Crib for 11/11/2000 Analytical Cume:

a. (20points) The different colored balls in the ballpit is analogous to an "ideal solution" problem. Thermodynamics concerns itself with the initial (mixed balls) and final (sorted balls) states. Since the interactions of the balls are independent of color, there is no difference in enthalpy between the initial and final states.

$\Delta H = 0$

To sort the balls from the completely disordered state to the ordered state requires overcoming the entropy of mixing. There is a decrease in entropy, therefore, in going from the initial state to the final state that can be quantified on the basis of the entropy of mixing:

$\Delta S_{mix} = k*\ln[(N_1 + N_2 + N_3 + N_4)!]/(N_1!N_2!N_3!N_4!)$

where N_n is the number of each color ball

Given that $\Delta H = 0$, $\Delta S = \Delta S_{mix} < 0$, and $\Delta G = \Delta H - T\Delta S$, the free energy change associated with sorting the balls is positive:

$\Delta G > 0$

Therefore, work must be done on the system to go from the unsorted to sorted states.

b. (40 points - 10 points/proposed approach) There are many possible answers to part b. In cases in which more than four approaches were suggested, only the first four proposed approaches were scored. The answers that were given were evaluated on the following bases:

1. How clearly was the approach described? Was it clear from the description how the balls would be separated/distinguished? Separating the balls on the basis of shape, for example, would be scored highly only if a clear description of how this would be done was given.

2. How effective would the approach be? Based on the description given, is it clear that the approach would work? Approaches that successfully separate/identify multiple components were scored more highly than ones that work on only a few components.

c. (40 points – 10 points/analogy) There are many possible analogies that might be drawn, depending upon the proposed approaches in b. These responses were evaluated on the following bases:

1. How clearly was the analytical approach described? Simply naming a common technique was not scored as highly as responses that indicated indicated a good understanding of the underlying phenomena.

2. How good is the analogy between the proposed approach to dealing with the mixture of balls and the "analogous" analytical technique?

3. How well was the analogy presented/defended?

Cumulative Exam Crib for

Biochemistry Division

November Exam

1. Signal transduction pathways must generally turn off once their stimulatory missions are completed. First, describe the sequence of steps in the signal transduction pathway leading from adrenaline release into the blood stream to activation of glycogen breakdown. Then, summarize the processes that result in inactivation of each step of the pathway and explain how these inactivation processes are regulated. (40 points)

Steps in activation pathway	Inactivation
1. Adrenaline binds to cell surface receptor	Receptor endocytosis
2. Coupled G protein exchanges GTP for GDP	G protein hydrolyzes GTP to GDP
3. Gα•GTP complex activates adenylate cyclase	----------
4. Active adenylate cyclase synthesizes cAMP	Phosphodiesterase hydrolyzes cAMP
5. cAMP binds and activates cAMP dependent protein kinase (PK-A)	----------
6. PK-A phosphorylates glycogen phosphorylase kinase	A phosphatase dephosphorylates the same enzyme
7. Glycogen phosphorylase kinase phosphorylates glycogen phosphorylase	A phosphatase dephosphorylates the same enzyme
8. Glycogen phosphorylase cleaves a glucose from glycogen generating glucose -1- phosphate	----------

2. Describe the major end-stage changes that lead to apoptotic cell death. Explain, where possible, the enzymes and upstream signaling components that activate the programmed cell death. (30 Points)

The end-stage changes that mark an apoptotic cell include i) DNA cleavage to nucleosome-size (~180bp) fragments (DNA laddering), ii) nuclear condensation, iii) phosphatidylserine flip-flop to the outer surface of the plasma membrane, iv) membrane blebbing, v) exposure of a number of "eat me" signals to trigger phagocytosis of the apoptotic cells.

Upstream signaling can be initiated by either external ligands such as FAS-ligand, CD95 ligand, granzyme B, tumor necrosis factor, or internal stimuli such as DNA damage or conflicting "divide"/ "don't divide" signals. Many of these signals converge on the family of Bc1-2 proteins (Bad, Bax, Bim, Bid, Bc1-2 and Bc1-x) that regulate release of cytochrome c from the mitochondrion. Cytochrome c in combination with an adaptor protein (Apaf-1) can activate caspase 9, leading to development of the above markers of apoptosis. Other signals (e.g. tumor necrosis factor) activate caspase 8 without assistance of Bc1-2 family members.

3. Briefly describe the optimal experimental method for assaying each of the following signal transduction events. (30 Points)

   a. a change in phosphorylation of an important protein
   b. influx of Ca^{++} into a cell
   c. a change in membrane potential
   d. activation of phospholipase C
   e. assembly of a signaling complex
   f. activation of a G protein.

   a. Use radiolabelled $^{32}PO_4\equiv$ and evaluate changes in protein phosphorylation by SDS polyacrylamide gel electrophoresis followed by autoradiography.

   b. Use $^{45}Ca^{++}$ to measure Ca^{++} influx, or use a Ca^{++}-specific fluorescent probe such as FURA-2 AM, INDO-1 AM, or Fluo-3AM.

   c. Use a membrane potential sensitive fluorescent dye (e.g. ANS or one of the cyanine dyes), or use a patch clamb measurement.

   d. Follow formation of phospholipase C hydrolysis products by TLC or use a fluorescent substrate of phospholipase C (e.g. NBD-PE).

   e. Immunoprecipitation of the organizing center of the complex followed by SDS-PAGE and immunoblotting.

   f. Inhibit inactivation with GTP γS or isolate and analyze GTP content of G protein.

Physical Chem

11/00

1. a). Sub-barrier emission is made possible by
8 points quantum mechanical tunneling through the barrier. Thus, the wavefunction of the α-particle extends beyond the barrier with much reduced amplitude. The phenomenon can also be understood by application of the uncertainty principle: by specifying the energy (or momentum) of the particle, an uncertainty in its position follows, i.e. it can be outside the barrier.

9 points b). $M_\alpha E_\alpha = M_{Pu} E_{Pu}$ where $E_{decay} = E_\alpha + E_{Pu}$

$$\text{So } E_{Pu} = \frac{M_\alpha E_\alpha}{M_{Pu}}$$

$$E_{decay} = E_\alpha \left(1 + \frac{M_\alpha}{M_{Pu}}\right)$$

$$= 5.38\left(1 + \frac{4}{242}\right) = 5.47 \text{ MeV}$$

c). The half-life is determined by the decay of a statistically significant number of atoms. One cannot determine a half-life based on the
8 points decay of a single atom, although ~~the~~ one can say that it is probably short.

8 points d) It is favorable energetically to reduce the nuclear charge of heavy elements because this reduces the Coulomb repulsion between the protons and thereby increases nuclear stability. A second decay mode of the heaviest elements is spontaneous fission - it also reduces the nuclear charge (2 points)

9 points e) $\Delta A = 238 - 206 = 32$

3 α-particle has $A=4$, so 8 α-particles are emitted.

$\Delta Z = 92 - 82 = 10$

8 α correspond to $\Delta Z = 16$

6 So, $16 - 10 = 6\beta^-$ are emitted

8 points f) The electron is created at the moment of emission as a neutron transforms into a proton and an electron (plus a neutrino)

2. a) $Q = (\sum M_r - \sum M_p)_{amu} \times 931.5\ MeV/amu$

8 points $Q = (14.0030744 + 4.0026036 - 16.999133 - 1.0078252) \times 931.5$

$Q = -1.193\ MeV$

b.) $Q > 0$, exothermic reaction
8 points $Q < 0$, endothermic reaction

c). By conserving momentum one obtains

$$E_{threshold} = \frac{M_{target} + M_{projectile}}{M_{target}} \times |Q| \quad \text{for } Q < 0$$

10 points For α incident on ^{14}N:

$$E_{th} = 1.193 \times \frac{18}{14} = 1.534 \text{ MeV}$$

For ^{14}N incident on ^{4}He

$$E_{th} = 1.193 \times \frac{18}{4} = 5.369 \text{ MeV}$$

d)(4) 1. $Q > 0$ is exothermic while $\Delta H < 0$ is exothermic.
8 points (4) 2. Q is expressed on a per atom basis while ΔH is expressed on a per mole basis.

8 points e) For both types of processes, spontaneity is determined by $\Delta G = \Delta H - T\Delta S$
For nuclei in their ground state (i.e. target nuclei) the nuclear temperature $T \simeq 0$. Thus ΔG reduces to ΔH, which corresponds to Q.

f). The 2 protons need to overcome the Coulomb
8 points barrier between + charged particles. The energy of H atoms on Earth ($\sim kT$) is way too low, in the Sun T is sufficiently high for

this reaction to occur. Chemical reactions are similar in that high T are often needed to overcome the activation barrier.