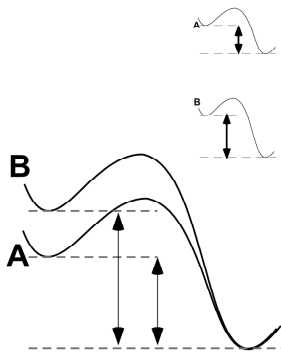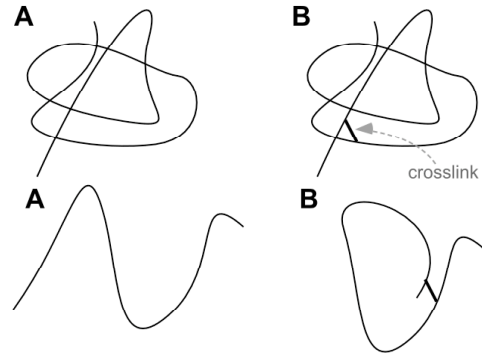Please show your work, and your thinking, in the space provided. Be brief, but complete. Long, wandering answers typically demonstrate a lack of understanding…
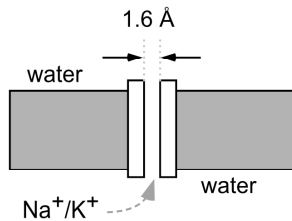
1. (25 points) For this question (*and this question only*), ignore entropic contributions from water. Consider the folding of a protein, (A) at right. The protein is stably folded (folding is energetically favored over the random chain). You find that introduction of a covalent (disulfide) cross link where indicated (B), does not alter the structure of the protein but does substantially *increase* its stability.
Explain this in thermodynamic terms (you do *not* need to know any details of protein structure to answer this question).

One must consider the energetics of the *unfolded* state (random chain). In case B, the (configurational chain) entropy of the unfolded state is reduced. It's energy is increased. Thus the difference in energy between the folded and unfolded states is greater. The folded protein is more stable. The effect of ΔH from the covalent bond is the same for folded and unfolded states and so has no effect on stability, as shown in the smaller illustration above.

2. (25 points) In a presentation on campus this week, Scott Auerbach talked about a transmembrane protein channel that selectively allows K^+, but not Na^+ to pass through the channel. The protein channel is negatively charged and has an inner *diameter* of 2.8 Å.
*Explain* why the channel allows K^+ to pass freely, but Na^+ passes through only very poorly, ie., the overall process of transport has a higher energy barrier. Think about what we talked about in class.

Ionic Radii (Å)	
Na^+	0.95
K^+	1.33

Atomic Radius (Å)	
O	0.73

The key here is that due to the dimensions of the channel and the size of the ions, either ion must become desolvated in order to pass through the channel. As we discussed in class, Na^+ is more highly solvated than K^+ (because Na^+ is smaller, with a larger charge density and so interacts more strongly with the water dipoles).
Since it takes more energy to desolvate, then the overall process has a higher energy barrier.

3. Consider the following reaction:

A + B ⇌ C
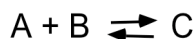
a) (15 points) Your friend has been collecting data for this reaction and fitting it using "LineWeaver-Burke" analysis (don't worry that you've never heard of this). This analysis takes the equation for ligand binding and rearranges it to fit the data and obtain the equilibrium constant. In this case, the required assumption that B is in large excess *is valid*. Assume that the uncertainty in each of the original measured values of [C] is constant at ±0.2. Without worrying about the precise derivation of the equation, ***decide*** which of the two fits is the better fit and ***explain*** why you chose the one you did. You may want to work through part (b) *first*.
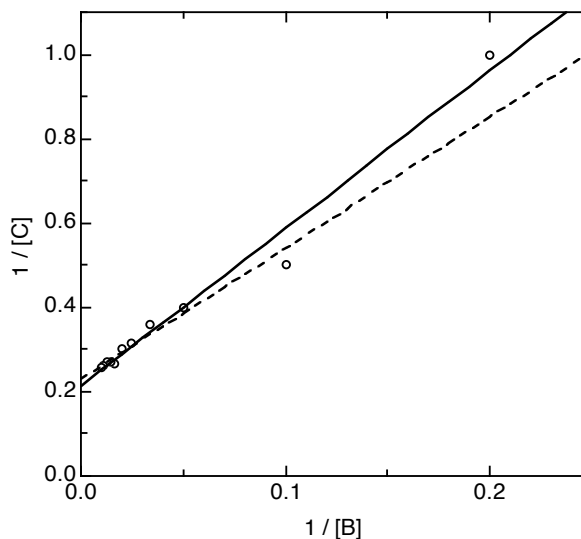
As we discussed in class, in taking the inverse of [C], the error of the inverse data points is larger for numbers arising from small values of [C] (large values of 1/[C]). So data toward the right of the plot should be weighted less in fitting.

The lower curve doesn't fit the far right data point as well, but fits the left most points better. Therefore, it is the better fit (indeed, it represents the parameters obtained from the direct fit of [C] vs [B]).

Whether or not you picked the right curve is not as important here as your explanation of why you picked it…

b) (10 points) Assume that the uncertainty in each of the original measured values of [C] is constant at ± 0.2, in the above graph, ***plot the trend in (y) errors***. You need not draw every error in the plot above, but just a few to illustrate the trend.

4. (15 points) Consider the following kinetic mechanism:

$$A + B \underset{k_2}{\overset{k_1}{\rightleftarrows}} C \underset{k_4}{\overset{k_3}{\rightleftarrows}} A + D$$
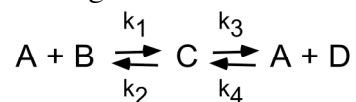
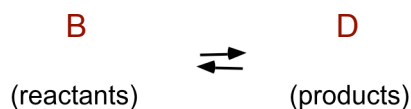Write the differential equations that describe the kinetics:

$$\frac{\partial A}{\partial t} = -k_1 AB + k_2 C + k_3 C - k_4 AD$$

$$\frac{\partial B}{\partial t} = -k_1 AB + k_2 C$$

$$\frac{\partial C}{\partial t} = k_1 AB - k_2 C - k_3 C + k_4 AD$$

$$\frac{\partial D}{\partial t} = k_3 C - k_4 AD$$

b) (5 points) Write the overall stoichiometry for the complete reaction

B   D

$$\rightleftarrows$$

(reactants)   (products)

c) (5 points) In this reaction, species A is called what?

A catalyst
("enzyme" would also be acceptable, but catalyst is more general)