Week 5 problem solving

+ equations, + applications

Drug binding: K_d vs ΔG, ΔH, ΔS

(in addition to Lecture 9 examples)

Decay, Radioactivity, gamma-rays

K_d calculation from equilibrium concentrations

- **Problem:** A 4 μM target protein solution is made. Then drug is added to achieve 3:5 molar ratio. In equilibrium 2.33 μM of 1:1 complexes are formed. Find the dissociation constant K_d.
- **Solution:**
  - The molar ratio of 3:5 means that $[L_{tot}] = 4\ \mu M\ \frac{3}{5} = 2.4\ \mu M$
  - Since 2.33 μM of complexes was formed, unbound concentrations are:
    - $[P] = [P_{tot}] - [PL] = 4\ \mu M - 2.33\ \mu M = \mathbf{1.67\ \mu M}$
    - $[L] = [L_{tot}] - [PL] = 2.4\ \mu M - 2.33\ \mu M = \mathbf{0.07\ \mu M}$

  - $K_d = [P][L] / [PL] = 1.67 \times 0.07 / 2.33 \approx 0.05\ \mu M = 50\ nM$

K_d to ΔG, $\Delta G = \Delta H - T\Delta S$

- **Problem:** When performed at 300K, an endothermic 1:1 drug/target binding reaction with K_d = 58 nM absorbs the molar heat of 1.4 kcal/mol. What is the molar entropy change of this reaction, ΔS^0? Steps: 1) ***K_d* to** ΔG_0 2) ΔH_0=1.4 3) ΔS_0= ..

- **Solution:**
  - Find molar ΔG_{bind}: $\Delta G = RT \ln Kd$ = 0.6 kcal/mol $\times$ ln (58×10^{-9}) = -10 kcal/mol
  - Molar ΔH_{bind} of +1.4 kcal/mol is given
  - $\Delta G = \Delta H - T\Delta S$; therefore, $\Delta S = (\Delta H - \Delta G) / T$ = (1.4 + 10 kcal/mol) / 300 K = 11400 cal/mol / 300 K = **38 cal/(mol K)**
  - In this problem, **entropy change upon binding must be positive!** Given that ΔH is positive, this is the only way to achieve negative ΔG. It may happen due to hydrophobic nature of binding (the number of water molecules with restricted motion is reduced upon binding).

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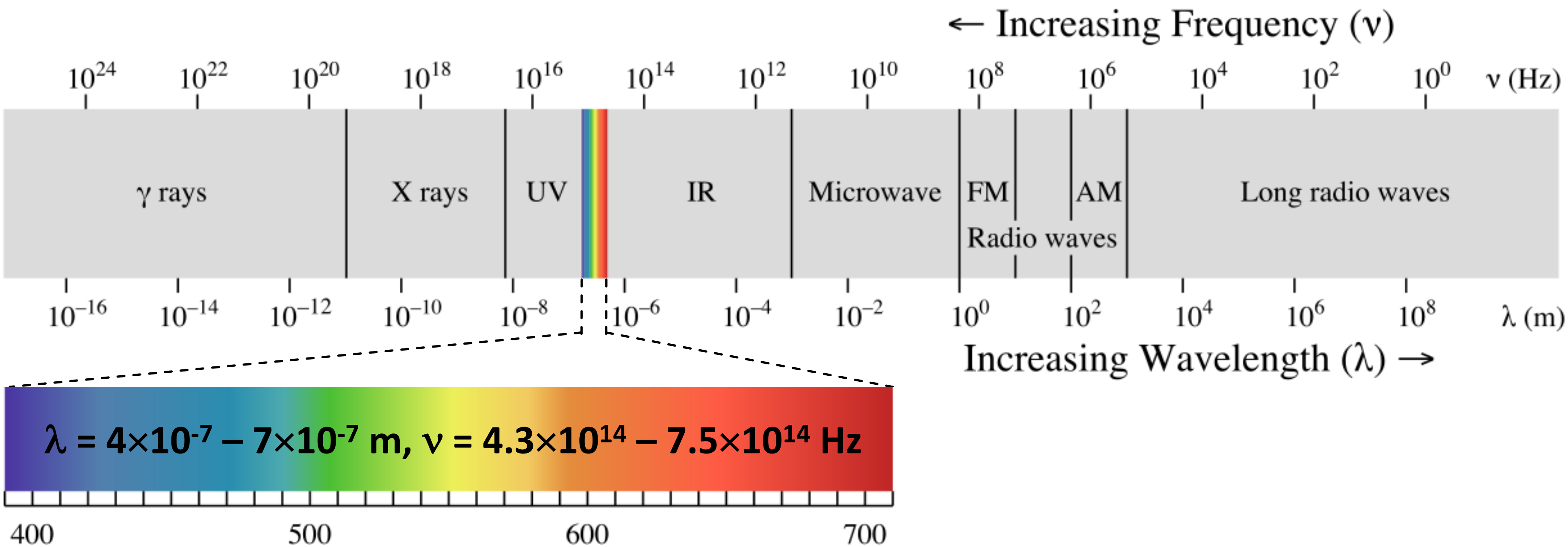
EM radiation, fluorescence, radioactivity

EM bands & photon energies



Note that energy of ONE photon need to be compared with **kT (not RT).**
RT may be compared with energy of $N_{Avogadro}$ of photons.

$$h \approx 4.1357\times10^{-15}\ \text{eV}\cdot\text{s}$$
$$h \approx 6.6262\times10^{-34}\ \text{J}\cdot\text{s}$$
(Planck constant)

$$1\ \text{eV} = 1.6022\times10^{-19}\ \text{J}$$

Energy vs Frequency relation:

Photon $E = h\nu$

$$\nu \times \lambda = c$$

$c \approx 3\times10^{8}$ m/s (speed of light)

Wavelength, frequency and energy of a single photon

- At room temperature **kT** , (energy of one vibration) is equal to

25.8 meV (or milli eV)

To break a chemical bond, one needs at least 20 kT of energy

Range	λ	ν	Photon E, [eV]
Radio	1 m-10^5 km	3 Hz-300 MHz	12.4 feV-1.24 μeV
Microwave	1 mm-1 m	0.3-300 GHz	1.24 μeV-1.24 meV
Far IR	15-1000 μm	0.3-20 THz	1.24-82.7 meV
IR	1.5-15 μm	20-200 THz	82.7-827 meV
Near IR	700-1500 nm	200-430 THz	0.83-1.77 eV
VIS	400-700 nm	430-750 THz	1.77-3.1 eV
Near UV	300-400 nm	0.75-1 PHz	3.1-4.13 eV
UV	200-300 nm	1-1.5 PHz	4.13-6.2 eV
Far UV	10-200 nm	1.5-30 PHz	6.2-124 eV
X-ray	0.01-10 nm	30 PHz-30 EHz	0.13-124 keV
Gamma	<10 pm	>30 EHz	>124 keV

Gamma, X-ray and visible Light Radiation: wavelength to frequency

- ***Problem***: The longest wavelength of EM radiation that is needed to break a C=C bond is 200 nm.
- Calculate the frequency of this radiation in Hz
  A. 1.5 PHz
  B. 1.5 THz
  C. 0.66 GHz
  D. 60 Hz

- ***Solution***:
  - $\nu = \frac{c}{\lambda} = \frac{3\times10^{8} m/s}{2\times10^{-7} m} = 1.5 \times 10^{15}\ Hz$ = 1.5 PHz

T is Tera (12)
P is Peta (15)

- ***Answer***: 1.5 PHz

Ultraviolet (UV) radiation: from **frequency** to **photon energy**

- The longest wavelength of UV radiation that is needed to break a C=C bond is 200 nm
- Calculate the frequency of this radiation in Hz
- Calculate the energy of a single photon in eV
  - A. 47 meV
  - B. 6.2 eV
  - C. 3.1 keV
  - D. 9.3 MeV

- ***Solution***:
  - Have just found that frequency ν = 1.5 PHz
  - $E_{photon} = h\nu = (4.1357\times10^{-15}$ eV·s$) \times (1.5\times10^{-15}$ Hz$)$ = 6.2 eV
- ***Answer***: 6.2 eV. , keep in mind that thermal energy at room temperature kT ~ 0.0258 eV

Activity of radiopharmaceuticals

- Counting the *rate of radionuclei disintegration*
- 1 Bq (Becquerel) = 1 event per second = 1 s^{-1}
- 1 Ci (Curie) = 37 GBq = $37 \cdot 10^9$Bq
- Energy released depends on the specific nuclei and disintegration mode
  - an average value may be associated with each radionuclide and decay mode
- Activity goes down as the radionuclide decays
  - provided values are "*at time of calibration*"
- **Radiopharmaceuticals are prescribed as *activity* in Bq**

Sodium Iodide (^{131}I) Solution

Therapeutic Oral

USES: Compounding of Oral Therapeutic Solution or Capsules

Each ml contains: Carrier-free $Na^{131}I$
Inactive Ingredients:
0.05M Sodium Hydroxide and 0.02M Sodium Thiosulfate
Store upright in a shielded container at 2° - 25° C
Calculate dosage from Calibration date

RX Only

^{131}I HALF LIFE= 8.025 DAYS

CAUTION
RADIOACTIVE MATERIALS

Order # Lot #:
Calibration Date:
Calibration Time: 12:00 (MST)
Total radioactivity @ calibration: GBq (mCi)
Total Volume @ calibration: ml
Radioconcentration @ calibration: GBq/ml (mCi/ml)
Expiration Date:
NDC Code:

Caution-Radioactive Material

Manufactured by
International Isotopes, Inc.
Idaho Falls, ID

Table 2. Solution Strengths

Total Radioactivity* per Vial		
Concentration*	**Volume of Solution**	**Total Radioactivity* per Vial**
185 MBq/mL (5 mCi/mL)	1 mL	185 MBq (5 mCi)
	2 mL	370 MBq (10 mCi)
	3 mL	555 MBq (15 mCi)
	4 mL	740 MBq (20 mCi)
	5 mL	925 MBq (25 mCi)
	7 mL	1295 MBq (35 mCi)
925 MBq/mL (25 mCi/mL)	2 mL	1850 MBq (50 mCi)
	3 mL	2775 MBq (75 mCi)
	4 mL	3700 MBq (100 mCi)
	6 mL	5550 MBq (150 mCi)

* *At time of calibration*

Source: FDA

Dosimetry-related quantities

- **Radiation source, Exposure:** a measure of ionization
  Electric charge freed by radiation per **kg of air**
  1 R (Roentgen) = 0.000258 C/kg (Coulomb per kg)
- **Absorbed dose** (energy/body mass)**:**
  - ❖ 1 Gy (gray) = 1 J/kg
  - ❖ 1 rad = 0.01 Gy
  - ❖ Depends on the type of matter that absorbs the radiation, e.g. for an exposure of 1 roentgen by 1 MeV γ-rays:
    - the dose in air = 0.877 rad
    - the dose in water = 0.975 rad
    - the dose in averaged human tissue = 0.965 rad
- **Dose equivalent:**
  - ❖ Different radiation types have different biological effects for the same deposited energy
  - ❖ W_R **is a corrective *radiation weighting factor***:
    - dependent on radiation type
    - converts the absorbed dose into an estimate of tissue damage
  - ❖ 1 Sv (Sievert) = $W_R \times$Gy = $W_R \times$[J/kg]
  - ❖ 1 rem (roentgen equivalent man) = 0.01 Sv
- **Ionizing radiation is prescribed as *absorbed dose* in Gy**

Activity of radio-pharmaceuticals

- **Problem:** ^{131}I decay releases energy in the form of **β** and γ radiation. The average energy release per nucleus is **192 keV for β** and 364 keV for γ.

Given a sample of ^{131}I with total activity of 5 mCi, how much energy does it emit per second in the form of β-radiation? Give your answer in J/s.

A. 57 kJ/s
B. 28.4 J/s
C. 13.2 mJ/s
D. 5.68 μJ/s

- **Solution:**
  - 1 Bq = 1 nucleus per second = 1 s^{-1}; 1 Ci = 37 GBq
  - 5 mCi = 0.005 × 37 GBq = 185 MBq (1.85×10^8 nuclei disintegrate per second) : converting Curie units to Bq units.
  - For β: (1.92×10^5 eV) × (1.85×10^8 Bq/s) × (1.6×10^{-19} J/eV) = 5.68×10^{-6} J/s

Beta-energy x Number of decays x eV to J conversion

- **Answer:** 5.68 μJ/s