No Analytical crib available
August 25, 2012
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No Organic crib available
August 25, 2012
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Biochemistry Cumulative Exam

Title: Signal Transduction

August 25th, 2012

1. (10 points). Provide any one mechanism by which Src kinase is inhibited.

   Src is inhibited by Csk-mediated phosphorylation at Y527, which triggers the binding of phospho-Y527 its own SH2 domain, which closes the active site, rendering it inactive.

2. (10 points) What is the purpose of A-kinase associated proteins (AKAP)?

   AKAPs are a group of structurally diverse proteins. They have a common function of binding to the regulatory subunit of PKA kinase, thereby confining the PKA holoenzyme to discrete locations within the cell.

3. (10 points). How does PKA regulate long term change in protein composition in a cell?

   Activation of PKA often leads to phosphorylation of nuclear CREB protein, which together with CBP/300 co-activator stimulates transcription of genes, thus initiating a long term change in cell's protein composition.

4. (20 points) Provide the mechanism by which GPCR can increase Ca^{++} concentration in the cells via intracellular stores and extracellular media.

   GPCR containing $G_{\alpha o}$ or $G_{\alpha q}$ can activate phospholipase C, which increases Ca^{++} concentration in cells. In response to hormone stimulation $G_{\alpha o}$ or $G_{\alpha q}$ subunit separates from $\beta\gamma$ subunits and bind PLC in the membrane, activating it. Activated PLC cleaves PIP_2 into diacylglycerol (DAG) and inositol triphosphate (IP_3). IP_3 binds to the calcium channel located on ER membrane (IP_3 gated channels), which opens these channels and release calcium in the cytoplasm. When Ca^{++} levels in ER stores are depleted, STIM proteins from ER relocate to areas close to the plasma membrane and trigger opening of Ca^{++} channels in the membrane, allowing influx of extracellular Ca^{++}.

5. (20 points) Why the activation of NFκappaB is considered irreversible as compared to receptor tyrosine kinase activation? How is this pathway downregulated?

   In unstimulated cells, NFκappaB is localized in the cytoplasm bound to the inhibitor protein IκappaB. In response to different extracellular signals, phosphorylation-dependent ubiquitination and degradation of IκappaB in proteasomes releases active NFκappaB, which translocates to the nucleus. Since IκappaB is degraded, this pathway

is considered relatively irreversible as compared to receptor tyrosine kinase activation, which is phosphorylation-dependent. NFκappaB pathway is inhibited when newly synthesized IκappaB enters into the nucleus and brings back NFκappaB in the cytoplasm inactivating it.

6. (20 points) With what technique could you measure the amount of activated G protein in ligand-stimulated cells? Explain using an example.

   Activated G proteins can be quantified by measuring their binding with corresponding effector proteins in unstimulated and ligand-stimulated cells. For example, activated Ras binds Raf, therefore, Ras can be pulled down using Ras antibody from unstimulated and ligand-stimulated cells, and bound Raf levels in Ras immunoprecipitates can be analyzed using western blotting.

7. (10 points) Grb2 protein lacks enzymatic activity, still it is a critical component of Ras signaling pathway. Provide the mechanism by which it activates Ras pathway.

   Grb2 is an adapter protein that possesses two SH3 domains and one SH2 domain. When a ligand binds receptor tyrosine kinase, it dimerizes and autophosphorylates itself at several tyrosine residues, creating a binding site for the SH2 domain of Grb2. Grb2 bound to the receptor, then binds SOS via its two SH2 domains, which activates SOS. SOS is an exchange factor which exchanges GDP from Ras for a GTP activating it.

1. symmetry operations:

a. E = identity = leaves molecule unchanged +3

b. n-fold rotation = C_n

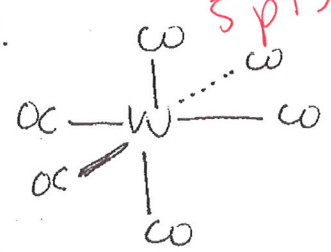
= molecule appears unchanged after a rotation of 360°/n. +3

= line about which rotation is performed

+3

c. σ = reflection across a plane such that the molecule appears unchanged

2. 5 pts.



$W(CO)_6$

Valence e⁻: 18e⁻ ← 5 pts

C_4 : 3 axes

C_3 : 4 axes

C_2 : 6 axes

13 axes ← 5 pts

3. a) D_3

b) C_{2h}

c) D_{4h}

d) C_{2h}

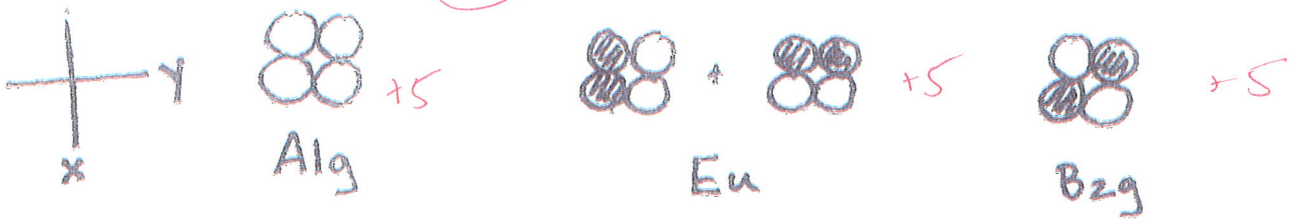
e) D_{2h}

f) C_2

42 pts

7 each

4. a. -34 drawing 4 pts.



point group = D4h +5

A1g : dz^2  +5

B2g :  dxy +5

Physical Chemistry Cume Exam August 2012

The expectation value of the *angular* kinetic energy of a hydrogen atom is $\frac{\langle L^2 \rangle}{2m_e}\left\langle \frac{1}{r^2} \right\rangle$, and its *total* kinetic energy is the sum of its *angular* and *radial* kinetic energies.

Useful fundamental constants and equations:

$\hbar = h/2\pi = 1.1 \times 10^{-34}$ J s $\qquad m_e = 9.1 \times 10^{-31}$ kg (electron mass)

$a_0 \approx 0.53\text{Å} \approx 5.3 \times 10^{-11}$ m $\qquad hcR_Z = Z^2 2.18 \times 10^{-18}\,\text{J} = Z^2 1{,}313$ kJ/mol

$$E_n = \frac{-hcR_Z}{n^2} \qquad hcR_Z = \frac{Z^2\hbar^2}{2m_e a_0^2} \qquad P_{nl}(r) = R_{nl}^2(r)r^2 \qquad \sqrt{\langle L^2 \rangle} = \hbar\sqrt{l(l+1)}$$

$$\Psi_{1s} = \Psi_{100} = \sqrt{\frac{Z^3}{\pi a_0^3}}e^{-Zr/a_0} \qquad P_{1s}(r)dr = |\Psi_{1s}|^2 4\pi r^2 dr = 4\left(\frac{Z}{a_0}\right)^3 e^{-2Zr/a_0} r^2 dr$$

$$\int_{-\infty}^{\infty} e^{-ax^2}dx = \sqrt{\frac{\pi}{a}} \qquad \int_{-\infty}^{\infty} x^2 e^{-ax^2}dx = \frac{1}{2a}\sqrt{\frac{\pi}{a}} \qquad \int_0^{\infty} x^n e^{-bx}dx = \frac{n!}{b^{n+1}}$$

$$\int x^2 e^{-cx}dx = -e^{-cx}\left[\frac{x^2}{c} + \frac{2x}{c^2} + \frac{2}{c^3}\right]$$

Virial Theorem: $\frac{\langle V \rangle}{\langle K \rangle} = \frac{2}{n}$ for any potential of the form $V(r) \propto r^n$

NOTE: The above information was not sufficient to obtain the radial probability density for the 2p state. I had intended to provide the following additional information.

$$R_{2,0} = \left(\frac{1}{2a_0}\right)^{3/2}\left(2 - \frac{r}{a_0}\right)e^{-r/2a_0}$$

$$R_{2,1} = \left(\frac{1}{2a_0}\right)^{3/2}\left(\frac{r}{\sqrt{3}\,a_0}\right)e^{-r/2a_0}$$

1) (30 points) Write down the integral which you would need to evaluate in order to determine $\langle 1/r^2 \rangle$ for hydrogen in a $2p$ state, and simplify it to a form that is equivalent to one of the integrals given above.

Solution: $\left\langle \frac{1}{r^2} \right\rangle = \int_0^{\infty} \frac{1}{r^2} P_{2,1}(r)dr = \int_0^{\infty} \frac{1}{r^2} R_{2,1}^2(r) r^2 dr = \left(\frac{1}{2a_0}\right)^3 \left(\frac{1}{3a_0^2}\right) \int_0^{\infty} r^2 e^{-r/a_0} dr$

2) (20 points) Evaluate the integral, and use your result to obtain the *angular* kinetic energy of hydrogen in a 2*p* state (and express your answer as a number in J units).

Solution: $\left\langle \frac{1}{r^2} \right\rangle = \left(\frac{1}{2a_0} \right)^3 \left(\frac{1}{3a_0^2} \right) 2!\, a_0^3 = \frac{2}{8 \cdot 3} \frac{1}{a_0^2} = \frac{1}{12 a_0^2}$

$$\frac{\hbar^2 l(l+1)}{2m_e} \left\langle \frac{1}{r^2} \right\rangle = \frac{\hbar^2}{m_e} \frac{1}{12 a_0^2} \approx 3.9 \times 10^{-19} \text{ J}$$

3) (20 points) Use the Virial Theorem to obtain the expectation value of the *total* kinetic energy of hydrogen in a 2*p* state.

Solution: The Virial Theorem implies that $\langle K \rangle = -\langle H \rangle \approx \frac{2.18 \times 10^{-18}}{2^2} \approx 5.4 \times 10^{-19}$ J

4) (20 points) Combine the above results to obtain the *radial* kinetic energy of hydrogen in 2*p* state.

Solution: The radial kinetic energy is $\langle \mathrm{K} \rangle - 3.9 \times 10^{-19}$ J $\approx 1.5 \times 10^{-19}$ J

5) (10 points) How would the above energies change for He^+?

Solution: The magnitude of all of the energies would increase by a factor of four (because He has a nuclear charge of Z=2)