

Due in class on Thursday Sept. 8th

1. For the following processes, identify whether ΔG° , ΔH° and ΔS° are positive (+), negative (-) or about zero (~ 0) at the standard state (gases 1 atm, solutes 1 M) and 298 K. Offer brief explanations.

Reaction	ΔG°	ΔH°	ΔS°	Explanation
$N_2(g) \rightarrow 2 N(g)$	+	+	+	Bond breaking is entropically favorable, but the enthalpic cost is huge and so it's not spontaneous at Room Temp.
$2 NH_3(aq) \rightarrow NH_3 \cdot NH_3(aq)^*$	>0	≈ 0	<0	No enthalpic value to H-bond since it's just replacing H-bonds with water. But NH_3 loses entropy (2 free molecules to 1 complex)
100 dodecyl sulfate** \rightarrow micelle	<0	>0	>0	Def. spontaneous, since 1 M (std state) is larger than cmc. Enthalpically unfavorable due to clustering of anionic head groups, so entropy gain due to releasing waters from clathrates likely drives process.

* The formation of an H-bonded dimer of ammonia in water

**The cmc for dodecyl sulfate is 150 μM .

2. Ethanol (C_2H_5OH) is highly soluble in water but propane (C_3H_8) is fairly insoluble, even though the molecules are about the same size. Why? Compare:

	ΔH° (kcal/mol)	ΔS° (cal/molK)	ΔG° (kcal/mol)
$C_2H_5OH(l) \rightarrow C_2H_5OH(aq)$	-2.9	+3.8	-4.0
$C_3H_8(l) \rightarrow C_3H_8(aq)$	-1.5	-13.3	+2.6

a. Does ethanol dissolve spontaneously in water (at the standard state)? How do you know? Explain the values of ΔH° and ΔS° associated with dissolution.

You bet it dissolves spontaneously ($\Delta G^\circ < 0$). Entropy is positive due to mixing (both ethanol and water will occupy a larger volume) and enthalpy is negative presumably because ethanol makes stronger H-bonds with water than itself and the water forms stronger vdW with the ethyl group than ethanol does.

b. Does propane dissolve spontaneously in water (at the standard state)? Why? Explain the values of ΔH° and ΔS° associated with dissolution.

No propane does not, as evidenced by positive ΔG° . ΔH° is still favorable (stronger vdW betw. water and propane than betw. propane & propane), but ΔS° is now negative due to the hydrophobic effect and formation of clathrates around propane surfaces.

3. There is a simple rule of thumb in calculating ΔG° as a function of changes in the equilibrium constant K .

a. Fill out the following table assuming a temperature of 298 K and remembering that R is either 0.00831 kJ/mol•K or 0.00199 kcal/mol•K.

K	ΔG° (kJ/mol)	ΔG° (kcal/mol)
100	-11.4	-2.7
10	-5.7	-1.4
1	0	0
0.1	+5.7	+1.4
0.01	+11.4	+2.7

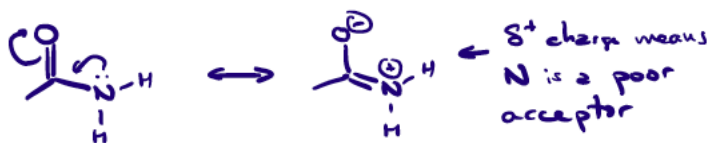
b. By how much does ΔG° increase or decrease (specify) in kJ/mol and in kcal/mol for every 10-fold change in K ?

If K increases 10x, ΔG° decreases by 5.7 kJ/mol or 1.4 kcal/mol

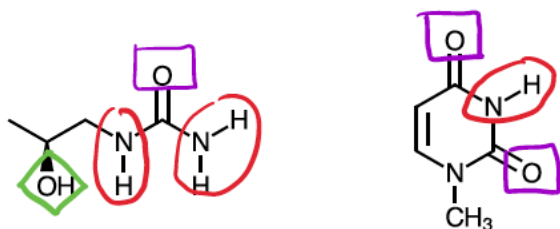
c. Scout's honor that you don't use a calculator for this. What is ΔG° for a reaction with an equilibrium constant of 1×10^{-3} ?

$11.4 + 5.7$ kJ/mol = 17.1 kJ/mol or $2.7 + 1.4$ kcal/mol = 4.1 kcal/mol

4. Amides have lone pairs on both the oxygen and nitrogen, yet only accept H-bonds at the oxygen. The nitrogen is unable to accept an H-bond. In the space below draw an amide with an accessible resonance structure and show why it does not accept H-bonds.

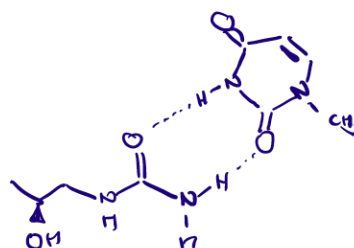


5. Consider molecules below. Note that the exocyclic amine cannot accept H-bonds (see question 4) because its lone pair is in resonance with the ring pi electrons.

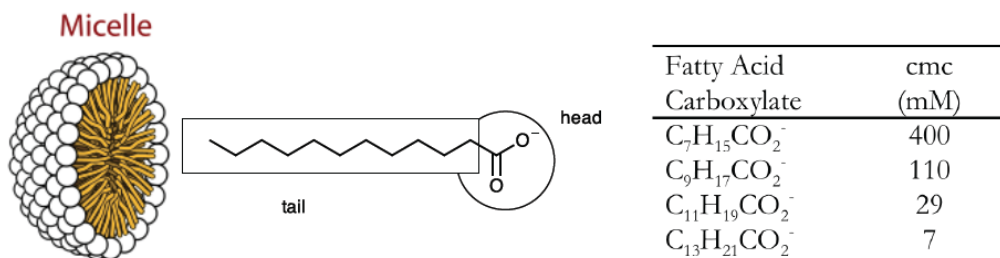


a. Identify heteroatoms (N & O) that can act as H-bond donors by circling them. If they can act as acceptors, draw a square around them. If they can both donate and accept, draw a diamond.

b. Redraw the molecules and orient them so that each molecule is both donating an H-bond to and accepting an H-bond from the other. *Be careful!* Make sure that the H-bond has a roughly 180° angle about the hydrogen atom. Note that there are multiple ways to achieve this.



5. Fatty acids are amphiphilic molecules possessing a polar “head group” and a non-polar “tail”. Most are sparingly soluble in water as individual molecules and above a particular concentration (the cmc, critical micelle concentration) they aggregate to form micelles – spherical aggregates of a few dozen to a few hundred molecules where the tails are buried from solution and the heads are exposed (see picture).



a. The cmc’s of several fatty acids are given above at pH 7. Given the values of cmc listed above, how does the free energy of micelle formation change with increasing number of carbons in the tail? Explain briefly.

ΔG of micelle formation is more negative as tail length grows. A lower concentration of free amphiphile is needed to form micelle. If less reactant present at equilibrium, K is larger and therefore ΔG is more negative.

b. Consider the enthalpic issues attached to aggregation and briefly state whether you expect them to be favorable or unfavorable:

i. ΔH for transfer of tail from water to micelle interior:

Slightly positive. Tail gives up dipole/induced dipole interaction for induced dipole/induced dipole interaction.

ii. ΔH for transfer of head group from water to micelle surface.

Positive. Negative charges packed on surface repel each other, which is enthalpically unfavorable.

c. What entropic considerations are responsible for that trend? Briefly discuss each of the following concerns and ID the one that

i. Conformational entropy of the chain:

Negative – loss of free rotations in C-C bonds is unfavorable.

ii. Entropy of aggregation

Negative – many free molecules aggregate to form one object. Loss of translational freedom.

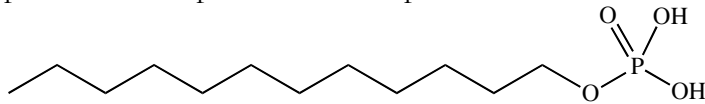
iii. Solvent entropy

Positive – clathrates disrupted by tails being segregated from water.

d. Given you analysis of enthalpic and entropic contributions to micelle formation, briefly identify the contribution that you think dominates the trend in free energy of micelle formation.

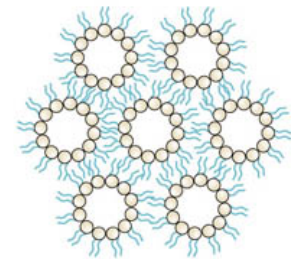
Only solvent entropy contributes to greater spontaneity of micelle formation as tail length grows.

6. Consider the following detergent. The pK_a 's of the head group are at 3 and 7. In **one or two** sentences, describe how the cmc of this detergent is likely to change with pH, specifically citing potential enthalpic and/or entropic effects.



At low pH the head group of this detergent molecule is neutral, but as pH increases it becomes increasingly anionic. Upon forming a micelle, the anionic headgroups will be placed in close proximity, leading to electrostatic repulsion. Thus, one would expect to see a higher cmc at higher pH due to disfavorable enthalpic effects that accompany micelle formation at high pH.

7. In addition to forming bilayered vesicles, phospholipids are capable of forming an *inverted hexagonal phase* (see diagram at right) in which the lipids form long tubes, with head groups facing inwards, that are filled with water.



Inverted hexagonal phase

a. Lipids with the PA head group can be induced to adopt the hexagonal phase at low pH **or** upon addition of Ca^{2+} at pH 7. Briefly suggest a structural/thermodynamic reason for that observation.

Phase requires close approach of head groups. Phosphate is protonated at low pH, leading to easier aggregation and avoiding neg charge repulsion. Calcium, Ca^{2+} , can also neutralize negative charge.

b. Predict whether saturated or unsaturated phospholipids are more likely to adopt the hexagonal phase, providing a short rationale for your answer.

Inverted phase needs “inverted cone” shape, where tails are thicker than heads. Arguably the unsaturated fatty acids broaden the tail so that it is “wider” than the head.

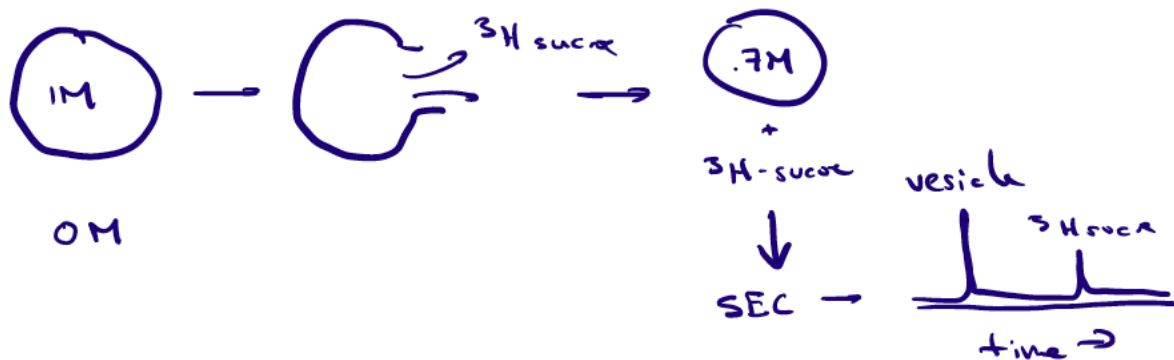
Chemistry 391 – PS #1 paper questions

Chen et al. (2004) The Emergence of Competition Between Model Protocells. *Science* **305**, 1474-6.

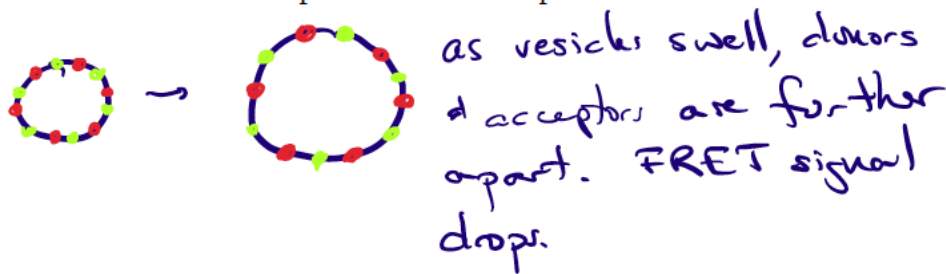
1. What is the chief *goal* of this work. They're wordy on this point – see if you can ID a single sentence that says it all. (Do not confuse goals with results. Find a hypothesis or some similar statement of what they seek to achieve, not what they did or did not achieve.)

We sought to detect the emergence of an adaptive cellular-level trait based on the physical properties of a model prebiotic vesicle system containing encapsulated nucleic acids.

2. Draw an image that illustrates how the surface tension of the fatty acid vesicles was determined. Consider this a task in manuscript illustration. You may include a 2-sentence caption.



3. Explain the FRET-based assay that is used to obtain the data shown in Figure 1. I'll let you choose to create an illustration or to use prose in the description.



4. For each panel, A-D, explain the experiment briefly and what the result indicates. Then provide a one sentence summary of the observations.

- A. FRET-labeled isotonic + unlabeled isotonic. No change in FRET signal. Indicates that the assay does not detect change in case where there is no difference in osmotic pressure.
- B. FRET-labeled isotonic + unlabeled swollen. Surface area decreases in the isotonic vesicles because they are losing fatty acids to the swollen vesicles.
- C. FRET-labeled swollen + unlabeled swollen. No change in FRET signal. Indicates that the assay does not detect change in case where there is no difference in osmotic pressure and vesicles are under stress.
- D. FRET-labeled swollen + unlabeled isotonic. Surface area decreases in the isotonic vesicles because they are losing fatty acids to the swollen vesicles.

Summary: In this competition assay, the swollen vesicles are able to gain resources from the isotonic vesicles, suggesting a mechanism whereby vesicles with stuff inside “win”.

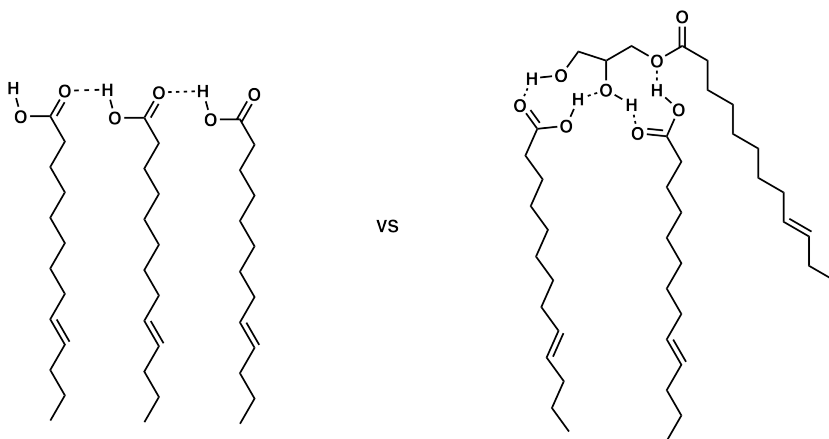
5. Provide explanations for the data in Figure 1 E & F, and the data in Figure 2 A.

1 E&F: Repeating the FRET assay with vesicles composed of phospholipids, we find no exchange of the membrane components, suggesting that the observed competition in B&D is a function of a primitive amphiphile.

2A: By observing differences in FRET signal, the authors conclude that an expected 35% gain/loss in membrane surface area is achieved.

6. The experiments with vesicles swollen with nucleotides have a different composition than those swollen with sucrose. Specify why the change was made and suggest a chemical hypothesis for why the MA:GMM vesicles behave in a superior fashion (it may be helpful to draw GMM).

Thanks Group 6. I'd note that at the moderate pH used in this study there are likely to be carboxylates mixed in, and the glycerol will be particularly useful in H-bonding with them.



7. In three sentences, suggest why the editor of *Science* was persuaded that this is high impact work that should be shared with a broad audience or... refute the editor's decision.

Well – I liked the paper. One definition of life suggests that it is any system capable of undergoing replication, variation and selection – that is, it can evolve over generations. This is an example of a chemical system demonstrating a capacity to compete and select for individuals who have succeeded in sequestering essential biological molecules. All you need to do now is get it to replicate...

