BC368, Spring 2018 Problem set #2 Due: Friday, February 16th

(All hand-in problems must be completed on separate pages & all short answer questions must be typed)

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1. The Scatchard analysis, like the Lineweaver-Burke method for enzyme kinetics, is an arcane linearization of experimental data that can be convenient for data analysis, but ultimately erroneous in its quantitative conclusions.

    a. Rearrange the Scatchard equation in Box 12-1 to reflect the true hyperbolic relationship between bound hormone, [LR] on the Y-axis, and total hormone [L] on the X-axis.

    b. Given the following experimental data for the binding of radiolabeled glucagon to cultured human hepatocytes (25,000 cells in each 3.00 mL sample), calculate the binding affinity (K_d) for glucagon binding to its receptor and the average number of glucagon binding sites per cell (n) using the least-squares method with your equation from part (a). **Attach your Excel data and charts.** ***Hint: 'B$_{MAX}$' in Box 12-1 can also be solved as B$_{MAX}$ = n•[cells]. Also, Solver may not work if your parameters are several orders of magnitude different from each other, so you may need to adjust units.***

$[L]_{tot}$ (M)	[RL] (M)
0.00E+00	0.00E+00
1.00E-08	1.91E-15
2.00E-08	3.36E-15
4.00E-08	5.16E-15
6.00E-08	6.33E-15
8.00E-08	7.10E-15
1.00E-07	7.75E-15
1.20E-07	8.19E-15
1.40E-07	8.51E-15
1.60E-07	9.80E-15

    c. The data in part (b) suggest that there is either one binding site per glucagon receptor or that receptors with multiple bindings sites bind glucagon without cooperativity. If, however, the glucagon receptors *did* exhibit cooperativity, sketch a plot ([RL] as a function of [L]) that would be consistent with positive cooperativity.

2. The 'Ras' proteins are G-proteins that act as switches for a variety of cellular processes involved in cell cycle, proliferation, and apoptosis. Nearly a quarter of human malignancies contain a Ras mutation, many of which render Ras constitutively active. Propose two unique strategies for pharmaceutical intervention for cancer patients with Ras mutations.