Week 2 problem solving

Heat Capacity (total, molar)

Enthalpy of Drug Binding

Enthalpy of Crystal Dissolution

Heat capacity, $C = q/\Delta T$

- How much *heat* is needed for a 1°K increase?
  - Substances with fewer atoms have low molar heat capacity
  - **C** is measured in J/K or cal/K, or derivative units (extensive)
- Where does the *heat* come from?
  - Internal (from a reaction in which Enthalpy changes)
  - External source
- *Normalized* Heat Capacity (per *mole , mass, volume*)
  - Introduce heat capacity *per unit amount of sample*
  - **specific heat** is per 1kg of mass C [J/(k**g**·K)], or [J/(g · K]
  - **molar heat capacity** is per mole C [J/(**mol**·K)]
- What is the heat capacity (specific heat) of water?
  - At STP, C_{H2O} **= 1 cal**/(g·K) = 4.1813 J/(g·K)

Heat content vs ΔT : $q=C\Delta T$ or $C=q/\Delta T$

- **Problem**: Specific heats of ethanol and water at STP are equal to 2.44 J/(g·K) and 4.18 J/(g·K), respectively. Their densities are 0.8 g/cm³ and 1 g/cm³, respectively. Compare temperature increases of 1 mL samples of ethanol and water after 1 cal = 4.18 J of heat is transferred to them.

  A. $\Delta T(C_2H_5OH) = \Delta T(H_2O)$
  B. $\Delta T(C_2H_5OH) = \Delta T(H_2O) \times 1.71$
  C. $\Delta T(C_2H_5OH) = \Delta T(H_2O) \times 2.14$

  Q1: weight of 1mL?
  Q2: C of 1m?
       (c_p*mass)
  Q3: $\Delta T = q/C$

- **Solution**:
  - 1 mL of water = 1 g $\Rightarrow$ total C of 1 mL water is 4.18 J/K
  - 1 mL of ethanol = 0.8 g $\Rightarrow$ C of 1 mL ethanol is 0.8×2.44 = 1.95 J/K
  - ΔT for water = q/C_{water} = 4.18 J / 4.18 J/K = 1 K
  - ΔT for ethanol = $q/C_{ethanol}$ = 4.18 J / 1.95 J/K = 2.14 K

C$_p$ and C$_v$ heat capacities

At const. volume, C_V
- The system does not perform work
- All heat transferred to the system is added to its internal energy and translates into *T* increase

$$q = \Delta U = C_V \Delta T$$

Isobaric: at constant pressure: C_P
- The system *may* perform work
  - ❖ E.g. if gas is produced in the reaction and allowed to expand
- Heat transferred to the system is spent in two ways :
  - ❖ partially on work
  - ❖ partially on *T* increase

$$q = \Delta H = \Delta U + P\Delta V = C_P \Delta T$$

- *T* increase is lower than it would be w/o work
- $C_P > C_V$, by $P\Delta V / \Delta T$:
  - ❖ Liquids and solids: $P\Delta V \approx 0$
    $$C_P \approx C_V$$
  - ❖ Ideal gas: work = $P\Delta V = nR \times \Delta T$
    Per mole, $C_P \approx C_V + R$

Heat capacities of common substances

Substance	Phase	Isobaric specific heat capacity C_P J/(g·K)	Isobaric molar heat capacity $C_{P,m}$ J/(mol·K)	
Oxygen	gas	0.918	29.38	
Carbon dioxide CO_2	gas	0.839	36.94	
Air (dry, 1 atm, 0°C)	gas	1.0035	29.07	
Ethanol	liquid	2.44	112	
Human tissue	mixed	3.5		
Water steam at 100°C	gas	2.08	37.47	
Water at 25°C	liquid	4.18	75.33	
Water ice at -10°C	solid	2.05	38.09	

Reaction/transition thermochemistry

- Enthalpy change (ΔH) in a reaction or transition:

  Reactants (R) $\Rightarrow$ Products (P)

- Heat of reaction is defined by enthalpy change

  - $\Delta H = H$(products) $- H$(reactants)

  - $\Delta H < 0$ means "$\Rightarrow$" is *exothermic* (produces heat)

  - $\Delta H > 0$ means "$\Rightarrow$" is *endothermic* (absorbs heat)

- Heat can be measured in a (micro)calorimeter, and used to:

  - Characterize the reaction (Endothermic/exothermic? Molar ΔH^0? Strength and number of bonds vs ΔH^0 sign)

  - Find the extent of reaction from ΔH and ΔH^0 (how much product is formed?)

Exothermic vs endothermic

- **Problem:** Calorimetric data on binding of several anti-HIV drugs to their common target, HIV protease, at T=300K is presented in the table. For how many drugs in the list, is the binding reaction endothermic?

  A. 1
  B. 2
  C. 3
  D. 4
  E. 5
  F. 6

Drug	ΔH binding (kcal/mol)
Nelfinavir	3.1
Indinavir	1.8
Saquinavir	1.2
Tipranavir	-0.7
Lopinavir	-3.8
Atazanavir	-4.2
Ritonavir	-4.3
Amprenavir	-6.9
Darunavir	-12.7

- **Answer:** 3 drugs. *Endothermic* means $\Delta H > 0$, which is the case for Indinavir, Saquinavir, and Nelfinavir

(Quantitative) ΔH of reaction/transition

Reaction	Equation	ΔH_m(react) = molar ΔH(react) = heat produced/absorbed when…
Dissolution	$D_{solid} + H_2O \leftrightarrow D_{aq}$	1 mole of drug/substance dissolves in infinite amount of water
Neutralization	$OH^- + H^+ \leftrightarrow H_2O$	1 mole of OH^- interacts with 1 mole of H^+ to form 1 mole of H_2O
1:1 protein/ligand binding	$P + L \leftrightarrow PL$	1 mole of L binds to 1 mole of P to form 1 mole of PL complex

- ΔH(react) = ΔH_m(react)$\times n_{moles}$
- n is the extent of reaction:
  - Dissolution: n = amount of substance dissolved
  - Neutralization: n = amount of limiting reactant
  - **Protein/ligand binding: n = amount of complex (not necessarily equal to limiting reactant!)**
- $n = \Delta H / \Delta H_m$

# Acid-base neutralization heat

Reaction: HCl(aq) + NaOH(aq) --> NaCl(aq) + H_2O(l) + Energy

- **Problem:** Molar enthalpy of neutralization reaction between HCl and NaOH at 25°C is -55.9 kJ/mol. When 25 mmol HCl was added to 10 ml of NaOH solution in a calorimeter, the evolved heat was measured to be 1 kJ. What was the concentration of NaOH in the solution?

   A. 25 mM

   B. 25 M

   C. 0.55 M

   D. 1.79 M

   E. 17.9 mM

- **Solution:** If 25 mmol of HCl were completely neutralized by NaOH, ΔH would be equal to 0.025 mol × -55.9 kJ/mol ≈ -1.4 kJ. However, we only observed heat of 1 kJ.

   - NaOH was a limiting reactant
   - Only 1/55.9 = 0.0179 mol (17.9 mmol) of reaction products was formed
   - Therefore 17.9 mmol NaOH was present in the solution in the beginning
   - This corresponds to NaOH concentration of 1.79 M (17.9 mmol/10mL=1.79m/L).

- **Answer:** 1.79M
- **Note:** Acid/base neutralization involves formation of H_2O from OH- and H+; covalent bonds are formed, exothermic.
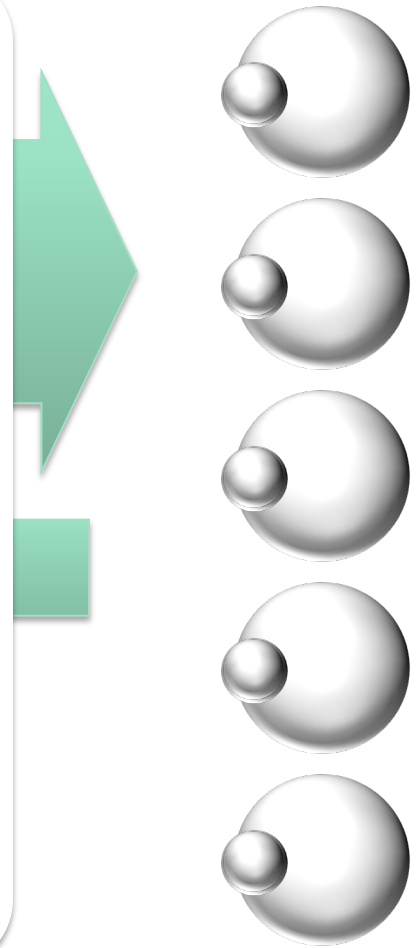
Protein-ligand binding equilibrium

binding

dissociation
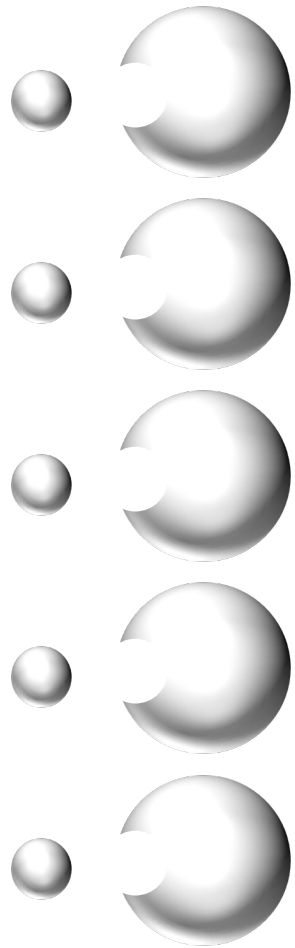
1 mole of protein
1 mole of ligand
unbound
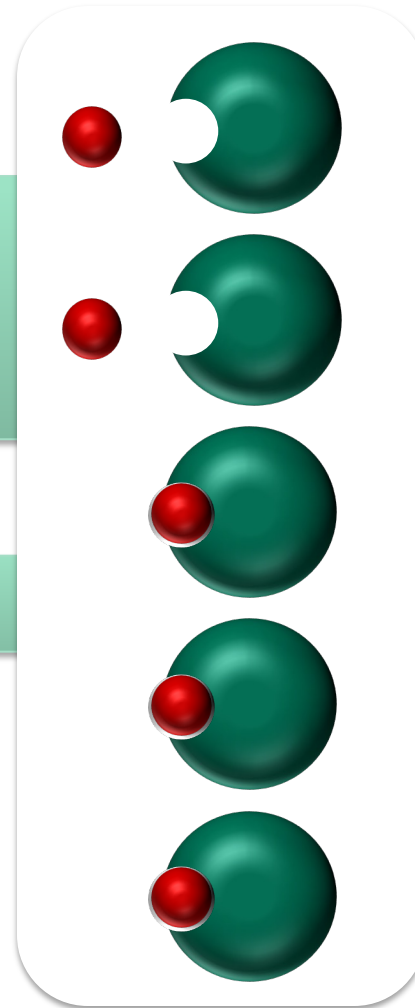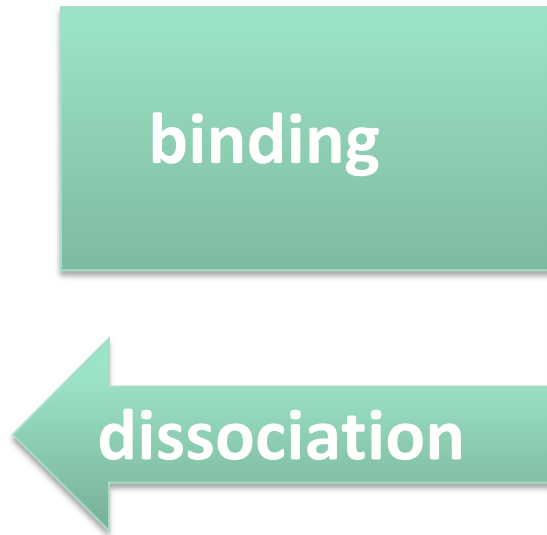
0.4 mole of unbound protein
0.4 mole of unbound ligand
0.6 mole of bound complex
EQUILIBRIUM

d complex
bound

Enthalpy of drug binding - I

- **Problem:** 0.3 mL of 1 mM solution of a drug is added to a tube with a protein solution. Some of the drug reacts with the protein to form 1:1 protein-drug complex. The reaction produces heat of -2.4×10^{-3} cal. Estimate molar enthalpy of binding ΔH_m.
  - A. -8 kcal/mol
  - B. -12 kcal/mol
  - C. 24 kcal/mol
  - D. 3.6×10^{-3} cal/mol
  - E. impossible to tell because the extent of reaction is not known
- **Solution:** The total molar amount of drug is 0.3 10^{-3}L x 10^{-3}mol/L = **0.3 μmol** – but how much of it is bound to the protein? And how much product (complex) was formed, in moles?
  - If n = 0.3 μmol, $\Delta H_m = \Delta H/n = -2.4 \times 10^{-3}$ cal / (0.3×10^{-6} mol) = -8 kcal/mol
  - If n = 0.2 μmol, $\Delta H_m = \Delta H/n = -2.4 \times 10^{-3}$ cal / (0.2×10^{-6} mol) = -12 kcal/mol
  - If n = 0.1 μmol, $\Delta H_m = \Delta H/n = -2.4 \times 10^{-3}$ cal / (0.1×10^{-6} mol) = -24 kcal/mol
- **Answer:** impossible to tell b/c the extent of reaction is not known
  - However, we know that the reaction is exothermic
  - And that $\Delta H_m \leq -8$ kcal/mol

Enthalpy of drug binding - II

- **Problem:** 0.3 mL of 1mM solution of a drug is added to a tube with a protein solution, and the drug reacts **entirely** with the protein to form a 1:1 protein-drug complex (**no unbound drug is left**). The reaction produces heat of -2.4×10^{-3} cal. Estimate molar enthalpy of binding.

  A. -8 kcal/mol

  B. -12 kcal/mol

  C. 12 kcal/mol

  D. 3.6×10^{-3} cal/mol

  E. impossible to tell because the extent of reaction is not known

- **Solution:**
  - ❖ The total molar amount of drug is 0.3 μmol
  - ❖ All of it reacted, so 0.3 μmol of complex was formed ($n = 0.3$ μmol)
  - ❖ $\Delta H_m = \Delta H / n = -2.4 \times 10^{-3}$ cal $/ (0.3 \times 10^{-6}$ mol$) = -8$ kcal/mol

- **Answer:** -8 kcal/mol

- **Note:** It is important that all 0.3 μmol of drug was bound

Dissolution heat vs T changes

- **Problem:** After dissolving some amount of Lidocaine HCl in 1 ml pure water at room temperature, the ampule cooled down by 1.04 K. How much drug was dissolved? Molar enthalpy of Lidocaine HCl dissolution is 43.5 kJ/mol. Consider the density and the heat capacity of the solution approximately equal to those of pure water.
  - A. 1 mol
  - B. 100 mmol
  - C. 10 mmol
  - D. 1 mmol
  - E. 100 μmol
- **Solution:** Two processes:
  - (1) endothermic dissolution of Lidocaine (absorbs heat)
  - (2) where is that heat subtracted from? This is why the ampule cools down!
  - Specific heat capacity of water is 4.184 J/(g·K)
  - To decrease temperature of 1 ml of water by 1.04K:
    - heat of 4.184 J/(g·K) × 1.04K × 1g ≈ 4.35 J must be absorbed
  - Equal to dissolution of 4.35 J ÷ 43.5 kJ/mol ≈ 0.1 mmol of the drug
- **Answer:** 100 μmoles

Thermodynamic cycle & Hess law

- The enthalpy change for a reaction carried out in a series of steps is equal to the sum of the enthalpy changes for the individual steps.

- In a reaction:

  Reactants (R) $\Rightarrow$ Products (P)

- Enthalpy change for the reaction can be found from enthalpies of formation of R and P:

  $$\Delta H_f°(R) + \Delta H_r = \Delta H_f°(P)$$
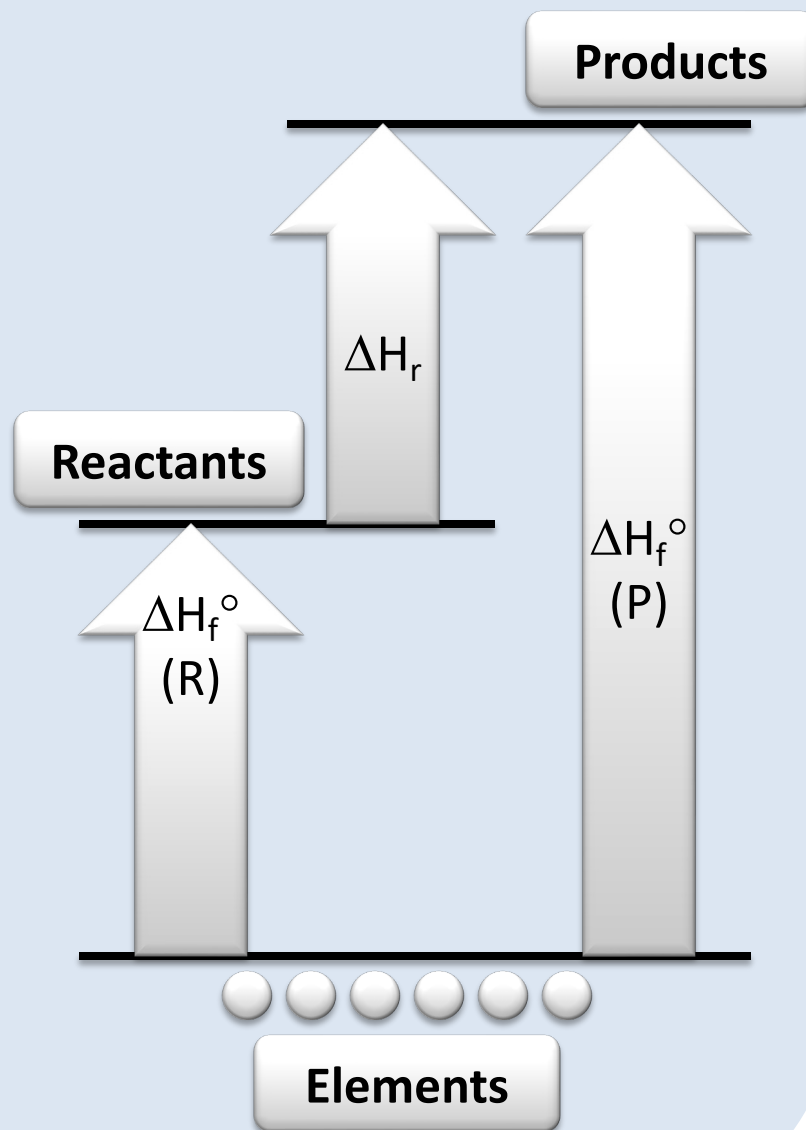
Deriving Dissolution Enthalpy from Enthalpies of Formation

- **Problem:** Standard enthalpy of formation of ammonia at 25°C is -80.8 kJ/mol for its aqueous form and -45.9 kJ/mol for its gaseous form. What is the enthalpy of dissolution of 2 moles of gaseous ammonia in water at 25°C?

  A. +34.9 kJ

  B. −34.9 kJ

  C. +69.8 kJ

  D. −69.8 kJ

  E. +126.7 kJ

  F. −126.7 kJ

- **Solution:** Molar enthalpy of dissolution is the difference between standard enthalpies of formation:

  - -80.8 – (-45.9) = -34.9 kJ/mol
  - The enthalpy of dissolution of 2 moles is 2 × -34.9 = -69.8 kJ
  - Ammonium dissolution is exothermic!

- **Answer:** -69.8 kJ

Kirchhoff's Law : H(T)

- Relates enthalpies at different temperatures
- $H_{T2} - H_{T1} = C_p \times (T_2 - T_1)$
  - assuming that C_p is approx. constant within ΔT
- H_{T2} is H_{T1} plus energy needed to heat the sample
- Find enthalpy at a different temperatures:
  - $H_{T2} = H_{T1} + C_p(T_2 - T_1)$
- Find heat capacity within the given temp. range:
  - $C_p = (H_{T2} - H_{T1}) / (T_2 - T_1) = \Delta H / \Delta T$
- Find a new temperature given corresponding enthalpy:
  - $T_2 = T_1 + (H_{T2} - H_{T1}) / C_p$

Kirchhoff's Law

- **Problem:** Molar enthalpies of formation of gaseous CO_2 are -393 kJ/mol at 293K and -391.89 kJ/mol at 323K. Approximately how much heat is needed to raise the temperature of a 3 mol sample of CO_2 from 30°C to 40°C at constant pressure?
  - 1.11 kJ
  - ~1 J
  - 37 J
  - -10 kJ
  - 1179 kJ
- **Solution 1:** $\Delta_f H_{T1}$, $\Delta_f H_{T2}$, Kirchhoff's Law $\Rightarrow$ molar hear capacity of CO_2 at constant pressure and 20-50°C:
  - $C_{p,m}$ = (-391.89 kJ/mol+393 kJ/mol)/30K ~ 37 J/(mol K)
  - Heating a 3 mol sample by 10°C will require:
    $$\Delta T \times n \times C_{p,m} = 10 \text{ K} \times 3 \text{ mol} \times 37 \text{ J/(mol K)} \sim 1.11 \text{ kJ of heat}$$
- **Solution 2:** Heating 3 moles by 10°C is ~ the same as heating 1 mole by 30°
  - Simply take the difference $\Delta_f H_{T2} - \Delta_f H_{T1}$ = 1.11 kJ
- **Answer:** 1.11 kJ