Department of Chemistry
Cumulative Examinations
November 17, 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 1-2
2) Biochemistry Cumulative Examination, Pages 3-6
3) Inorganic Cumulative Examination, Page 7
4) Organic Cumulative Examination, Pages 8-11
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

1. You are asked to determine the concentration of a particular species that you know fluoresces with a relatively high quantum efficiency. Assuming there are no significant matrix effects and that you can work under conditions in which the product of pathlength, molar absorptivity, and concentration is < 0.05, answer the following questions:

   a) Assuming a constant incident radiative power, how will the fluorescence signal vary with analyte concentration? (5 pts.)

   b) How will sensitivity depend upon concentration? (5 pts.)

   c) For a fixed indeterminate (random) measurement error, how will concentration error vary with concentration? (5 pts.)

   d) For a fixed inderminate measurement error, how will relative concentration error vary with concentration? (5 pts.)

2. You are determining the concentration of the substrate of a particular enzyme via an approach based on Michaelis-Menten kinetics. That is, you are measuring a reaction rate or velocity, v, between the enzyme and substrate that obeys the relation:

$$v = \frac{v_{\max}[S]}{K_M + [S]}$$

   where K_M is the Michaelis constant.

   a) Draw the mechanism upon which Michaelis-Menten kinetics is based. (5 pts.)

   b) What determines the Michaelis constant for a given enzyme? (5 pts.)

   c) What conditions are best suited for determining the concentration of substrate and what conditions are best suited for determining the concentration of enzyme? (10 pts.)

3. How are UV/visible absorbance measurements different from IR absorbance measurements:

   a) From the standpoint of implementation. (10 pts.)

   b) From the standpoint of application. (10 pts)

4. The determination of an analyte of interest was accomplished by reacting it with excess iodide, I^-, to form triodide, I_3^-, with subsequent quantitation of triiodide. The determination of triiodide concentration can be accomplished via a variety of means, including potentiometrically.

$E^0_{I3-/I-} = 0.536$ V, $[I^-] = 0.202$ M, $I_3^- + 2e^- \rightarrow 3I^-$, $RT/F = 0.0257$ V-M^{-1}, $E_{SCE} = 0.244$ V

   Write the expected relationship between cell potential, E_{cell}, and triiodide concentration if the potential of a platinum electrode placed into the analyte solution is measured against the standard calomel electrode (SCE). (20 pts)

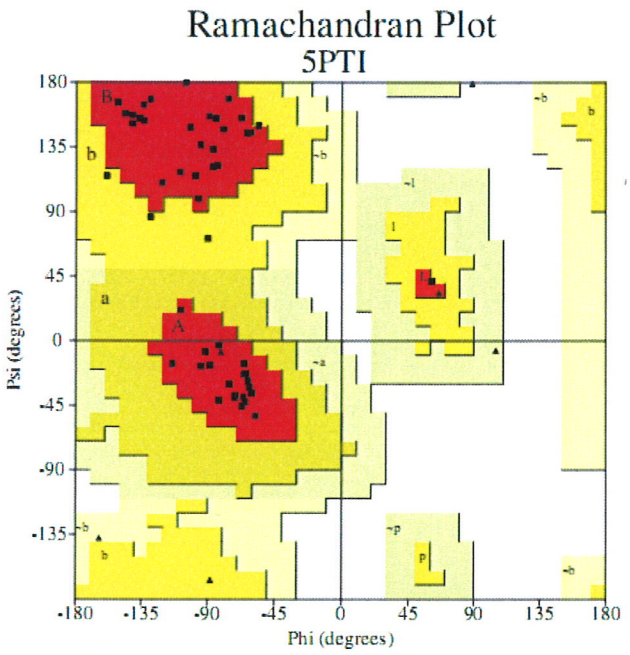
5. Assume that you will be measuring the concentration of a compound in the gas phase via its proton transfer reactions with a reagent ion. You begin with a fixed number of reagent ions in the presence of a constant concentration of analyte species. You are able to measure the abundances of the remaining reagent ion at two fixed times (which you know). Assuming you also know the rate constant for the reaction and that there are no other loss mechanisms for the reagent ion, answer the following questions:

   a) Write the relationship you would use to determine the analyte concentration. (10 pts.)

   b) Draw a plot of the measured quantity versus concentration to show the qualitative shape of the relationship. (10 pts.)

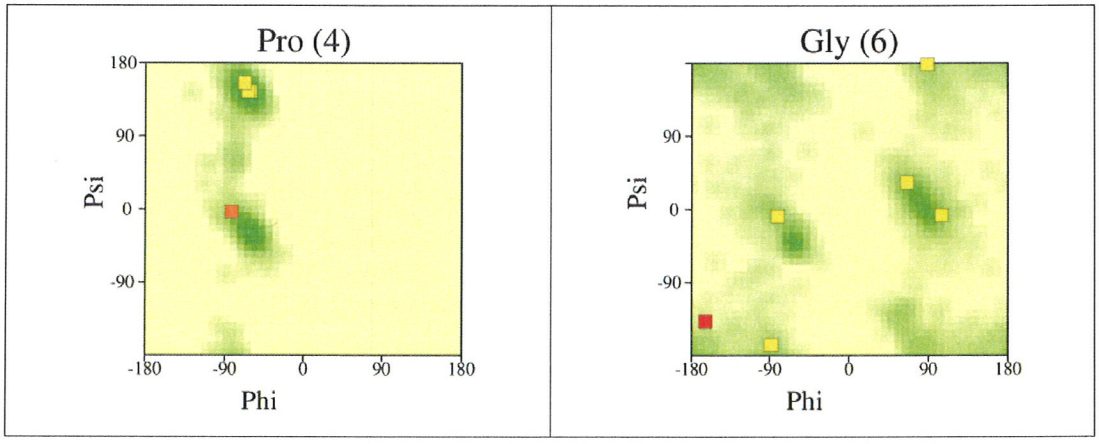
CUMULATIVE EXAMINATION IN BIOCHEMISTRY
November 2012

1. The plot below represents a Ramachandran map, with the symbols in the plot (squares and triangles) derived from the protein structure 5PTI.



Please explain the meaning of the three areas in the plot that are colored red.

2. The Ramachandran map shown above (question 1) presents the information on all residues in the structure 5PTI. In contrast, the maps below show only proline residues (left panel) and only glycine residues (right panel) from 5PTI.



Please rationalize and discuss the distribution of Pro and Gly residues on the Ramachandran map.

3. The coordinates 5PTI in the above plot represent a small protein called Bovine Pancreatic Trypsin Inhibitor (BPTI). BPTI binds to trypsin with incredible affinity constant of $6 \cdot 10^{-14}$ M. Please provide a biological rationale for this extraordinary affinity constant.

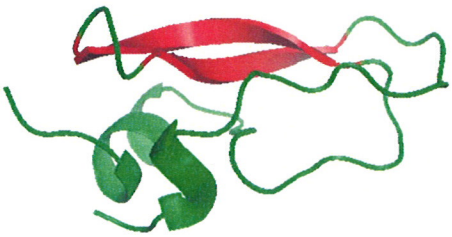
4. I have run the primary sequence of BPTI through the BLAST engine, and obtained the following hit:

```
GENE ID: 515917 LOC515917
Score = 73.9 bits (180),  Expect = 4e-15, Method: Composition-based stats.
Identities = 33/56 (59%), Positives = 37/56 (66%), Gaps = 0/56 (0%)

Query    RPDFCLEPPYTGPCKARIIRYFYNAKAGLCQTFVYGGCRAKRNNFKSAEDCMRTCG
Sbjct    KPAFCLKPKSIGPCKGRKIRYFYNAKTRQCQRFFYGGCKGNLNNFYTMALCMNTCG
```

While many residues differ between the two sequences, all six cysteins (C) are conserved. What may be the structural reason for this cysteine conservation?

5. The picture on the right shows a 3D structure based on the coordinates 5PTI. This structure includes 2-strand β-sheet (colored red in the plot). Is this a parallel or anti-parallel β-sheet? Please justify your answer.



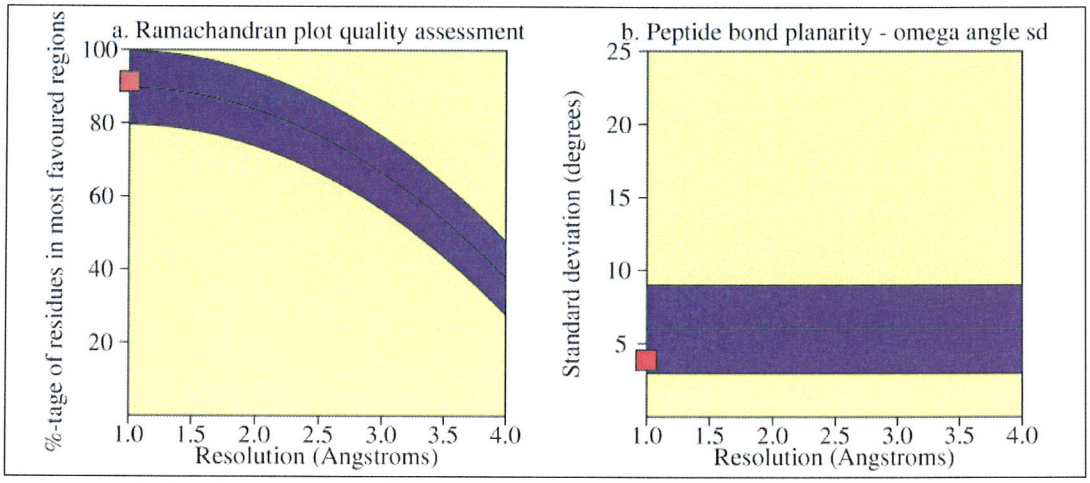
6. The table below is taken from the paper by Kim et al. (*Prot. Sci.* 2, 588). The second column in the table lists melting temperatures, T_m, of the wild-type BPTI and several BPTI mutants. The third column describes thermodynamic stability of the BPTI and its mutants. Part of the information is deliberately concealed (pink rectangle).

Table 4. *Stability of WT BPTI and its mutants*

	T_m[a] (°C, pH 2)	ΔG(25 °C)[a] (kcal/mol, pH 2)
WT	87	9.0
F22A		7.8
Y23A		3.1
Y35G		4.0
N43G		3.3
F45A		2.1

Based on the available information, please rank the wild-type protein and the mutants according to T_m, beginning from the one that shows the highest T_m value.

7. Running the structure validation program ProCheck over the set of coordinates 5PTI produces a number of quality assessment metrics. Two of such metrics are illustrated in a form of the graphs (shown below). Please deduce and explain the meaning of these graphs.



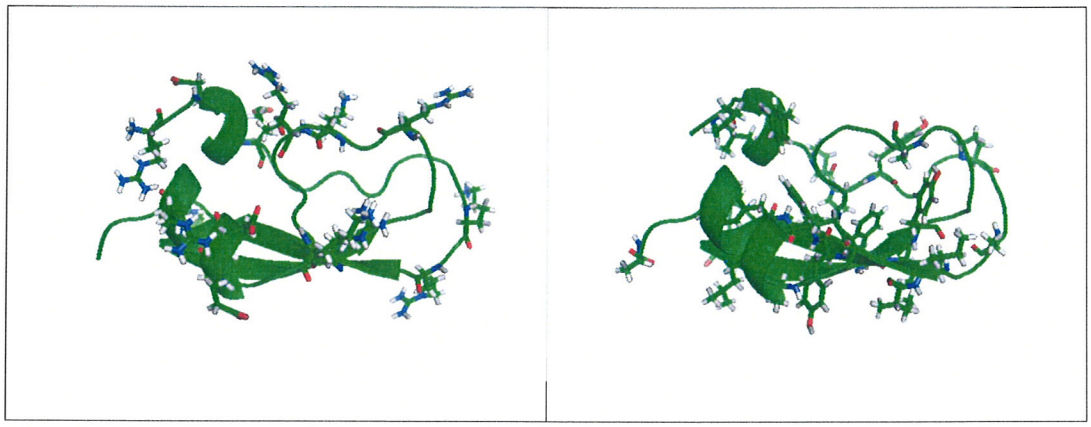
8. The program *hbplus* uses protein coordinates to detect and parameterize hydrogen bonds. Applying this program to the coordinate set 5PTI produced the following output (excerpt shown below):

```
HBPLUS Hydrogen Bond Calculator v 3.15          Nov 07 22:46:41 EST 2012
(c) I McDonald, D Naylor, D Jones and J Thornton 1993 All Rights Reserved.
Citing HBPLUS in publications that use these results is condition of use.
5PTI <- Brookhaven Code "5PTI.pdb" <- PDB file
<---DONOR---> <-ACCEPTOR-->
h    n   atom  resd res     DA  ||   DHA
n    s   type  num  typ    dist DA  angle

A0005-CYS N     A0002-PRO O     2.96 MM  150.1
A0006-LEU N     A0003-ASP O     3.12 MM  163.8
A0007-GLU N     A0004-PHE O     3.02 MM  166.4
A0043-ASN ND2   A0007-GLU O     2.85 SM  148.0
A0043-ASN N     A0007-GLU OE2   3.11 MS  151.0
A0036-GLY N     A0011-THR O     2.83 MM  165.9
A0011-THR OG1   A0034-VAL O     2.64 SM  170.0
A0016-ALA N     A0036-GLY O     2.92 MM  148.2
A0018-ILE N     A0035-TYR O     3.03 MM  161.7
A0020-ARG N     A0033-PHE O     2.93 MM  163.0
```

From this list please select the strongest hydrogen bond. Justify your choice.

9. The figures below represent the structure 5PTI with charged chains selected (left panel) or, alternatively, hydrophobic side chains selected (right panel).



Please rationalize and discuss the spatial distribution of charged and hydrophobic side chains in the protein structure.

10. The web server H++ (http://biophysics.cs.vt.edu/) predicts pK_a values of ionizable groups in proteins based on the protein 3D structure. I have run this program on the coordinate set 5PTI. The output is shown below:

Residue	pK_(1/2)
NTARG-1	7.422
argNT-1	>12.000000
ASP-3	3.438
GLU-7	3.944
TYR-10	9.565
LYS-15	10.590
ARG-17	>12.000000
ARG-20	>12.000000
TYR-21	10.258
TYR-23	11.161
LYS-26	10.404
TYR-35	8.864
ARG-39	>12.000000
LYS-41	10.724
ARG-42	>12.000000
LYS-46	10.154
GLU-49	3.851
ASP-50	2.761
ARG-53	>12.000000
CTALA-58	3.876

Based on these results, please estimate the net charge of BPTI molecule at pH 5.5. Explain how you came up with this estimate.

Inorganic Chemistry Cumulative Exam
Purdue University
Saturday, November 17, 2012

Question 1: (40 points)
The enzyme carbonic anhydrase catalyzes the hydrolysis of carbon dioxide according to the following equation:

$$CO_2 + H_2O \rightarrow HCO_3^- + H^+$$

A) Draw a picture of the enzyme active site. You do not need all the details, just provide the basics. (10 points)
B) Draw a catalytic cycle. About 5 steps are recommended to be shown. (30 points)

Question 2: (20 points)
In 1879, Chile, Bolivia, and Peru went to war over a precious natural resource.
A) What was this resource that led to war?
B) Modern chemistry has advanced to the point that we no longer need to wage war over such resources. What is the name, chemical reaction, and desired product of the process now used? Note that you do <u>not</u> need to provide a catalytic cycle nor mechanism for the reaction.

Question 3: (20 points)
In July 2012, a rouge "scientist" chartered a ship and dumped 100 tons of iron powder into the ocean waters off the Canadian west coast, northwest of Seattle. His activities were in violation of several laws, even though he set out on his activities "in the name of science." What was he trying to do (other than make money)? Explain the relevant chemistry.

Question 4: (20 points)
If you live a healthy, clean life (no late night benders at Harry's, no speed-induced all nighters cramming for exams) and remain free of both disease and accidents, you will still not live forever. About what is the oldest that you can hope to live to? Why does this limit exist? What is the chemical origin of aging?

Organic Chemistry Cumulative Exam
November 2012

INSTRUCTIONS: There are two separate sections to the exam.
YOU MUST PASS BOTH SECTIONS OF THE EXAM.

Section A: Questions in Section A were taken *verbatim* from CHM 115/116 exams, and are multiple choice. There are 8 questions in this section. *You must get at least 6 correct answers in this section in order to pass the exam.* Also, 5 points will be deducted from your score for Section B for each incorrect answer.

Section B: Section B is based on material discussed in the article by Andujar-De Sanctis and Singleton in *Org. Lett.* **2012**, *14*, 5238-5241. It is worth 100 pts, and you need to score at least 50 to pass (including any deductions due to incorrect answers in Section A)

SECTION A: General Organic Chemistry

A1. Which of the following statements is correct?

(a) Electronegativity increases as one moves down a group.
(b) Electronegativity increases as one moves to the right across a period.
(c) Electronegativity describes the desire of an atom to give up an electron.
(d) Electronegativity get smaller as more electrons are removed from an atom.
(e) None of the above

A2. On the basis of the VSEPR model, which of the following molecules is linear?

(a) AlF_3
(b) H_2O
(c) SO_2
(d) CO_2
(e) None of these

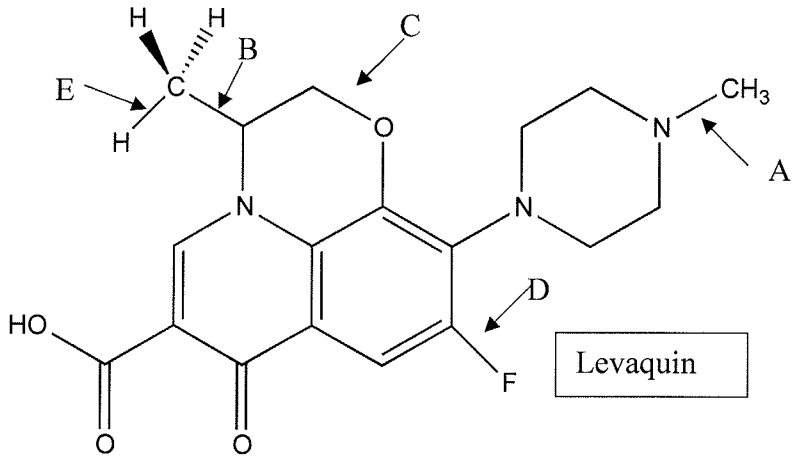
A3. What is the bond hybridization around the carbon atom in formaldehyde, CH_2O?

(a) sp^3
(b) sp^2
(c) sp
(d) sp^3d^2
(e) sp^3d

A4. Which one of the following functional groups is an amino group?

(a) $-NH_2$
(b) $-OH$
(c) $-COOH$
(d) $-C=O$
(e) None of the above

Use the molecular structure of Levaquin, a potent antibiotic, to answer questions A5 and A6 below.



Levaquin

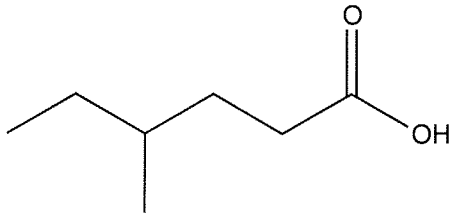
A5.___ How many sp^2 carbons are present in Levaquin?

(a) 6
(b) 8
(c) 10
(d) 12
(e) 18

A6.___ There are five bonds labeled with arrows in the structure above. Which arrow points to the **longest** bond?

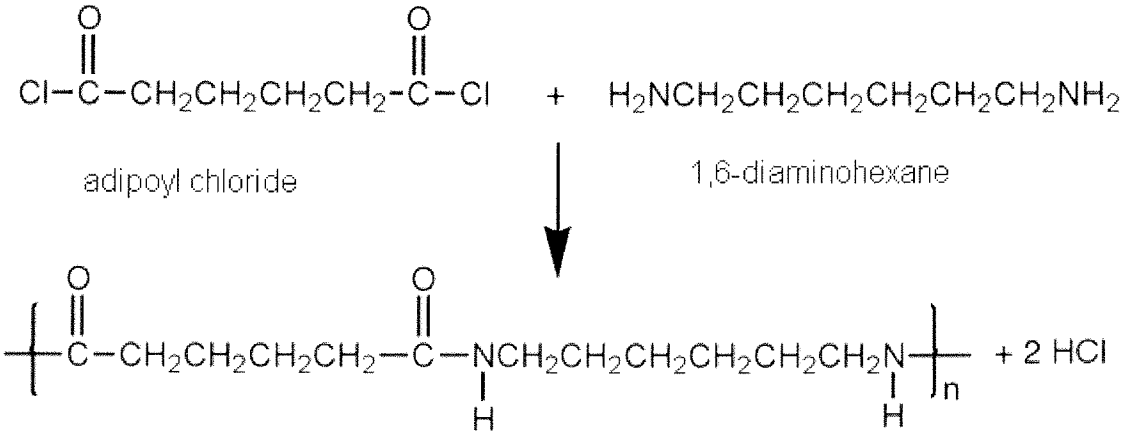
(a) A
(b) B
(c) C
(d) D
(e) E

A7.___ What is the correct formula for the organic molecule shown below?



(a) $C_7H_{12}O_2$
(b) $C_7H_{13}O_2$
(c) $C_6H_{14}O_2$
(d) $C_7H_{14}O_2$
(e) $C_8H_{14}O_2$

A8.___ In the nylon preparation process, NaOH was added to the reaction mixture even though it does not appear in the reaction equation. What function does NaOH have in the process?

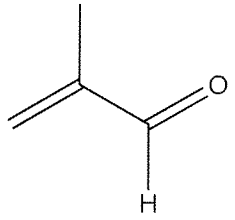


(a) It makes the reaction less toxic.
(b) It causes the adipoyl chloride to be more reactive.
(c) It neutralizes the HCl produced in the reaction.
(d) It eliminates gases produced in the reaction.
(e) It activates the carbonyl.

SECTION B: Physical Organic Chemistry from October issues of *Organic Letters*

100 points

In *Org. Lett.* **2012**, *14*, 5238-5241, Singleton and co-workers describe an investigation of the $^{12}C/^{13}C$ kinetic isotope effects on the dimerization of methacrolein, **1**.



1

B1. What is the product obtained upon dimerization of **1** at 70° C. Identify the two methacrolein units in the product.

B2. In the paper, the authors note that "In ordinary isotope effects…, ^{12}C usually undergoes σ-bonding making/breaking faster than ^{13}C." Explain why.

B3. The dimerization product of **1** is asymmetric, and the two monomer units end up in distinct positions. If the two reactants are identical, then they have a 50/50 chance of being either the diene or dienophile. However, if one of the reactants is isotopically labeled then its position in the product can be identified, and there can be a kinetic isotope effect on where it ends up.

a) Remarkably, although the product is asymmetric, and the two monomers are distinct, the transition state for the reaction is completely symmetric, and does not differentiate between either monomer. Draw this structure of the transition state.
b) Because the product is asymmetric, the potential energy surface bifurcates at the transition state toward the two products. Even though the energy paths for the two product structures are the same, the system with the ^{12}C "races" to the product faster than the one with ^{13}C. The authors describe it as a "Newtonian kinetic effect." Explain what this means.

B4. The authors were surprised by which position had the largest kinetic isotope effect. Which position was it, and why does it have such a big effect?

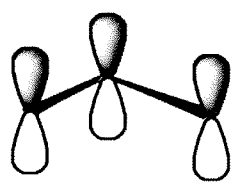
Physical Chemistry
Cumulative Examination

1. (50 pts) The Hückel model a simple linear combination of atomic orbitals molecular orbitals (LCAO MO) method for the determination of energies of molecular orbitals of π electrons in conjugated hydrocarbon systems. In the Hückel method the Hamiltonian matrix $H = (H_{ij})$ is parametrised in the following way:

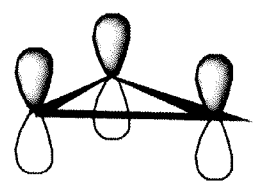
$H_{ii} = \alpha$ for C atoms;
$H_{ij} = \beta$ if the two C atoms are next to each other, $\beta<0$;
$H_{ij} = 0$ in any other case.

Use the Hückel model to obtain information on π orbitals in the allyl radical and the cyclopropenyl radical (see Figure 1). For each of these molecules, do the following:

a. (5) construct the Hückel Hamiltonian;
b. (5) calculate the orbital energies;
c. (15) calculate the normalized eigenvectors and plot the molecular orbitals;
d. (5) plot the molecular orbital diagram of the π system and show the electrons;
e. (10) calculate and compare the total energies in the allyl radical and the cyclopropenyl radical. Rationalize your observation.
f. (10) calculate and compare the total energies in the corresponding anions. Rationalize your observation.



allyl radical



cyclopropenyl radical

2. (50 pts) The π-orbitals of benzene, C_6H_6, may be modeled very crudely using the wave functions and energies of a particle on a ring. Suppose that a particle of mass ***m*** is constrained to move on a circle (of radius ***r***) in the xy plane. Further assume that the particle's potential energy is constant (choose zero as this value).

a. (10) Write down the Schrödinger equation in the normal Cartesian coordinate representation. Transform this Schrödinger equation to cylindrical coordinates where x = ***r***cosϕ, y = ***r***sinϕ, and z = z (z = 0 in this case). Use $\frac{\partial^2}{\partial x^2} + \frac{\partial^2}{\partial y^2} = \frac{1}{r^2}\frac{\partial^2}{\partial \phi^2}$
b. (5) Taking ***r*** to be held constant, write down the general solution, $\Phi(\phi)$, to this Schrödinger equation.
c. (15) The "boundary" conditions for this problem require that $\Phi(\phi) = \Phi(\phi + 2\pi)$. Apply this boundary condition to the general solution.

This results in the quantization of the energy levels of this system. Write down the final expression for the normalized wave functions and quantized energies.

d. (5) What is the physical significance of these quantum numbers that can have both positive and negative values? Draw an energy diagram representing the first five energy levels.

e. (10) Treat the six π-electrons of benzene as particles free to move on a ring of radius 1.40Å, and calculate the energy of the lowest electronic transition. Make sure the Pauli principle is satisfied! What wavelength does this transition correspond to?

f. (5) Suggest some reasons why this differs from the wavelength of the lowest observed transition in benzene, which is 2600 Å.

$m_e = 9.1 \times 10^{-31}$ kg (electron mass)
$\hbar = h/2\pi = 1.054 \times 10^{-34}$ J·s
$e = 1.60 \times 10^{-19}$ C
1 Å = 0.1 nm = 10^{-10} m
$c = 3.0 \times 10^{8}$ m/s
$\Delta E = h\nu = hc/\lambda$

Periodic Classification of the Elements

I A	II A	III B	IV B	V B	VI B	VII B	VIII			I B	II B	III A	IV A	V A	VI A	VII A	O
1 H 1.00797																	2 He 4.0026
3 Li 6.939	4 Be 9.0122											5 B 10.811	6 C 12.01115	7 N 14.0067	8 O 15.9994	9 F 18.9984	10 Ne 20.183
11 Na 22.9898	12 Mg 24.312											13 Al 26.9815	14 Si 28.086	15 P 30.9738	16 S 32.064	17 Cl 35.453	18 Ar 39.948
19 K 39.102	20 Ca 40.08	21 Sc 44.956	22 Ti 47.90	23 V 50.942	24 Cr 51.996	25 Mn 54.9380	26 Fe 55.847	27 Co 58.9332	28 Ni 58.71	29 Cu 63.54	30 Zn 65.37	31 Ga 69.72	32 Ge 72.59	33 As 74.9216	34 Se 78.96	35 Br 79.909	36 Kr 83.80
37 Rb 85.47	38 Sr 87.62	39 Y 88.905	40 Zr 91.22	41 Nb 92.906	42 Mo 95.94	43 Tc (99)	44 Ru 101.07	45 Rh 102.903	46 Pd 106.4	47 Ag 107.870	48 Cd 112.40	49 In 114.82	50 Sn 118.69	51 Sb 121.75	52 Te 127.60	53 I 126.9044	54 Xe 131.30
55 Cs 132.905	56 Ba 137.34	57 La* 138.91	72 Hf 178.49	73 Ta 180.948	74 W 183.85	75 Re 186.2	76 Os 190.2	77 Ir 192.2	78 Pt 195.09	79 Au 196.967	80 Hg 200.59	81 Tl 204.37	82 Pb 207.19	83 Bi 208.980	84 Po (210)	85 At (210)	86 Rn (222)
87 Fr (223)	88 Ra (226)	89 Ac† (227)															

*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 164.930	68 Er 167.26	69 Tm 168.934	70 Yb 173.04	71 Lu 174.97
†Actinides	90 Th 232.038	91 Pa (231)	92 U 238.03	93 Np (237)	94 Pu (242)	95 Am (243)	96 Cm (247)	97 Bk (247)	98 Cf (249)	99 Es (254)	100 Fm (253)	101 Md (256)	102 No (256)	103 Lw (257)

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