LV}\cos\theta^* = \phi(\gamma_{SV} - \gamma_{SL}) - (1-\phi)\gamma_{LV} = \phi\,\gamma_{LV}\cos\theta_E - (1-\phi)\gamma_{LV}$

$\Rightarrow \cos\theta^* = \phi\cos\theta_E - (1-\phi)$

(b) $\theta_E = 69\ for\ SU-8\ and\ \theta_E = 115\ for\ Teflon.$ Teflon is more super hydrophobic.

(c) Now you can implement the formula in an Octave code.

```
clc
close all
clear
%%
theta_E=69 *pi/180;
% theta_E is ~69deg for SU-8 and
%           ~115deg for teflon

phi_mat=linspace(0,1,100);

theta_CB=acos(cos(theta_E)*phi_mat…
            -(1-phi_mat)) *180/pi;
%%
figure;
plot(phi_mat,theta_CB)
xlabel('\phi')
ylabel('\theta* (deg)')
```



Problem 2.3: ***Beating the diffusion limit by flow. (Ref. Lecture 8)***

Consider a disk sensor embedded in fluidic channel with w=4um, h=1um. The analyte concentration is ρ_0 = 1fM and its diffusion coefficient is D=150 um^2/s.

(a) Write the expression for Pe and I.
(b) Plot the total flux I as a function of the sensor radius a. Calculate for both volumetric flow Q= 0.1 and 10 uL/min.
(c) From the lecture slides, you should expect ln(I)=(5/3)ln(a) + c. Confirm this approximated relationship from the plots.

Solution:

(a)

$$Pe = 6\,\frac{Q}{wD}\left(\frac{a}{h}\right)^2$$

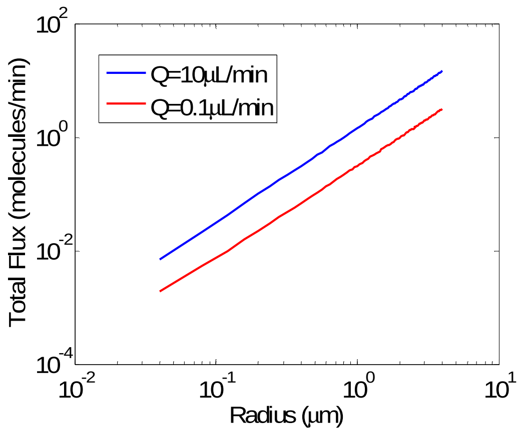
$$I = \rho_0 \cdot \mathrm{a} \cdot \mathrm{D} \cdot \frac{(4 - 0.123 \cdot Pe^{\frac{3}{2}})}{(1 - 0.203 \cdot Pe^{\frac{1}{2}})} \qquad (\mathrm{Pe}<1)$$

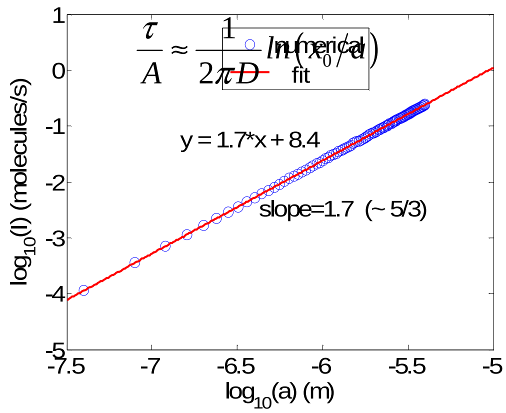
$$I = \rho_0 \cdot \mathrm{a} \cdot \mathrm{D} \cdot (2.157 \cdot Pe^{\frac{1}{3}} + \frac{3.55}{Pe^{\frac{1}{6}}}) \qquad (\mathrm{Pe}>1)$$

(b)&(c) The flowrate and the radius-flux relationship is calculated based on the following Octave code.

```
clc
close all
clear

%%
NA=6.22e23; % Avogedro's number
```

```
c0=1e-15; % molar
rho0=c0 * NA; % # of molecules /L
rho0=rho0*1e3; % # of molecules /m3


Q= 10* 1e-6 * 1e-3 /60; % 1* 1e-6 * 1e-3 /60 m^3/s = 1uL/min

% a=1 * 1e-6;
w=4 * 1e-6;
a_mat=linspace(w/100,w, 100);
h=1 * 1e-6;

D=150 *(1e-6)^2;

for k=1:length(a_mat)
   a=a_mat(k);
Pe=6*Q/w/D *(a/h)^2;

if(Pe<1)
   I=rho0*a*D* (4-.123*Pe^(3/2))/(1-.203*Pe^(1/2));
else
   I=rho0*a*D* (2.157*Pe^(1/3)+3.55/Pe^(1/6) );
end

I_mat(k)=I;

end

%%

figure;
loglog(a_mat/1e-6,I_mat*60)
xlabel('Radius (\mum)')
ylabel('Total Flux (molecules/min)')
```





Problem 2.4: ***Diffusion in confined geometries.***

Consider two concentric cylinders of radius a and b, respectively. The cylinder (with radius a) is a perfect sink. The particles are being injected at a radius x_0 from the center.

(a) Use the charge control model to find the exact MFPT is

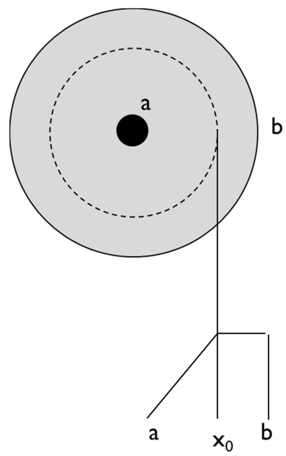
$$\tau = \frac{b^2}{2D} ln\left(x_0/a\right) + \frac{1}{4D}\left(a^2 - x_0^2\right)$$

(b) Show that when b>>a, then the result reduces to that calculated based on the approach of diffusion equivalent capacitance.

$$\frac{\tau}{A} \approx \frac{1}{2\pi D} ln\left(x_0/a\right)$$

Solution.

MFPT in 2D – Exact Result



Concentric cylinders

$$Q_1/\rho_0 = 2\pi\int_0^{x_0} rdr \frac{ln(r/a)}{ln(x_0/a)} = \pi x_0^2 + \frac{\pi}{2}\frac{a^2 - x_0^2}{ln(x_0/a)}$$

$$Q_2/\rho_0 = \pi\left(b^2 - x_0^2\right)$$

$$I = C_{D,ss} \times \rho_0 = \frac{2\pi D\rho_0}{ln(x_0/a)}$$

$$\tau = \frac{Q_1 + Q_2}{I} = \frac{b^2}{2D} ln(x_0/a) + \frac{1}{4D}\left(a^2 - x_0^2\right)$$

To compare with the approximate solution, note that

$$\frac{\tau}{\pi b^2} = \frac{1}{2\pi D} ln(x_0/a) + \frac{1}{4\pi D}\left(\frac{a^2 - x_0^2}{b^2}\right)$$

$$\frac{\tau}{A} \approx \frac{1}{2\pi D} ln(x_0/a)$$

This completes the solution set for HW2