Department of Chemistry
Cumulative Examinations
March 5, 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, Pages 2-3
3) Inorganic Cumulative Examination, Page 4
4) Organic Cumulative Examination, Pages 5-6
5) Physical Cumulative Examination, Pages 7-8

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. Characterization of large saturated hydrocarbons in mixtures is of great interest to petroleum chemists. Why do you think this is so?
2. What sort of information could be obtained for such mixtures by using mass spectrometry? Give at least three answers.
3. What issues cause problems when attempting to analyze mixtures of large saturated hydrocarbons by mass spectrometry?
4. What evaporation and ionization method(s) would you choose for such analysis? Justify.
5. How would you provide structural information? Discuss at least two different approaches.
6. How would you provide quantitative information? Outline the difficulties in obtaining quantitative information on unknown mixtures by using mass spectrometry.
7. Define mass accuracy, mass resolution and linear dynamic range. Illustrate with drawings.
8. Explain why it would be good to be able to carry out measurements on complex mixtures at high mass accuracy and resolution and with a large linear dynamic range.
9. Describe one mass spectrometer that is capable of very high resolution and highly accurate mass measurements, and explain how it is done.
10. Explain why ion trap mass spectrometers do not have as great linear dynamic range as other mass spectrometers.
Protein folding, unfolding, misfolding, and disorder

It is expected that the answer should contain 1-4 succinct straight-to-the-point sentences. If you feel like elaborating, please stay within an 8 sentence limit anyway. All questions carry the same weight.

1. A single-residue mutation has been made in the hydrophobic core of a globular protein, Leu → Ala. Predict the most likely effect of this mutation on protein stability. Justify.

2. Amyloid plaques are the signature of neurodegenerative diseases, such as Alzheimer and Parkinson disease. The structure of the amyloid is quite regular, a cross-beta sheet. Yet, there are essentially no high-resolution x-ray crystallographic structures of amyloids. Why?

3. What is “molten globule”?

4. By analyzing the protein primary sequence, one can make a good prediction on whether this particular chain is going to be folded or, alternatively, disordered under the physiological conditions. For instance, a certain sequence with unusually high content of Glu residues is likely to be disordered. Please, explain why.

5. Binding of a (disordered) peptide to a (globular) protein typically occurs with association rate \( k_{\text{on}} \sim 10^6 \text{ M}^{-1}\text{s}^{-1} \). Sometimes, however, extremely high rates, \( k_{\text{on}} \sim 10^9 \text{ M}^{-1}\text{s}^{-1} \), are observed. This exceeds the estimates based on the model of diffusion-controlled binding. What is the mechanism behind these very high on-rates?

6. Assume that you have successfully prepared and purified a new protein sample (1 ml of protein solution with 100 μM concentration). The first thing that you want to determine is whether the protein is folded or not. How would you make this determination (suggest suitable experimental methods)?

7. What is prion and how does it cause disease (e.g., mad cow disease)?
8. Radius of gyration of a protein can be approximately expressed as follows: 
\[ R_g \approx \left( \frac{1}{\sqrt{6}} \right) hN^p. \] 
Here \( h \) is the so-called effective monomer length, \( N \) is the number of residues in the protein, and \( p \) is the exponent (a number). Please, estimate the (typical) value of \( p \) for (i) folded proteins and (ii) denatured proteins. Please, explain and justify your choice of \( p \).

9. The scheme on the right (© Martin Chaplin) illustrates different contributions into free energy of the transition from the native (N) state to the denatured (D) state,
\[ \Delta G_N^D = \Delta G_N^D - T \Delta S_N^D. \]
According to this diagram, how does the folding status of the protein change as a function of temperature?

10. Using the diagram from Question 9, discuss the entropy term associated with non-polar side chains in the protein interior (continuous blue curve).

11. Many human proteins cannot be successfully expressed in E.coli for the purpose of in vitro studies. For instance, this is the case for folate receptor \( \beta \), 255 aa protein which is glycosylated, features 8 disulfide bonds and the GPI anchor. Why E.coli is not a suitable organism for expressing this protein*?

12. Consider a sample of a certain protein (purified and dissolved in an aqueous buffer); the protein is known to be folded at room temperature. As we raise the temperature, the protein becomes unfolded. After that we start lowering the temperature and eventually bring the system back to the room temperature. What will happen to the protein – will it become folded again or not?

* Insect cells with baculovirus expression system actually do the trick
Dinitrogen oxide or N₂O has C₂ᵥ symmetry and an interesting chemistry.

A. What oxidation states of nitrogen appear to the immediate right and immediate left of N₂O in a standard Latimer diagram wherein the oxidation number increases from right to left?

B. Outline the commercial synthesis of N₂O which involves comproportionation and a material often used as fertilizer in agriculture. For extra credit, cite the principal hazard associated with the process.

C. The 4 contour plots a-d given below depict the HOMO and LUMO orbitals of N₂O. Predict which two represent the HOMO’s and explain why both sets of levels are degenerate. The NNO lettering shows the orientation of the molecule.

D. The van der Waals radius of O is smaller than that of N, yet N₂O exhibits an NN bond distance of 1.128 Å and an NO bond distance of 1.184 Å. Use MO or valence bond theory concepts to rationalize why the NN distance is shorter.

E. Isoelectronic with CO₂, dinitrogen oxide poses environmental issues because on an equimolar basis it is 300 times more effective as a greenhouse gas than carbon dioxide. Postulate an explanation.

F. Identify a medicinal or commercial use of N₂O.

G. Bacteria produce N₂O via an enzyme known as nitric oxide reductase which has an active site that includes heme and non-heme iron centers. Workers suspect the hyponitrite ion [ONNO]²⁻ is an intermediate in the pathway. Draw a Lewis structure of the ion, and explain why there are two isomers.
An article published in JACS in late 2010 (volume 132, pp. 17933-17944), titled "Indolyne Experimental and Computational Studies: Synthetic Applications and Origins of Selectivities of Nucleophilic Additions", and co-authored by Ken Houk and Neil Garg with their students at the University of California, Los Angeles, focuses on addition reactions to indolynes and other unsymmetrical ortho-benzyne analogs. This research led to the design of a substituted 4,5-indolyne that exhibits enhanced nucleophilic regioselectivity. In order to demonstrate your understanding on the fundamental properties of benzyynes and nucleophilic additions to benzyynes, please answer the following questions related to this paper.

1) Draw proper Lewis structures for the ortho-, meta- and para-benzyynes.

2) These three biradicals have singlet electronic ground states. Explain what this means. Illustrate by an energy diagram showing the formally unpaired electrons distributed on the formally singly occupied orbitals. Also show an energy diagram for a biradical with a triplet ground state.

3) Explain why each of the above three biradicals has a singlet electronic ground state. Illustrate your answer by showing how electrons in the formally singly occupied orbitals couple (show the orbitals).

4) Define singlet-triplet gap.

5) Which of the above benzyynes has the largest singlet-triplet gap and why?

6) Indole and 4,5-indolyne are shown below. Which is which?

7) Draw the structures of 5,6- and 6,7-indolynes.

8) The indole heterocycle is usually exploited for its nucleophilic character. In contrast, the indolyynes can act as electrophiles. Explain why.
9) The electrophilic behavior of indolynes is of interest because it allows
derivatization of the benzenoid ring as opposed to the pyrrole ring of indole. In
order to illustrate how, draw a mechanism for the reaction of NH$_3$ with 4,5-
indolyne and give the most likely products.

10) Give the most likely product for the Diels-Alder reaction of furan with 4,5-
indolyne.

11) Nucleophilic addition to 4,5-indolyne was found in this paper to be
regioselective. The addition occurs more readily to the carbon with a more
distorted angle. Considering the calculated structure of 4,5-indolyne shown
below, which is the carbon atom predominantly attacked by nucleophiles?

![4,5-indolyne (29)](image)

12) As opposed to ortho-benzyne analogs, what sort of reactions would you expect
to dominate for para-benzyne analogs, and why?

13) How about meta-benzyne analogs? Why?
The Pauli spin matrices $\sigma_x, \sigma_y, \sigma_z$ can be defined by the way they act on the $\frac{1}{2}$-spin orthonormal states $\keta{\uparrow}$ and $\keta{\downarrow}$:

\[
\begin{align*}
\sigma_x \keta{\uparrow} &= +\ket{\downarrow} \\
\sigma_x \keta{\downarrow} &= +\ket{\uparrow} \\
\sigma_y \keta{\uparrow} &= +i\ket{\downarrow} \\
\sigma_y \keta{\downarrow} &= -i\ket{\uparrow} \\
\sigma_z \keta{\uparrow} &= \ket{\uparrow} \\
\sigma_z \keta{\downarrow} &= \ket{\downarrow}
\end{align*}
\]

There are two spins in the ground-state of the Hydrogen atom: The spin of the proton and the spin of the electron. We can therefore define four base kets in the following way:

\[
\begin{align*}
\keta{1} &= \keta{\uparrow, \uparrow} & \text{The electron and proton are both spin "up"} \\
\keta{2} &= \keta{\uparrow, \downarrow} & \text{The electron is "up" and the proton is "down"} \\
\keta{3} &= \keta{\downarrow, \uparrow} & \text{The electron is "down" and the proton is "up"} \\
\keta{4} &= \keta{\downarrow, \downarrow} & \text{The electron and proton are both "down"}
\end{align*}
\]

We can also define operators $\sigma^p$ and $\sigma^e$ acting independently on the proton and the electron respectively, so that, for example,

\[
\sigma_z^e \sigma_z^p \keta{2} = -\keta{4}
\]

The Hamiltonian for the ground-state of the Hydrogen atom is given by:

\[
H = A \sigma^e \cdot \sigma^p
\]

Where $A$ is a constant energy ($A = 2.35 \times 10^{-25}$ J) and $\sigma^e \cdot \sigma^p$ is the dot product:

\[
\sigma^e \cdot \sigma^p = \sigma_x^e \sigma_x^p + \sigma_y^e \sigma_y^p + \sigma_z^e \sigma_z^p
\]

1. (20 points) Complete the following matrix representation of $H$ using the base kets defined above:

\[
H = \begin{pmatrix}
A & 0 & 0 & 0 \\
0 & ? & ? & 0 \\
0 & ? & ? & 0 \\
0 & 0 & 0 & A
\end{pmatrix}
\]

2. (20 points) An arbitrary state $\ket{\psi}$ representing the ground state of Hydrogen can be written as the linear combination $\ket{\psi} = C_1 \keta{1} + C_2 \keta{2} + C_3 \keta{3} + C_4 \keta{4}$.

Schrödinger's equation $i\hbar \frac{\partial}{\partial t} \ket{\psi} = H \ket{\psi}$ leads to four equations for the coefficients $\{C_i\}$. Write down these equations.
3. (20 points) Find the four stationary states of $H$ and their corresponding energies.

4. (20 points) Explain why astronomers have observed pervasive microwave radiation of 21cm-wavelength throughout the universe. (Note: Planck’s constant is $6.63 \times 10^{-34}$ J.s, and the speed of light in vacuum is $3 \times 10^8$ m/s).

5. a. (10 points) What is the Zeeman effect?

   b. (10 points) Indicate how you would calculate the Zeeman splitting for the energy levels of the ground state of Hydrogen.
### Periodic Classification of the Elements

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*Lanthanides*:
- Ce (140.12)
- Pr (140.97)
- Nd (144.24)
- Pm (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 (171.04)
- Lu (174.97)

†Actinides:
- Th (232.038)
- Pa (238.03)
- U (238)
- Np (239)
- Pu (242)
- Am (243)
- Cm (247)
- Bk (249)
- Cf (251)
- Es (254)
- Fm (253)
- Md (256)
- No (256)
- Lw (257)

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