

1. Any measurement that seeks to determine the concentration of an unknown via an instrumental technique such as electrochemistry, spectroscopy, mass spectrometry, etc., relies upon a relationship between the actual measured quantity (e.g., a voltage, a current, absorbance/transmittance) and concentration. The following questions relate to the error associated with the measured quantity and its relationship to the resulting error in concentration. We assume here that there is only random or indeterminate error.

- a) A common means for determining the concentration of an analyte species in solution is to compare the radiant power of light transmitted through the analyte solution,  $P$ , with radiant power,  $P_0$ , transmitted through a solution with negligible analyte present (i.e., a blank solution) under otherwise identical conditions. What is the relationship between concentration,  $C$ , in the limit of low concentration, and  $P/P_0$ ? Define all symbols that you provide. (5 pts)

$$P/P_0 = 10^{-\epsilon b C}$$

$P$  = radiant power transmitted through the sample solution

$P_0$  = radiant power transmitted through the blank solution

$b$  = path length

$\epsilon$  = molar absorptivity

Also,  $P/P_0 = e^{-2.3(\epsilon b C)}$

$$C = (-\log P/P_0)/(\epsilon b) \text{ or } C = (-\ln P/P_0)/(2.3\epsilon b)$$

Equivalently, since  $\log u = 2.303 \ln u$

Also,  $P/P_0 = T$

$T$  = transmittance

$A = -\log T$

$A$  = absorbance

$A = \epsilon b C$

$C = A/(\epsilon b)$

- b) Provide a relationship for the sensitivity associated with this measurement? (10 pts)

sensitivity =  $d(P/P_0)/dC$       note:  $d(e^u)/dx = e^u du/dx$

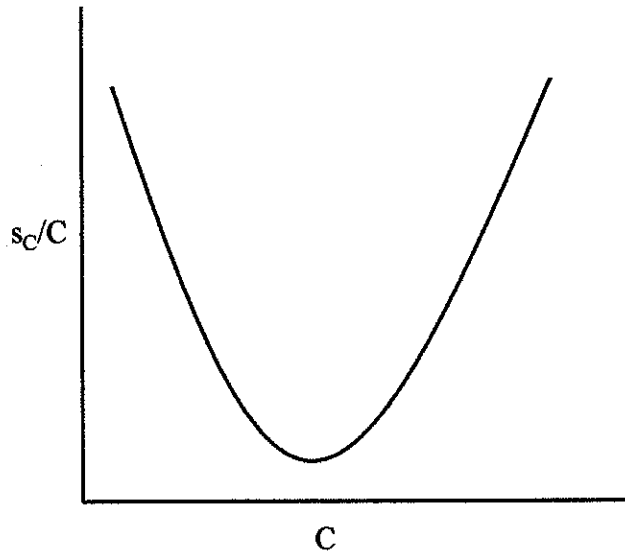
$$d(e^{-2.3(\epsilon b C)})/dx = (-2.3\epsilon b)e^{-2.3(\epsilon b C)}$$

- c) For a fixed error in the measurement of  $P/P_0$  (i.e.,  $s_{P/P_0} = \text{constant}$ ) what is the relationship between the error in concentration,  $s_C$ , that arises from the error in  $P/P_0$ ? (10 pts)

$$s_C = (s_{P/P_0})/\text{sensitivity}$$

$$s_C = (s_{P/P_0})/ [(-2.3\epsilon b)e^{-2.3(\epsilon b C)}] = -e^{-2.3(\epsilon b C)}/(2.3\epsilon b)$$

- d) For  $s_{P/P0} = \text{constant}$  with concentration, draw the shape of a plot of  $s_C/C$  versus  $C$  (i.e., a plot of the relative concentration error versus concentration). (10 pts)



- e) Based on the dependence of relative concentration error on concentration in this type of measurement, where is the relative concentration error minimized? (5 pts)
- a) at low concentration
  - b) at intermediate concentration
  - c) at high concentration
  - d) relative concentration is independent of concentration in this measurement

answer: b (see plot of part d)

2. The titration of  $50.00(\pm 0.02)$  mL of a strong acid required  $42.4(\pm 0.2)$  mL of a  $0.1034(\pm 0.0002)$  M strong base to reach the equivalence point.

- a) what is the concentration of the strong acid? (5 pts)

$$C = (0.0424 \text{ L})(0.1034 \text{ M}) / (0.050000 \text{ L}) = 0.0877 \text{ M}$$

- b) what is the error associated with the value of the acid determined by this titration? (Show how you arrived at the result) (10 pts)

$$\frac{s_y}{y} = \sqrt{\left(\frac{0.02}{50.00}\right)^2 + \left(\frac{0.2}{42.4}\right)^2 + \left(\frac{0.0002}{0.1034}\right)^2} = 0.005$$

$$s_y = (0.005)(0.0877 \text{ M}) = 0.0004$$

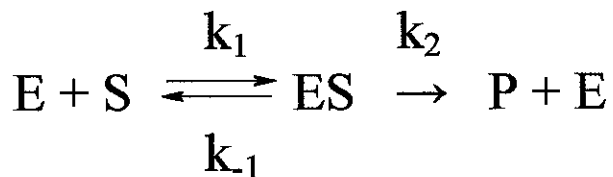
$$y = 0.0877 \pm 0.0004 \text{ M}$$

3. The EPA monitors contract labs that analyze environmental samples. A standard sample containing lead at a concentration of 16.40 ppm was sent to the contract lab for analysis. The contract lab measured the standard sample 6 times and determined an average concentration of 16.23 ppm with a standard deviation of 0.1378 and a sum of the squares of deviation from the mean of 0.095. Does the contract lab's method show bias at the 95% confidence level? Show the work you use to justify your answer. (10 pts)

$$t = \frac{\bar{x} - \mu}{\frac{s}{\sqrt{N}}} = \frac{16.23 - 16.40}{\frac{0.1378}{\sqrt{6}}} = -3.03$$

$$t_{5,95} = -2.57 \quad -3.03 < -2.57, \text{ bias is indicated}$$

4. The behavior of an enzyme catalyzed reaction is often consistent with the generalized mechanism



where E is the enzyme, S is the substrate, ES is an enzyme-substrate complex, and P is the product.

- a) Two scientists are associated with proposing this mechanism. What are their last names? (5 pts)

(Leonor) Michaelis and (Maude) Menten

- b) The relationship that gives the rate of product formation,  $v$ , (sometimes referred to as the velocity of the reaction) is given below:

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

In terms of rate constants and concentrations, what is the relationship for the maximum rate,  $v_{\max}$ ? (5 pts)

$$v_{\max} = k_2[E]_0$$

- c) What conditions will make the measured rate pseudo-first order in initial enzyme concentration? (5 pts)

$$v = \frac{v_{\max} [S]}{K_M + [S]} = \frac{k_2[E]_0[S]}{K_M + [S]}$$

when  $[S] \gg K_M$ ,  $v = k_2[E]_0$

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

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

- a) Write the expected relationship between cell potential,  $E_{\text{cell}}$ , and triiodide concentration if the potential of a platinum electrode placed into the analyte solution is measured against the standard calomel electrode (SCE). (10 pts)

$$E_{I_3^-/I^-} = E^0 - \frac{RT}{nF} \ln \frac{[I^-]^3}{[I_3^-]} = 0.536 - (0.0128)(3 \ln(0.202) - \ln[I_3^-])$$

$$E_{\text{cell}} = 0.536V - \frac{RT}{2F} \ln \frac{[I^-]^3}{[I_3^-]} - E_{SCE} = 0.354V + 0.0128 \ln[I_3^-]$$

- b) What is the mathematical relationship between the random error associated with the cell potential measurement,  $s_{E_{\text{cell}}}$ , and the resulting error in concentration,  $s_c$ , assuming  $s_{E_{\text{cell}}}$  to be constant with concentration? (10 pts)

$$s_C = s_{E_{\text{cell}}}/\text{sensitivity}$$

$$\text{sensitivity} = dE_{\text{cell}}/dC = 0.0128 d \ln[I_3^-]/d[I_3^-] = 0.0128/[I_3^-]$$

$$s_C = [I_3^-] s_{E_{\text{cell}}}/(0.0128)$$

Useful relationships:

$$\frac{de^u}{dx} = e^u \frac{du}{dx} \quad \frac{d \ln u}{dx} = \frac{1}{u} \frac{du}{dx}$$

TABLE 7-4

Critical Values of  $F$  at the 5% Probability Level (95% confidence level)

Degrees of Freedom (Denominator)	Degrees of Freedom (Numerator)								
	2	3	4	5	6	10	12	20	$\infty$
2	19.00	19.16	19.25	19.30	19.33	19.40	19.41	19.45	19.50
3	9.55	9.28	9.12	9.01	8.94	8.79	8.74	8.66	8.53
4	6.94	6.59	6.39	6.26	6.16	5.96	5.91	5.80	5.63
5	5.79	5.41	5.19	5.05	4.95	4.74	4.68	4.56	4.36
6	5.14	4.76	4.53	4.39	4.28	4.06	4.00	3.87	3.67
10	4.10	3.71	3.48	3.33	3.22	2.98	2.91	2.77	2.54
12	3.89	3.49	3.26	3.11	3.00	2.75	2.69	2.54	2.30
20	3.49	3.10	2.87	2.71	2.60	2.35	2.28	2.12	1.84
$\infty$	3.00	2.60	2.37	2.21	2.10	1.83	1.75	1.57	1.00

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TABLE 7-5

Critical Values for the Rejection Quotient,  $Q^*$ 

Number of Observations	$Q_{crit}$ (Reject if $Q > Q_{crit}$ )		
	90% Confidence	95% Confidence	99% Confidence
3	0.941	0.970	0.994
4	0.765	0.829	0.926
5	0.642	0.710	0.821
6	0.560	0.625	0.740
7	0.507	0.568	0.680
8	0.468	0.526	0.634
9	0.437	0.493	0.598
10	0.412	0.466	0.568

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**TABLE 7-3****Values of  $t$  for Various Levels of Probability**

Degrees of Freedom	80%	90%	95%	99%	99.9%
1	3.08	6.31	12.7	63.7	637
2	1.89	2.92	4.30	9.92	31.6
3	1.64	2.35	3.18	5.84	12.9
4	1.53	2.13	2.78	4.60	8.61
5	1.48	2.02	2.57	4.03	6.87
6	1.44	1.94	2.45	3.71	5.96
7	1.42	1.90	2.36	3.50	5.41
8	1.40	1.86	2.31	3.36	5.04
9	1.38	1.83	2.26	3.25	4.78
10	1.37	1.81	2.23	3.17	4.59
15	1.34	1.75	2.13	2.95	4.07
20	1.32	1.73	2.09	2.84	3.85
40	1.30	1.68	2.02	2.70	3.55
60	1.30	1.67	2.00	2.62	3.46
$\infty$	1.28	1.64	1.96	2.58	3.29

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**TABLE 7-1****Confidence Levels for Various Values of  $z$** 

Confidence Level, %	$z$
50	0.67
68	1.00
80	1.28
90	1.64
95	1.96
95.4	2.00
99	2.58
99.7	3.00
99.9	3.29

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# Biochemistry Cumulative Examination

## Title: Signal Transduction

August 27, 2005

1. (15 pts) Provide brief general definitions for the following terms.
  - (i) RNAi  
**RNA interference (RNAi) is a process in which double-stranded RNA triggers the degradation of a homologous messenger RNA (sharing sequence-specific homology to particular "target" mRNAs).**
  - (ii) Antagonists  
**Substances that bind to a receptor, but fail to elicit a response.**
  - (iii) Desensitization  
**Adaptation to long term stimuli by reducing their response to them.**
  - (iv) GTPase activating protein  
**An enzyme which assists in the hydrolysis of GTP to GDP.**
  - (v) SH3 domain  
**Src-Homology 3 domain is a domain commonly found in tyrosine kinases. It specifically binds ProX-X-Pro motif.**
  
2. (40 pts) Provide concise answers to the following questions.
  - (i) Why receptor tyrosine kinases possess multiple autophosphorylation sites, compared to cytoplasmic kinases like Src and Abl, which have only one autophosphorylation site?  
**Receptor tyrosine kinases provide a platform for different signaling proteins to come together upon stimulation. By autophosphorylating multiple tyrosine residues, they provide binding sites for different SH2 containing proteins. These proteins when assembled upon the receptor interact with each other and thus turn on different signaling cascades. This mechanism is absent in cytoplasmic kinases like Src and Abl.**

- (ii) What is senescence?  
**A stage when cells stop dividing.**
- (iii) Src kinase gets phosphorylated at Y416, is this event stimulatory or inhibitor. Explain the mechanism.  
**Phosphorylation at Y416 is stimulatory, because it opens up the catalytic site that binds ATP.**
- (iv) Mutations in G proteins active sites are often oncogenic. Explain a plausible mechanism.  
**Often mutations in G proteins break the on/off control provided by GTP and GDP binding respectively. Since the cellular concentration of GTP is 10 times higher than GDP, more often GTP is bound in the active site, thus making the protein oncogenic.**
- (v) What are the main kinases that constitute the MAP kinase cascade?  
**MAPKKK, MAPKK and MAPK.**
- (vi) If rasGAP protein is degraded by RNAi, predict the effect on G protein signaling pathway when it is specifically activated?  
**It will be constitutively activated.**
- (vii) Define the functional consequences of activating Ras with GTP $\gamma$ S versus GTP $\alpha$ S.  
**GTP $\gamma$ S will activate it constitutively, whereas GTP $\alpha$ S will behave just like GTP and will get hydrolyzed to GDP over the course of time.**
- (viii) What is the molecular target of Gleevec?  
**Bcr-Abl**

3. (15 pts) Explain briefly.

- (i) Define WW domain.  
**~40 residue module that binds proline rich sequences on target proteins.**
- (ii) What is the function of islets of Langerhans?  
**It is an endocrine gland that maintains energy metabolite homeostasis.**
- (iii) What is the function of a PLC $\beta$ ?  
**PLC $\beta$  are activated by heterotrimeric G proteins and hydrolyze PIP2 to IP3 and DAG.**
- (iv) How are PLC $\beta$  and PLC $\gamma$  activated?  
**PLC $\beta$  are activated by heterotrimeric G proteins and PLC $\gamma$  is activated by protein tyrosine kinases.**

- (v) What are the hallmarks of cancer?  
**Uncontrolled proliferation.**

4. (30 pts) Provide concise answers to the following questions.

- (i) Explain the molecular mechanism that leads to bubonic plague.  
**The Bubonic Plague is a disease that is caused by a germ called Yersinia pestis. It is spread to humans by fleas from infected rodents.**
- (ii) EGTA is a chelating agent with high specificity and affinity towards calcium. How would EGTA microinjection affect a cell's response to (a) vasopressin  
**Vasopressin acts by elevating cytosolic  $Ca^{2+}$  to  $10^{-6}$  M, activating PKC. EGTA injection will block vasopressin activation.**  
b) glucagon?  
**It should not affect the response to glucagons, which use cAMP, not  $Ca^{2+}$  as second messenger.**
- (iii) Explain two key differences between Jak/Stat and Receptor Tyrosine Kinase pathways?  
**Jak itself is not a receptor kinase, it binds to cytokine receptor which is stimulated upon binding cytokines. Receptor tyrosine kinases (RTK) bind ligands themselves.**  
**Jak kinase phosphorylates Stat which is a transcription factor. RTKs usually do not phosphorylate transcription factors directly.**
- (iv) Both kinases and ATPases require ATP as a cofactor, how do they differ?  
**Kinases use ATP to phosphorylate the substrate proteins at a Y, S or T residue. ATPases hydrolyze ATP to ADP and release energy that is used in the cell.**
- (v) What is the key difference between PTP and PTEN?  
**PTP is a tyrosine phosphatase and PTEN is inositol polyphosphate 3-phosphatase.**

**-Answer Key-**  
**Inorganic Chemistry Cumulative Exam**  
Purdue University  
August 27, 2005

**Question 1:**

It's a *d-d* transition. The octahedral compound  $[\text{Ti}(\text{OH}_2)_6]^{3+}$  has Ti in the +3 oxidation state, with one *d* electron. This one *d* electron moves between the  $e_g$  and  $t_{2g}$  set of orbitals in the octahedral field splitting scheme.

**Question 2:**

The  $\text{Cl}^-$  and  $\text{I}^-$  ligands each have a different effect upon splitting of the crystal field.  $\text{Cl}^-$  is a stronger field ligand than  $\text{I}^-$ , thereby creating a larger energy gap and a different color of light to be absorbed.

**Question 3:**

Although  $\text{TiBr}_4$  has no *d* electron, and hence no *d-d* transitions to bring about color, there are bromide-to-titanium charge-transfer bands. These charge-transfer bands are in the visible region, thus giving this compound color.

**Question 4:**

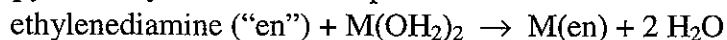
Ethylenediaminetetraacetic acid. Consisting of 4 carboxylate and 2 amine ligands, EDTA is a very strong chelator of metals. EDTA is used often when a generic strong metal chelator is needed.

**Question 5:**

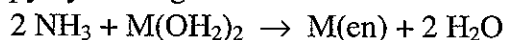
Paramagnetic metal ions have unpaired electrons and diamagnetic metal centers do not.

**Question 6:**

The chelate effect states that a ligand with multiple donor atoms will bind to a metal center with higher affinity than monodentate ligands. For example, ethylenediamine ( $\text{H}_2\text{NCH}_2\text{CH}_2\text{NH}_2$ ) will bind to a metal center with a significantly higher affinity than two ammonias. The driving force for the chelate effect comes from increased entropy in the system. For example:



increases entropy by starting with two molecules and yielding three. Whereas:



begins with 3 molecules and ends with 3 molecules.

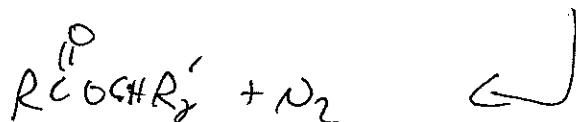
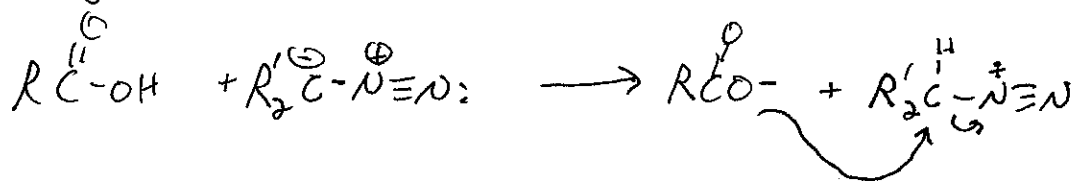
# ORGANIC CUME ANSWER KEY

AUGUST 27, 2005

- 1)
- 1) B
  - 2) D
  - 3) C
  - 4) E
  - 5) A

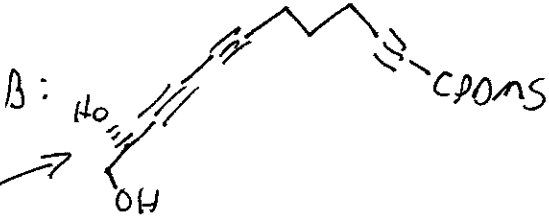
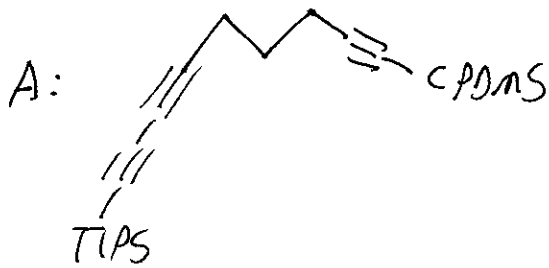
- 2) a) Animal Fat: typically long chain, <sup>nearly</sup> saturated fatty acids - solid  
 Vegetable Oil: unsaturated fatty acids - liquid  
 Tropical oils: saturated but short chain fats - liquid  
 b) Butter is natural animal fat - <sup>mostly</sup> saturated  
 Margarine is hydrogenated vegetable oil: still mostly saturated but from vegetable source

- 3) A typical mechanism for the reaction of carboxylic acids + diazomethanes is,

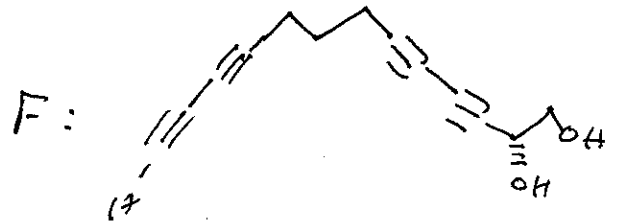
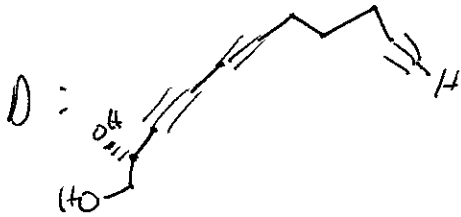
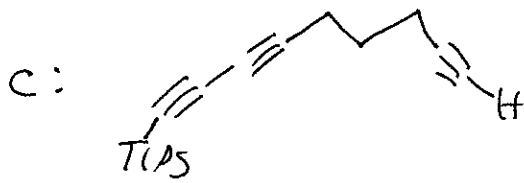


The difference in  $p$  values likely reflects the difference in the ability of the solvent to ~~stabilize~~ solvate the carboxylate in ~~the~~ ~~the~~ methanol, the carboxylate is <sup>more</sup> stabilized by solvation, but ion ~~stabilization~~ substitution is more critical in non-solvating solvent

4)



Stereo-chemistry is important



c) cyanopropyl dimethyl silane

6)

I: f

II: a, e

III: b

IV: c

5) Small rings,  $n=4, 5$ , are more highly strained due to bond angles. For things this large the isn't a lot of strain in  $n=7, 8$

However, smaller rings are also  
However, large rings are entropically disfavored  
compared to small rings

note:

2 hexamers  $\rightarrow$  3 tetramers  $\Delta S > 0$

4 hexamers  $\rightarrow$  3 tetramers  $\Delta S < 0$

Hexamers & Pentamers have the best balance of enthalpy & entropy

Compared to hexamers:

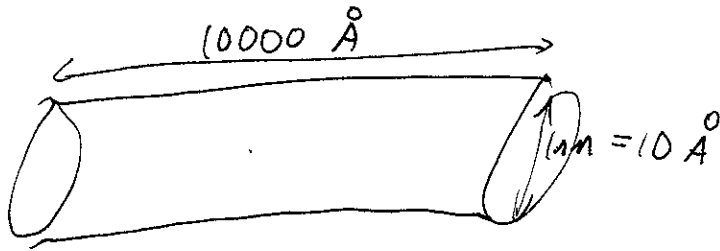
tetramer: favorable entropy, very bad enthalpy

pentamer: high enthalpy, high entropy (close)

heptamer: ~~higher~~ higher enthalpy, ~~higher~~ lower entropy

octamer: ditto

56)



$$\text{circumference} = \pi d = 31.4 \text{ \AA}$$

Assuming the bond length in graphite is about  $1.4 \text{ \AA}$ , that means there are about 22 carbons around the circumference

Assuming  $1.4 \text{ \AA}$  between carbon rings means there are about

$$\frac{22 \text{ carbons}}{1.4 \text{ \AA}} \times \frac{10000 \text{ \AA}}{1.4 \text{ \AA between rings}} \approx 15 \times 10000 = 150000 \text{ carbons}$$


①  $i\hbar \frac{\partial \Psi}{\partial t} = H \Psi \quad \Psi = \psi(x) F(t)$

$i\hbar \frac{1}{F(t)} \frac{\partial F}{\partial t} = \frac{1}{\psi(x)} \hat{H} \psi(x) = E$

$i\hbar \frac{\partial F}{\partial t} = E_n F(t) ; \quad H\psi = E_n \psi$   
 $f_n(t) = e^{iE_n t/\hbar} \quad \psi_n(x) e^{iE_n t/\hbar}$

②  $\langle \Psi | H | \Psi \rangle = \sum_n C_n^* C_n E_n$   
 $P = \frac{C_n^* C_n}{\sum_n C_n^* C_n}$

③ a  $\Rightarrow P(x) = \frac{1}{L} \left( \sin^2 \frac{\pi x}{L} + \sin^2 \frac{2\pi x}{L} \right)$



c  $\Rightarrow |\Psi(x,t)|^2 = \frac{1}{L} \left[ \sin^2 \frac{\pi x}{L} + \sin^2 \frac{2\pi x}{L} + \sin \frac{\pi x}{L} \sin \frac{2\pi x}{L} \left( e^{i(E_1-E_2)t/\hbar} + e^{i(E_2-E_1)t/\hbar} \right) \right]$

d  $\Rightarrow T = \frac{2\pi\hbar}{E_2-E_1} = \frac{8mL^2}{3h}$

④  $\langle p \rangle = 0$  ,  $KE = \frac{h^2}{8mL^2} \quad \langle x \rangle = \frac{L}{2}$