Department of Chemistry
Cumulative Examinations

December 5, 2015

You may choose to answer any exam from any area covered in the examination booklet. Each exam may contain multiple parts. You may answer more than one exam but each exam is scored separately and is treated as an individual examination result. Thus, answering parts of two exams with a score of 50% would not yield a 100% grade for this cumulative exam. Instead you would receive 50% on each examination attempted.

This booklet contains five examinations.

1) Analytical Cumulative Examination, Pages 1-2
2) Biochemistry Cumulative Examination, Pages 3-4
3) Inorganic Cumulative Examination, Pages 5-6
4) Organic Cumulative Examination, Page 7
5) Physical Cumulative Examination, Page 8

On your examination booklet:

1) Print your student ID number.
2) Print the Exam Booklet number.
3) Print the question number you are answering.
4) Print the Exam Date.

Do not write your name anywhere on the examination booklet. Each exam will be scored anonymously. If you attempt more than one exam, you must use a separate examination booklet for each examination.

When you complete the examination, return the examination and your answer booklet to the proctor. Exam results will be posted on bulletin board #2B on the north side of the hall near BRWN 2124.
1. A variety of detectors have been used in gas chromatography. Answer the following questions regarding two common detectors:

   a) Provide an equation that gives the response of an electron capture detector (ECD) to an analyte at low concentrations and in the absence of any instrumental discrimination effects. (5 pts)

   b) Provide an equation that gives the response of a photoionization detector (PID) to an analyte at low concentrations in the absence of any discrimination effects. (5 pts)

   c) Under what circumstances would you choose to use an ECD? (5 pts)

   d) Under what circumstances would you choose to use a PID? (5 pts)

2. Any measurement that seeks to determine the concentration of an unknown via an instrumental technique relies upon a relationship between the measured quantity (e.g., a voltage, a current, absorbance/transmittance) and concentration. The following questions relate to the random error associated with the measured quantity and its relationship to the resulting random error in concentration. (Assume no systematic error.)

   a) A common means for determining the concentration of an analyte species in solution is to compare the radiant power of light transmitted through the analyte solution, P, with radiant power, P₀, transmitted through a solution with negligible analyte present (i.e., a blank solution) under otherwise identical conditions. What is the relationship between concentration, C, in the limit of low concentration, and P/P₀? Define all symbols that you provide. (5 pts)

   b) Provide a mathematical relationship for the sensitivity associated with this measurement? (10 pts) (note: sensitivity $\neq$ detection limit)

   c) For a fixed error in the measurement of P/P₀ (i.e., $s_{P/P₀} = constant$) what is the relationship between the error in concentration, $s_C$, that arises from the error in P/P₀? (10 pts)

   d) For $s_{P/P₀} = constant$ with concentration, draw the shape of a plot of $s_C/C$ versus C (i.e., a plot of the relative concentration error versus concentration). (10 pts)

3. What is a coulometric titration? Describe the principle behind the measurement and a typical way to conduct such a measurement. Compare and contrast a coulometric titration with the more traditional volumetric titration. What are the relative advantages/disadvantages of a coulometric versus volumetric titration? (10 pts)
4. Some analytical methods are based on the establishment of equilibrium (i.e., equilibrium methods) and some are based on the measurement of rates of reactions (i.e., kinetic methods).

   a) List two advantages of kinetic methods over equilibrium methods. (5 pts)

   b) List two disadvantages of kinetic methods relative to equilibrium methods. (5 pts)

   c) Glucose is the most widely determined biomarker in the world. Many of the approaches used for glucose determination are kinetic methods. Why is this so? (5 pts)

   d) Species A reacts with species B in an essentially irreversible reaction with 1:1 stoichiometry and with a rate constant of $1.80 \times 10^{-2} \text{ M}^{-1}\text{s}^{-1}$. After rapid mixing of solutions containing A and B, 50.0% of A was converted to products after 30.0 s. If the concentration of B was significantly higher than that of A such that the concentration of B was essentially constant over 30s, what was the concentration of B? (10 pts)

5. Hypothesis testing is commonly used in quantitative chemical analysis. Name and describe the relevant statistical tests used to address the following questions: (10 pts)

   a. Is there bias in my method?

   b. Are the precisions of two different methods the same?

   c. Am I justified in considering a data-point to be an outlier?

   d. Are the quantities of active ingredients in these two tablets the same?

   e. How well does the model I have chosen fit the data?
1. Is it possible to correctly fold a protein \textit{in silico}? 

2. Please explain the difference between polarizable and non-polarizable force fields.

3. ROSETTA is the best-known computational tool for predicting protein structure. Briefly, ROSETTA assembles a new structure from various 9-residue (3-residue) fragments extracted from Protein Data Bank. Many candidate structures obtained in this manner are ranked using an empirical knowledge-based scoring function (in other words, ROSETTA tests whether candidate structures are consistent with the established structural patterns seen in the Protein Data Bank). The best-scoring candidate structure is selected to become a chosen ROSETTA model. For smallish proteins ROSETTA achieves the backbone accuracy of 5 Å. Relatively recently an enhanced version of ROSETTA, called CS-ROSETTA (Chemical Shift ROSETTA) has been released. What is the mode of operation of CS-ROSETTA? Please speculate.

4. Explicit water models in Molecular Dynamics can be classified into 3-, 4-, and 5-centered. What does this mean?

5. After experimental NMR data have been collected, they are used as an input for a computer program that builds a structural model (i.e. solves protein structure). Please describe general principles of this structure-building process (as done on the computer).

6. After experimental X-ray diffraction data have been collected, they are used as an input for a computer program that builds a structural model (i.e. solves protein structure). Please describe general principles of this structure-building process (as done on the computer). Assume that phase problem has been successfully solved prior to the model-building step.

7. Two (sufficiently long) protein sequences have been aligned and showed the identity of 30%. What can be said about the structures of these two proteins – do we expect these structures to be similar or dissimilar?

(continued on the next page)
8. The figure to the right shows the empirical potential functions that is an integral part of all conventional MD force fields. What is the meaning of this potential function?

9. The enzyme Superoxide Dismutase (SOD) catalyzes conversion of highly reactive superoxide radical to far less damaging hydrogen peroxide. Is it possible to study the mechanism of SOD catalysis using Molecular Dynamics? Is it possible to study the mechanism of SOD catalysis using Density Functional Theory? What would be your preferred choice of computational method to study the mechanism of SOD catalysis?

10. MD simulations of biomolecules in explicit solvent are normally performed under periodic boundary conditions (PBCs). The most popular simulation cell is a truncated octahedron (shown on the right). Please, explain why PBCs are needed and how they are implemented with the truncated octahedron. Use a graphic sketch if necessary.
Inorganic Chemistry Cumulative Exam
Purdue University
December 5, 2015

Question 1: 25 points
Carbonic anhydrase is an important enzyme for catalyzing the following reaction:
\[ \text{CO}_2 + \text{H}_2\text{O} \rightarrow \text{H}^+ + \text{HCOO}^- \]
Carbonic anhydrase is one of the very few metalloenzymes for which synthetic mimics of the active site can actually exhibit full, catalytic activity. (Albeit at a slower rate.) Design a functional, small molecule mimic of carbonic anhydrase. Draw a picture of your new compound. Describe all of the important features that you have incorporated.

Question 2: 25 points
Alkaline phosphatase catalyzes the following reaction:
\[ \text{R-OPO}_3^{2-} + \text{H}_2\text{O} \rightarrow \text{ROH} + \text{HPO}_4^{2-} \]
Here is what the enzyme active site looks like with the R-OPO$_3^{2-}$ substrate bound:

Note that charges are not shown and bond orders may differ from the drawing.
After the shown substrate binding, the next step in catalysis is attack of the serine alkoxide (shown in blue) onto the alkylphosphate substrate (shown in red). (If I can get this exam printed in color.)
A) How could you redesign this active site to accelerate the serine attack on the phosphate? Feel free to propose any changes that you would like. Do not worry about how difficult it may or may not be to actually produce such an altered protein.
B) What problem have you just created by making these changes?
**Question 3: 25 points**
Your apartmentmate has taken to wearing capes, only going out at night, and sleeping in a coffin that she got during the great Black Friday sale at vampirecoffins.com. She claims to be a vampire. What kind of chemical and/or biochemical test could you run to see whether or not your apartmentmate really is a vampire? She is quite accommodating and willing to provide you with blood or other samples if you wish.

**Question 4: 25 points**
Speaking of blood... Why is your blood red? Describe the relevant biochemistry, compounds, and electronic transition.
In a recent seminal and highly publicized paper, Plata and Singleton (J. Am. Chem. Soc., 2015, 137 (11), pp 3811–3826) reported an investigation of the mechanism of the Morita Baylis-Hillman reaction shown below.

In the paper, they carried out an extensive experimental study of the mechanism, and compared it to the mechanisms examined in theoretical studies. They concluded that the theoretically predicted mechanisms were so worthless that they were "not even wrong," because they couldn't make any legitimate testable predictions. Moreover, increasing the quality of the calculations didn't help, because they were all based on incorrect mechanisms in the first place, and missed key features. The questions on this exam refer to that paper, which you have hopefully read.

An important conclusion of the paper is that the experimental evidence supports a very mundane, simple mechanism, consistent with the type that we would draw based on first principles, like those you would learn in an introductory graduate level organic course.

1) Write an “arrow pushing” mechanism for the reaction, assuming methanol as the solvent

2) To a large extent, the published theoretical mechanisms derided by Plata and Singleton agreed with the typical mechanism, with one important difference. Draw the theoretical mechanism, and highlight where it is different.

3) Among the evidence used to determine the mechanism were the carbon kinetic isotope effects (KIEs).  
   a) Identify the positions on molecules 5 and MA that you would expect to have the largest kinetic isotope effects, based on the mechanism.  
   b) Plata and Singleton describe that the KIEs “were determined at natural abundance by NMR methodology.” Explain how this experiment is done.

4) Proton KIEs were also very important. One experiment, in particular, is very illuminating. When MA was allowed to equilibrate in CD$_3$OD (HINT: Think H/D exchange), they found a solvent KIE of 3.1 (CH$_3$OH vs CD$_3$OD). As they argue, this result can be used to identify the rate-limiting step of the reaction (at that temperature). Which step in the mechanism from part 1 is the rate-limiting step, and how is it consistent with the measured kinetic isotope effect?

5) Plata and Singleton list some of the theoretical methods that have been used to investigate the mechanism of the reaction, including MPW1K, CBS-4M, G3MP2, B3LYP and M06-2X methods. For each of these 5, indicate whether they are ab initio based or Density Functional Theory (DFT) (it’s either one or the other).

(Extra Credit 5 points) What's the difference between ab initio and DFT?
The following questions pertain to the statistical thermodynamic description of a system with two energy levels $\varepsilon_0 = 0$ and $\varepsilon_1$ of degeneracy $g_0$ and $g_1$, respectively, and application of the results to molecular conformational equilibria.

**Fundamental Constants:**

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<th>Name</th>
<th>Symbol</th>
<th>Value (in SI units)</th>
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<tr>
<td>Avogadro's Number</td>
<td>$N_A$</td>
<td>$6.02 \times 10^{23}$ molecules/mol</td>
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<tr>
<td>Boltzmann's Constant</td>
<td>$k_B$</td>
<td>$1.38 \times 10^{-23}$ J/K</td>
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<tr>
<td>Gas Constant</td>
<td>$R = N_A k_B$</td>
<td>$8.31$ J/(K mol)</td>
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1) (10 points) Write an expression for the partition function of the above system, in terms of the variables $\Delta \varepsilon = \varepsilon_1 - \varepsilon_0 = \varepsilon_1, g_0, g_1$, and the temperature of the system $T$ (K).

2) (10 points) What is the limiting value of partition function when the temperature is very low, expressed in terms of $g_0$ and/or $g_1$?

3) (10 points) What is the limiting value of partition function when the temperature is very high, expressed in terms of $g_0$ and/or $g_1$?

4) (10 points) How are the above results related to the number of states that are thermally populated at various temperatures?

5) (10 points) Write an expression for the probability of finding the system in its ground state, in terms of the variables $\Delta \varepsilon = \varepsilon_1 - \varepsilon_0 = \varepsilon_1, g_0, g_1$, and the temperature of the system $T$ (K).

6) (10 points) Write an expression for the ratio of the probabilities of finding the system in the upper and lower energy levels, in terms of the variables $\Delta \varepsilon = \varepsilon_1 - \varepsilon_0 = \varepsilon_1, g_0, g_1$, and the temperature of the system $T$ (K).

In answering the following questions, use the above two-level model to describe of the conformational isomerization n-butane, whose two-fold degenerate gauche conformation is approximately 3.7 kJ/mol higher in energy than its non-degenerate trans conformation.

7) (10 points) Predict the probability of finding the system in the trans state at 293K.

8) (10 points) Predict the trans to gauche equilibrium constant at 293K.

9) (10 points) Predict the Gibbs free energy of the trans to gauche reaction at 293K.

10) (10 points) Predict the entropy of the trans to gauche reaction at 293K.
### Periodic Classification of the Elements

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*Numbers in parentheses are the mass numbers of the most stable isotopes.*

(Names of elements are in the top row, and atomic numbers are in the leftmost column.)