Department of Chemistry
Cumulative Examinations
April 2, 2005

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, Pages 4-5
4) Organic Cumulative Examination, Pages 6-7
5) Physical Cumulative Examination, Page 8

On your examination booklet:

1) Print your student ID number.
2) Print this 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
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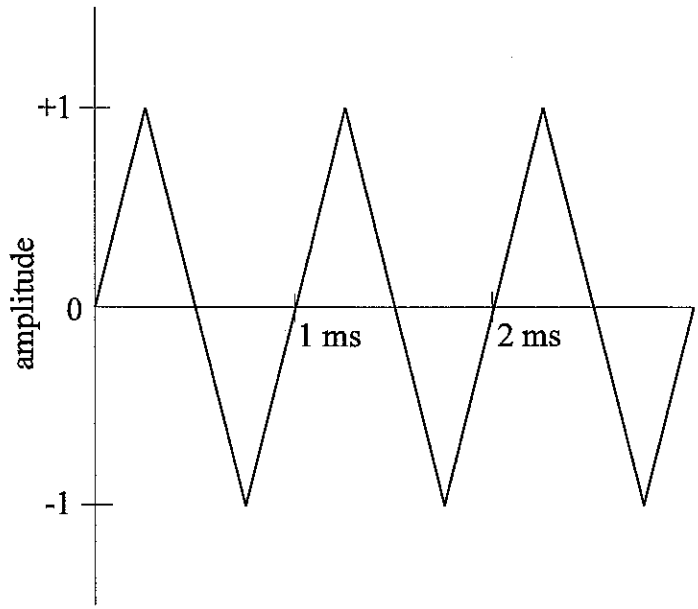
Analytical Cumulative Exam April 2, 2005

Triangular waves are used many places in chemical instrumentation, e.g. cyclic voltammetry. The waveform at the right represents a portion of an odd triangular wave that extends from $-\infty$ to $+\infty$ in time. The goal is to obtain the spectrum of this waveform. Each part of the question is worth 20%.



Start by considering an even triangular wave having the same amplitude and period (not shown). Such a wave can be constructed from a comb, triangle and a y-axis offset.

a) Draw the temporal comb function clearly labeling any characteristic time and amplitude (10%). What is the Fourier transform of the comb (5%)? Give both the amplitude and any characteristic frequency (5%). Use numeric values, not symbols such as t^0.

b) A triangle function is not one of the basis set pairs of transforms. How is a triangle function generated from the basis set pairs? To answer this part of the question let the full-width-at-half-maximum of the triangle be denoted Δt. Give the Fourier transform of the triangle knowing how it is generated from the basis set pairs (10%). For this part use symbols. Finally, give both the amplitude and any characteristic frequency for the triangle required to create the even triangular wave (10%). For this part use numeric values.

c) What is the temporal waveform resulting from the convolution of the triangle in part (b) and the comb in part (c) (5%)? From this waveform determine the y-axis offset needed to create an even triangular wave (5%). What is the Fourier transform of the offset (5%). Give both the amplitude and any characteristic frequency (5%). Use numeric values for all parts.

d) From the answers to (a) through (c) give the Fourier transform of the even triangular wave (10%). Label your answer with the amplitude and any characteristic frequencies (10%).

The odd triangular wave (shown) can be obtained by a temporal shift applied to the even triangular wave.

e) Use the shift theorem to obtain the Fourier transform of the odd triangular wave (5% for correctly stating the shift theorem). Hint: The shift theorem will map the spectrum from the real axis of the complex plane to the imaginary axis in a frequency dependent way. The trick is determining the numeric sign of the amplitudes, i.e. it doesn't simply convert cosines into sines.

Biochemistry Cumulative Examination
Title: Proteolysis

April 2, 2005

1 (15 pts) Provide a brief general definitions (with aid of illustrations, if necessary) for the following terms describing enzyme catalysis:

i. 'kinetic mechanism'
ii. 'chemical mechanism'
iii. 'Michaelis complex'
iv. 'suicide inhibitor'
v. 'zymogen'

2 (15 pts) Proteases are often key players in a wide range of biological processes and are therefore common targets for therapeutic intervention Name key proteases (or protease classes) involved in the following processes and classify them as serine, cysteine, aspartic proteases, or metalloproteinases:

i. Angiogenesis (matrix remodeling)
ii. Apoptosis
iii. Neurodegeneration in Alzheimer's disease
iv. HIV replication
v. Blood clotting

3 (20 pts) Describe the chemical mechanism of hydrolysis of specific peptide bonds in chymotrypsin by answering the following questions:

a. Describe substrate binding, including the role and chemical nature of the "specificity pocket" in chymotrypsin and trypsin, as well as other binding interactions between a peptide substrate and the enzyme.
b. Draw the structure of the catalytic triad found in all serine proteases (including structures of the amino acid side chains and hydrogen bonds. What is the role of each member of the catalytic triad in the reaction?
c. What is the nucleophile that attacks the carbonyl group in acylation? In deacylation?
d. Draw the structures of each of the tetrahedral intermediates in the reaction. Indicate the leaving group in each structure.
e. What is the role of the "oxyanion hole" in the mechanism?

4 (20 pts) A substantial residual activity of trypsin is maintained even when the catalytic triad is absent. (($k_{cat}/k_{uncat} \approx 10^3$ JACS **1992**, 114, 1784). Provide a plausible explanation for this observation.

5 (10 pts) In 1954, while examined reaction of chymotrypsin with *p*-nitrophenyl acetate, B. S. Hartley and B. A. Kilby, noted that the release of *p*-nitrophenol involved an initial "burst", equal in magnitude to the concentration of the enzyme. Provide a plausible explanation for that observation.

6 (10 pts) A major difficulty in investigating the properties of the pancreatic serine proteases is that these proteases being proteins themselves are self-digesting. This problem is less severe, however, for solutions of chymotrypsin than it is for solutions of trypsin or elastase. Explain.

7 (10 pts) The protease from the human immunodeficiency virus possesses a catalytic diad of two aspartate residues (one residue in each of two identical domains: Asp-25, $pK_a = 3.3$, and Asp-25', $pK_a = 5.3$. In the first step of a peptide bond hydrolysis, one aspartate acts as a base, and the other aspartate acts as an acid. The resulting tetrahedral intermediate is <u>not</u> covalently bound to the enzyme. Write a mechanism for this protease.

Inorganic Cumlative Exam
April 2, 2005

Answer both 1 and 2.

1. The following mechanism is proposed for the reaction of ozone with excess bromide ion in acidic solutions, where $BrOOO^-$ is a steady-state intermediate:

$$O_3 + Br^- \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} BrOOO^- \quad (1)$$

$$BrOOO^- + H^+ \xrightarrow{k_2} HOBr + O_2 \quad (2)$$

$$BrOOO^- + H_2O \xrightarrow{k_3} HOBr + O_2 + OH^- \quad (3)$$

$$HOBr + Br^- + H^+ \xrightarrow{fast} Br_2 + H_2O \quad (4)$$

$$H^+ + OH^- \xrightarrow{fast} H_2O \quad (5)$$

(a) Give the equation of the overall reaction. Is this reaction (1) acid catalyzed or (2) acid assisted, or (3) neither?

(b) Derive the rate expression for the rate of O_3 loss and rate of Br_2 formation.

(c) What is meant by a "steady-state intermediate"?
How does this differ from transition states? What is the composition of the transition state(s) for this mechanism?

(continued)

2. The gas phase decomposition of acetaldehyde at 480 °C is a classic example of a chain reaction.

The Rice-Herzfeld mechanism is:

$$CH_3CHO \xrightarrow{k_1} CH_3\bullet \; + \; \bullet CHO \qquad (1)$$

$$CH_3\bullet \; + \; CH_3CHO \xrightarrow{k_2} CH_4 \; + \; \bullet CH_3CO \qquad (2)$$

$$\bullet CH_3CO \xrightarrow{k_3} CH_3\bullet \; + \; CO \qquad (3)$$

$$2CH_3\bullet \xrightarrow{k_4} C_2H_6 \qquad (4)$$

(1) What are the chain centers for this mechanism?

(2) Which steps generate the main reaction products?
What are these products? What is the general terminology for these steps?

(3) What minor or trace species are formed? What is the terminology for each of these steps?

(4) The first example of a chain reaction was found for the reaction of $H_2(g)$ and $Br_2(g)$.

(a) What are the reaction products?

(b) What are the chain centers?

Organic Cumulative Exam

April 2, 2005

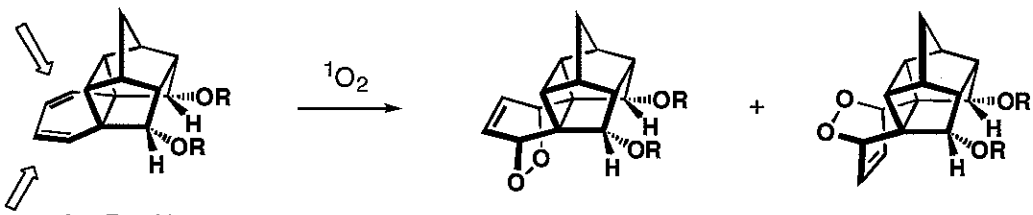
I.1 (16 pts) Provide general definitions (with aid of illustrations, if necessary) for the following terms:

i. 'stereoelectronic effects'
ii. 'anomeric effect'
iii. 'Bürgi-Dunitz angle'
iv. 'orbital hyperconjugation'

I.2 (20 pts) The conformational equilibrium of spiroketal **1** overwhelmingly favors only one out of three possible arrangements. Which one? Give an explanation by drawing all three contributors.

1

I.3 (14 pts) Explain the following observations (*Chem. Comm.* **1998**, 1813):



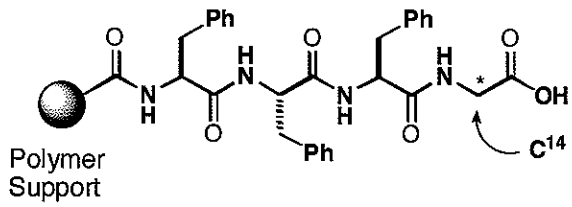
2a: R = H
2b: R = Ac
2c: R = Me

3a: 79%
3b: 79%
3c: 0%

4a: 21%
4b: 21%
4c: 100%

II.1 (15 pts) Provide names and chemical structures of 20 genetically encoded amino acids. Any of the three ways: a full name, a three-letter or one-letter abbreviations will work. Spelling WILL affect your score. **Extra credit (5 pts)** for the less common 21st one (name + structure)

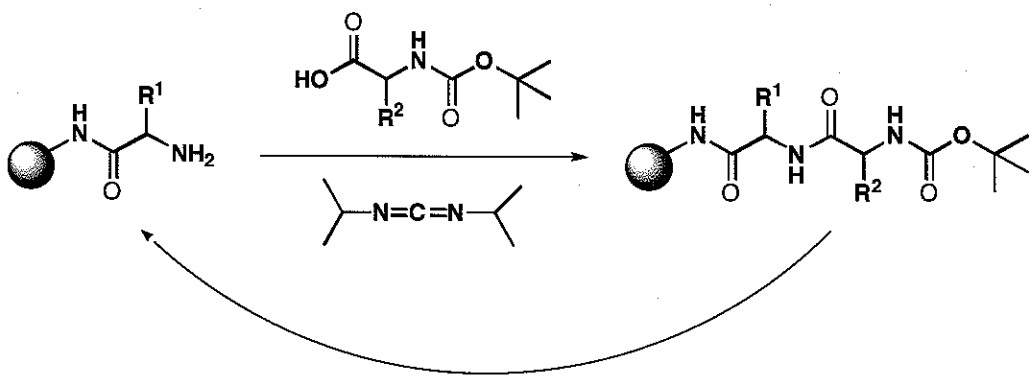
II.2 (15 pts) A few years ago Kahne & Still reported an ingenious method for measuring the rate of peptide bond hydrolysis at room temperature and neutral pH. In this experiment, a C^{14}-labelled peptide is attached covalently to a polyacrylamide support and the immobilized peptide is incubated with a buffer. The release of radiolabel into the media is periodically assayed to provide the half-time of hydrolysis at the ambient conditions of seven years (*J. Am. Chem. Soc.* **1988**, *110*, 7529).



a) Why is this paper an important contribution ton the field of Bioorganic Chemistry.

b) Several competing processes other than peptide bond hydrolysis might lead to the observed bleed of radioactivity. These are:
   i. mechanical degradation of the polymeric support;
   ii. noncovalently adsorbed radioactive peptide;
   iii. enzymatic contaminants.
   Describe the *control experiments* you might perform to distinguish each of these possibilities from the hydrolysis of the terminal peptide bond.

II.3 (20 pts) R. Bruce Marrifield has been awarded the Nobel Prize in Chemistry in1984 for his development of a straightforward method for obtaining peptides through iterative synthesis. The basic methodology is presented below:



Further cycles of deprotection (H^+) and acylation

a) **Briefly**, discuss the importance of this development to life sciences.

b) While the ribosomal polypeptide biosynthesis is in the N to C direction, solid phase peptide synthesis works best in the opposite C to N direction. Why? Provide the mechanistic rationale confirming your answer.

c) Write a detailed mechanism for the carbodiimide-mediated peptide coupling.

Physical Chemistry Cumulative Exam

$T\ (K) = T\ (^0C) + 273$ $\quad$ $R = 8.3\ J/(K\ mol) = N_0\ k$
$N_0 = 6 \times 10^{23}$ molec/mol $\quad$ $k = 1.4 \times 10^{-23}\ J/K$

Experimental studies of the staphylococcal nuclease protein have determined the following equilibrium concentration ratios of the unfolded (u) to the folded (f) states:

$T\ (^0C)$	$K = [u]/[f]$
20	0.004
40	0.2

1) As a first approximation one may represent the protein unfolding process as a simple statistical mechanical two-level system with energies, ε_f and ε_u and degeneracies g_f and g_u.
   a. (20 points) Write an expression for K in terms of the parameters, ε_f, ε_u, g_f, g_u, and the temperature of the system, T.
   b. (10 points) If you assume that the folded and unfolded states have the same effective degeneracy, use the experimental value of K at 20°C to estimate $\Delta\varepsilon = \varepsilon_u - \varepsilon_f$ (in kJ/mol units).
   c. (10 points) Alternatively, if you assume that the folded and unfolded states have exactly the same energy, use the experimental value of K at 20°C to estimate the ratio of the effective degenacies of the two states, g_u/g_f.
2) The following questions pertain to the experimental protein unfolding process. In answering these question you may assume that the experimental enthaply, $\Delta H = H_u - H_f$, and entropy, $\Delta S = S_u - S_f$, of unfolding are temperature independent.
   a. (10 points) What is the experimental value of the Gibbs free energy of the unfolding reaction, $\Delta G = G_u - G_f$, at 20°C ?
   b. (20 points) Use values of K at 20°C and 40°C to determine experimental enthalpy, ΔH, and entropy, ΔS, of unfolding ?
3) The following questions pertain to the relationship between the results obtained in questions (1) and (2). In answering these questions, you may safely assume that at ambient pressure the enthalpy and energy of unfolding are essentially equivalent to each other, $\Delta H = \Delta U$.
   a. (20 points) Relate the experimentally derived ΔU and ΔS to the parameters introduced in question (1).
   b. (10 points) Briefly (in no more than one notebook page) discuss the physical significance of the above results.

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.)