**BMB/BI/CH174 Spring 2017**

**Problem Set 2: Physical Biology**
**Due: 4/25/2017 at the beginning of class**
**Office hour: 4/24/2017, 6pm, Broad 300 Conference room**

**Problem 1. (20 points total)**
**1.1 (10 points)**
There are roughly 3 million proteins in a E. coli cell, one-third of them are membrane proteins. Please make an estimate about how much membrane area does each membrane protein occupy, and what is the average distance between two neighboring proteins on the same membrane? Show your steps of estimation.
*Hint:* you may use "bionumbers" website (*bionumvers.hms.harvard.edu*) to find out the typical surface area for each E. coli cell. And keep in mind that E. coli has outer membrane and inner membrane.
**1.2 (10 points)**
Given that a phospholipid molecule has molecular weight of about 800 Daltons and takes roughly 0.5 $nm^2$ of membrane area. The table below shows estimated protein-to-phospholipid mass ratios of various types of membranes. Use this table to calculate the areal density of membrane proteins (Daltons per $nm^2$ of membrane) and their mean distances (*Hint: calculate areal density of phospholipids first. And keep in mind membrane's bilayer property*).

**Table 1. Protein-to-phospholipid mass ratios of membranes used in SXS experiments**

| Membranes | Protein/phospholipid, mg/mg |
|---|---|
| ER membranes*† | 2.6 |
| Untreated ER | 2.4 ± 0.2 |
| Protease-treated ER‡ | 0.12 ± 0.01 |
| Cholesterol-depleted ER§ | 0.15 ± 0.02 |
| ER liposomes | ND¶ |
| Golgi membranes* | 1.8 |
| Untreated Golgi | 1.7 ± 0.09 |
| Protease-treated Golgi | 0.08 ± 0.01 |
| Cholesterol-depleted Golgi§ | 0.09 ± 0.01 |
| Golgi liposomes | ND |
| BPM*‖ | 2.2 |
| Untreated BPM | 2.8 ± 0.3 |
| Protease-treated BPM | 0.16 ± 0.2 |
| Cholesterol-depleted BPM§ | 0.17 ± 0.1 |
| BPM liposomes | ND |
| APM*,** | 1.5 |
| Untreated APM | 1.7 ± 0.2 |
| Protease-treated APM | 0.11 ± 0.01 |
| Cholesterol-depleted APM§ | 0.11 ± 0.01 |
| APM liposomes | ND |
| *E. coli* cytoplasmic membranes* | 2.0 ± 0.2 |
| Untreated *E. coli* membranes | 1.8 ± 0.2 |
| Protease-treated *E. coli* membranes | 0.13 ± 0.2 |
| *E. coli* membrane liposomes | ND |

**Problem 2. (60 points total)**

**2.1 (15 points)**

Cytoplasmic membrane is permeable to small molecules, though it has different permeability to different types of molecules. Membrane permeability can be described as the number of molecules crossing a unit membrane area per unit time, or the "flux":

$$\text{flux } j = - P * \Delta C$$

in which P is the permeability coefficient (length/time), and C is the concentration inside or outside the cell.

Molecules can diffuse across the membrane because of concentration difference, in other words, diffusion would reach equilibrium once $\Delta C = 0$. For simplicity, let's imagine that a bacterial cell is a "sphere" with radius equals to 1μm; and for simplicity, let's also assume that flux stays constant irrespective of change in molecule's concentration difference across the membrane. Using the information given above, give an equation to estimate the time required for a certain type of molecule to reach zero flux.

**2.2 (15 points)**

Take glucose for example, it's permeability coefficient is in the range of $10^{-8}$ cm/sec, use the relationship you derived from above, find out how long it will take for glucose to leak out the cell?

**2.3 (15)**

Ions have lower permeability across the membrane because of their charges, membrane potential can thus be built across axon neurons. If a glucose is phosphorylated and thus charged, and its permeability becomes 100-fold smaller than the unphosphorylated glucose, how much longer will it take for phosphorylated glucose to reach flux equilibrium?

**2.4 (15 points)**

Write a simple differential equation for molecules' rate of change of concentration, given that the initial concentration in the cell is $C_0$ and concentration outside the cell is $C_{out} = 0$. Solve the differential equation and find the time scale for glucose to diffuse out of the cell.

**Problem 3 (20 points)**

Mechanosensitive channels are activated upon change in membrane tension. Eukaryotic channels such as TRAAK (also known as KCNK4), like bacterial MscL and MscS, is gated open by membrane tension, but has different structural basis. Recently, structures of mechanosenstive potassium channel TRAAK let us hypothesize the molecular mechanisms of how these channels are gated open from a structural perspective, a model that is different from the classic bacterial Msc channels. Read the review paper by Phillips et al. and go through figures in these papers by Brohawn et al.: [1] doi: 10.1038/nature14103 and [2] doi: 10.1073/pnas.132076811), briefly describe the structural features in Msc and TRAAK, what particularly interesting structural features are emphasized by Brohawn et al. in terms of TRAAK gating? Based on these results, briefly explain your opinions on the impacts of lipid composition, mechanical forces applied to membrane, and membrane protein crowdedness on TRAAK gating.