Department of Chemistry
Cumulative Examinations

February 6, 2016

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, Page 7
4) Organic Cumulative Examination, Pages 8-9
5) Physical Cumulative Examination, Page 10

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. (10 pts) Please calculate the output $V_o$ of the following amplification circuit.

![Amplification Circuit Diagram]

2. (10 pts) Please calculate the cutoff frequencies of the band pass filter circuit below.

![Band Pass Filter Diagram]

3. (10 pts) The spectrum below is one of the very first set of spectra recorded for biomolecules using electrospray ionization mass spectrometry. This was a synthetic polynucleotide that was analyzed in the negative mode. Please use the deconvolution method to calculate the average molecular weight of this polynucleotide.

![Mass Spectrum Image]

For the question 4 – 8, please keep your answers as concise as possible. Most of the answers only need 1 or 2 sentences.

4. (25 pts) Almost every manuscript about mass spectrometry used to start with “Mass spectrometry is the most sensitive and specific analytical technique for general purpose chemical analysis.”
   a. Please defend/justify this claim using 5 sentences or fewer. (10 pts)
   b. Specificity – What contributes to the specificity provided by mass spectrometry?
c. Now adding an ion mobility section to a mass spectrometer is popular. What does this bring to the “already-fantastic” mass spectrometry? (5pts)
d. Complex mixture analysis – would chromatography or some kind of pre-separation still be needed if we use a mass spectrometer with unlimited high mass resolution? Explain why or why not. (5pts)

5. (20 pts) Please answer the following questions:
a. Why a much lower pressure is required for operation of TOF or a sector, in comparison with a quadrupole filter? (5pts)
b. All are trap-type mass analyzers, but why do orbi-trap and ion cyclotron resonance trap operate at much lower pressures, in comparison with a quadrupole ion trap? (5pts)
c. What type of mass spectrometer is used on the rover Curiosity that is currently in operation on Mars? (5pts)
d. During the Manhattan Project, the isotopes of uranium were separated using a mass spectrometer. It was built based on one of the following inventions. Which one then? (5pts)

6. (15 pts) Quadrupole ion trap is a great device as a mass analyzer as well as a reactor for gas phase reactions. Please list three methods for increasing the m/z range of an ion trap, including at least one method that does not compromise the resolution for mass analysis. Explain why. Also, can this method be used to extend the m/z range without limitation? If not, what is the limiting factor?

7. (10 pts) Waters and Advion both put out a desktop size, single quadrupole mass spectrometer product to the market around the same time. Advion was advertising its product for direct analysis with minimum sample preparation and no chromatographic separation. For example, the organic chemists could now analyze their synthesized products themselves. Waters, however, went to the opposite direction and was selling its product as the detector for their HPLC. From technical aspect please predict which product would sell better or have a greater potential in the future; or which one would
have a fatal problem in its marketing strategy.

**Bonus Questions**

8. (10 pts) In a Q-TOF mass spectrometer with an atmospheric pressure interface, a plastic tube (made from a material that does not degas) is used to connect a pressure gauge to the first differential pumping stage. The tubing has a thin wall but is strong enough to not be deformed due to the pressure difference (the pressure outside the tube is 760 torr while the inside pressure of the tube is the same as in the vacuum chamber). Do you think it is safe to use this tubing to connect a pressure gauge to the Q section? What about the TOF section? Please explain why.

**Bonus questions for future leaders in Analytic Chemistry.**

9. (20 pts) The current platform for chemical/biological analysis using mass spectrometry has been built on the concept of abstaining definitive answers. For instance, multi-dimension separation techniques are combined to sort analytes out; it has always been a major push in the technical development to make the instruments to separate analytes with high resolution and high accuracy. This no doubt has been critical for analytical chemists to draw better conclusions based on the information obtained from the experiments. Now, suddenly the big data concept is everywhere. How do you think it would affect the future development of the chemical/biological analysis related to mass spectrometry?

**Note:** You would likely NOT get any partial credit unless your answer comprehensively addresses a set of important or interesting points. So if you have never thought about the “big data” problem, save your time to try other exam questions.

10. (10 pts) If you are an assistant professor starting your career on research and development of ambient ionization mass spectrometry, what areas would you think that deserve the most attention for academic research in the next five years?

**Note:** You will not get credit for mentioning general ideas like “no sample prep”, “tissue imaging”, “biofluid analysis”, or “use of miniature mass spectrometer”, etc. What's needed here is an in-depth analysis of the technical developments that might make a significant impact in the field of ambient mass spectrometry.
Cumulative Examination in Biochemistry

6 February, 2016

Metabolism and Systems Thinking: Using thermodynamics and metabolic regulation processes to predict and explain the behavior of living systems in health and disease

Instructions: Use the attached metabolic pathway chart as well as your own diagrams and appropriate examples to answer the following questions.

1. Use a specific example to explain the meaning of:
   a. A metabolic pathway;
   b. A metabolic system.

2. Use the first Law of Thermodynamics to explain how metabolic pathways play a major role in thermoregulation during fever in humans.

3. Discuss the multiple ways in which metabolism is regulated at the molecular, genetic, cellular and whole-body levels to achieve integrated whole body functioning of the human “machine”. Illustrate your answer with specific examples.

4. Many metabolic reactions are not spontaneous under standard conditions of temperature, concentration and pH. Use equations and calculations to explain how the cell manipulates such conditions to render such reactions spontaneous.

5. Show how the second Law of Thermodynamics can be used to:
   a. Predict the direction of metabolic pathways in cellular systems.
   b. Predict whether a metabolic reaction will likely be controlled by EITHER changes in cellular concentrations of substrate; OR by inhibition or activation of enzymes.
   c. Which of the two types of control mentioned in b. above are likely to play the major role in determining pathway direction and flux? Explain why and how?

6. Suggest ANY ONE experiment that you could use to study any aspect of a metabolic pathway. Clearly state the goal of the experiment; a brief overview of the protocol you would use and the type of data you would expect to get to enable you to achieve the goal.
Information Sheet Biochemistry Cume (6 Feb 2016): Metabolism and Systems Thinking

Note: All enzymes can function physiologically in the reverse direction except those marked with an asterisk.
Summary of the regulation of carbohydrate and fat metabolism
Inorganic Cumulative Exam: Famous Molecules of 2015

Each of the molecules below was published in JACS, Angew. Chem., Nature, or Science in 2015

Choose 3 of the 6 molecules, and answer the questions below:

(a) Provide a plausible oxidation state for the metal and the corresponding number of d electrons.

(b) Provide a qualitative d-orbital splitting diagram, and predict the overall spin state of the molecule.

(c) Provide a brief description (approx. 2–5 sentences) of what is unusual or unique about the compound relative to more routine molecules that are reported in the literature. You may comment on any aspect of the structure, electronic structure, or both.

(d) Provide a brief description (approx. 2–5 sentences) of the broader significance of the compound to the field of chemistry. You may discuss a variety of things including, but not limited to, fundamental bonding and electronic structure, catalytic applications, biological cofactors, etc.

(e) Identify a spectroscopic technique (besides X-ray diffraction!) that would provide a critical piece of information about the structure of the molecule. Provide a description of what you expect to see in the spectrum and what those spectroscopic features would tell you about the molecule (the more detail the better! eg. approximate position of signals, number of signals, splitting patterns, etc.). Use a different technique for each of your three molecules.

(f) BONUS: Name the corresponding author of the manuscript describing the compound.

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2

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4

5

6
Cumulative Exam – Organic Chemistry (2016)
Department of Chemistry, Purdue University

Topic: Mechanistic Aspects of (Hetero)Aryl C-C Bond Formation through C-H Activation and Direct Arylation Polymerization (JACS, 2006, 128, 16496; 2010, 132, 11420; 2015, 137, 15636)

(25 pts) Aryl-aryl cross-coupling has a profound impact in organic synthesis. It is widely practiced in a wide range of fields, such as pharmaceuticals, agrochemicals and high performance materials. The Nobel Prize in Chemistry 2010 was awarded jointly to Richard F. Heck, Ei-ichi Negishi and Akira Suzuki "for palladium-catalyzed cross couplings in organic synthesis".

a) (15 pts) Please name 5 different conventional aryl C-C bond formation reactions, mark their functional groups, and list key reaction ingredients.

The conventional cross-couplings, however, are not free from disadvantages in organic synthesis. A common issue for these methods is the need to prepare often unstable, reactive or toxic activated functional substrates, which necessitates additional synthetic steps to prepare and form stoichiometric reaction byproducts. An emphasis on global reaction efficiency has prompted the development of reactions that are less reliant on pre-activation. Direct arylation, which substitutes one of the activated arenes with an unfunctionalized arene, provides a viable solution as an alternative or replacement to the conventional aryl C-C bond formation.

b) (10 pts) Please list at least two of such direct arylation reactions, mark their activated functional groups, and list all necessary reaction ingredients.

(30 pts) Fagnou et al. (JACS, 2006, 128, 16496) reported palladium-catalyzed Benzene arylation and achieved excellent cross-coupling efficiency. One key contribution in this study was to introduce catalytic pivalic acid as a proton shuttle.

![Catalytic Cycle Diagram]

a) (25 pts) Please draw the proposed catalytic cycle and highlight the role of pivalic acid.

b) (5 pts) Explain why pivalic anion is superior to bicarbonate anion in this process.
(15 pts) Conjugated polymers are generally prepared by transition-metal catalyzed cross-coupling reactions (i.e. Suzuki, Stille and Negishi coupling) involving aryl halides and aryl organometallic species. Direct arylation polymerization (DArP) of heteroarenes with aryl halides has recently emerged as a promising alternative for the synthesis of conjugated polymers, because it allows to circumvent the need to prepare sensitive, often toxic organometallic species, avoid the generation of excessive waste, and use less reaction steps. Despite the first case for DArP preparation of poly(3-hexylthiophene) (P3HT) was reported in 1999 by Lemaire, DArP had not received much attention for more than a decade. It was possibly because only low molecular weight oligomeric species were obtained. The change came in 2010 when Ozawa et al. reported DArP synthesis of P3HT with high regioselectivity, high molecular weight and high yield (*JACS*, 2010, 132, 11420). A rapidly increasing numbers of publications on DArP have been thus noticed in the following years.

a) (5 pts) Please list the polymerization and its condition for synthesis of head-to-tail P3HT.

b) (10 pts) Please rationalize the success of Ozawa’s synthesis of highly regioregular P3HT and explain how the authors verify the high regioselectivity in P3HT.

(30 pts) Cross-couplings proceeding via double C–H activation would be ideal to form aryl C-C bond, as there would be no need to pre-functionalize any substrates. To date, several methods for oxidative cross-coupling of arenes have been reported using Cu, Rh, and, most frequently, Pd catalysts. Larrosa et al reported the first methodology for Au(I/III)-catalyzed oxidative cross-coupling of arenes via double C–H with high selectivity between electron-rich hetero-/carbocyclic arenes and electron-poor arenes bearing relatively acidic C–H bonds. (*JACS*, 2015, 137, 15636).

a) (5 pts) Please give an example of Pd-catalyzed oxidative cross-coupling and provide key reaction ingredients.

b) (20 pts) Please give an example of Au-catalyzed oxidative cross-coupling and draw the proposed catalytic cycle.

c) (5 pts) Highlights the rationales for the high selectivity in Au-catalyzed oxidative cross-coupling.
Physical Chemistry Cume

1. (5 points each) Explain the following acronyms:
   SCF:
   HF:
   CIS:
   CCSD(T):
   MP2:
   B3LYP:
   FCI:

2. (65 points) CH₂ diradical belongs to C₂ᵥ symmetry group (see character table for C₂ᵥ). Molecule lies in y-z plane.

<table>
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<tr>
<th>C₂ᵥ</th>
<th>E</th>
<th>C₂</th>
<th>σᵥ(xz)</th>
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<td>B₂</td>
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<td>−1</td>
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</table>

The ground state of CH₂ is the triplet ³B₁ state with electronic configuration (¹A₁)² (²A₁)² (¹B₂)² (³A₁)¹ (¹B₁)¹.

(30) Construct MO diagram for CH₂ in this state. Label orbitals with symmetry labels. Sketch orbital shapes.

(5) Construct Slater determinant wave function for this triplet state.

(5) The lowest singlet state is ¹A₁ with the electronic configuration (¹A₁)² (²A₁)² (¹B₂)² (³A₁)². Construct Slater determinant wave function for this singlet state.

(10) Using MO diagram as a guide, predict significant geometrical change between the ³B₁ and ¹A₁ states.

(15) Both singlet and triplet states of diradicals can be often observed in photoelectron spectra of the corresponding anion. Construct Slater determinant wave function for the CH₂⁻ anion and show pictorially that both ¹A₁ and ³B₁ can indeed be accessed in the photoelectron experiment.
# Periodic Classification of the Elements

<table>
<thead>
<tr>
<th>I A</th>
<th>H (1.00797)</th>
<th>II A</th>
<th>Li (6.939) Be (9.0122)</th>
<th>III B</th>
<th>IV B</th>
<th>V B</th>
<th>VI B</th>
<th>VII B</th>
<th>I B</th>
<th>II B</th>
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<td>K (39.102)</td>
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<td>Ti (47.90)</td>
<td>V (50.942)</td>
<td>Cr (51.996)</td>
<td>Mn (54.938)</td>
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<td>Nb (92.906)</td>
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### *Lanthanides*

| 58 Ce (140.12) | 59 Pr (140.907) | 60 Nd (144.24) | 61 Pm (147) | 62 Sm (150.35) | 63 Eu (151.96) | 64 Gd (157.25) | 65 Tb (158.924) | 66 Dy (162.50) | 67 Ho (164.93) | 68 Er (167.26) | 69 Tm (168.934) | 70 Yb (173.04) | 71 Lu (174.97) |

### †Actinides

| 90 Th (232.038) | 91 Pa (233.21) | 92 U (238.03) | 93 Np (237) | 94 Pu (242) | 95 Am (243) | 96 Cm (247) | 97 Bk (249) | 98 Cf (254) | 99 Es (253) | 100 Fm (256) | 101 Md (256) | 102 No (256) | 103 Lw (257) |

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