Department of Chemistry
Cumulative Examinations
March 3, 2012

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 1-3
2) Biochemistry Cumulative Examination, Pages 4-6
3) Inorganic Cumulative Examination, Pages 7-8
4) Organic Cumulative Examination, Pages 9-11
5) Physical Cumulative Examination, Pages 12-13

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.

Purdue University
Analytical Chemistry Cume

1) N,N-dimethylformamide (DMF) is widely used as a solvent in chemistry for solid phase peptide synthesis, the development and production of pharmaceuticals, and the manufacture of multiple biological compatible materials. It is miscible with water. One graduate student was asked to prepare for 500 mL of stock aqueous solution that contains 25% (w/w) of DMF. DMF is provided with a commercial source and its label is illustrated. Please describe the experimental steps to prepare the stock solution. In his chemical experiment, the graduate student used 150 mM DMF as the experimental solvent. Please calculate the volume of stock solution the student needed to prepare for 2.0 ml of the experimental solvent.

2) Monosodium glutamate (MSG) is commonly used as food additive for better taste.

(i) If you dissolve 5.0 mg of MSG in water, what is the pH of the solution?

(ii) Given the pKa values of the glutamic acid, please write down the structure of MSG in water.

(MW of MSG: 169.1)

3) H₃PO₄ is a polyprotic acid frequently used to neutralize basic solutions. It was prepared in the lab as 1.0 M stock solution. Calculate the pH change when you add 0.50 mL of stock H₃PO₄ solution into (pKa1=2.15; pKa2=7.20; pKa3=12.35):

(i) 100 mL of 50 mM NaOH solution;

(ii) 100 mL of 50 mM Na₂HPO₄ solution.
4) Reverse phase HPLC is widely used in separating biological molecules. In reverse-phase HPLC the stationary phase is typical silica modified with C18. A few years ago, PolyLC Inc. (established by our Purdue alumns) introduced a new type of HPLC, termed hydrophilic HPLC. According to the name, it is based on hydrophilic interactions between the stationary phase and the sample. The new HPLC type can be used efficiently to isolate peptides and other biological molecules. Please answer the following questions:

(i) Design the stationary phase that can be used for hydrophilic HPLC (you may give one example by drawing its chemical structure)

(ii) If you use hydrophilic HPLC to isolate a mixture of peptides, what are the typical loading buffer and gradient mobile phase?

(iii) If the peptide mixture includes Ala-Gly-Phe, Arg-Glu-Lys, Arg-Glu-Gly, and Gly-Ala-Ala, what is the elution order? (see attached page for amino acid residues)

5) One Purdue research lab has a state-of-the-art mass spectrometer that has the capability of analyzing phosphorylated proteins in high efficiency and sensitivity. However, the lab does not allow the introduction of radioactive isotopes (above 1 μCi) into the instrument. In an in vitro kinase assay, one graduate student ordered 100 μCi hot ATP-\(^{32}\)P from the company. Based on the information provided by the company, the student determined that the purity of hot ATP was 85% when he received the radioisotope reagent due to the radioisotope decay during the transportation and handling process. The student immediately started the experiment once he received the radioisotope. The experiment only lasted a few hours, and the sample was subsequently stored in the refrigerator for a period of time before being analyzed by the mass spectrometer.

(1) Write the reaction equation for the \(^{32}\)P decay to emit β particle and form stable isotope.

(2) What is the minimum time the graduated needed to wait before the sample could be introduced into the instrument? The half-live of \(^{32}\)P is 14 days.
Twenty standard Amino Acids

Nonpolar, aliphatic R groups

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Leucine | Methionine | Isoleucine

Aromatic R groups

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Positively charged R groups

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Negatively charged R groups

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<td>Glutamate</td>
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CUMULATIVE EXAMINATION IN BIOCHEMISTRY
March 3, 2012

It is expected that each answer should contain 1-4 succinct straight-to-the-point sentences. The exam consists of 10 questions + 2 bonus questions. Each question is worth 10 points. To successfully answer most of the questions you only need a broad background in the field + sound logic and reasoning. In most cases, it is not necessary to know any technical details.

1. Blood is buffered through carbonic acid / bicarbonate / carbon dioxide equilibrium. For this equilibrium, one can write an analogue of the Henderson-Hasselbalch equation:

\[ \text{pH} = pK + \log \left( \frac{[\text{HCO}_3^-]}{[\text{CO}_2]} \right) \]

This equation sheds light on some interesting aspects of human physiology. For example, a person experiencing a panic attack is often advised to breath in and out of a brown paper bag. Please, establish a connection between the brown-bag treatment and the above equation.

2. Asp amino-acid in solution can be found in a protonated or deprotonated state (side chain \( \text{CH}_2-\text{COOH} \) or \( \text{CH}_2-\text{COO}^- \), respectively). For free Asp in solution, the corresponding pKa value is 4.0. In a protein, however, one can often find pKa values that are significantly different from 4.0.

Consider, for example, a situation where Asp forms a salt bridge with Lys residue (side chain \( (\text{CH}_2)_2-\text{NH}_3^+ \)). Predict (qualitatively) the pKa value of Asp residue in such situation and justify your prediction.

3. pKa values of amino-acid side chains can be determined experimentally.

Consider, for example, free Asp amino-acid (pKa=4, see previous question). The protonated carboxyl shows a ‘signature’ IR absorption band at around 1730 cm\(^{-1}\). On the other hand, the deprotonated carboxylate group shows two characteristic bands near 1400 and 1570 cm\(^{-1}\).

Based on this information, please design a simple experiment to determine the pKa value of free Asp. Briefly describe your experiment and how it leads to quantitative determination of pKa.
4. *E. coli* is used as a platform for many biochemical experiments. The growth of *E. coli* in LB media is usually monitored via OD600 parameter (i.e. the absorbance of light at wavelength 600 nm). This measurement allows for determination of the concentration of *E. coli* in solution. However, the result is error-prone. The graph on the right shows the dependence of the relative error in determined concentration vs. the actual concentration. Please, discuss and rationalize the shape of this graph.

5. Many animals and insects that live in the Arctic region are capable of producing massive amounts of glycerol and/or sorbitol, erythritol, etc. (in quantities that far exceed what can be found in tropical species). Please explain this observation.

6. An enzyme that catalyzes the reaction S → P is isolated from two bacterial species. As it turns out, the version of the enzyme from *Escherichia coli* displays $K_M = 1 \mu$M, whereas the version of the enzyme from *Clostridium botulinum* displays $K_M = 3 \mu$M. All other things being equal, which of the two enzyme should be chosen for industrial catalysis of $S \rightarrow P$ reaction in biotechnology industry? Please, justify your answer.

   [For your information, Michaelis-Menten equation reads: $v = \frac{V_{max}[S]}{K_M + [S]}$.]

7. Food packaging normally carries a label that lists the caloric value of the product. Speculate on how this caloric value can be defined and determined.

8. Peptide Sos forms a complex with protein Crk with dissociation constant $K_d = 2.7 \mu$M. The structural study of the complex found that residue S186 from Crk forms a hydrogen bond with residue P2 in Sos. It was further determined that this hydrogen bond contributes 1.3 kcal/mol (5.4 kJ/mol) to the stability of the complex (in terms of free energy).

   Point mutation S186A abolishes the said hydrogen bond. Based on this information please estimate the dissociation constant $K_d$ for the complex between Sos and the mutant protein, Crk S186A.
9. The figure below illustrates the concept of an ITC experiment which characterizes binding of a certain ligand to a protein (assume 1:1 binding). Please, explain the concept of this experiment and how the binding enthalpy, ΔH, is obtained.

![Isothermal Titration Calorimetry (ITC)](http://www.endocytosis.org/)

ΔG = -14.1
ΔH = -19.9
TΔS = -5.8

10. Using the same graph as in the previous question, please explain how the dissociation constant $K_d$ is determined.

11. Using the same graph as in question 9, explain how one obtains the values of $ΔG$ and $TΔS$.

12. What is conformational entropy of a polypeptide chain? Consider peptide A which consists of ten Gly residues (i.e. polyglycine) and peptide B which consists of ten proline residues (i.e. polyproline). Which of the two will have higher conformational entropy? Please justify.
Inorganic Cumulative Exam
This cumulative exam covers the molecular orbitals of some inorganic systems.

A. (40 points) The Figure below provides a qualitative MO energy-level diagram for the valence orbitals of the cyanide ion. The Figure assumes that the internuclear axis defines the z-direction and that the plane of the page is the yz plane.

The following are crude sketches (contour plots) of two of the occupied orbitals from the scheme above. Identify the two MO's and all contributing atomic orbitals in each. The black dots represent nuclei.

B. (40 points) Cyanide ion complexes to Fe⁺ to give a linear molecule, and here the focus is on the carbon-linked isomer. If free Fe⁺ starts out with the [Ar]4s¹3d⁶ electronic configuration, MO calculations suggest the MO scheme of the complex contains elements of the scheme presented above. (DeYonker, N. J. et al., J. Chem. Phys., 2004, 120, 4726) In fact, the energy level scheme for FeCN predicts the ground state to be a ⁶Δ state with an electronic configuration we could write as:

\[ 2σ²\gamma²\pi⁴\sigma²\alpha⁴\beta²\delta³\delta¹ \]

The energy of the orbitals increases from left to right, and the bold lettering identifies energy levels of FeCN derived mostly from MO's based on cyanide and much like
orbitals found in the scheme in A. The non-bold lettering designates the next higher energy levels of FeCN which turn out to have mainly iron character, account for the paramagnetism, and exhibit sigma, pi, or delta symmetry.

i. Assume that FeCN lies on the z-axis of the coordinate system, and list all valence atomic orbitals of Fe⁺ capable of sigma bonding to the cyanide ligand.

ii. Identify the iron orbitals with delta symmetry.

iii. Assume that back-bonding to cyanide is responsible for the energy difference between the br and co orbitals. Identify the orbitals of cyanide from the scheme in part A that engage in back-bonding with the metal, and sketch contours of the two bonding molecular orbitals of FeCN that result. Be sure to include the iron orbitals involved and label axes in your drawings.

C. (20 points) The SF₆ molecule has a positive electron affinity and forms a stable anion. The contour provided describes the singly occupied molecular orbital of the resulting anion. (Eisfeld, W. et al. J. Chem. Phys. 2011, 134, 054303)

i. Identify all the valence atomic orbitals involved in the contour and indicate the atoms and shells from which they come.

ii. Calculations suggest S-F bond elongation occurs with formation of the anion. Explain why.

iii. Theory also suggests the anion spontaneously distorts from octahedral symmetry. Does this system satisfy the criterion for a standard Jahn-Teller distortion? Explain why or why not.
In a February issue of JACS (J. Am. Chem. Soc. 2012, 134, 2856–2859; Diastereoselective Construction of syn-1,3-Dioxanes via a Bismuth-Mediated Two-Component Hemiacetal/Oxa-Conjugate Addition Reaction), Andrew Evans presented a new synthetic strategy for the generation of syn-1,3-dioxanes shown below:

In order to demonstrate your knowledge on naming and presenting stereoisomeric compounds, please answer the following questions (we will get back to Evans’ paper in the end).

1. Give the absolute configuration for the stereocenter in this compound:

2. Same here:

3. Below are two isomers, one of which is a sedative and the other one a teratogen (causes birth defects). Years ago, a combination of these isomers was given to many pregnant women to sedate them, which resulted in the birth of many terribly misformed babies. This is a good example of why organic chemists need to be able to distinguish between isomeric molecules. Are these two molecules constitutional isomers, cis-/trans-isomers, geometric isomers, diastereomers, enantiomers, and/or (E)/(Z)-isomers?
4. Consider again thalidomide and its isomer shown above. Assign the absolute configuration for each.

5. Give the full IUPAC name for the molecule shown on right (remember to indicate stereochemistry).

6. Same here:

7. Consider the molecules shown below. If present, identify two enantiomers, two diastereomers, two identical molecules, and two different molecules.


10. Consider cholesterol (shown right). How many stereocenters does it contain? Assign the absolute configuration for the stereocenter far left and the one on very top.

This is the stereoisomer found in human metabolism.
11. Going back to Evans’ synthesis, give the number of stereocenters and assign the absolute configuration of each stereocenter for the final product of this reaction:

(i) 1.5 mol% HG-II
\[ \text{CH}_2=\text{CHCHO, DCM, } \Delta \]
98%

(ii) TESOTf
\[ 2,6\text{-lutidine, } -78 \^\circ \text{C} \]

\[ ^7\text{Bu}_3\text{SnCH}_2\text{CH}=\text{CH}_2 \]
\[ \text{cat. (S)-BINOL:TiCl}_4:Ti(O^\text{OPr})_4 \]

\[ (4:1:3), \text{cat. Ag}_2\text{O} \]

\[ \text{DCM, } 0 \^\circ \text{C} \]
87%

\[ \text{Bi(NO}_3)_3\text{5H}_2\text{O} \]
\[ \text{CH}_3\text{CHO} \]
\[ \text{DCM, RT} \]
71%

\[ \text{Me} \]

1 mol% HG-II
\[ \text{CH}_2=\text{CHCOMe, DCM, } \Delta \]
87%

\[ \text{Me} \]

\[ \text{cat. Bi(NO}_3)_3\text{5H}_2\text{O} \]
\[ \text{CH}_3\text{CHO} \]
\[ \text{DCM, RT} \]
91%
Physical Chemistry

1. (30) Consider the one-dimensional problem of a particle of mass $m = 1\, a.u.$ in a potential (atomic units (a.u.)) $m = \hbar = e = a_0 = 1$

$$V(x) = \infty \quad \text{for} \quad x < 0, \quad V(x) = 0 \quad \text{for} \quad 0 \leq x \leq 1,$$

and $V(x) = 5 \quad \text{for} \quad x > 1$

The bound state energies are given by the equation

$$\tan\sqrt{2E} = -\sqrt{\frac{E}{5-E}}$$

Without solving the Schrodinger equation:

(a) (20) Sketch the ground state wave function, $\Psi_0$, for $E < 5$ and for $E > 5$. Explain your results.

(b) (10) What happens to the eigenvalues if you add the momentum operator, $p = -i\frac{d}{dx}$, as perturbation (the new Hamiltonian is $H = H_0 + \lambda p$, where $H_0$ is the original Hamiltonian with the above potential and $\lambda$ is the strength of the perturbation)

2. (30) Assuming that two protons of $H_2^+$ molecule are fixed at their normal separation of 1.06\,\text{Å}:

(a) Sketch the potential energy of the electron along an axis passing through the protons

(b) Sketch the electron wave functions for the two lowest states

(c) Explain the formation of the chemical bond for this system, what is ground state binding energy (just an order of magnitude!)

(d) What happens to the two lowest energy levels in the limit that the protons are moved far apart

(e) Explain the Born-Oppenheimer approximation for molecular systems, when do you think this approximation will break down, give an example

3. (20) The wave function for an electron in a one-dimensional potential $V(x)$ at time $t$ is given by the expression

$$\Psi(x, t) = \sqrt{\frac{2}{a}} \sin\left[\frac{\pi x}{a}\right] e^{i\gamma t/\hbar}, \text{ for } 0 \leq x \leq a$$

where $a$ and $\gamma$ are constants
(a) (5) Is the particle bound? Explain
(b) (5) Sketch the potential for this wave function
(c) (5) Find the lowest energy eigenvalue of $V(x)$ in terms of the given quantities
(d) (5) Can we use this wave function and model potential to describe the motion of a $\pi$-electron in conjugated molecules

4. (20) Spectroscopy

(a) (10) Different regions of the electromagnetic spectrum (Microwave, Far Infrared, Infrared, Visible and Ultraviolet) are used to investigate different molecular processes. Which regions of the electromagnetic spectrum correspond to (a) Rotation of small molecules (b) vibrations of flexible bonds (c) Rotation of polyatomic molecules and (d) Electronic transitions, explain.

(b) (5) Explain what is the fundamental line and second overtone line in the observed vibrational spectra.

(c) (5) What is the main difference between Frank-Condon Principle and Born Oppenheimer approximation for diatomic molecules.
# Periodic Classification of the Elements

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*Lanthanides*  
*Ce* 140.12  
*Ce* 140.97  
*Nd* 144.24  
*Pr* 147  
*Sm* 150.35  
*Eu* 151.96  
*Gd* 157.25  
*Tb* 158.924  
*Dy* 162.50  
*Ho* 164.930  
*Er* 167.26  
*Tm* 168.934  
*Yb* 173.04  
*Lu* 174.97  

†Actinides  
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*Lw* 257  

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