# Biophysical Chemistry for Life Scientists

Biotechnology Research Center, National Taiwan University
Fall 2000
Instructor: Sunney I. Chan
Vice President & Distinguished Research Fellow, Institute of Chemistry,Academia Sinica
[Telephone: 2-2789-9402; e-mail: chans@chem.sinica.edu.tw]

Lectures 2 and 3
Date: Friday, October 20, 2000 and Monday, October 23, 2000

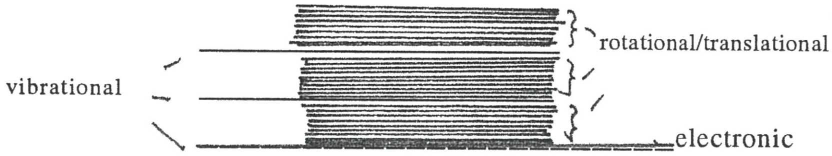
## Suggested Readings

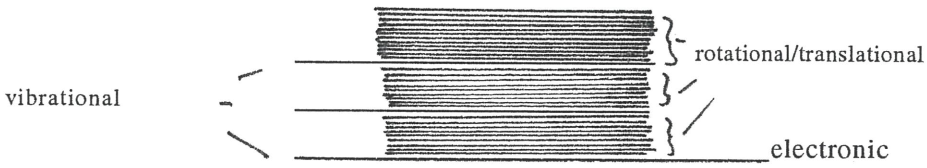
Raymond Chang, "Physical Chemistry for the Chemical and Biological Sciences" (University Science Books) 2000, Chapter 4.

## Molecular energy levels and molecular energy states

- Associated with molecules are molecular energy levels and molecular energy states (derived from quantum mechanics and solving the Schroedinger equation for the molecule).
- These molecular energy levels are well defined for an isolated molecule, or molecules in the gas phase at low pressures.
- They become less well defined for molecules in a high-pressure gas, or in a liquid, due to intermolecular forces or interactions.
- In the solid, the intermolecular interactions are sufficiently strong that the energy levels involve collections of molecules.

**Molecular energy levels/states when the molecules interact only weakly**




**Molecules are distributed among the molecular energy levels/states to the extent that these energy levels/states are thermally accessible.**

So, $E$ = energy of the system

$$= \sum_J \varepsilon_J n_J$$

where $\varepsilon_J$ is the energy of the molecule in quantum state J, and $n_J$ denotes the number of molecules in this quantum state.

Also, if N is the total of molecules in the system, we have

$$N = \sum_J n_J$$

## Molecular interpretation of energy

If define K.E. denotes the kinetic energy of molecules
P.E. denotes the potential energy of molecules,

then,

$n\,\underline{E}$ (per mole)

$$= nN_A(<K.E.>+<P.E.>)$$ if molecules ar interacting weakly only

average per molecule (arrows point to $<K.E.>$ and $<P.E.>$) ($N_A$ = Avogadro's number)

## Things we could do to the system

We could do a number of things to the system, namely, our collection of molecules:

- Apply heat to the system: change the distribution of molecules among the molecular energy levels/states.

- Do work on the system: change the energy levels/states of the system, and possibly alter the distribution of molecules among the various molecular energy levels/states.

- Add molecules to the system or take molecules away from the system: change N, and hence $n_J$.

## Chemical Thermodynamics

- Motivation:

(1) Can't describe cellular properties and cellular processes properly without the concepts of Energy (E), Enthalpy (H), Entropy (S), Free Energy (G), Heat (H), Work (W), etc. Also, Temperature (T) and Pressure (P).

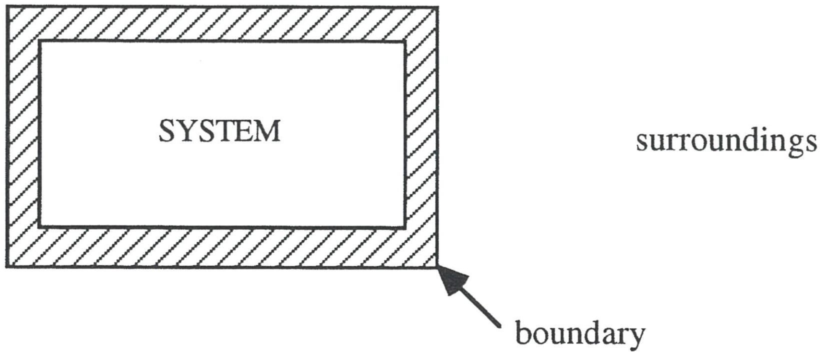
(2) Can't understand these concepts without the Laws of Thermodynamics.

(3) Laws are completely general, applicable to gases, liquids, solids, in fact any system, and not restricted to ideal or perfect gases, as discussed earlier.

**Thermodynamic system or System:**

- Focus of attention
- Various types of systems
  - (i) physical system
  - (ii) chemical system
  - (iii) biological system (in this course) ⟵

**Region around the system is called the surroundings:**




**All interactions of a system with surroundings occur across the boundary:**

(1) Matter may cross boundary.

(2) Two forms of energy can cross boundary:
- heat
- work

**Systems in thermodynamics are classified by the permeability of the boundary to matter, heat and work:**

| | |
|---|---|
| (1) Open system | Matter, heat, work free to pass |
| (2) Closed system | No transport of matter, but passage of heat and work allowed |
| (3) Adiabatic system | impermeable to matter and heat |
| (4) Isolated system | impermeable to matter, heat and work |

**Isothermal system:**

$T_{\text{system}} = T_{\text{surrounding}}$,

where T = temperature.

## System is characterized by its Properties

- Properties can be intensive (independent of size of system)
  extensive (proportional to size of system)

- A system is said to be in a defined state when all its properties have specified values.

- A system is said to be in thermodynamic equilibrium if its properties are independent of time and there is no flow of mass or energy across its boundary.

- When there is flow of matter or energy through a system and yet no change of properties with time, the system is said to be in steady state.

## Equation of State

A mathematical relationship between some of the properties of a system (empirical relationships devised to fit experimental data, or relationships derived from molecular theory).

| • Simple Examples | Equation of State |
| --- | --- |
| Ideal gas | $PV = nRT$ |
| Van der Waal gas | $\left(P + \frac{n^2 a}{V^2}\right)(V - nb) = nRT$ |
| Virial eq. for gas | $pV = nRT\left(1 + \frac{nB'}{V} + \frac{n^2 C'}{V^2} + \cdots\right)$ |

- Also other properties!

  e.g. E(V,T) or S(V,T)

- Usually only a few properties need to be specified to specify the state of a system.

e.g., for a single pure and homogeneous substance, such as liquid $H_2O$,

one extensive property (such as mass)
two intensive property (such as temp. & pressure)

are sufficient to specify the state of the system. All other properties are then automatically fixed, i.e., there are no further degrees of freedom.

- The number of properties that have to be specified in order to define the state of a system is given by the Gibbs phase rule.

## Process

An event in which a property of a system changes:

| | |
|---|---|
| physical process | (thermal expansion of liquid water) |
| chemical process | (chemical reaction) |
| biological process | (cellular differentiation) |

- A process is reversible if change proceeds through a succession of equilibrium states, each differing from the last by an infinitesimal change in a property of the system. (Idealized; difficult to achieve!! Infinitesimal slow rates.)

- Otherwise, process is irreversible.

- These two kinds of processes are fundamentally different, even if in the two scenarios, the system started from the same initial state and ended up in the same final state following the change. The important difference is that the amounts of heat and work that cross the boundary during the process are different for the two processes.

## Work (W)

Concept familiar to most of you.

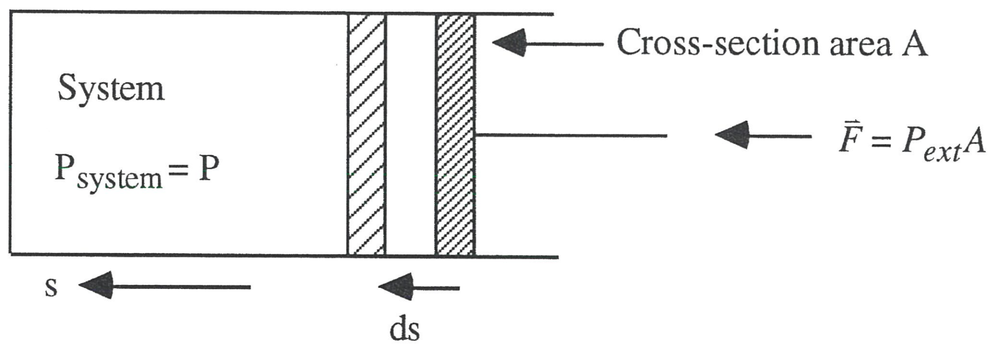
- Work = force x distance

$\vec{F}$ = force applied on system
$\vec{s}$ = distance traversed by system

$dW = \vec{F} . d\vec{s} > 0$

when work is done on system by surroundings

- Pressure-volume work




$dW = \vec{F}\, ds$
$= P_{ext}A\, ds$
$= -P_{ext}d\, V$

If compression is reversible, $P_{ext} = P_{system} = P$

irreversible, $P_{ext} > P$

- Other forms of Work

Electrical work

intensive variable

dW = voltage difference x increment amount of charge transferred through voltage charge

extensive variable

$= (\Delta\Phi)\, dq$

Chemical work

$$dW = \mu_A \underbrace{dn_A}$$

$\mu_A$: chemical potential of component A

$dn_A$: change in # of moles of A

Surface work

$$dW = \gamma \underbrace{dA}$$

$\gamma$: surface tension

$dA$: change in surface area

**Heat**

Concept should be familiar to you also.

Heat = Thermal energy that one can transfer from one system to another.

**First Law of Thermodynamics**

- Relates Heat, Work and Energy

$$dE = dQ + dW \qquad \text{differential form}$$

E = energy or energy content of system

• <u>E is a state function</u> (a property!)

i.e., $E(T,P)$, or $E(V,P)$, or $E(V,T)$ for a pure homogeneous substance

↑ extensive variable

$\Delta E = E_f - E_i = [E(V_f, T_f) - E(V_i, T_i)]$ if $V$ and $T$ are the independent variables.

The result is independent of path

It follows then that dE is an <u>exact</u> differential.

If system involves more than 1 component, then E(V,T composiiton), or E(T,P, composition), and so on.

• <u>dQ, dW inexact differentials</u>

(1) Q and W do not follow a mathematical relationship

(2) These quantities are <u>path</u>-dependent

Many workers prefer DQ, DW to distinguish them from dE, i.e., to denote that they are <u>inexact</u> differentials.

• <u>Integrated form of First Law</u>

$$\boxed{\Delta E = Q + W}$$

$$\uparrow \qquad\qquad \uparrow \qquad\qquad \uparrow$$

$$\int_i^f dE = \sum_i^f dQ + \sum_i^f dW$$

This is merely a statement of conservation of energy!

## Two simple applications

• Heating of a system at constant volume or constant pressure, but PV work only

1) Heating at Constant Volume

PV work only $\Rightarrow dW = - P_{ext}\, dV$

$\therefore\ dE = dQ - P_{ext}\ dV$

But constant $V$, $\therefore\ dV = 0$

so $dE = dQ_V$

and $\Delta E = Q_V$

From this, it follows that

$$\left(\frac{\partial E}{\partial T}\right)_V = \frac{dQ_V}{dT} = C_V \equiv \text{heat capacity at constant volume}$$

$\Rightarrow$ a measure of the system to store energy at constant volume

2) <u>Heating at Constant Pressure</u>

Again, $dE = dQ - P_{ext}\, dV$

Because $P_{ext}$ constant

$$\therefore \ \Delta E = Q_P - P_{ext}\, \Delta V$$

$$\text{or } Q_P = \Delta E + P_{ext}\, \Delta V$$

- <u>Enthalpy</u>

Definition $\qquad H = E + PV$

↑ (P) pressure of <u>system</u>

<u>Return to heating at constant pressure</u>

At constant pressure,

$$dH = dE + pdV + VdP$$

($VdP$) $= O$

Also, when heating at constant pressure, typically $P = P_{ext}$

$$\therefore \ \Delta H = \Delta E + P_{ext}\, \Delta V$$

and comparing result obtained at top of page

$$\Delta H = Q_P$$

from this it follows that $\left(\dfrac{\partial H}{\partial T}\right)_P = \dfrac{dQ_P}{dT} = C_P$

heat capacity at constant pressure

## A Few More Complex Applications

(1) Isothermal Expansion (PV work nonzero) of an ideal gas (also perfect gas)

First Law

$$dE = dQ + dW$$
$$= dQ - P_{ext}\,dV$$

Ideal Gas

$$PV = nRT$$

*also* $$PV = \frac{2}{3}E$$

$$\therefore E = \frac{3}{2}(nRT)$$

| Thus, for an ideal gas, E(T) only. In general, however, E(T,V) |
|---|

So

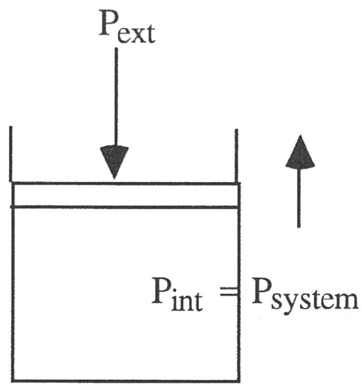
$$dE = \left(\frac{\partial E}{\partial T}\right)_V dT + \left(\frac{\partial E}{\partial V}\right)_T dV$$
$$= C_V T + 0.\,dV$$

isothermal $\Rightarrow dT = 0$

$$\therefore dE = 0$$
$$\therefore \boxed{\Delta E = 0}$$

Work

$$dW = -\,P_{ext}\,dV$$




a) Irreversible expansion $\quad P_{int} > P_{ext}$
system

Need to know path to calculate work, i.e., how $P_{ext}$ varies during process

b) Reversible expansion

$$P_{ext} = P_{system} = \frac{nRT}{V}$$

$$dW = -P_{ext}dV = -\frac{nRT}{V}dV$$

$$W = -nRT\int_{V_i}^{V_f}\frac{1}{V}dV = \boxed{-nRT\ln\frac{V_f}{V_i}}$$

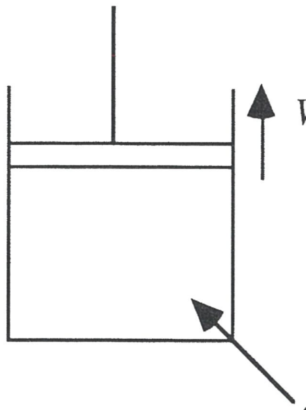
$$\frac{V_f}{V_i} > 1,\ W < 0$$

or, work is done by system on surroundings (expansion)

Because $\Delta E = 0$ for ideal gas

$$\boxed{Q = -W = nRT\ln\frac{V_f}{V_i}}$$

**Final Result**




Clearly $|W_{rev}| > |W_{irrev}|$

Thus, during reversible isothermal expansion, one obtains <u>maximum</u> transfer of heat into PV work (compared with irreversible isothermal expansion).

(2) Adiabatic Expansion of an Ideal Gas

<u>Adiabatic</u> $\therefore\ dQ = 0,\qquad \boxed{Q = 0}$

<u>First Law</u> $dE = \underbrace{-P_{ext}dV}_{DW\ or\ dW}$

<u>$\Delta E$</u>

Now gas must cool following expansion

<u>Recall</u>

$$dE = \left(\frac{\partial E}{\partial T}\right)_V dT + \left(\frac{\partial E}{\partial V}\right)_T dV$$

$$= C_V dT \qquad \textit{for ideal gas}$$

$$\therefore \Delta E = \int_{T_i}^{T_f} C_V dT = C_V\left(T_f - T_i\right)$$

$T_f$ will depend on path (i.e., reversible *vs* irreversible)

Reversible expansion

$$C_V dT = -P_{ext} dV = -P dV \quad \underline{\text{reversible}}$$

$$C_V dT = -\frac{nRT}{V} dV$$

$$\frac{C_V}{T} dT = -\frac{nR}{V} dV$$

$$C_V \ln\frac{T_f}{T_i} = nR \ln\frac{V_i}{V_f}$$

$$\text{or} \quad \frac{T_f}{T_i} = \left(\frac{V_i}{V_f}\right)^{nR/C_V}$$

## Molecular Interpretation of *H*

- E = energy content

  K.E. = kinetic energy of molecules

  P.E. = potential energy of molecules

  E = $nN_A(<K.E.>+<P.E.>)$ if molecules ar interacting weakly only

  average per molecule $N_A$ = Avogadro's number

- H = heat content = enthalpy

$$H = E + \boxed{PV}$$

P = pressure = pressure of system

V = volume <u>accessible</u> to molecules

PV gives a measure of the capacity of the system to do pressure-volume work

## Enthalpy Changes - physical processes

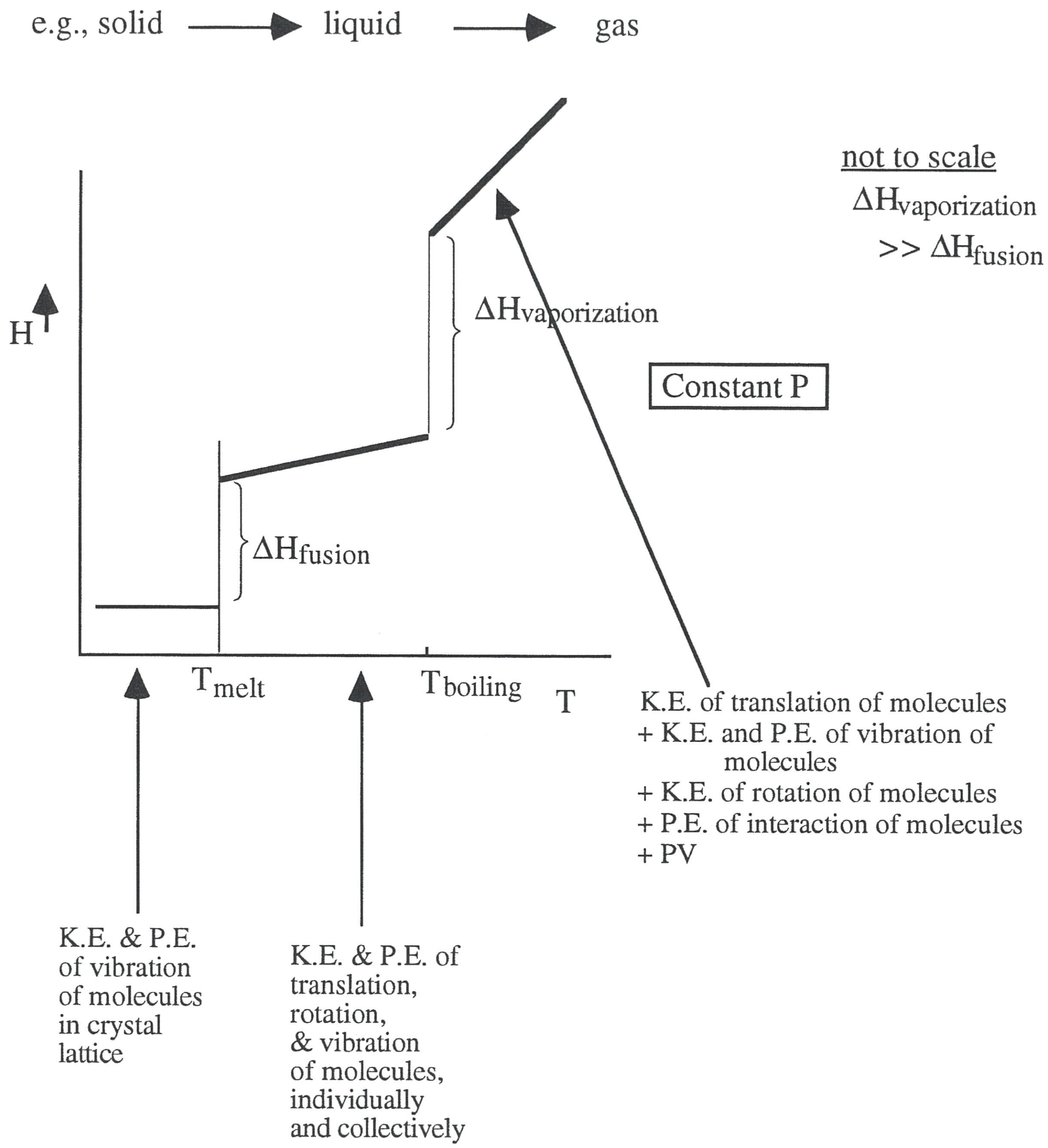
- Change T, change average K.E. and P.E. of molecules

  Change P change capacity of molecules of system to do pressure-volume work

Usually H(T,P) increases with increasing T and P with

$$\left(\frac{\partial H}{\partial T}\right)_P \text{ and } \left(\frac{\partial H}{\partial P}\right)_T > 0.$$

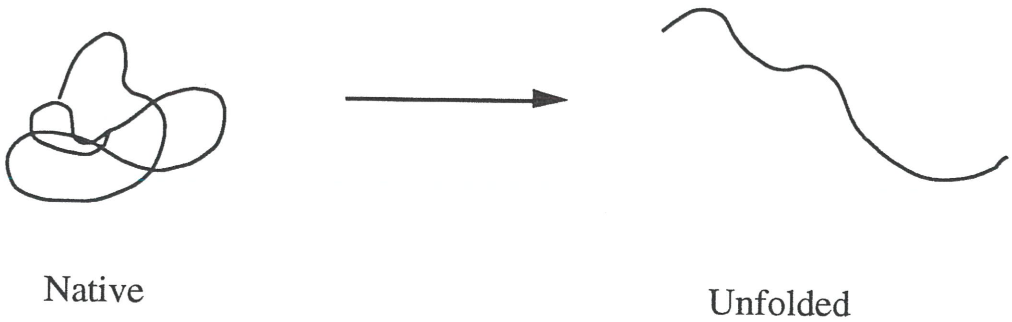
For physical processes involving a single component system (pure homogeneous substance), largest change occurs at phase transitions.

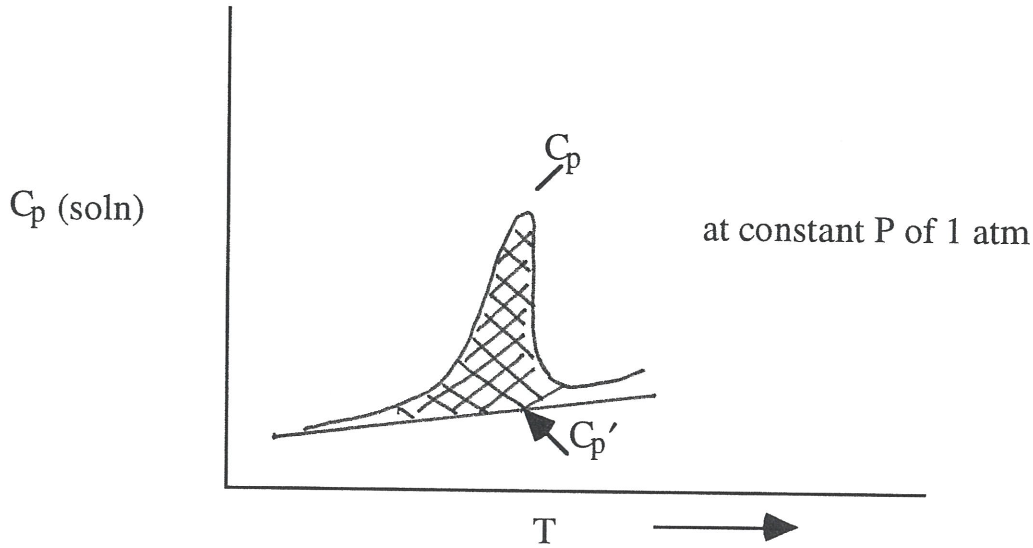



• Note that $C_p$ <u>infinite</u> at phase transitions ($T_{melt}$ & $T_{vap}$ are well-defined temperatures at constant P), since there is a $\Delta H$ without a temperature change accompanying the phase transitions.

## Enthalpy changes for a simple biological/biochemical process

### (1) Thermal unfolding of a protein or macromolecule




$$dH = \left(\frac{\partial H}{\partial T}\right)_P dT + \left(\frac{\partial H}{\partial P}\right)_T dP \qquad \text{closed system}$$

$$= \left(\frac{\partial H}{\partial T}\right)_P dT \qquad \text{at constant P}$$

$$\Delta H_{process} = \int_{T_{lower}}^{T_{upper}} C_p^{\ protein}\, dT = \int_{T_1}^{T_2} \left(C_p - C_p'\right) dT$$

area under curve

- Two Points

(a) $C_p$ not infinite at transition:
Protein unfolding not as cooperative as melting of ice

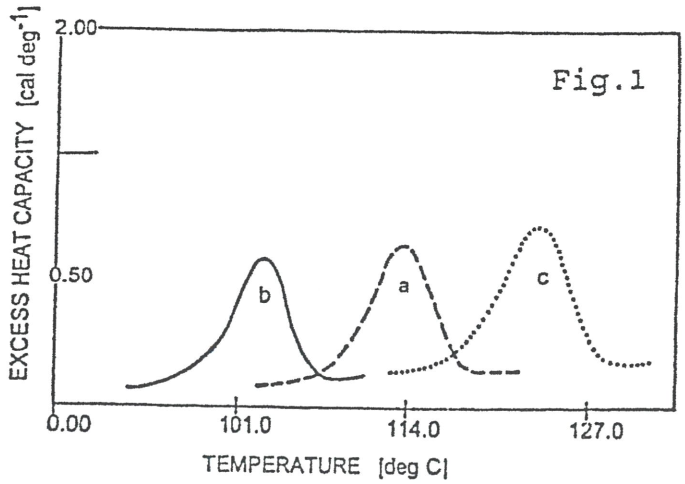
The more cooperative the process, the larger the $C_p$.

(b) Orders of magnitude for enthalpy of protein unfolding

| Protein | $\Delta H$/kJ mol$^{-1}$ |
|---|---|
| α-chymotrysin | 560 |
| ribonuclease A | 400 |
| lysozyme | 370 |
| metmyoglobin | 285 |
| cytochrome c | 210 (~44 kcal/mole) |

| | |
|---|---|
| typically | 200-600 kJ/mole |
| $T_m$ typically | 40-90°C |

Recently, a number of hyperthermophilic proteins have been discovered that do not "melt" until ~110°C, e.g., rubredoxin from *Pyrococcus furiosus*, Pure & Applied Chem. 66, 485-489 (1994), H.H. Klump, M.W.W. Adams and F.T. Robb.



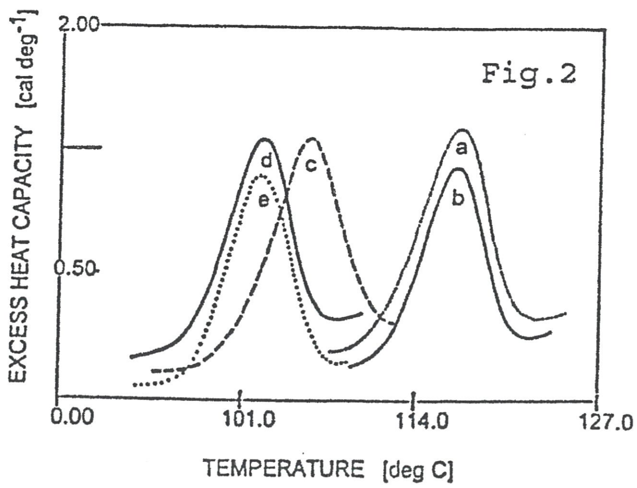
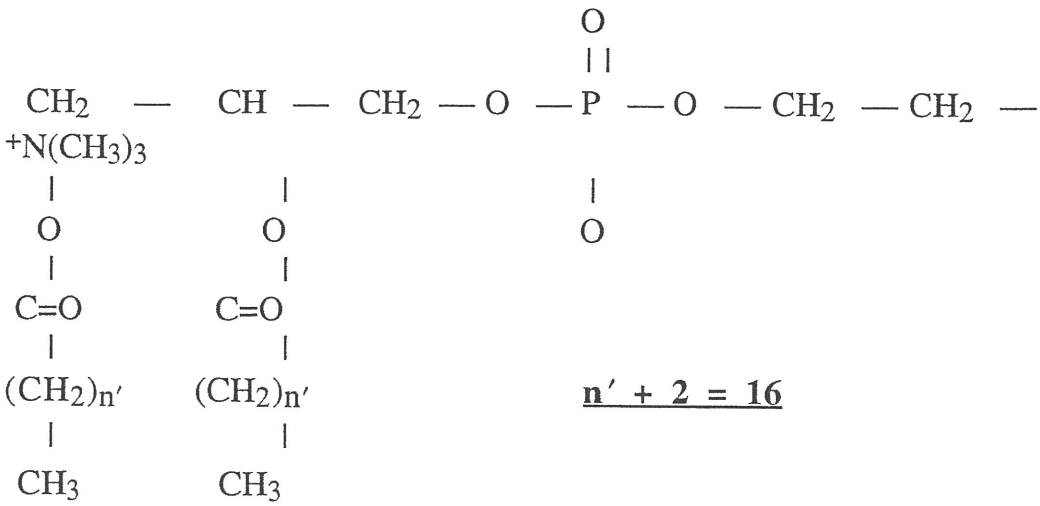




Fig.1 shows the excess heat capacity vs. temperature scans for the three different rubredoxin samples. The corresponding scans for the five ferredoxins are given in Fig.2.

| Denaturation | ΔHcal | ΔScal | Tm | Fig. |
|---|---|---|---|---|
| Rubredoxin (ox) | 22.5 kcal/mole | 57.0 | 113 | 1a |
| Rubredoxin (red.) | 20.2 | 53.8 | 102 | 1b |
| Rubredoxin (Zn) | 23.8 | 60.0 | 123 | 1c |
| Ferredoxin (ox/4Fe) | 11.5 | 29.3 | 117.5 | 2a |
| Ferredoxin (red/4Fe) | 11.4 | 29.0 | 117.0 | 2b |
| Ferredoxin (ox/3Fe) | 11.0 | 29.3 | 105 | 2c |
| Ferredoxin(therm*/ox/3Fe) | 11.0 | 29.3 | 102.5 | 2d |
| Ferredoxin(therm/red/3Fe) | 11.0 | 29.3 | 102.0 | 2e |

*Thermotoga

(2) Thermal melting of a phospholipid bilayer
single component dispersion in $H_2O$.
e.g., dipalmitoylphosphatidylcholine (DPL)




n′ + 2 = 16

These molecules aggregate to form bilayer membranes in $H_2O$

Pure bilayer dispersions exhibit a thermal phase transition corresponding to "melting" of hydrocarbon chains.

solid or
gel phase $L_\beta$
phase

fluid or
liquid crystalline
$L_\alpha$

For DPL, the transition temperature is 42°C, and ΔH = 9 kcal/mole.

## Phospholipid phase transitions

### Saturated lipids (PC)

| *n* | $T_m$ | ΔH | |
|---|---|---|---|
| 12:0 | ~0°C | | DLL |
| 14:0 | 23 | 6.7 kcal/mole | DML |
| 16:0 | 41 | 9 | DPL |
| 18:0 | 58 | 10.5 | DSL |
| 22:0 | 75 | 14.9 | |

### Unsaturated lipids (PC)

| $n_1$ | $n_2$ | $T_m$ | ΔH |
|---|---|---|---|
| 16:1$\Delta^9$ | 16:1 $\Delta^9$ | -36°C | 9.1 |
| 18:1$\Delta^2$ | 18:1 $\Delta^2$ | 41 | 9.6 |
| 19:1 $\Delta^5$ | 19:1 $\Delta^5$ | 11 | 7.8 |
| 18:1 $\Delta^9$ | 18:1 $\Delta^9$ | -22 | 7.6 |

### Different Heatgroups (Saturated)

| n | $T_m$ | ΔH | |
|---|---|---|---|
| PE 16:0 | 60°C | 8.5 | $-CH_2-CH_2-NH_3^+$ |
| PC 16.0 | 41 | 9 | $-CH_2-CH_2-{}^+N(CH_3)_3$ |
| PS 16:0 (pH~7) | 55 | 9 | $-CH_2-CH(NH_2)-COO^-$ |

## Enthalpy change for a chemical reaction

- Example: oxidation of glucose to carbon dioxide and water

Chemical equation

$$C_6H_{12}O_6(s) + 6O_2(g) \quad \rightarrow \quad 6CO_2(g) + 6H_2O(g)$$

| Reactants | | Products |
|---|---|---|
| a) Set of chemical bonds, 0 K<br>b) Thermal energy<br>Kinetic: vibrations rotation, translation;<br>Potential: bond vibrations, inter-and intramolecular interactions | → $\Delta H$ | a) New set of chemical bonds, 0 K<br>b) Thermal energy<br>Kinetic: vibrations, rotation, translation;<br>Potential: bond vibrations intermolecular & intramolecular interactions |

- If process is carried out at constant temperature and pressure

$\Delta H_{RX} = Q_P =$ heat of reaction at that temperature and pressure

and $\Delta H_{RX}(\mathrm{T,P}) = \underline{c}H_c(T,P) + \underline{d}H_D(T,P) - \underline{a}H_A(T,P) - \underline{b}H_B(\mathrm{T,P})$

if we write reaction as

$\underline{a}A + \underline{b}B \rightarrow \underline{c}C + dD$ chemical reaction equation or chemical equation.

or $\Delta H_{RX}(T,P) = \sum_{\text{Products}} \nu_P H_P(T,P) - \sum_{\text{Reactants}} \nu_R H_R(T,P)$

if we write chemical equation as

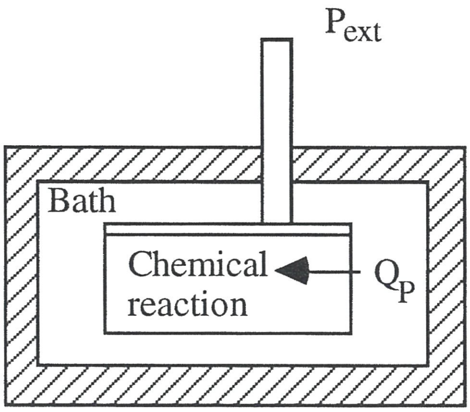
$\sum_{\text{reactions}} \nu_R S_R = \sum_{\text{products}} \nu_P S_P$ $\quad S \equiv$ molecular species

• Standard Conditions:

$$\left.\begin{array}{l} T = 25^\circ C \quad \text{or} \quad 298\ K \\ P = 1\ \text{atmosphere} \end{array}\right\}$$

$$\Delta H_{RX} \Rightarrow \Delta H^\circ_{RX}$$

• Measurement of $\Delta H_{RX}$ in a bomb calorimeter




Open bomb calorimeter

$$\Delta H_{RX} = Q_P = -C_P(\text{bath})\Delta T$$

$Q_P$ $> 0$ endothermic rx (heat is absorbed from bath)

$Q_P$ $< 0$ exothermic rx (heat is produced by reaction)

• If closed calorimeter is used and reaction is carried out at constant V, then one measures $Q_V = \Delta E_{RX}$

Note that $T_i \neq T_f$ and one must correct for this to obtain $\Delta E_{RX}(T, V)$.

Similarly for $\Delta H_{RX}(T, P)$