Equation Sheet

- Mole, Avogadro (6): $N_A \sim 6.022 \bullet 10^{23}$, 1 mole of carbon atoms 12g
- Length of a C-C single bond: ~ 1.54Å (from 1.4Å in benzene, shorter for double bonds)
- Kinetic energy = ½ mv^2 ; Energy units: J ≡ kg m^2 s^{-2} ; 1 cal = 4.184 J; Cal ≡ kcal;
- 1eV = 1.6 10^{-19} J (λ~1240 nm). $E=mc^2$; c ≈ 3×10^8 m/s , E= hf (f is freq.in hertz [hertz] ≡ $[sec]^{-1}$)
- 1 eV of one particle translates into ≈ 100 kJ for a mole of particles
- Force, Newton's 2nd law, **F** =m **a** , Units: N ≡ kg m s^{-2},
- 1 kg-force (or kgf) ≡ 1 kg m s^{-2} = 9.8 N; 1 pound-force ≈ 4.45 N
- 1 **psi** ≡ pound-force-per-square-inch = 6894.76 Pa ≈ 0.068 atm ; 1 atm ≈ 14.7 psi;
- unit of psi**g** (g for gauge) means **in addition** to the external pressure.
- Momentum **P** =m **v** , Δ**p** = **F** Δt
- Celsius /Kelvin conversion °K = 273.15 + °C
- Gas constant **R** 8.314 J/(K•mol) 1.986 (≈2) cal/(K•mol) ; 0.08205746 L atm / (K mol) ; 5.189×10^{19} eV/(K mol)
- RT at room temperature of 302K is ≈ 0.6 kcal/mol or 2.5 kJ/mol
- Boltzmann constant (one molecule): $k_B = R/N_A$
- Mean translational movement energy molecules in gas: $E = (1/2)mv^2 = (3/2)RT$
- Graham's Law (effusion rate vs mol. mass): $Rate_1 / Rate_2 = (M_2 / M_1)^{½}$
- Gas Law: PV = nRT , n = m/*M* , eg mass (m) in [g] and molar mass *M* in [g/mol]
- Density = mass/volume, [kg/m^3]
- Pressure units: 1 Pa= 1 $kg\cdot m^{-1} \cdot s^{-2}$ = 1N/m^2 ; 1 atm ≈ 10m of water = 760mmHg ≈ 1bar = 100,000 Pa; 1atm = 101,325 Pa ; 1bar= 14.5 psi.
- Barometric Formula: $P_h = P_0 \bullet Exp(-Mgh/RT)$, *M* –molar mass [kg/mol]; g = 9.8 m/s^2 ; h height [m]
- 1st law of thermodynamics: ΔU = q - w
- Enthalpy H = U + PV
- Heat capacity, C ≡ q / ΔT = ΔH / ΔT, at constant P or V
- $C_P \equiv \partial H / \partial T$, $C_V \equiv \partial U / \partial T$, $C_P \sim C_V$ for liquids and solids ; molar: $C_P = C_V + R$ for gases
- Dulong-Petit: for any solid substance the high T limit of C is $3R \bullet N_{atoms}$ (3 vibrations per atom)
- Water:heat capacity = 4.184 J/(g K), or 1 cal/(g K) or 1 kcal/(kg K), 1 ml weighs 1g, 1L weighs 1kg
- Enthalpy at T, Kirchhoff: $H_{T2} = H_{T1} + C_P (T_2 - T_1)$
- Calorimetry: ΔH = s m ΔT, m is mass, s is *specific heat*.
- Entropy measurement and classical definition: ΔS = q/T
- Entropy at T, ($C_P \approx$ const) : $S_{T2} = S_{T1} + C_P \ln (T_2 / T_1)$
- Boltzmann for entropy: $S=k_B \ln(N_{total})$, $S_m = R\ln(n_1)$ (n_1 is the number of states of ONE molecule)
- Gibbs free energy: G = H – TS = U + PV – TS; dG = PdV – SdT
- Estimate of ligand entropic cost of binding $-T \times \Delta S_{conformational} \approx 0.6 n_{rotatable\_bonds}$ [kcal/mol]
- Phase equilibrium: $G_{phase1} = G_{phase2}$; $\Delta H_{trs} = T_{trs} \Delta S_{trs}$
- Trouton's rule: $\Delta S_{vap} \sim$ 85-89 J/(K mol) for many liquids (except water), hence ΔH_{trs} is proportional to T_{trs}
- Clausius-Clapeyron equation: $\ln(P_2 / P_1) = (\Delta H_{vap} / R) \bullet (1/T_1 - 1/T_2)$
- Hess: $\Delta H_{reaction} = \Delta H_f$ (products) - ΔH_f (reactants) ; same for ΔS and ΔG

- Fundamental equation dG of a mixture: $dG = VdP - SdT + \mu_A dn_A + \mu_B dn_B + ...$

- Molar fraction: $x_A = n_A / \Sigma n_i$, n_i is the number of moles of component *i*
- Dalton's Gas Mixture Law: $P_A = x_A \bullet P_{total}$, x_A is a molar fraction
- Chemical potential changes from the reference state 0 (value at partial pressure P_0 or V_0 or C_0):
  - $\mu_A (V) = \mu_{A0} - RT \bullet \ln(V_A / V_0)$ (gas)
  - $\mu_A (P) = \mu_{A0} + RT \bullet \ln(P_A / P_0)$ (gas)
  - $\mu_A (C) = \mu_{A0} + RT \bullet \ln(x_A / x_0)$ (solution)
- Chemical equilibrium: $\ln K = -\Delta G^0_{reaction} / RT$, or $\Delta G^0 = -RT\ln K$, or $K = \exp(-\Delta G^0 / RT)$
- $K \approx C_A^{\nu A} \bullet C_B^{\nu B} \bullet .. , \nu_i$ - stoichiometry coefficients, negative for reactants
- $K \approx ([C]^c [D]^d) / ([A]^a [B]^b)$ for $aA + bB \Leftrightarrow cC + dD$. Stoichiometry (*a,b,c,d)* define the unit of K
- van't Hoff : $\ln(K_1 / K_2) = (\Delta_r H^0 / R)(1/T_2 - 1/T_1)$
- van't Hoff : $\log_{10}(K) = -(\Delta_r H^0 / 2.3\ RT) + (\Delta_r S^0 / 2.3\ R)$

Colligative Properties

- Entropy of binary mixing (x + y = 1 mole): $\Delta S_{mix} = -R (x \ln x + y \ln y)$; 0.7R for 0.5:0.5
- μ of water in solution: $\mu_w = \mu_{w\_pure} + RT \ln x_w \approx \mu_{w\_pure} - RT\ x_{solute}$ ($x_{solute} << 1$)
- Raoult's law: $\Delta P_{w\_vapor} = x_{solute} \bullet P_{w\_pure}$ (non-volatile solute)
- Henry's law: $P_{A\_vapor} = x_A \bullet K_{H\_A}$ (A is a volatile solute or dissolvable gas)
  - oxygen (O_2) : $K_H = 769.2$ L·atm/mol
  - carbon dioxide (CO_2) : $K_H = 29.41$ L·atm/mol
  - hydrogen (H_2) : $K_H = 1282.1$ L·atm/mol
- Freezing: $\Delta T_f = K_f \bullet c_{solute}$. $K_{f\_water} \approx 1.853$ K·L/mol.
- Boiling : $\Delta T_b = K_b \bullet c_{solute}$. $K_{b\_water} \approx 0.512$ K·L/mol.
- x_A and c_A take van't Hoff factors ***i*** (or dissociation) into account. $i = x_1 + 2 \bullet x_2 + 3 \bullet x_3$ ..
- Molarity and Osmolarity (per L of solution): M ≡ mole/L , Osm ≡ osmole/L .
- Plasma osmolarity: 285 ± 10 mosmoles/L (mOsm)
- Simple osmosis rules: 1) water follows stuff; 2) pressure is proportional to the total molar concentration difference
- Pressure: $\Delta_{osm} P = \Delta M_{solute} \bullet RT \approx 25.4 \bullet \Delta M_{solute}$ [atm], or 25.7 ..[bar] (C_{solute} in Osm, $T_{body} = 309.75K$) , $M \rightarrow iM$
- Water: 55.5 mol/L (1000g L^{-1} / 18g/mol)

Binding reaction (dissociation and association)

- $K_{eq} = \exp(-\Delta G_0 / RT)$; $pK_d \approx 0.7 * \Delta G_0$ [kcal/mole]; $\Delta G_0 \approx 1.4\ pK_d$
- $PL \leftrightarrow P + L$; $K_d = [P][L]/[PL]$; $K_a = 1/K_d$; $\Delta G_a = -\Delta G_d$; $\Delta G_a = RT\ \mathrm{Ln}\ K_d$
- $x = [PL]$; $(P_0 - x)(L_0 - x) = x \bullet K_d$
- $x = ½ \bullet (P_0 + L_0 + K_d - ((P_0 + L_0 + K_d)^2 - 4P_0 L_d)^{½})$
- **Non-abundant protein target** $P_0 << K_d$: $[PL]/[P] \approx L_0 / K_d$ (50% inhibition @ $L_0 = K_d$)
- Fraction_of_receptor_bound $\approx L_0 / (K_d + L_0)$,where L_0 is total ligand concentration.
- **Protein in excess** $[PL] << P_0$: $[PL]/[L] \approx P_0 / K_d$, fraction_drug_bound $\approx P_0 / (P_0 + K_d)$

Quantum Mechanics, Waves, Radioactivity, Fluorescence

- $E = h\nu = \hbar\omega$, ν - cycles per second, ω - radians per second, $E=mc^2$

Planck constant: h=6.626 10^{-34} J•s , $\hbar \approx 10^{-34}$ J•s

- wavelength λ ; $\lambda = c/\nu$; $E = h\, c/\lambda$ ($c = 3.\bullet 10^8$ m/s)
- $E=mc^2$ The speed of light: $\approx 3.\bullet 10^8$ meters per second (299,792,458 $m \cdot s^{-1}$).
- 1 eV = $1.6 \bullet 10^{-19}$ J ; 1 J = $6.2415 \bullet 10^{15}$ keV
- 1eV corresponds to 1240 nm (nano meter,infrared) λ = 1240 nm/ E[eV]
- charge e = $1.60217 \bullet 10^{-19}$ C (coulomb or s·A)

Interaction Energetics

- $U = (1/4\pi\varepsilon_0)(q_1\, q_2 /(\varepsilon d))$, d : distance, ε : is dielectric constant
- Units: U [kcal/mole] = C ($q_1\, q_2 /(\varepsilon d)$) , if C=332, d in Å q in A.U.
- Formal_charge = N_valence_electrons – N_electrons_in_lone_pairs - N_bonds
- Solvation energies: $U_{m\text{-}w} \approx C\,(q^2/2r_q)(\,1/\varepsilon_w - 1/\varepsilon_m\,)$; $U_{w\text{-}m} = \text{Const} \times Z^2/r_q$
- Van der Waals: $U_{vw} \approx A/d^{12} - B/d^6$, d is distance
- Hydrophobic effect $U_{hp} = \sigma\, A_{area}$
- Polar surface area (PSA): PSA < 120-140 $Å^2$; $PSA_{BBB} < 75\ Å^2$
- Conformational entropy loss estimate: $\Delta N_{states} \approx 3^{\Delta Ntor}$, $\Delta S_{conf} \approx R \bullet \Delta N_{tor} \bullet \ln(3)$

Acid-Base equilibrium, LogP

- $LogP \equiv Log_{10}\,(C_{oct} / C_{water})$
- $pH \equiv -Log_{10}\,([H+])$; pOH = 14 − pH
- $pKa = -Log_{10}\,([A-][H+]/[AH])$, $Ka = [A-][H+]/[AH]$
- $pKa_{base} = -Log_{10}\,([B][H+]/[BH+])$, $Ka_{base} = [B][H+]/[BH+]$
- Henderson-Hasselbalch (Log_{10} ..):
  - Log([A-]/[AH]) = pH − pKa
  - Log([B]/[BH+]) = pH − pKa
- logD = Log10 (all_forms_in_octanol / all forms in water)
- acids: $logD = logP - Log_{10}\,(1+10^{\,pH-pKa}) \approx logP - (pH - pKa)$ (for pH > pKa+1, mostly charged)
- bases: $logD = logP - Log_{10}\,(1+10^{-(pH-pKa)}) \approx logP + (pH - pKa)$ (for pH < pKa-1, mostly charged)

Drug solutions, pH, solubility

- Strong acid: pH = -log c ; strong base: pH ~ 14+log C (C >> 10^{-7} M)
- Weak acid: pH = ½ pKa − ½log(C) , (C >> 10^{-7} M)
- Weak base: pH = 7 + ½ pKa + ½log(C) , (C >> 10^{-7} M)
- More accurate (acid): $(c-x)K_A = x(x+10^{-7})$, solve for x ≡ [A-]
- Solubility: $\mu_{0\_aq} + RT \ln S_w = \mu_{0\_crystal}$
- Solubility w.acid: $S_0 \equiv [AH]$, $[A-]=S-S_0$; $Log((S - S_0)/S_0) = pH - pK_A$; $S = S_0\,(1+10^{pH-pKa})$
- Solubility w.base: $S_0 \equiv [B]$, $[BH+]=S-S_0$; $Log((S - S_0)/S_0) = pK_A - pH$; $S = S_0\,(1+10^{pKa-pH})$
- $LogSw \equiv Log_{10}\,(S)$

Kinetics. Rates

- $d[A]/dt = k\times([A]^x \times [B]^y, ...)$, reaction order is x + y + .., e.g.
- Zero order: $d[A]/dt = -k$; $[A] = [A_0] - kt$; $t_{½} = [A_0]/2k$
- First order: $d[A]/dt = -k[A]$; $[A] = [A_0] \times \exp(-kt)$; $t_{½} = \ln(2)/k$

- Second order: $d[A]/dt = -k[A]^2$; $1/[A] = 1/[A_0] + kt$
- $k \sim \exp(-\Delta G_{act} / RT)$
- reversible reactions: $A \leftrightarrow B : K = [B]/[A] = k_f / k_r$
- drug-target dissociation: $K_d = k_{off} / k_{on}$; $k_{off} = 1 / \tau$,(τ is residence time; $t_{1/2}=\tau \ln 2$)
- Absorption: Amount absorbed: $\propto$ Area $\times$ (ΔC) $\times$ Time
- Dissolution rate (R_D) $\propto$ Area $\times$ ($C_{saturated}$ - C)

Methods

- X-ray: distances (d) to reflection angles (θ) : $2d \sin(\theta) = n\lambda$
- Mass.Spec: $\mathbf{F} = q(\mathbf{E} + \mathbf{v} \otimes \mathbf{B})$, $R = (m/q) \times (v/B)$
- Units of B: Tesla (T) = 1 Newton/(Ampere · meter) = $kg/(A \cdot s^2)$
- For a 21.1 tesla magnet, the resonant frequency of H+ is about 900 MHz. Earth: 5 to 65 μT

Target binding free energies, enthalpies and entropic contributions for 9 HIV drugs

Generic Name	MW	ΔG (kcal/mol)	ΔH (kcal/mol)	-TΔS (kcal/mol)
Nelfinavir	567.8	-12.8	3.1	-15.9
Indinavir	613.8	-12.4	1.8	-14.2
Saquinavir	670.8	-13	1.2	-14.2
Tipranavir	602.7	-14.6	-0.7	-13.9
Lopinavir	628.8	-15.1	-3.8	-11.3
Atazanavir	704.9	-14.3	-4.2	-10.1
Ritonavir	720.9	-13.7	-4.3	-9.4
Amprenavir	505.6	-13.2	-6.9	-6.3
Darunavir	547.7	-15	-12.7	-2.3

Periodic Table (fragment)