Practice, Week 1

Therapeutic substance

Gases

Metric prefixes

Prefix	Symbol	Factor	Factor (sci. notation)
peta	P	1,000,000,000,000,000	$\times 10^{15}$
tera	T	1,000,000,000,000	$\times 10^{12}$
giga	G	1,000,000,000	$\times 10^{9}$
mega	M	1,000,000	$\times 10^{6}$
kilo	k	1,000	$\times 10^{3}$
hecto	h	100	$\times 10^{2}$
deca	da	10	$\times 10^{1}$
(none)	(none)	1	$\times 10^{0}$
deci	d	0.1	$\times 10^{-1}$
centi	c	0.01	$\times 10^{-2}$
milli	m	0.001	$\times 10^{-3}$
micro	µ (=u)	0.000 001	$\times 10^{-6}$
nano	n	0.000 000 001	$\times 10^{-9}$
pico	p	0.000 000 000 001	$\times 10^{-12}$
femto	f	0.000 000 000 000 001	$\times 10^{-15}$

Pharm-related quantities and units

Quantity	SI unit	Pharmacology & practice	Comment
Length	**m**	Å, nm, μm, cm	1 Å = 0.1 nm
Mass	**kg**	g, mg, μg	
Time	**s**	s	
Temperature (absolute: K, relative: C,F)	**K**	K, °C	ΔT [°C] = ΔT [K] T [°C] = T [K] – 273.15 **Convert F to C**
Amount of substance	**mol**	mol	6×10^{23} molecules
Area	m^2	m^2	
Volume	m^3	1 L = 1 dm^3, 1 mL = 1 cm^3	
Density	kg/m^3	1 g/cm^3 = 1 g/mL	Density of pure H_2O is 1 g/mL
Concentration		1 M = 1 mol/L; nM, μM, …	**Avoid g/L**
Unified atomic mass		1 Da corresponds to 1 g/mol	

Pharm-related quantities and units

Quantity	SI unit	Pharmacology & practice	Comment
Speed	m/s		
Acceleration	m/s^2		
Force	$N = kg \times m/s^2$	Newton, pound, ..	Newton
Pressure	$Pa = N / m^2$	1 bar = 100,000 Pa = 100 kPa 1 atm = 101,325 Pa $\approx$ 1 bar 1 mmHg* = 1 atm / 760	Pascal Hg is mercury
Energy	$J = N \times m$	1 cal $\approx$ 4.184 J [energy need to heat 1 g H_2O by 1°C] 1 eV $\approx 1.6 \times 10^{-19}$ J [Δ energy when 1 electron moves through 1 V potential difference]	Food calorie: 1 Cal = 1 kcal **Avoid ambiguity, use kcal**

*Blood pressure is a *gauge pressure*, not an *absolute pressure*

- 1 atm = 760 mmHg
- Blood (gauge) pressure of 140 mmHg = absolute P of 900 mmHg $\approx$ 1.184 atm
- Blood (gauge) pressure of 80 mmHg = absolute P of 840 mmHg $\approx$ 1.105 atm

Constants

- **STP** = Standard Temperature and Pressure:
  - T = 0 °C = 273.15 K
  - P = 1 bar = 100 kPa
- **RT** = room Temperature ≈ 300 K
  - not to be confused with the other RT below
- **Avogadro number N_A** = 6.022×10^{23}
- **Gas constant, *R***:

$R \approx 8.314$	J / (K·mol)
$R \approx 5.189\times10^{19}$	eV / (K·mol)
$R \approx 0.082$	L·atm / (K·mol)
$R \approx 1.9872 \approx 2$	cal / (K·mol)

- **Boltzmann constant, k_B** = $R / N_A \approx 1.38 \times 10^{-23}$ J/K
- "***RT***" = $R\times T$ is the thermodynamic "currency"
  - at room temp., $RT \approx$ 0.6 kcal/mol ≈ 2.5 kJ/mol
- Air is 78% N_2, 21% O_2, <1% Ar, 0.04% CO_2 (numbers rounded)
- **Gravitational acceleration (g)** near Earth's surface, g = 9.8 m/s^2

SI units

- ***Problem***: The SI unit for density is
  - g/m^3
  - $0.1Kg/m^3$
  - m/Kg^3
  - g/mL
  - Kg/m^3

- ***Answer***: Kg/m^3

Unit conversion

- ***Problem***: The density of oxygen at room temperature is about 1.3 kg/m^3. Express its density in g/cm^3.
  - 0.013
  - 13
  - 1300
  - 130
  - 0.0013
- ***Solution***:
  - $1\ kg = 10^3\ g$
  - $1\ m^3 = 100 \times 100 \times 100\ cm^3 = 10^6\ cm^3$
  - $1.3\ kg/m^3 = 1.3 \times 10^3 / 10^6 = 0.0013\ g/cm^3$

Energy unit conversion

- ***Problem***: 1 Joule is close to the following value:
  - 4.2 kcal
  - 2.092 cal
  - 0.24 cal
  - 8.314 cal
  - 1.035 cal
  - 4.184 cal
- ***Answer***: 1 Joule = 0.24 cal; 1 cal = 4.184 Joule

Kelvin vs Celsius

- ***Problem***: A patient's body temperature is determined to be 313 K. The patient is most likely
  - healthy
  - sick
  - dead
- ***Answer***:
  - 313 K $\approx$ 313-273 = 40°C
  - The patient has a fever therefore he/she is sick.

Gas constant : from T to Energy

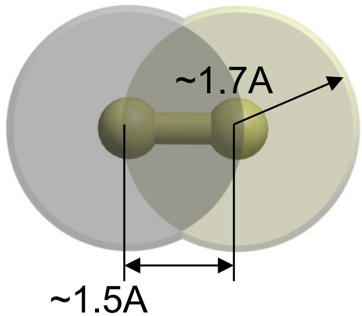
- ***Problem***: Calculate RT at 0°C in kcal/mol

- ***Solution***: Of the many faces of the gas constant R…
  - ❖ $R \approx 8.314$ J / (K · mol)
  - ❖ $R \approx 5.189\times10^{19}$ eV / (K · mol)
  - ❖ $R \approx 0.082$ L·atm / (K · mol)
  - ❖ $R \approx 1.986$ cal / (K · mol)
  - … choose $R \approx 1.986$ cal / (K · mol)
  - $T = 0°C \approx 273$ K
  - Therefore $RT = 1.986 \times 273 = 542.178$ cal/mol ~ 0.54 kcal/mol
- **Answer:** 0.54 kcal/mol
  - At room temp, *RT ~ 0.6 kcal/mol*

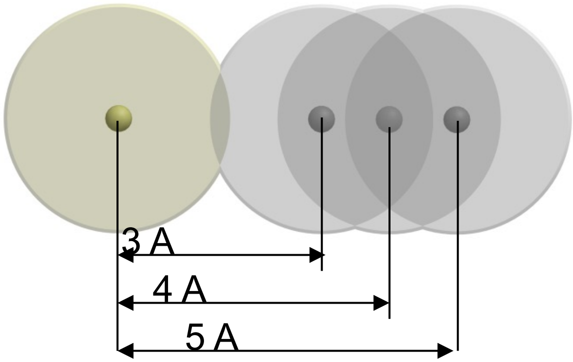
Sizes of therapeutics (from atoms to proteins to cells)

- ***Problem***: The distance between centers of two covalently bonded carbon atoms is close to:
  - 1.5 nm
  - 1.5 µm
  - 1.5 Å
  - 0.015 nm
  - 150 Å

- ***Answer***: 1.5 Å, same as 0.15 nm or 150 pm



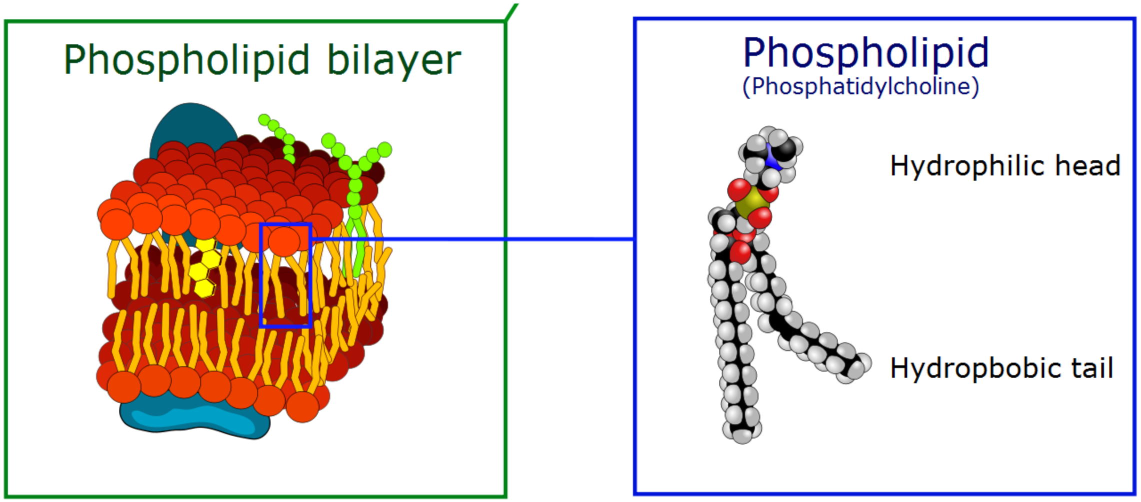
Covalent bond length is shorter than



Non-covalent interaction distance

Biological size scale cntd.

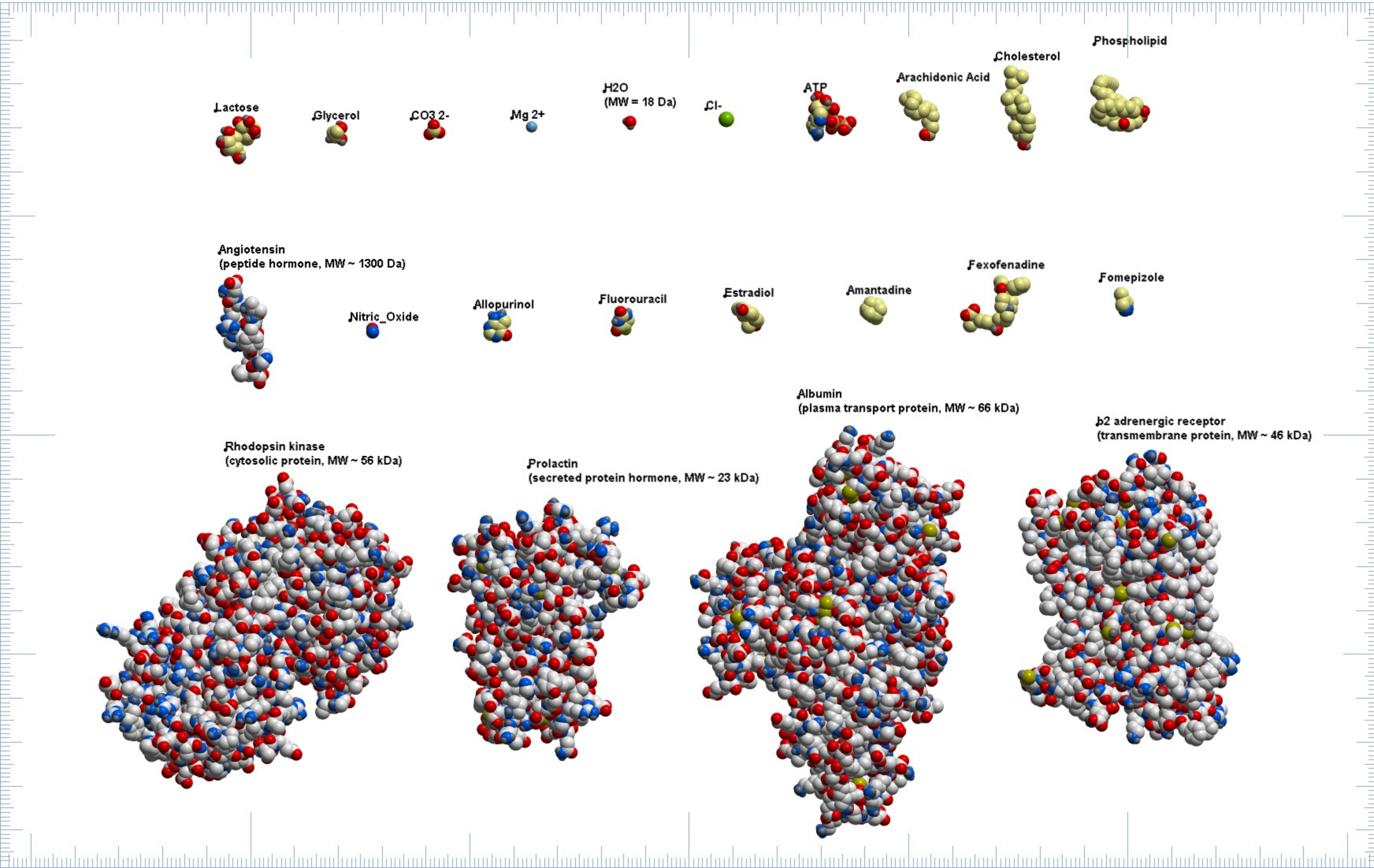
- ***Problem:*** Cell membrane and the membranes surrounding inner cell organelles are phospholipid bilayers about _____ thick
  - 5 nm
  - 100 pm
  - 1 Å
  - 5 Å
  - 50 nm
  - 5 µm



- ***Answer:*** 5 nm

- ***Hint:*** membrane is a bilayers of phospholipids
  - Each lipid has a head (~ 5 covalent bonds tall) and a hydrocarbon chain (~ 17-20 covalent bonds long)
  - $2 \times 25 \times 1.5$ A (for the length of C-C bond) = 75 Å = 7.5 nm
  - The actual answer is smaller, because bonds are connected at ~120^o angles.

Comparative sizes of drugs and targets

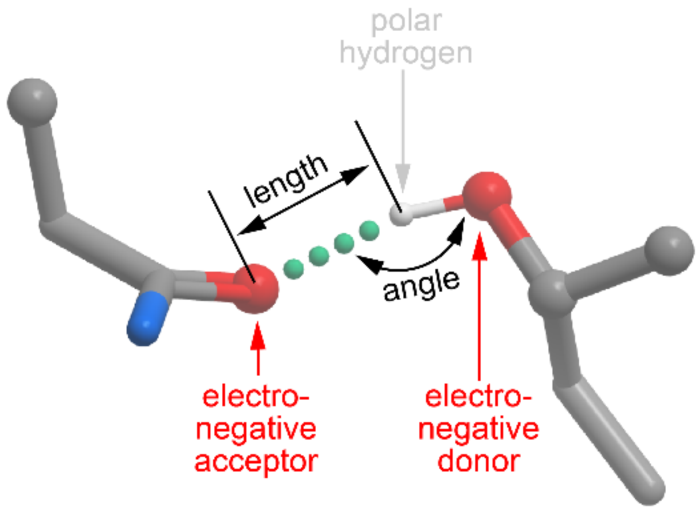


Biological energy scale

- ***Problem***: What is the best approximation for the energy of a covalent bond?
  - 25 kcal/mol to 100 kcal/mol
  - exactly 10.45 kcal/mol
  - 1 to 2 kcal/mol
  - about 0.1 kcal/mol
  - 1 to 5 kcal/mol

- ***Answer***: 25 kcal/mol to 100 kcal/mol

- ***Bonus problem:*** What about a hydrogen bond?
- ***Answer:*** In biological settings, a good estimate for a favorable hydrogen bond is ~2.5 kcal/mol

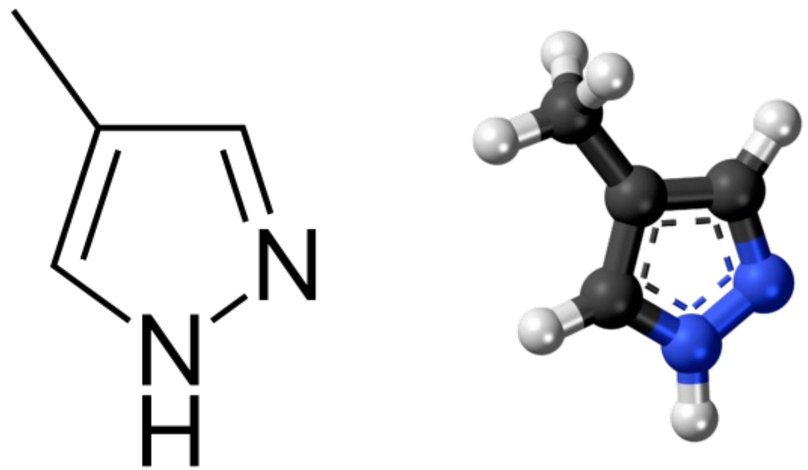


Concentrations, volumes, **molar** amounts…

- Concentration = molar amount / volume
  - measured in mol/L ≡ M, also mM, µM, nM, pM etc.
  - molar amount = volume × concentration
  - volume = molar amount / concentration
- MW = mass / molar amount
  - measured in g/mol ≡ Da
  - Mass = MW x molar amount
  - molar amount = mass / MW

Molar amount vs weight

- ***Problem:*** Fomepizole is used as an antidote in methanol and ethylene glycol poisoning. Estimate the weight of a 0.5 mmol sample of Fomepizole.
  - 0.04 g
  - 0.004 mg
  - 0.5 µg
  - 82 g
  - 4.05 g



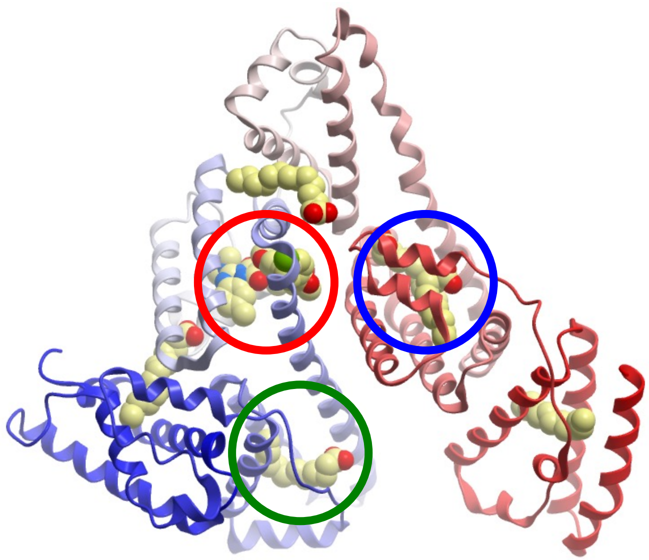
Fomepizole is a competitive inhibitor of the enzyme alcohol dehydrogenase

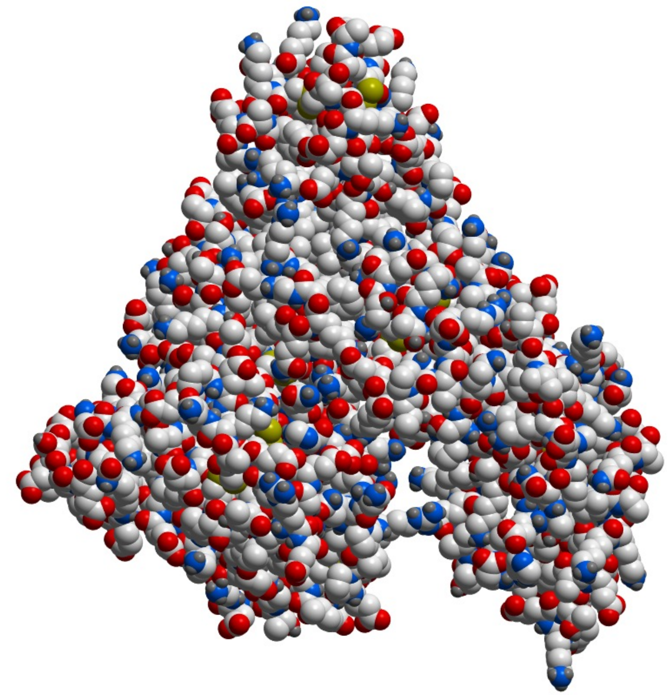
- ***Solution:***
  - MW(Fomepizole) is $4\times12(C) + 2\times14(N) + 6(H) = 82$
  - $0.5\ \text{mmol} \times 82\ \text{g/mol} = 0.5\times10^{-3} \times 82\ \text{g/mol} \approx 0.04\ \text{g}$

- ***Answer:*** 0.04 g

Molar amount vs weight (continued)

- ***Problem***: Albumin is the most abundant serum protein and carrier for various drugs. Its concentration in plasma ranges from 30 to 50 g/L. Given that MW for albumin is 67 kDa, estimate its molarity.
  - 440-740 nM
  - 4-7 uM
  - 440-740 uM
  - 4-7 mM
  - 44-74 mM





- ***Solution***:
  - 33.5 g/L ÷ 67,000 = 5×10^{-4} mol/L = 0.5 mM or 500 uM
  - The correct range includes this number: 440-740 uM

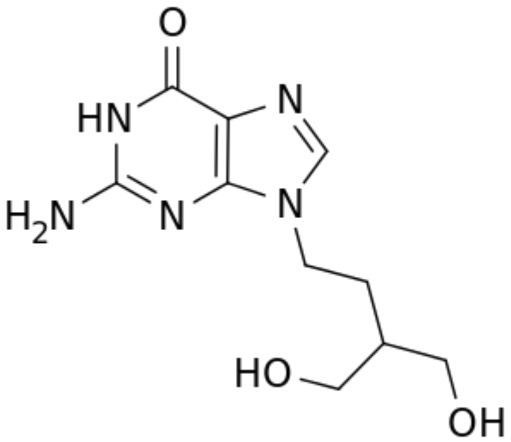
Concentration vs amount

- ***Problem***: What is the total molar amount of a compound in 0.3 mL of 1 mM solution of that compound?
  - 0.3 µmol
  - impossible to tell because the MW of the compound is not given
  - 3.33 mol
  - 0.3 mg
  - 0.3 mol
- ***Solution***:
  - **Molar amount = molar_concentration $\times$ volume**
  - $= (1 \times 10^{-3}) \times (0.3 \times 10^{-3}) = 0.3 \times 10^{-6} = 0.3$ µmol

Avogadro number, $N_A = 6\times10^{23}$

Remember: One mole is just an N_A –pack of molecules

- ***Problem:*** The approximate mass of one molecule of Penciclovir is 4.2×10^{-22} g. Calculate the molecular weight of the drug.
  - 252 g/mol
  - 172 g/mol
  - 326 g/mol
  - 472 g/mol
  - 504 g/mol



- ***Solution***:
  - $MW = 4.2 \times 10^{-22} \times 6 \times 10^{23} \sim 252$ g/mol

Week 1 equations

- **Kinetic energy vs *T***
  - $1/2\ Mv^2 = 3/2\ RT, \quad v=(3RT/M)^{1/2}$
  - Root mean square velocity:
    - Here *M* is the molar mass of the chemical
  - *Equipartition principle*: at thermal equilibrium, the energy is distributed equally between all available degrees of freedom
  - Only translational degrees of freedom matter for *T*
- **Graham's law:** effusion rates vs molecular mass of the gas
  - $\text{Rate1}/\text{Rate2} = (m2/m1)^{1/2}$
- **Ideal gas law**
  - $P \times V = n \times RT$ (n = # of moles); $V = n \times RT / P$
- **Barometric formula:** atmospheric pressure at altitude *h* [*m*]
  - $P_h = P_0 \exp(-Mgh/RT)$
  - Here *M* is molar mass [kg/mol] if we divide by R
- **Work** = Force × Distance [J] (or Pressure × Δ Volume)
- **Pressure** = Force / Area [Pa]

Kinetic energy vs temperature

- ***Problem*:** The Celsius temperature in a storage room was increased from 25°C to 50 °C. How much did the average kinetic energy of molecules in the room change? Mark the closest answer.
  - increased by 2½ times
  - decreased
  - increased by 8 %
  - increased by 2 times
  - the increase cannot be calculated without knowing the molecular mass
- ***Solution*:**
  - The kinetic energy is proportional to **Kelvin** temperature
  - Kelvin T was: 273 + 25°C = 298 K
  - Kelvin T now: 273 + 50°C = 323 K
  - Ratio: 323 K /298 K ~ 1.08
  - The temperature, as well as the average kinetic energy, increased by 8%.
- **Note:** Root mean square velocity will increase = 1.04 times, i.e. only by ~ 4%

Effusion rate (lecture 2)

- ***Problem*:** A mixture of oxygen (MW = 16) and helium (MW = 4) escapes through a porous membrane. Which of the gases escapes faster, and how much faster?
  - oxygen, 4x
  - oxygen, 2x
  - same rate
  - helium, 2x
  - helium, 4x

- ***Solution*:**
  - Use Graham's law: escape rate is inversely proportional to the square root of mass
  - MW(He) is 4 times lighter, therefore it escapes 2 times faster

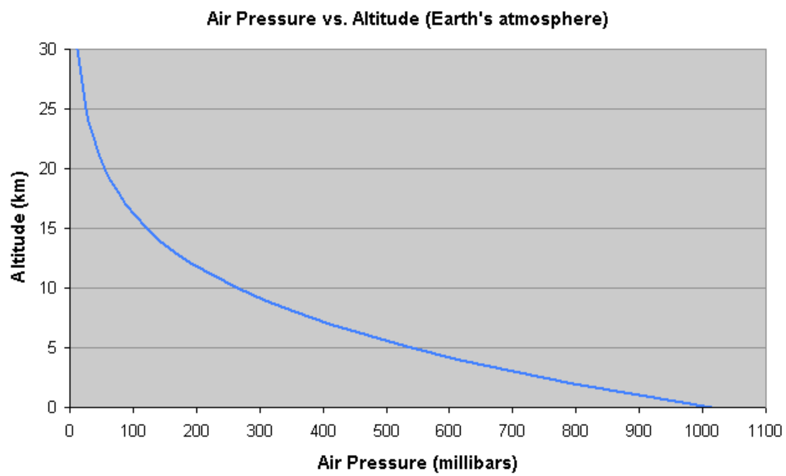
Volume of 1 mole of gas (lecture 2)

- ***Problem***: Estimate the volume of 1 mole of nitrous oxide at 0°C and at 27°C, assuming the atmospheric pressure.

- ***Solution***: Ideal gas law, $PV = nRT$
  - $V = RT / P$ (because $n = 1$)
  - Choose convenient units for R, R = 0.082 L·atm / (K·mol)
  - Then can use $P = 1$ atm, and $V = RT$
  - At 273 K, RT ≈ 22.4 L·atm / mol; **V ≈ 22.4 L**
  - At 300 K, RT ≈ 24.6 L·atm / mol; **V ≈ 24.6 L**
  - *Applies to any gas that can be approximated as ideal*

Atmospheric pressure at elevation

- ***Problem***: COPD patients experience worsening of symptoms (shortness of breath) when the atmospheric pressure drops by as little as 23 mmHg (3%). This atmospheric pressure corresponds to what elevation above the sea level? Use 29 g/mol for molar mass of air, assume T=300K (26.85C)
  - 11 km
  - 3 km
  - 1600 m (elevation of Denver – the "mile-high city")
  - 900 m
  - < 300 m

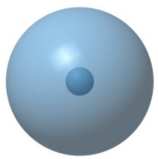
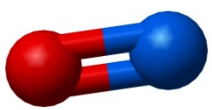
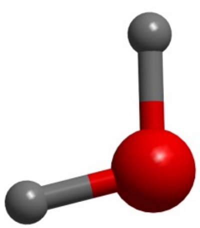
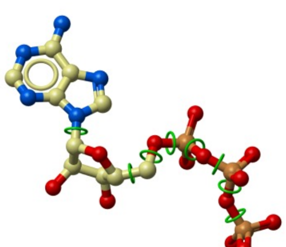


- ***Solution***:
  - $P_h = P_0 \exp(-Mgh/RT)$
  - Make sure to use SI metric units (R = 8.314 J / (K·mol))
  - $\mathrm{Exp}(-Mgh/RT)=0.97$; $Mgh/RT=-\mathrm{Ln}(0.97)$; $h = -RT*\mathrm{Ln}(0.97)/(0.029*9.8)$
  - $h \approx 268$ m < 300 m

Degrees of freedom (DF) (**advanced, optional)

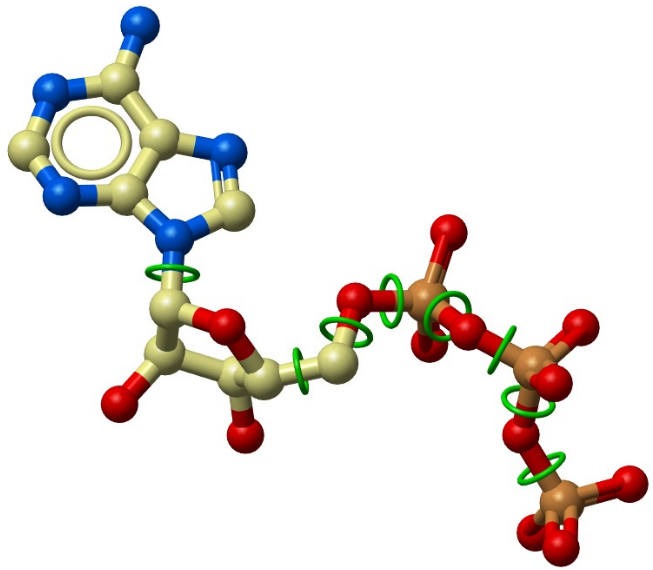
- DF are the elementary units of a molecular mixture ("*variables*") capable of storing kinetic or potential energy
  - 1 DF stores energy ½ ***kT***, 1 mole of DF stores energy ½ ***RT***
- # DF in a molecule depends on the # atoms, physical state…
  - # of DF inside a molecule increases with *T*
  - More variables get excited and capable of storing energy
- DF of a molecule in gas phase:
  - **# $DF_{trans} = 3$**
  - **# $DF_{rot} = 0, 2, \text{ or } 3$**
  - **# $DF_{vib} \leq 2 \times (3 \times N_{at} - 3_{trans} - N_{rot})$:**
    - In a fully excited state, a molecule with N_{at} is described by $3 \times N_{at}$ independent variables ⇒ # of vibrational modes: $3 \times N_{at} - 3_{trans} - N_{rot}$
    - Each vibrational mode contributes 2 DFs (can store potential and kinetic energy)
  - Some (slow) vibrations ARE excited at 300 K
    - E.g. collective motions involving rotatable sp_3-sp_3 torsional variables
  - Other (fast) vibrations are NOT excited at 300 K
    - Bond vibrations in most diatomic gases are not excited
    - Bond vibrations in Cl_2, Br_2, I_2 are partially or fully excited

Degrees of freedom in gas phase (**)

	Overall Movement and Rotation	If ALL vibrations are excited	T = 300K
	**3** Translational only	**3** No vibrations	**3**
	**5** # $DF_{trans}=3$ # $DF_{rot}=2$	$(3\times2-5)\times2+5=$**7** # $DF_{vib}=2$	**5** for most X_2 gases **6-7** for Cl_2, Br_2, I_2 *(based on $C_{v,m}$)*
	**6** # $DF_{trans}=3$ # $DF_{rot}=3$	$(3\times3-6)\times2 + 6 =$ **12** # $DF_{vib}=6$	**~7** *(based on $C_{v,m}$)* only 1 of 6 DF_{vib} is excited
	**6** # $DF_{trans}=3$ # $DF_{rot}=3$	**$(3\times N_{at}-6)\times2+6$** Many vibrations!	**>> 6** sp_3-sp_3 torsion vibrations are excited

Degrees of freedom (**)

- ***Problem:*** Determine the number of degrees of freedom of adenosine triphosphate (ATP) in gas phase at T=300K.
  - 1
  - 2
  - 3
  - 4
  - 5
  - 6
  - infinitely many
  - the correct answer not given



- ***Solution:***
  - $\#DF_{trans} + \#DF_{rot} = 3+3 = 6$...
  - At T=300K, collective motions involving the rotatable sp3-sp3 bonds are excited…
  - Therefore, the total #DF is finite but greater than 6.
  - *The correct answer is not given*.

** (preview) DF and heat capacity, $C_{v,m}$

Experimentally measured $C_{v,m}$ at 298K

Gas		$C_{v,m}$, J/(mol·K)	$C_{v,m}/R$	# DF
He	•	12.5	1.5	3
Ne	•	12.5	1.5	3
Ar	•	12.5	1.5	3
Kr	•	12.5	1.5	3
Xe	•	12.5	1.5	3
H_2	•–•	20.18	2.43	5
CO	•–•	20.2	2.43	5
N_2	•–•	20.8	2.50	5
O_2	•–•	21.03	2.53	5
Cl_2	•–•	24.1	3.06	~ 6
Br_2 (v)	•–•	28.2	3.39	~ 7
H_2O (v)*	•●•	28.49	3.43	~ 7
CO_2	•-•-•	28.5	3.43	~ 7
CH_4	∴●∴	27.1	3.26	~ 6-7

* Value for H_2O at 373K

- # of DF determines heat capacity of a substance:
  - ❖ Each rotational/translational DF contributes R/2 to $C_{v,m}$
  - ❖ Each (excited) vibrational mode contributes up to R to $C_{v,m}$
- Monoatomic gases have 3 DF: $C_{v,m} = 3/2R$
- Diatomic gases have 5 DF below T_{vib}
  - ❖ for H_2, CO, N_2, $T_{vib} >> 298K$
- When $T \geq T_{vib}$, vibrational DF's appear
  - ❖ for Cl_2, Br_2, I_2, $T_{vib} \leq 298K$