Department of Chemistry
Cumulative Examinations
April 30, 2011

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, Page 1
2) Biochemistry Cumulative Examination, Page 2
3) Inorganic Cumulative Examination, Pages 3-5
4) Organic Cumulative Examination, Pages 6-8
5) Physical Cumulative Examination, Page 9

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.
Analytical Cume April 2011

Bioanalytical NMR has developed significantly over the past decade. One important characteristic of NMR is its quantitative capabilities. The following questions are focused primarily on NMR based quantitation.

1. (16 pts) There are a number of methods of quantitation that involve the use of standards. Briefly describe the quantitation process using following:
   a) Internal standard
   b) External standard
   c) Standard addition
   d) Calibration curve

2. (10 pts) What is the difference between a primary and a secondary standard? Can you give an example of each?

3. (10 pts) Give an example of a common standard used for NMR. How would you make sure that it is a quantitative standard?

4. (10 pts) Why is it usually sufficient to use a single standard to quantitate all analytes of interest in the NMR spectrum?

5. (14 pts) Recently, it was shown that the solvent (water) could be used as a useful quantitative standard, instead of an added compound.
   a) Why can water be used as a quantitative standard in aqueous solution?
   b) Discuss one advantage of such an approach
   c) Discuss one possible disadvantage of this approach

6. (10 pts) Quantitation in samples such as urine is difficult because of a variable dilution problem. Can you think of a way to reduce this problem?

7. (10 pts) For quantitation of analytes in blood samples by NMR, a different problem exists, namely the presence of lipids and proteins that contribute large, broad lines to the spectrum and baseline. Can you think of a way to improve this situation?

8. (10 pts) How would you perform quantitation in an LC-NMR experiment, where there are dilution steps and where not all of the analyte may be present in the NMR detection coil at one time?

9. (10 pts) Describe the differences between relative and absolute quantitation for an analyte in a complex sample. Which do you think would be better for comparing across different samples sets over time or geography?
Biochemistry Cumulative Exam

Title: Signal Transduction

April 30, 2011

1. (20 points) What are the binding specificities for the following protein modules:
   (a) SH3 domain
   (b) SH2 domain
   (c) PH
   (d) WW

2. (15 points) How are signals transduced by GPCR? Provide a pathway.

3. (15 points) What is MAPK cascade? Explain using any one example where signal from a receptor is transmitted to the nucleus using MAPK cascade.

4. (15 points) How do G Proteins act as on/off switch? What are the accessory proteins that are required for G Protein activity/inactivity?

5. (15 points) How do Cholera toxin and Pertussis toxin (whooping cough disease) target G Protein signaling?

6. (10 points) Explain how mutations in R or C subunit of Protein Kinase A (PKA) might lead to a (a) constantly active PKA or a (b) constantly inactive PKA?

7. (10 points) What are the differences between Ras and Gs? What is the functional difference between Gs and Gi?
There are 100 possible points in this exam.

1. (10 points) Write Miller indices for each plane shown below.

2. (10 points) Metal X has a face-centered cubic structure with a cell parameter, \( a = 4.00 \text{ Å} \). Calculate the density of metal X (Atomic weight of X = 60.0 g/mol).

3. (20 points) Draw the atomic arrangement of X on the (100), (110), and (111) planes. Indicate interatomic distances in each plane. Which plane has the most densely packed X atoms? Show work.

4. (15 points) What is the distance between the nearest (100) planes of metal X? Repeat the question for (110) planes and (111) planes.

5. (15 points) (a) What is the shortest metal-metal distance in the crystal structure of metal X? How many neighboring metal atoms can be found with this distance from one metal atom?
(b) What is the second shortest metal-metal distance? How many neighboring metal atoms can be found with this distance from one metal atom?

(c) What is the third shortest metal-metal distance? How many neighboring metal atoms can be found with this distance from one metal atom?

6. (10 points) (a) Explain why metals usually have a good electrical conductivity.

(b) When the temperature increases, how does it affect the electrical conductivity of metal?

7. (20 points) A lattice is an infinite array of identical points (i.e. each one has exactly the same environment of other points) and the points are obtained one from another by translations only. This description is applicable, equally, in one-, two-, and three-dimensional space. A unit cell of a plane (2D) lattice is a parallelogram of two unit translations, a and b, with lattice points at the corners and is perfectly representative of the lattice. There are five 2D lattice types. They are:

- **Oblique**: \( a \neq b, \gamma \neq 90^\circ \)
- **Rectangle**: \( a \neq b, \gamma = 90^\circ \)
- **Hexagon**: \( a = b, \gamma = 120^\circ \)
- **Rhombus (= centered rectangle)**: \( a = b, \gamma \neq 90^\circ \)
- **Square**: \( a = b, \gamma = 90^\circ \)
Draw a unit cell for the following 2D patterns (convention: choose the smallest repeat unit that is the most symmetric. (Symmetry level: square, hexagon > rhombus, rectangle > oblique) and identify a lattice type. **Attach this page of the exam to your blue book.** (A stapler is available at the podium).
In a recently published full paper (J. Am. Chem. Soc. 2011, 113, 6114-6117) Pettus and coworkers report the total synthesis of (±)-γ-rubromycin, a natural product known to be a potent inhibitor of telomerase. Several synthetic schemes from the paper are reproduced below. Answer the following questions about them.

1. (15 points) Provide a stepwise mechanistic explanation for the conversion of 7 to 9 in Scheme 2 (below). Be sure to include all likely intermediates and use curved arrow formalism to account for the movement of electrons.

Scheme 2. Synthesis of Naphthoquinone 5 from R-Tetralone 7

```latex
\begin{align*}
    & \text{MeO} & \text{OMe} & \text{MeO} \\
    & \text{OMe} & \text{OMe} & \text{OMe} \\
\end{align*}
```

(a) LiHMDS (2.4 equiv), THF, -78°C, then NBS (2.06 equiv); DBU (1.23 equiv), -78°C to rt, 78% yield. (b) CAN (2.14 equiv), MeCN/H₂O, 0°C, 60% yield. (c) NaN₃ (1.46 equiv), THF/H₂O, rt. (d) Cs₂CO₃ (1.5 equiv) PhCH₃/MeOH, rt, 65% yield for 2 steps. (e) KOH (21.4 equiv), MeOH/H₂O, 84% yield.

2. (20 points) The authors mention that 7 can be made in three steps from 1,2,4-trimethoxybenzene. Propose a synthetic conversion of 1,2,4-trimethoxybenzene to 7 that includes all reagents. You may use any reagent of 4 carbons or less in your synthesis. Also provide an explanation for any issues of selectivity that arise in your synthesis.
3. (15 points) Provide a stepwise mechanistic explanation for the conversion of 15 to 16 in Scheme 3 (below). Be sure to include all likely intermediates and use curved arrow formalism to account for the movement of electrons.

Scheme 3. Preparation of Methyleneated Isocoumarin 6

(a) Pd(OAc)$_2$, PPh$_3$, methyl acrylate (1.9 equiv), LiCl, NEt$_3$ (1.81 equiv), DMF, 80°C, 93% yield. (b) H$_2$ (1 atm), Pd/C, EtOAc, 94% yield. (c) p-TsOH (cat.), PhMe, reflux, 82% yield. (d) 14 (1.03 equiv), LiHMDS (1.0 equiv), THF, -78°C, then 13 (1.0 equiv), 60% yield, E/Z = 6/1. (e) CpTiMe$_2$ (2.19 equiv), PhMe, 70°C, 72% yield, E/Z = 8/1. (f) TBAF (1.03 equiv), THF, -78°C, 94% yield.

4. (10 points) Account for the selectivity of the reaction that converts 15 to 16 for only one of the three carbonyls present in 15.
5. (25 points) Provide a stepwise mechanistic explanation for the reaction of 5 with 6 to form 17 and 18 as shown in Scheme 4 (below). Be sure to include all likely intermediates and use curved arrow formalism to account for the movement of electrons. Feel free to abbreviate.

Scheme 4. Conclusion of the Total Synthesis of (±)-γ-Rubromycin (1)

\[ 5 + 6 \xrightarrow{{\text{CAN \ NaHCO}_3 \ NaHCO}_3 \ THF, \ 1 \ hr, \ r.t.}} (58\%) \]
\[ 17 : 18 = 1 : 2 \]

\[ 17 \]

\[ 18 \]

\[ \xrightarrow{{\text{BBR}_3(6 \text{ equiv}) \ -78 ^\circ C \ to \ -20 ^\circ C \ \ 1.5 \ hr, \ (61\%)}} \gamma-\text{rubromycin (1)} \]

\[ \xrightarrow{{\text{BBR}_3(8 \text{ equiv}) \ -78 ^\circ C \ to \ -20 ^\circ C \ \ 1.5 \ hr, \ (50\%)}} \]

6. (15 points) Provide a stepwise mechanistic explanation for the reaction of 17 to form γ-rubromycin (shown below). Be sure to include all likely intermediates and use curved arrow formalism to account for the movement of electrons.

\[ γ-\text{rubromycin (1)} \]
In the following problems an answer alone is not sufficient. You must show all work and give all reasoning to get any credit.

1. Consider the molecule anthracene. Recall it is comprised of three benzene rings.
   How many normal modes does anthracene possess?

2. This problem concerns the statistical thermodynamics of a hypothetical “atom” with only three energy levels $\varepsilon_0 = 0 < \varepsilon_1 = \varepsilon < \varepsilon_2 = 2\varepsilon$. The respective degeneracies of the levels are $g_0 = 1$, $g_1 = 2$, $g_2 = 1$. Defining $\Theta \equiv k^{-1}\varepsilon$, the partition function of the atom is

$$Q(T) = 1 + 2\exp\left[-\Theta/T\right] + \exp\left[-\Theta/T\right].$$

Below you will be asked to find (a) $P_i(T)$, the probability that the atom is in level $i = 0$, 1, or 2, (b) the internal energy $E(T) = kT^2 \sum_{i=0}^{2} \frac{d\ln Q(T)}{dT} \varepsilon_i P_i(T)$, (c) the heat capacity $C(T) = \frac{dE(T)}{dT}$, and (d) the entropy $S(T) = \frac{E(T) - A(T)}{T}$.

a. This part concerns the level probabilities $P_i(T) = Q^{-1}(T)g_i\exp(-\varepsilon_i/kT)$. What is

   (i) $\lim_{T \to 0} P_0(T)$
   (ii) $\lim_{T \to \infty} P_1(T)$
   (iii) the temperature $T^*$ in terms of $\Theta$ for which $P_0(T^*) = P_1(T^*)$?

b. This part concerns $E(T)$ and $C(T)$. What is

   (i) $\lim_{T \to 0} E(T)$
   (ii) $\lim_{T \to \infty} E(T)$
   (iii) $\lim_{T \to 0} C(T)$
   (iv) $\lim_{T \to \infty} C(T)$?

c. Explain why your two limiting results for $C(T)$ in part b are to be expected.

d. This problem concerns $S(T)$. What is

   (i) $\lim_{T \to 0} S(T)$
   (ii) $\lim_{T \to \infty} S(T)$?

e. Why is your result for $\lim_{T \to 0} S(T)$ expected?
**Periodic Classification of the Elements**

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*Lanthanides*  
58 Ce 140.12  
59 Pr 140.907  
60 Nd 144.24  
61 Pm 147.04  
62 Sm 150.35  
63 Eu 151.96  
64 Gd 157.25  
65 Tb 158.924  
66 Dy 162.50  
67 Ho 164.930  
68 Er 167.26  
69 Tm 168.934  
70 Yb 173.04  
71 Lu 174.97

†Actinides  
90 Th 232.038  
91 Pa 238.03  
92 U 238.03  
93 Np 237.04  
94 Pu 242.04  
95 Am 243.04  
96 Cm 247.04  
97 Bk 247.04  
98 Cf 251.04  
99 Es 252.04  
100 Fm 253.04  
101 Md 256.04  
102 No 256.04  
103 Lw 257.04

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