Exam 2 – Fall 2019 – Solutions / Rubric – Peer Review

BCH 341 - Physical Chemistry with a Biological Focus

Professor Jeff Yarger

September 24-26, 2019

Exam 2 DUE Monday September 23, 2019 by 11:59 PM (UTC-7). Turn in completed exam as a typeset single PDF document into the assignment link on ASU Canvas. Please make sure the completed exam is organized, self-contained and all text, equations, numbers, units, figures and images are typeset, clear and legible. **Peer Review DUE Thursday September 26, 2019 by 11:59 PM (UTC-7).**

Student Required Identification:

Last 4-Digits of my ASU ID #:___1234_____
(typically starting with 12xxxx**xxxx** or 10xxxx**xxxx**)

Student OPTIONAL Identification:

Email: _____biopchem@gmail.com_____
(*email address that does not provide obvious personal identification*)

Exam General Instructions
To aid in the optional anonymous peer review process (after the due date for this exam, Sept 24-26), you do NOT need to include your full name, just the last 4 digits of your ASU student ID. There is the **option** of including an email address for contact purposes (which is really helpful). It is recommended that you use an email address that does not contain any obvious personal information (e.g., first or last name).

There are 5 multi-component exercises/projects on this exam. Pick 4 of the 5 problems to complete. Each of the multi-component numbered exercises/projects (problems) is worth 25 points. Hence, the exam is worth a total of 100 points. If you do not include a number in the space below and provide answers for all 5 questions on the exam, then the first 4 will be graded. You are required to explicitly show all equations, numerical calculations and associated units. All points are associated with explicitly showing all your work and no points are awarded for just determining the correct numerical answer. All assumptions need to be clearly and concisely stated. If thermodynamic parameters are used, the citation, reference or link to where this thermodynamics data came from must be stated. Appropriate units should be associated with all numerical problem solving. The completed exam should be typeset (no handwriting of equations or numerical values and associated units).

Problem number student **omitted (not graded)**: __5__ (1, 2, 3, 4 or 5)

Evaluation Section (filled in my peer reviewers and instructors)
Peer-Review Information
This is a new feature and a trial in ASU Canvas as an additional option for an 'assignment' (exam 2 in Canvas). Details about the peer review process will be provided immediately after the due date for this exam.

Summary Peer Review Comment:
Students are welcome to comment on the solution set. Feedback is always welcome and appreciated._____
_____
_____
_____

Instructor Grading Summary:
Exam Score: __100___ / 100 pts Peer Review Score: __15____ / 15 pts

Instructor Comment:
_This is the solution guide (rubric) for exam 2, BCH 341 Fall 2019.

1. This exercise will explore the use of temperature-composition (T-χ) diagrams in the study of biological (lipid) systems.

(A) In numerous experimental study of model membrane-like assembly, a T-χ phase diagram of dielaidoylphosphatidylcholine (DEL) and dipalmitoylphosphatidylcholine (DPL) is often used as an example 'ideal' miscible binary system. A schematic T-χ phase diagram is reproduced from Atkins as Fig. 1 below. Explain what happens as a liquid mixture of composition χ_{DEL}=0.5 is cooled from 45°C to 0°C. (5 pts)

This problem is similar to suggested homework project question 3.39 (P. Atkins et. al., Physical Chemistry for the Life Sciences, 2nd Ed.). In fact, part (A) is the exactly taken from Atkin's project 3.39(c). The exact answer provided by the solution manual is provided below:

"Above about 33°C the membrane has the highly mobile liquid crystal form. At 33°C the membrane consists of liquid crystal in equilibrium with a relatively small amount of the gel form. Cooling from 33 °C to about 20°C, the equilibrium persists but shifts to a greater relative abundance of the gel form. Below 20°C the gel form alone is stable."

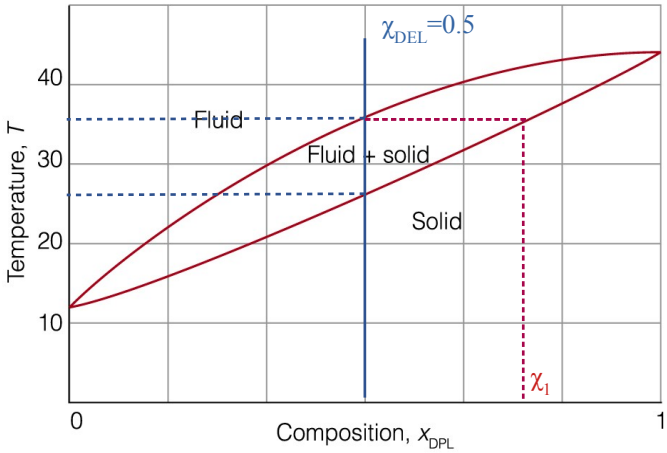


Fig. 1 – Schematic phase diagram (Atkins, 3.40)

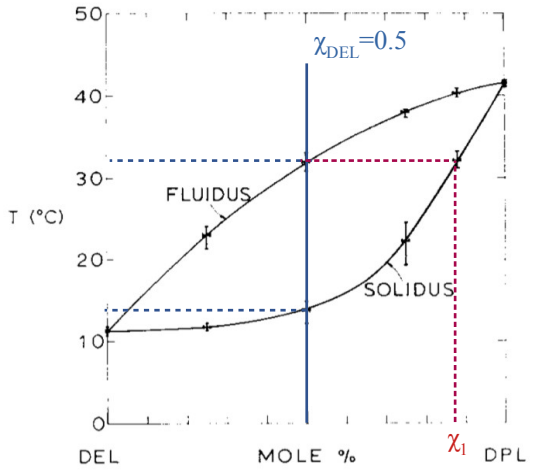
Comments about Atkin's solution manual answer:

- From fig 1 (fig 3.40 in Atkins book), my estimate would be 35°C for the initial Fluid/Solid transition (instead of 33°C) and the gel from alone being stable below 26°C (instead of 20°C).
- The figure labels the phases as fluid and solid, but then refers to it as a liquid crystal and gel in the description of the phase transition. This is confusing and not explained well.

I personally thing that this is much easier to illustrate with more graphically referencing the phase diagram. For example, I put a solid blue line showing the path that χ_{DEL}=0.5 is cooled from 45°C to 0°C is referring too. Also, I put dotted lines to show the estimate of the temperature and the start and end of the transition at the 0.5 mole fraction.

More importantly, the Atkin's solution set does NOT mention the critical aspects of what really happens between ~35°C and 26°C, during the phase transformation from a liquid crystal phase to a gel phase (or from a fluid to a solid, using the labels on the fig. 1). On cooling a mixture of composition χ_{DEL}=0.5 and χ_{DPL}=0.5 initially in the fluid (or liquid crystal) phase, there is no change until the temperature is lowered to around 35°C, when an infinitesimal amount of 'solid' (or gel) first appears with composition χ_1. The solid formed therefore contains a larger proportion of the higher melting component (DPL) than the original fluid (liquid crystal mixture). On further cooling, there is an interaction between the already formed gel (solid) and the fluid (liquid crystal), so that more gel is produced and the gel containing a gradually increasing proportion of the lower melting component (DEL). This can only happen by a preferential absorption of DEL from the fluid and the diffusion of DEL into the gel formed previously at higher temperature. The amount of fluid is reduced, while it also becomes enriched in DEL. The relative proportion of fluid to gel is given by a simple lever rule. Finally, as all the fluid is converted to gel at a temperature ~26°C (lower blue dotted line is my estimate) and below this temperature the gel is cooled without any further change in composition (the gel being at the same concentration as the original fluid started (χ_{DEL}=0.5 and χ_{DPL}=0.5). This concept is very well illustrated in A. Lee, Lipid Phase Transitions and Phase Diagrams II. Mixtures Involving Lipids, *Biochemica et Biophysica Acta*, **472** (1977) 285-344 (fig 3.).

(B) One of the best ways to better understand a topic is to go back to the experimental (or computational) studies and its associated data analysis and interpretation. The experimental T-χ phase diagram for DEL:DPL was first published by C. Grant et. al., *Biochimica et Biophysica Acta,* 363 (1974) 151-158. Figure 2 from this publication is reproduced below (as Fig. 2). Explain what happens as a fluid ('liquid') mixture of composition χ_{DEL}=0.5 is cooled from 45°C to 0°C. (5 pts)



I have drawn the same lines that I used above to describe fig 1 onto fig 2. The same description as above applies, but the transition temperature estimates are clearly different between figures 1 and 2. In fig 2, the initial fluid to gel transition is around ~32°C and the final solidus (gel) ~13°C. Also, the transition has a much different phase transition 'gap', which indicates different changes in enthalpy for the two components.

Fig. 2. Experimental phase diagram (Grant, et. al.)

The general description of a phase diagram for a binary system with complete miscibility in the liquid and solid phases is well described in most thermodynamic textbooks. Also, it is well described in the review article by A. Lee, Lipid Phase Transitions and Phase Diagrams II. Mixtures Involving Lipids, *Biochemica et Biophysica Acta*, **472** (1977) 285-344. I have reproduced fig 3. from this paper below.

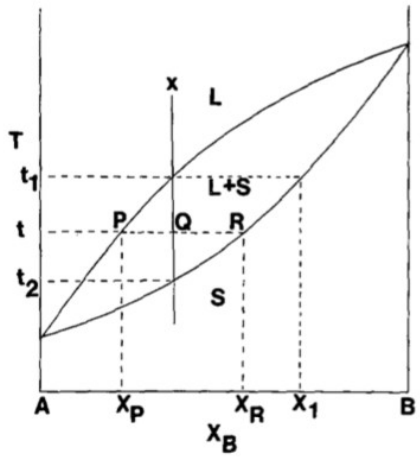


Fig. 3. The phase diagram for a binary system with complete miscibility in the liquid and solid phases.

The detailed description of this graph is given on p 293-295. Also, an ideal gas-liquid binary phase diagram also classically has this same shape and similar thermodynamic description (enriching the gas phase in the lower boiling point component, which is the basis for purification via distillation).

(C) This binary lipid system (DEL:DPL) has been extensively studied and is one of several that commonly gets used as model system for understanding lipid phase transitions and phase diagrams. There are many thermodynamic values and physical properties that can be determined directly or indirectly from phase diagrams. Its really useful to try and estimate (or calculate) as many different thermodynamic parameters of DEL and DPL as possible using the above experimental phase diagram (Fig. 2). However, to be specific for exam purposes, estimate (or calculate) the change in enthalpy (ΔH, latent heat of 'melting' or 'fusion') expected for this phase transition (for both components). This is one of the most useful and molecularly insightful thermodynamic energies you can determine from a standard T-χ binary phase diagram. Also, report your estimate of the phase transition temperature for each component (lipid). (15 pts)

Primary condition for phase equilibrium at a specific temperature is that the chemical potentials of each component in both phases are equal:

$$\mu_{DEL}^{gel} = \mu_{DEL}^{fluid} \quad \text{and} \quad \mu_{DPL}^{gel} = \mu_{DPL}^{fluid}$$

assuming ideal liquid/gel and mixing behavior

$$\mu_{DEL}^{fluid} = \mu_{DEL}^{fluid^o} + RT \ln X_{DEL}^{fluid} \quad \text{and} \quad \mu_{DEL}^{gel} = \mu_{DEL}^{gel^o} + RT \ln X_{DEL}^{gel}$$

At equilibrium, $$\ln \frac{X_{DEL}^{fluid}}{X_{DEL}^{gel}} = \frac{-\mu_{DEL}^{fluid^o} + \mu_{DEL}^{gel^o}}{RT} = \frac{-\left(\Delta H_{fus,DEL}\right)_{T_{fus}}}{R}\left(\frac{1}{T} - \frac{1}{T_{fus}}\right)$$

so, $$\frac{X_{DEL}^{fluid}}{X_{DEL}^{gel}} = \exp\left[\frac{-\left(\Delta H_{fus,DEL}\right)_{T_{fus}}}{R}\left(\frac{1}{T} - \frac{1}{T_{fus,DEL}}\right)\right] = e^{-A}$$

This is making the assumption that $\Delta C_P = 0$, which is often reasonable over a small temperature range. See A. Lee, Lipid Phase Transitions and Phase Diagrams II. Mixtures Involving Lipids, *Biochemica et Biophysica Acta*, **472** (1977) p. 288 for the full general derivation (or Prof. Yarger's lecture notes).

A similar derivation can be written from DPL, resulting in:

$$\frac{X_{DPL}^{fluid}}{X_{DPL}^{gel}} = \exp\left[\frac{-\left(\Delta H_{fus,DPL}\right)_{T_{fus}}}{R}\left(\frac{1}{T} - \frac{1}{T_{fus,DPL}}\right)\right] = e^{-B}$$

and in this binary system, $X_{DEL}^{fluid} = 1 - X_{DPL}^{fluid}$ and $X_{DEL}^{gel} = 1 - X_{DPL}^{gel}$

and with a little rearranging of equations (*Biochem. Biophys. Acta*, **472** (1977) p. 292),

$$X_A^{fluid} = \frac{e^{-A}\left(e^{-B} - 1\right)}{e^{-B} - e^{-A}} \quad ; \quad X_B^{fluid} = \frac{e^{-B}\left(e^{-A} - 1\right)}{e^{-A} - e^{-B}} \quad ; \quad X_A^{gel} = \frac{\left(e^{-B} - 1\right)}{e^{-B} - e^{-A}} \quad ; \quad X_B^{gel} = \frac{\left(e^{-A} - 1\right)}{e^{-A} - e^{-B}}$$

where A is DEL and B is DPL.

Estimating the transition temperatures from fig 2: 11°C and 42°C, for DEL and DPL, respectively, we can solve to determine the associated change in enthalpies for both lipids. You will get different values for each of the temperature data points and taking the average gives a reasonable estimate of ΔH, which is +30-70 kJ/mol for each of the components (quite a large range!!).

This is where a graphical method can be MUCH more illustrative and in my opinion, instructive!!

The easiest way to illustrate the effect that the latent heat of fusion (change in enthalpy for the lipid phase transition) has on the binary phase diagram is to make an interactive graph/plot. I have done this in google sheets and created a publicly sharable link: https://docs.google.com/spreadsheets/d/15JcmCSOWwEfYrW4NX58ruI0ibOuJTjfAxoN2P1rPnV0/edit?usp=sharing

Below is a screenshot from the google sheet I made and publicly shared.

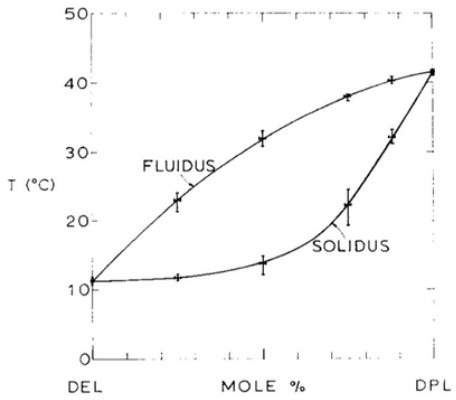
Estimate Data from the binary phase diagram (Grant et. al., Biochimica et Biophysica Acta, 363 (1974) 151-158, fig. 2)

Fluidus Data Points (Estimated from phase diagram)

Temp (C)	Mole Fraction DPL	exp(-A)	exp(-B)	Estimated Mol % DPL
11	0	1.0000	0.1010	0.00
23	25	3.0527	0.2597	19.09
32	50	6.6553	0.5023	46.17
38	75	10.9129	0.7633	74.55
40	88	12.8145	0.8744	86.52
42	100	15.0168	1.0000	100.00

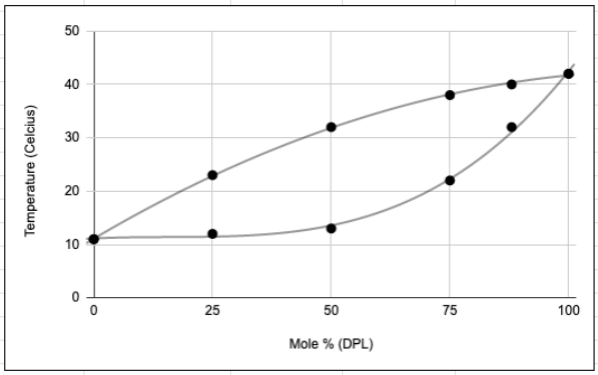
Solidus Data Points (Estimated from phase diagram)

Temp (C)	Mole Fraction DPL	exp(-A)	exp(-B)	Estimated Mol Frac DPL
11	0	1.00	0.1010	0.00
12	25	1.10	0.1096	10.23
13	50	1.21	0.1189	19.42
22	75	2.79	0.2408	70.23
32	88	6.66	0.5023	91.91
42	100	15.02	1.0000	100.00

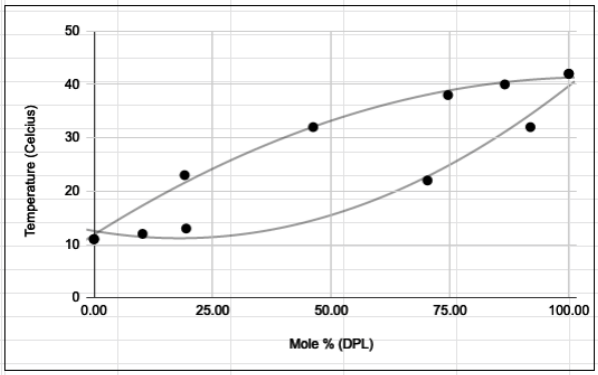


Estimate of thermodynamic Parameters			'Melting Temp'
ΔH(DEL)	65	kJ/mol	284 K
ΔH(DPL)	55	kJ/mol	315 K
R	0.008314	kJ/Kmol	

Reproduce Fig 2 from Exam 2 problem 1.



Enthalpy Plot Estimate



This spreadsheet and associated plots are editable so that you can change the estimated value of the enthalpies of the phase transition for both binary components, A & B, which in our case is DEL and DPL. I have highlighted the values in yellow.

Making a copy of this spreadsheet, understanding the equations programmed into the cells and varying the enthalpy values is a good way to start to better understand the effect that thermodynamic parameters like the enthalpy have on idea binary phase diagrams.

2. A thermodynamic treatment allows predictions of the stability of DNA. Thermodynamic parameters for calculating double-strand stability typically provide the standard Gibbs free energies (ΔG), enthalpies (ΔH) and entropies (ΔS) of formation at 310 K of short sequences of base pairs as two polynucleotide chains come together. These thermodynamic parameters vary significantly with pH, ionic strength and other common solution conditions. An example of a table of thermodynamic parameters for calculating double-strand stability is provided in the thermodynamic data and tables link at biopchem.education. To estimate the standard Gibbs free energy of formation of a double-stranded piece of DNA, $\Delta_{DNA}G^{o}$, we sum the contributions from the formation of the sequences and add to that quantity the standard Gibbs free energy of initiation of the process.

$$\Delta_{DNA}G^{o} = \Delta_{init}G^{o} + \Delta_{seq}G^{o}(\text{sequences})$$

Similar procedures lead to $\Delta_{DNA}H^{o}$ and $\Delta_{DNA}S^{o}$.
(A) Provide a molecular explanation for the fact that $\Delta_{init}G^{o}$ is most commonly found to be positive and $\Delta_{seq}G^{o}$ values are always found to be negative. (5 pts)
(B) Estimate the Gibbs free energy, enthalpy and entropy changes as well as the 'melting' temperature for the following reaction:

5′-A-G-C-T-G-3′ + 5′-C-A-G-C-T-3′ → $\begin{matrix} 5'-A-G-C-T-G-3' \\ 3'-T-C-G-A-C-5' \end{matrix}$

and please cite the source of any standard thermodynamic parameters. (5 pts)

This problem is similar to suggested homework project question 3.21 (P. Atkins et. al., Physical Chemistry for the Life Sciences, 2nd Ed.). In fact, part (A) and (B) are taken exactly from Atkin's exercise 3.21(a&c). The answer provided by the solution manual is provided below:

The Gibbs free energy of initiation of the process, $\Delta_{init}G^{o}$, is positive because by bringing together the two strands to form DNA, $\Delta_{init}S^{o}$ should be negative, resulting in a positive value for the Gibbs free energy. The Gibbs free energy of formation of DNA is negative because of hydrogen bonding and π-stacking interactions between base pairs. They hydrogen bonding is greater for G-C base pairs because of 3 hydrogen bonds.

Atkins textbook provides a thermodynamic table (which is not complete, nor does it describe the solution conditions, which is critical). Hence, biopchem.education provides a more detailed thermodynamic table. We will look at both here. The Atkin's table for exercise 3.21 is given below:

Sequence	5′–A–G 3′–T–C	5′–G–C 3′–C–G	5′–T–G 3′–A–C
$\Delta_{seq}G^{\ominus}$/(kJ mol^{-1})	−5.4	−10.5	−6.7
$\Delta_{seq}H^{\ominus}$/(kJ mol^{-1})	−25.5	−46.4	−31.0
$\Delta_{seq}S^{\ominus}$(kJ mol^{-1})	−67.4	−118.8	−80.8

$$\Delta_{DNA}G^{o} = \Delta_{init}G^{o} + \sum_{seq}\Delta_{seq}G^{o}$$
$$\Delta_{DNA}G^{o} = \Delta_{init}G^{o} + 2\Delta_{seq}G^{o}(AG/TC) + \Delta_{seq}G^{o}(GC/CG) + \Delta_{seq}G^{o}(TG/AC)$$
$$\Delta_{DNA}G^{o} = +14.2\,kJ/mol + (-10.8 - 10.5 - 6.7)\,kJ/mol = -13.8\,kJ/mol$$

In a similar manner, the standard enthalpy and entropy changes are calculated below:

$$\Delta_{DNA}H^{o} = \Delta_{init}H^{o} + \sum_{seq}\Delta_{seq}H^{o}$$
$$\Delta_{DNA}H^{o} = \Delta_{init}H^{o} + 2\Delta_{seq}H^{o}(AG/TC) + \Delta_{seq}H^{o}(GC/CG) + \Delta_{seq}H^{o}(TG/AC)$$
$$\Delta_{DNA}H^{o} = +2.5\,kJ/mol + (-51.0 - 46.4 - 31.0)\,kJ/mol = -126\,kJ/mol$$

$$\Delta_{DNA} S^o = \Delta_{init} S^o + \sum_{seq} \Delta_{seq} S^o$$
$$\Delta_{DNA} S^o = \Delta_{init} S^o + 2\,\Delta_{seq} S^o(AG/TC) + \Delta_{seq} S^o(GC/CG) + \Delta_{seq} S^o(TG/AC)$$
$$\Delta_{DNA} S^o = -37.7\,J/Kmol + (-134.8 - 118.8 - 80.8)\,J/Kmol = -372\,J/Kmol$$

Atkin's fig 3.17 shows that the melting temperature changes linearly with the fraction (*f*) of G-C base pairs.

$$T_{melting} = 325 + 39.7\,x\,f$$

The faction of G-C base pairs in this example is 3/5. Thus an estimate of the melting temperature of the piece of DNA shown above is:

$$T_{melting} = 325 + 39.7\,x\,(3/5) = 349\,K$$

Using the biopchem.education table we can get a separate calculation for these thermodynamic parameters for calculating double-strand stability in DNA at pH=7 and 1 M NaCl, which are more specific conditions.

$$5'-A-G-C-T-G-3' + 5'-C-A-G-C-T-3' \rightarrow \begin{matrix} 5'-A-G-C-T-G-3' \\ 3'-T-C-G-A-C-5' \end{matrix}$$

$$\Delta_{DNA} G^o = \Delta_{init} G^o + \sum_{seq} \Delta_{seq} G^o(nearest\ neighbors)$$
$$\Delta_{DNA} G^o = \Delta_{init} G^o + \Delta_{seq} G^o(AG/TC) + \Delta_{seq} G^o(GC/CG) + \Delta_{seq} G^o(CT/GA) + \Delta_{seq} G^o(TG/AC)$$
$$\Delta_{DNA} G^o = +8.1\,kJ/mol + (-5.4 - 9.3 - 5.4 - 6.0)\,kJ/mol = -18.0\,kJ/mol$$

Similar calculations for enthalpy and entropy changes:

$$\Delta_{DNA} H^o = +0.8\,kJ/mol + (-32.7 - 41.0 - 32.7 - 35.6)\,kJ/mol = -141.2\,kJ/mol$$
$$\Delta_{DNA} S^o = -23.4\,J/Kmol + (-87.9 - 102.2 - 87.9 - 95.0)\,J/Kmol = -396.4\,J/Kmol$$

The 3' and 5' direct can vary the values for the enthalpy and entropy changes by a small amount, as shown in the more complete thermodynamic table.

(C) Estimate the equilibrium constant for the above reaction. (5 pts)

The more accurate Gibbs free energy calculation is from the biopchem.education table and this is at a temperature of 37°C. So, the calculation for the equilibrium constant will be for 37°C. There will be a temperature dependence to the Gibbs free energy and the resulting equilibrium constant that must me taken into account if another temperature for this equilibrium is desired. A temperature of 37°C is an important temperature because this is a common temperature for DNA in living systems.

$$K_{310} = e^{-\Delta_{DNA} G^o / RT} = 1079$$

* This is for pH=7 and 1 M NaCl solution.

(D) Add one additional nucleotide at any position in both single-strand 5 nucleic acid molecules used in the reaction above (left side), with the goal of making the resultant DNA complex (right side) have the highest possible stability. Show the resulting DNA complex formed from the new 6 nucleotide molecules and thermodynamically determine the additional stability. (10 pts)

Adding 5'-G-C with the associated 3'-C-G provides the most stability and the highest melting point. This can be seen by looking at the ΔG^e value which is the most negative, -9.3 kJ/mol for the 5'-G-C / 3'-C-G pair.

$$5'-A-G-C-T-G-C-3' + 5'-G-C-A-G-C-T-3' \rightarrow \begin{matrix} 5'-A-G-C-T-G-C-3' \\ 3'-G-T-C-G-A-C-5' \end{matrix}$$

The stability is also increased by the addition of one more base pair.

$$\Delta_{DNA}G^o = +8.1\,kJ/mol + (-5.4-9.3-5.4-6.0-9.3)\,kJ/mol = -27.3\,kJ/mol$$
$$\Delta_{DNA}H^o = +0.8\,kJ/mol + (-32.7-41.0-32.7-35.6-41.0)\,kJ/mol = -182.2\,kJ/mol$$
$$\Delta_{DNA}S^o = -23.4\,J/Kmol + (-87.9-102.2-87.9-95.0-102.2)\,J/Kmol = -498.6\,J/Kmol$$

$$K_{310} = e^{-\Delta_{DNA}G^o/RT} = 4.0\,x\,10^4$$

$$T_{melting} = 325 + 39.7\,x\,f = 325 + 39.7\,x\,(4/6) = 351\,K$$

A spreadsheet can be made to interactively put in new nucleotides and calculate the resulting melting temperature, equilibrium constant and thermodynamic parameters shown above. I suggest doing this independently, especially if you are going to take the final exam in BCH341.

3. Show graphically the variation with pH of the composition of a 1.0 millimolar (1.0 mM) aqueous alanine (5 pts) and a 1.0 millimolar (1.0 mM) aqueous glutamic acid (10 pts) solution. Try to minimize assumptions and calculate all concentrations as accurately as possible (5 pts). Show all your work and state any assumptions (5 pts).

This problem is exactly like the suggested homework exercise 4.40 (P. Atkins et. al., Physical Chemistry for the Life Sciences, 2nd Ed.) and graphically is like figures 4.15 and/or 4.16 in the textbook.

* Minimizing assumptions would mean solving for the concentration of ALL possible species (molecular components) in solution at all pH values. This definitely requires a computer or spreadsheet program. The common assumption that gets used a lot is to assume as you get 3-4 pH units away from the pKa value, that the associated species are zero (<< than all other species). This can greatly simplify the calculation of concentrations. Also, if all the pKa values are far apart, it is common to use the Henderson-Hasselbalch equation. Your suggested homework discussion question 4.7 covers this topic.

I made a publicly accessible google sheet that is general enough to allow a someone to change the 3 pKa values and see the resulting graph. I have it setup explicitly for Glu, but it can be changed to show any tri-protic amino acid. I leave it as a general fractional concentration vs. pH. However, in this case you can substitute the fractional concentration for mM concentration. I even provide an example of the concentration of all species at pH=7.4

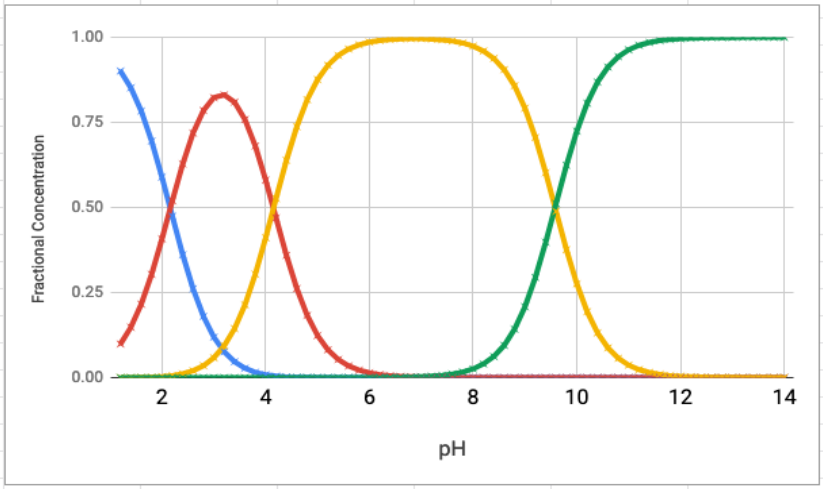
https://docs.google.com/spreadsheets/d/1F_pLgvhRseNwaFyE79oiKVOYti5QN9VgpY_rs2TCm2U/edit?usp=sharing

A screenshot is shown below:

Table for deprotonation reaction of 3 Acid Constants (pKa's) Amino Acids

pH	H3AA+	H2AA	HAA-	AA2-
1	0.94	0.06	0.00	0.00
1.2	0.90	0.10	0.00	0.00
1.4	0.85	0.15	0.00	0.00
1.6	0.78	0.22	0.00	0.00
1.8	0.70	0.30	0.00	0.00
2	0.59	0.41	0.00	0.00
2.2	0.47	0.52	0.01	0.00
2.4	0.36	0.63	0.01	0.00
2.6	0.26	0.72	0.02	0.00
2.8	0.18	0.79	0.04	0.00
3	0.12	0.82	0.06	0.00
3.2	0.08	0.83	0.09	0.00
3.4	0.05	0.81	0.14	0.00
3.6	0.03	0.76	0.21	0.00
3.8	0.02	0.68	0.30	0.00
4	0.01	0.58	0.41	0.00
4.2	0.00	0.47	0.53	0.00
4.4	0.00	0.36	0.64	0.00
4.6	0.00	0.26	0.74	0.00
4.8	0.00	0.18	0.82	0.00
5	0.00	0.12	0.88	0.00
5.2	0.00	0.08	0.92	0.00
5.4	0.00	0.05	0.95	0.00
5.6	0.00	0.03	0.97	0.00
5.8	0.00	0.02	0.98	0.00
6	0.00	0.01	0.99	0.00
6.2	0.00	0.01	0.99	0.00
6.4	0.00	0.01	0.99	0.00
6.6	0.00	0.00	1.00	0.00
6.8	0.00	0.00	1.00	0.00
7	0.00	0.00	1.00	0.00
7.2	0.00	0.00	0.99	0.00
7.4	**0.00**	**0.00**	**0.99**	**0.01**
7.6	0.00	0.00	0.99	0.01

pKa1	pKa2	pKa3
2.16	4.15	9.58



Blue	H3AA+	H3Glu+
Red	H2AA	H2Glu
Yellow	HAA-	HGlu-
Green	AA2-	Glu2-

1 mM Glutamic Acid (at pH 7.4)

[H3O+]	0.000000000398	M
[H3Glu+]	0.00	mM
[H2Glu]	0.00	mM
[HGlu-]	0.99	mM
[Glu2-]	0.01	mM

* Ala can be looked at in a similar fashion… and you can combine both onto one (clustered) plot, if you want.

4. (A) Use the Boltzmann distribution to describe the molecular features that determine the magnitude of equilibrium constants and their variation with temperature (10 pts). (B) Provide a detailed molecular equilibrium example that helps illustrate your explanation. Include a graphical, visual or animated component in your example. Your example can't be the same or similar to examples, brief illustrations or case studies shown in Atkin's textbook, chapter 4. (15 pts)

This problem suggested homework discussion question 4.5 (P. Atkins et. al., Physical Chemistry for the Life Sciences, 2nd Ed.) and an excellent discussion can be found in the textbook section 4.3(c).

Also, I will record a screencast on this topic (like we have for many of the discussion questions in Atkin's textbook).

The example in the textbook is the binding of oxygen to myoglobin and hemoglobin on pages 144-146 (case study 4.1). I will work on posting a few other examples on biopchem.education as well as in screencasts. Also, I am hopeful that students come up with some really good examples and will give me permission to publish their examples at biopchem.education.

Graphically, the textbook uses fig. 4.6 and 4.7 showing below:

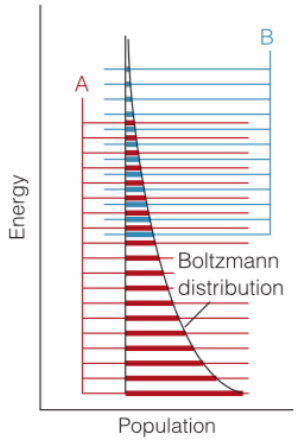


Fig. 4.6 The Boltzmann distribution of populations over the energy levels of two species A and B with similar densities of energy levels; the reaction A → B is endothermic in this example. The bulk of the population is associated with the species A, so that species is dominant at equilibrium.

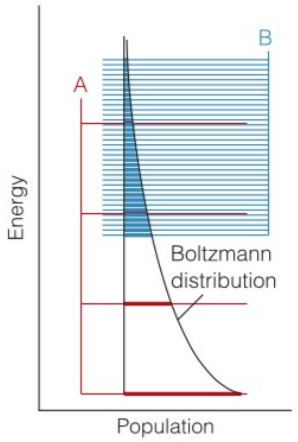


Fig. 4.7 Even though the reaction A → B is endothermic, the density of energy levels in B is so much greater than that in A, the population associated with B is greater than that associated with A; hence B is dominant at equilibrium.

5. Find a paper in the scientific literature that expands on one of the above exercises/projects (5 pts). Use the additional experimental, computational or theoretical thermodynamic information to further expand upon the thermodynamic concepts in one of the problems above (15 pts). Please provide a proper scientific citation and link for the chosen journal article. (5 pts)

I really hope that students find some interesting articles that expand on these take-home exam problems/projects. As an example, I found a ton of articles that expand on problem/project #1. As an example, I will talk about the one I posted on YellowDig and helps in creating example binary phase diagrams in lipid systems:

A. Lee, Lipid Phase Transitions and Phase Diagrams II. Mixtures Involving Lipids, *Biochemica et Biophysica Acta*, **472** (1977) 285-344.

Biochimica et Biophysica Acta, 472 (1977) 285–344

BBA 85178

LIPID PHASE TRANSITIONS AND PHASE DIAGRAMS

II. MIXTURES INVOLVING LIPIDS

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(Received January 11th, 1977)

CONTENTS

This paper and its associated references made it easy to construct a google sheets spreadsheet/plot for looking at the effect of enthalpy changes of the binary phase DEL:DPL under ideal conditions. I provide a link to this spreadsheet and associated plots in problem 1 solutions.

Building on the original work of Grant et. al., there have been several different molecule spectroscopy and calorimetry methods used to look at binary phase separation. For example,

R. McElhaney, Chem. Phys. Lipids 30 (1982) 229-259. This can be looked up and downloaded in PDF format from web of science at ASU.

A screenshot of the first section is shown below:

Chemistry and Physics of Lipids, 30 (1982) 229–259
Elsevier/North-Holland Scientific Publishers Ltd.

THE USE OF DIFFERENTIAL SCANNING CALORIMETRY AND DIFFERENTIAL THERMAL ANALYSIS IN STUDIES OF MODEL AND BIOLOGICAL MEMBRANES

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Differential scanning calorimetry (DSC), and to a lesser extent differential thermal analysis (DTA), are powerful yet relatively rapid and inexpensive thermodynamic techniques for studying the thermotropic phase behavior of lipids in model and biological membranes, without the introduction of exogenous probe molecules. In this review the principles as well as the scope and limitations of DSC and DTA are discussed first. The application of these techniques to the study of the thermotropic phase behavior of aqueous dispersions of various single synthetic phospholipids are then summarized, and the effects of cholesterol, free fatty acids, lysophospholipids, drugs, anesthetics and proteins on the gel to liquid-crystalline phase transitions exhibited by these model systems are discussed. The phase mixing properties of model membranes consisting of mixtures of two or more synthetic or natural phospholipids are considered next. Finally, the thermotropic phase behavior of prokaryotic plasma membranes and of the plasma, microsomal and mitochondrial membranes of eukaryotic cells are reviewed, and the applications of DSC and DTA to study the thermal behavior of specific membrane proteins, as well as the physical properties of the membrane lipid phase, are summarized.

Keywords: differential scanning calorimetry; differential thermal analysis; lipids; biomembranes.

This paper (and a bunch of others) show more updated phase diagrams and using DSC they are able to look at the change in enthalpy directly. Also, a much more detailed explanation is given for the molecular details of the phase transformation (liquid-crystal to gel phase, being the most appropriate description).

I could keep on with 10-20 other journal articles I looked at just on binary lipid phase diagrams and the addition of cholesterol, which is an obvious important addition to lipid-membrane systems in human health. However, I think this is best done in a blog post on biopchem.education

Extra Credit: After your exam is turned in, it will be put into an anonymous peer review system (in Canvas) and students will have 1-2 days to peer review three randomly assigned exams. Students who provide insightful comments will receive 15 extra credit points (5 pts/exam). These points will only be given to students that provide detailed corrections and comments on each of the 3 assigned exams and for each problem within the submitted exam. I think it is possible to leave comments directly in the Canvas LMS. However, it is recommended that the peer reviewer directly comment on the students pdf exam document.

The peer review (NOT peer grading) is open Sept 24-26th at ASU-Canvas for students. All discussion about exam questions and peer review will be done on YellowDig.

Also, please please send me comments at YellowDig or an email to yarger@biopchem.education if you have any suggestions for improving this rubric/solution set or you find any errors/typos.

Cheers, Jeff Yarger