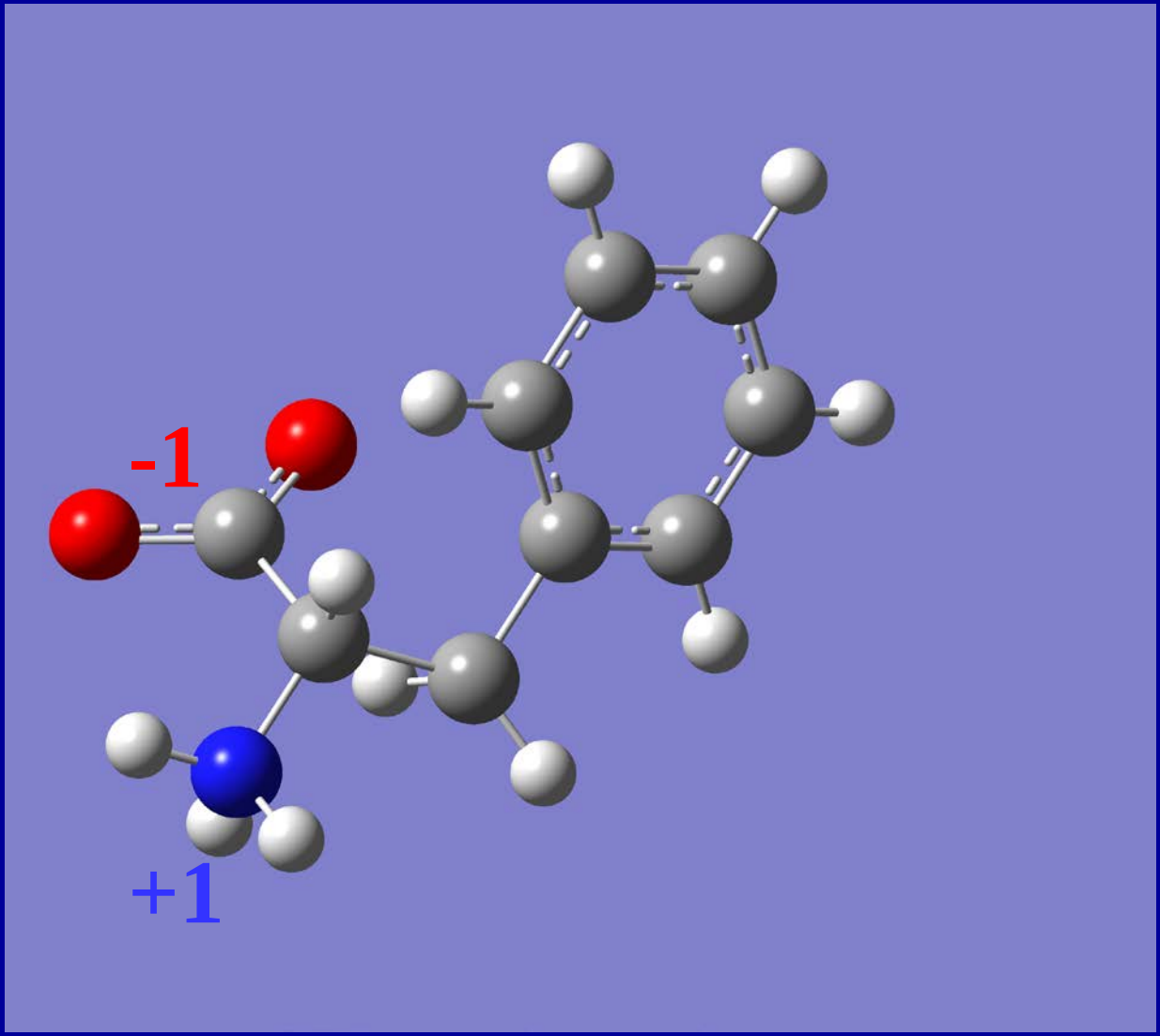
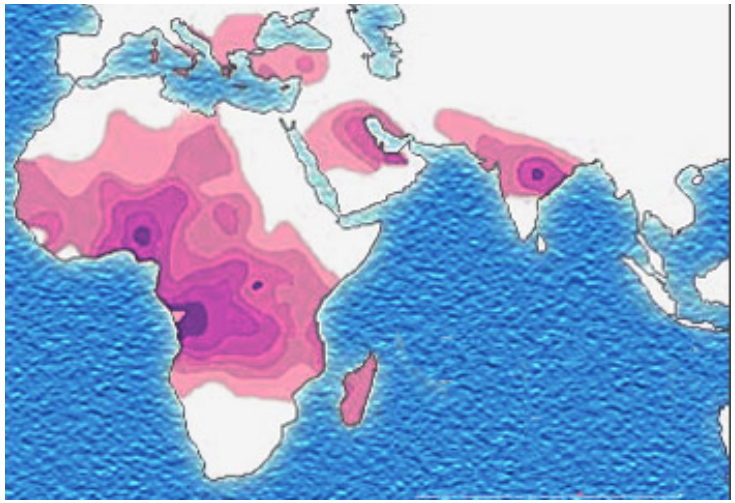
Office hours??

I am free 9:15-10, 11:30-12;
2:30-5

All free amino acids are ZWITTERIONS
That is why phenylalanine is water-soluable
and also NOT poisonous





Distribution of the **sickle-cell trait** shown in pink and purple

Historical distribution of **malaria** (no longer endemic in Europe) shown in green

The sickle cell trait was found to be 50% protective against mild clinical malaria, 75% protective against admission to the hospital for malaria, and almost 90% protective against severe or complicated malaria.[20] --Wikipedia

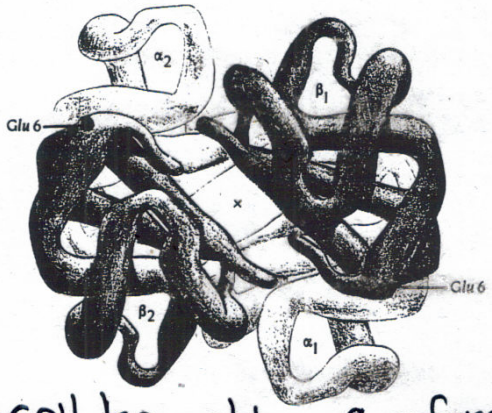


Figure 3.7 The hemoglobin molecule is built up of four polypeptide chains: two α chains and two β chains. Compare this with Figure 1.1 and note that for purposes of clarity parts of the α chains are not shown here. Each chain has a three-dimensional structure similar to that of myoglobin: the globin fold. In sickle-cell hemoglobin Glu 6 in the β chain is mutated to Val, thereby creating a hydrophobic patch on the surface of the molecule. The structure of hemoglobin was determined in 1968 to 2.8 Å resolution in the laboratory of Max Perutz at the M.R.C. Laboratory of Molecular Biology, Cambridge.

Sickle-cell hemoglobin confers resistance to MALARIA (natural selection)

Sickle-cell hemoglobin confers resistance to malaria

Sickle-cell anemia is the classical example of an inherited disease that is caused by a change in protein structure. Linus Pauling proposed in 1949 that it was caused by a defect in the hemoglobin molecule, and he coined the term **molecular disease**. Seven years later Vernon Ingram showed that the disease was caused by a single mutation, a change in residue 6 of the β chain of hemoglobin from Glu to Val.

Hemoglobin is a tetramer, built up of two copies each of two different

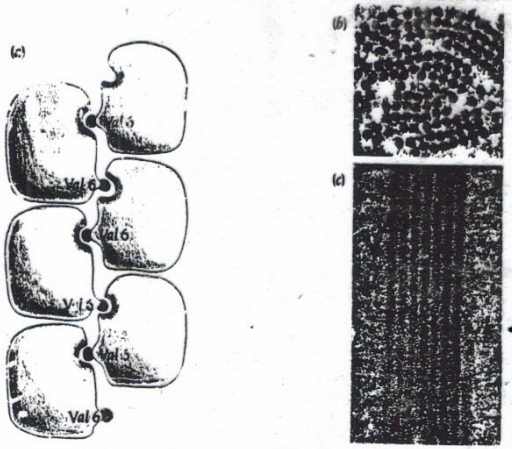
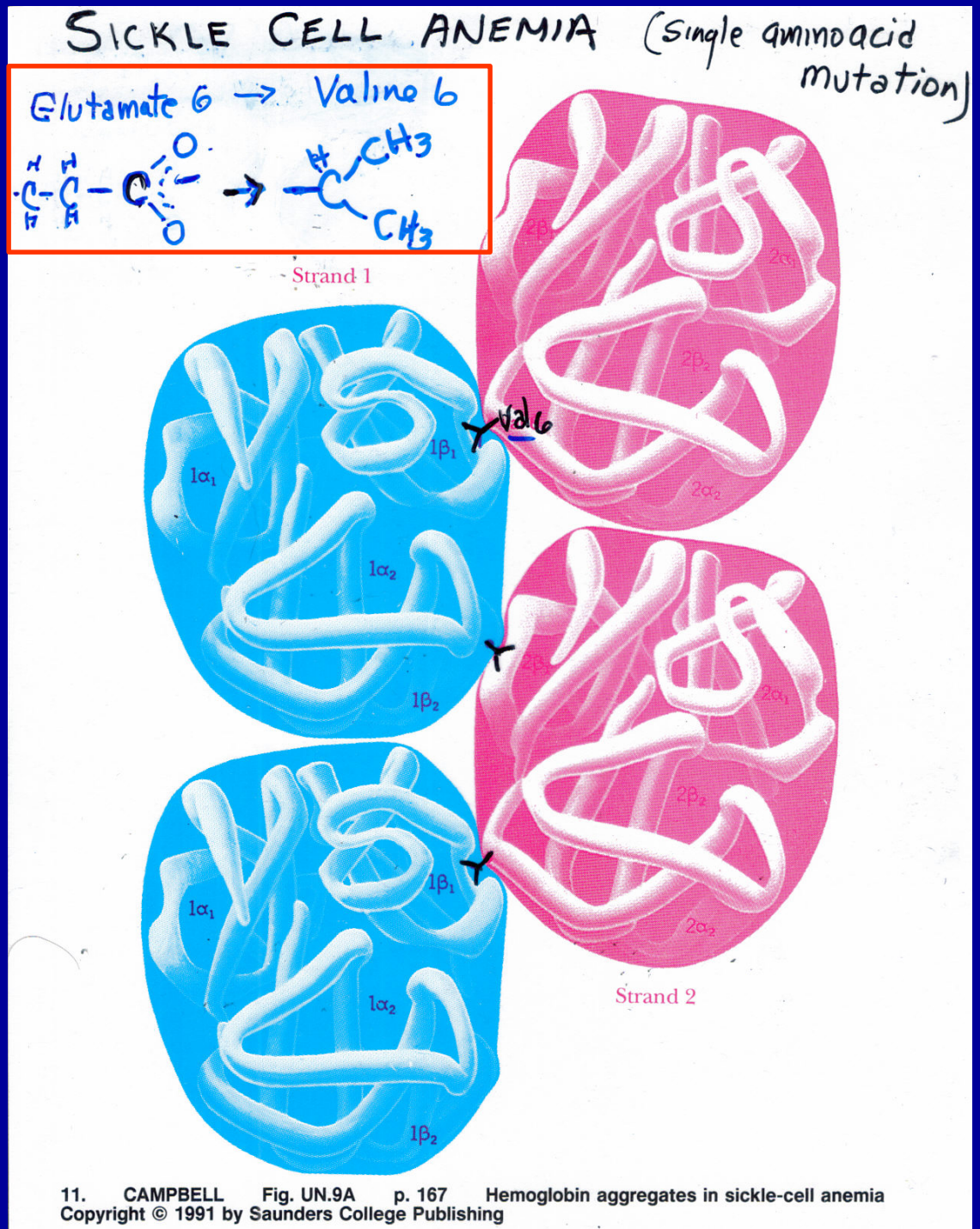


Figure 3.8 Sickle-cell hemoglobin molecules polymerize due to the hydrophobic patch introduced by the mutation Glu 6 → Val in the β chain. The diagram (a) illustrates how this hydrophobic patch (green) interacts with a hydrophobic pocket (green) in a second hemoglobin molecule, whose hydrophobic patch interacts with the pocket in a third molecule, and so on. Electron micrographs of sickle-cell hemoglobin fibers are shown in cross-section in (b) and along the fibers in (c). [(b) and (c) from J. T. Finch et al., *Proc. Natl. Acad. Sci. USA* 70. 718, 1973.]

← fibers of polymerized hemoglobin.

pH of the host cell slightly, but sufficiently to make the cell more prone to sickling. When sickling occurs, the cell membrane becomes more permeable to potassium ions, which leak out into the surroundings. This drop in potassium ion concentration kills the malarial parasite. The resistance to malaria due to this mechanism has had a high survival value for heterozygotes, especially in Africa. In evolutionary terms, the death of homozygotes has been an acceptable price to pay for increased survival of heterozygotes in a malarial environment.

make blood cell sickle-shaped



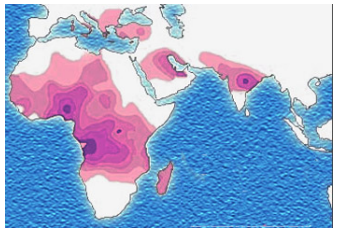
Caused by single mutation from ionic to hydrophobic amino acid on surface

Hemoglobin

Sickle Cell Trait

First "molecular disease":

Linus Pauling



Distribution of the **sickle-cell trait** shown in pink and purple

Although the precise mechanism for this phenomenon is not known, several factors are believed to be responsible.

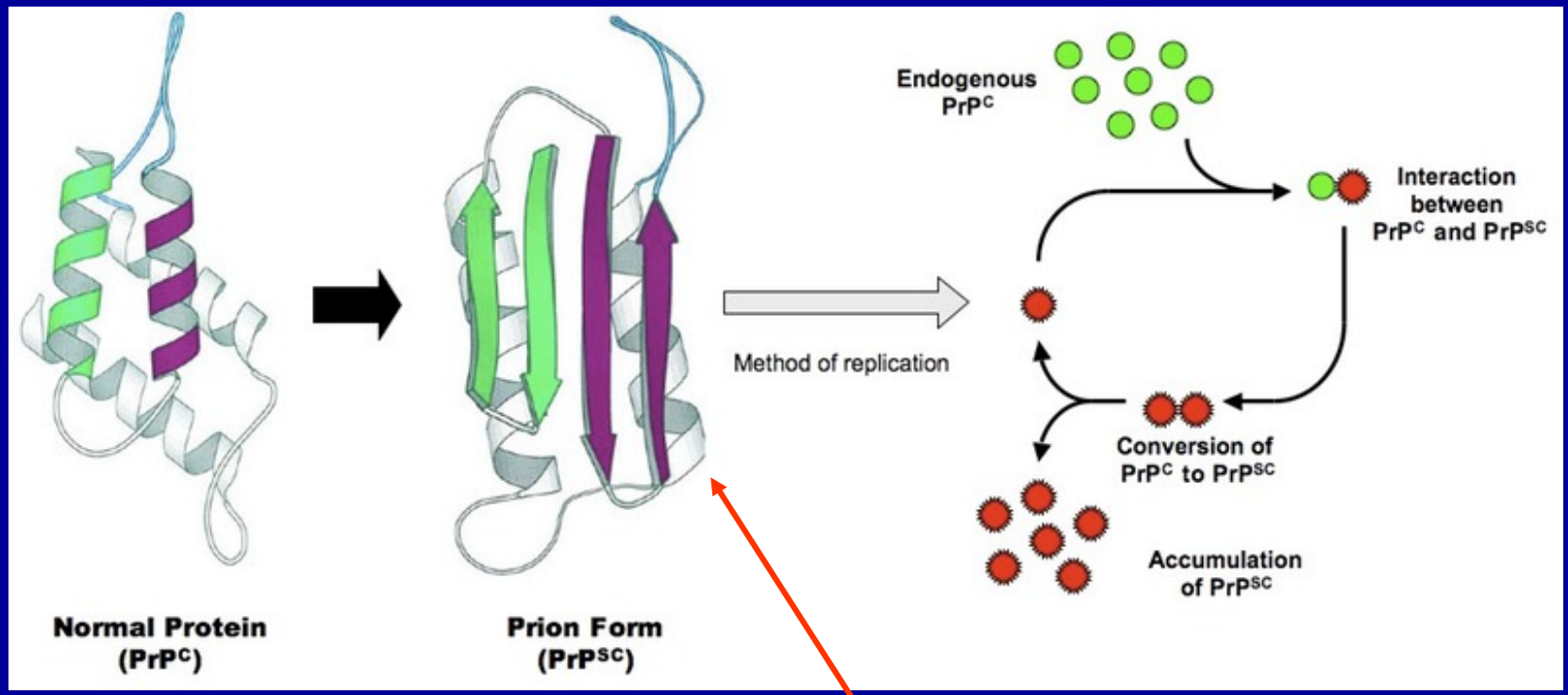
•Infected erythrocytes (red blood cells) tend to have lower oxygen tension, because it is significantly reduced by the parasite. This causes sickling of that particular erythrocyte, signaling the **phagocytes to get rid of the cell and hence the parasite within.**

•Since the sickling of parasite-infected cells is higher, these selectively **get removed by the reticulo-endothelial system, thus sparing the normal erythrocytes.**

•Excessive vacuole formation occurs in those parasites infecting sickle cells.

•Sickle trait erythrocytes produce **higher levels of the superoxide anion and hydrogen peroxide than normal erythrocytes** do, both are toxic to malarial parasites.[19]

PRION PROTEIN and Mad Cow "Disease": protein misfolding



CAUTION: this may be more **"artist conception"** than science.

The above image is one of dozens from Wikipedia, all differing significantly from one another!

Beta sheet structures are known to form fibrils.

Nucleic Acids

DNA and RNA

DNA (DOUBLE STRANDED)

POLY ANION

$\Delta G = \Delta H - T\Delta S$

MELTS, i.e., becomes Single Stranded

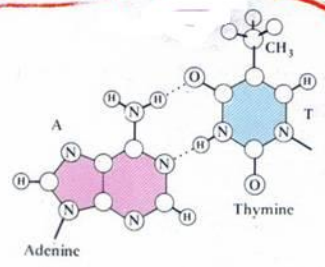
if: a) high temperature

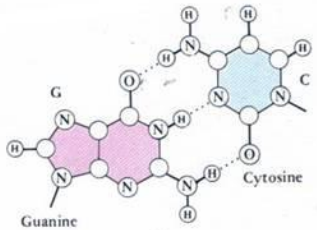
b) low Salt Concentration

$\Delta H_{melt.} \cong +35 \frac{kJ}{basepair}$

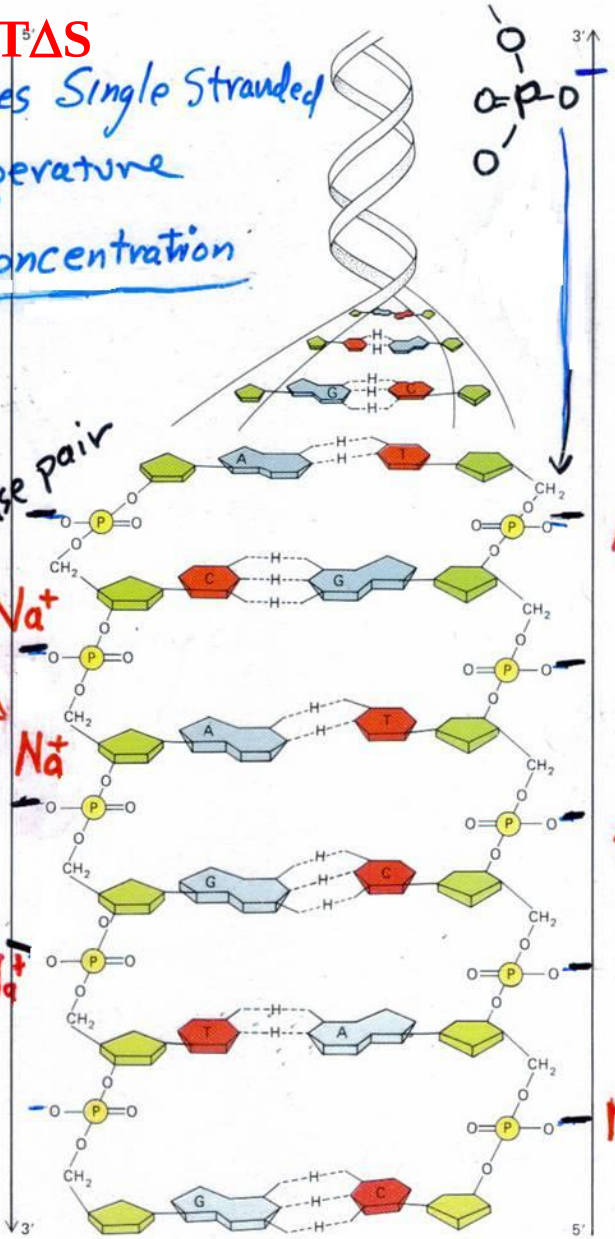
$\Delta S_{MELT.} \cong +88 \frac{J}{K}/base\ pair$

Counter ions → Na^+





(a)



(b)

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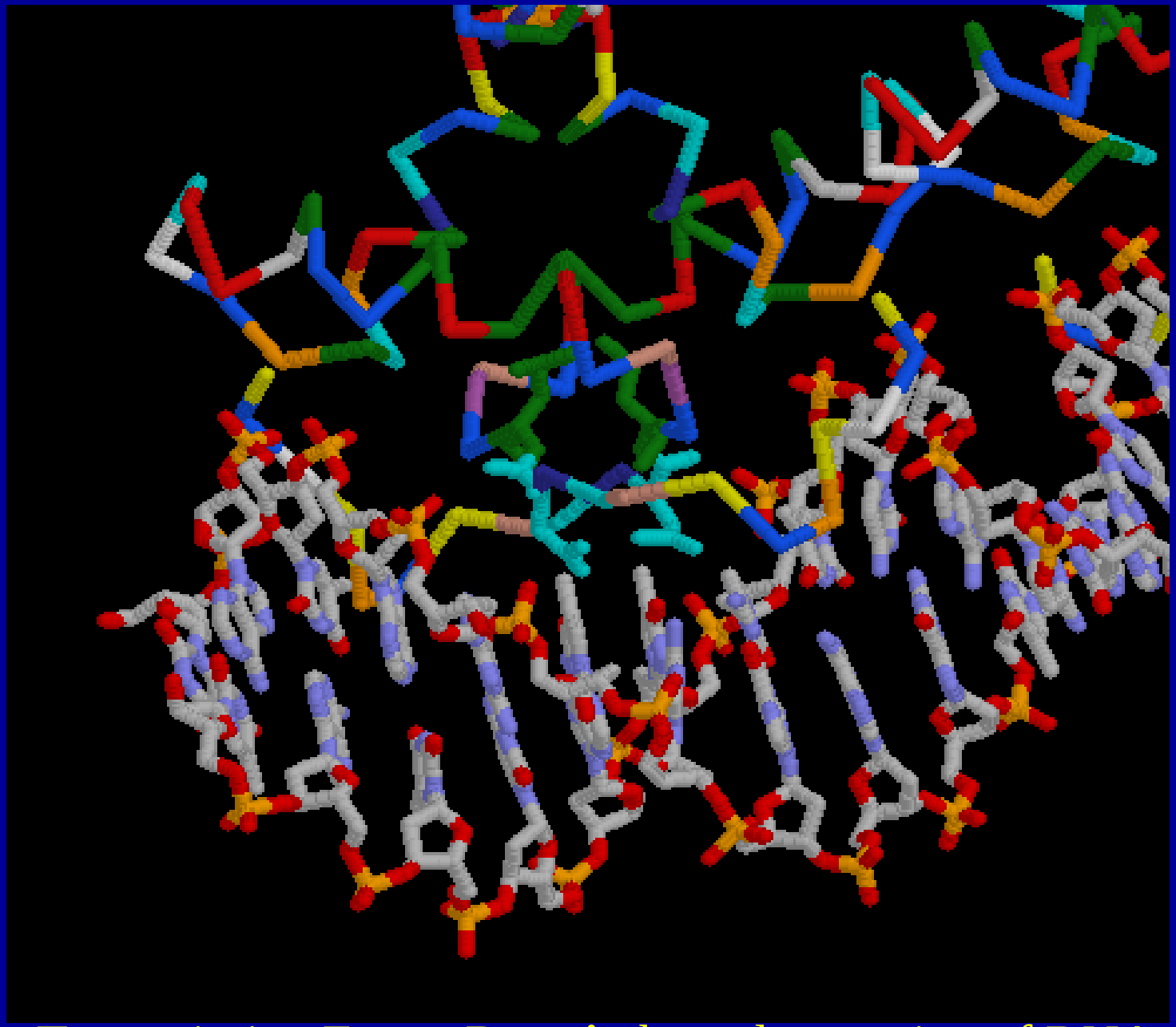
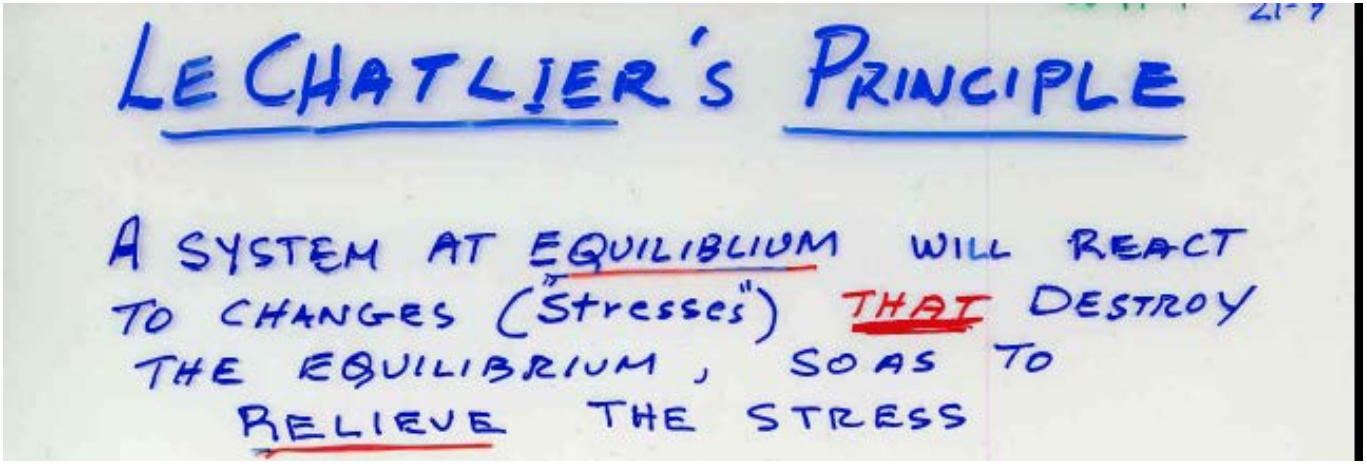
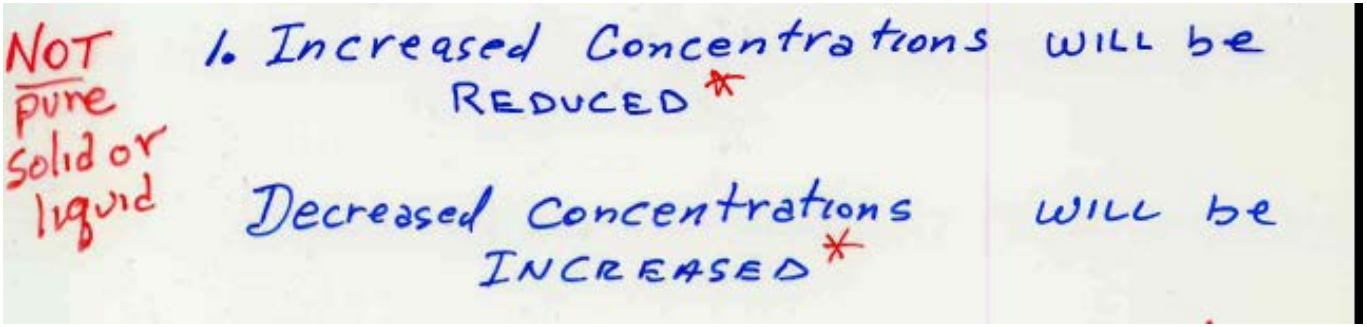


Transcription Factor **Protein** bound to section of DNA

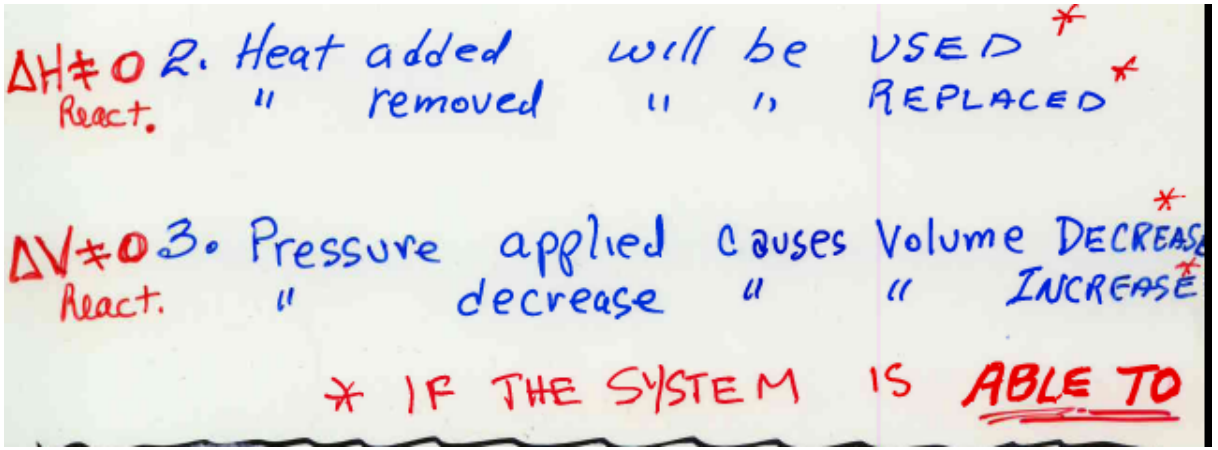
We are about to embark on the quantitative version of

Lechatelier's principle





all about **"Q"**



Van't Hoff Equation

Homework problem: **Graphite→ Diamond**

Chapter 4: Free Energy and ***Chemical*** Equilibria
Chapter 5: Statistical Foundations of Biophysical Chemistry
Chapter 6: Free Energy and ***Physical*** Equilibria

In both chapters **4** and **6** the same guiding principle applies:
Equilibrium is reached as a result of ***each chemical species*** *in the system*
seeking its most negative Gibbs energy.

The REAL reason, **always**, is because $\Delta S + \Delta S_{surr}$ **is positive!**
Because $\Delta S_{surr} = -q/T = -\Delta H/T$
$\Delta G_{A,m}$ the ***molar Gibbs energy change*** for substance A, therefore plays such and important role that it has been given a special name and symbol:

$$\Delta G_{A,m} \equiv \mu_A \equiv \left(\frac{\partial G}{\partial n_A}\right)_{T,P,n_B,B\neq A} \equiv \textit{chemical potential}$$

In other words, μ_A is the ***partial molar Gibbs energy*** of substance A

What is potential?

Some examples:

Gravitational potential energy = mgh Joules (extensive) **Divide energy by MASS**

Gravitational *potential* = gh Joules/kg (intensive)

Electrical potential = volts = Joules/coulomb **Divide energy by CHARGE**

Chemical potential (of substance A) = μ_A =Gibbs free energy in Joules/mol A **Divide energy by MOLES OF A**

μ_A = ΔG when tossing 1 mol of A into a swimming pool of solution (T, P, and the moles of other stuff are effectively kept constant)

Chapter 4: Free Energy and Chemical Equilibrium

$$n_A A + n_B B \rightarrow n_C C + n_D D$$

In an ***open*** system or when chemical ***reactions*** happen in a closed system:
moles of A,B,C,D, i.e., n_A, n_B, n_C, n_D are ***additional thermodynamic variables***.

Therefore:

$$dG = \left(\frac{\partial G}{\partial T}\right)_{p,n_A,n_B\ldots} dT + \left(\frac{\partial G}{\partial p}\right)_{T,n_A,n_B,\ldots} dp + \left(\frac{\partial G}{\partial n_A}\right)_{p,T,n_B,n_C\ldots} dn_A +$$

$$\left(\frac{\partial G}{\partial n_B}\right)_{p,T,n_A,n_C\ldots} dn_B + \ldots..$$

The names of these partial derivatives are found in the expression:

$$dG = -S\ dT + V\ dp + \mu_A dn_A + \mu_B dn_B + \mu_C dn_C + \mu_D dn_D \ldots$$

Where: $\mu_A = \left(\frac{\partial G}{\partial n_A} \right)_{p,T,n_B,n_C \ldots}$ i.e., **"The number of moles" SLOPE**

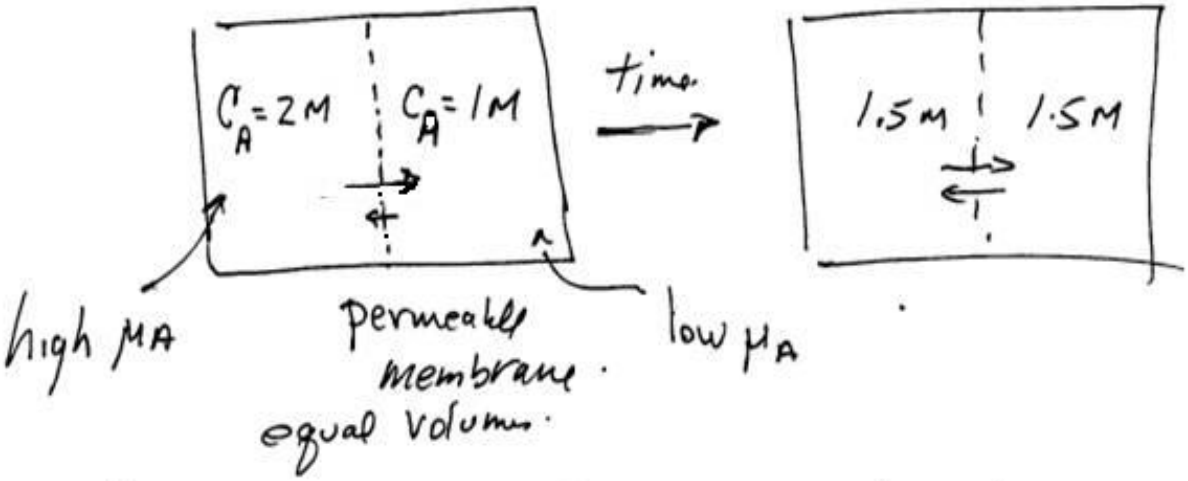
is the partial molar free energy of species A, and has been given the common name

"Chemical potential" of A

For ideal gases and solutes, $\Delta\mu_A = RT \ln\left(\frac{C_{A2}}{C_{A1}} \right)$

where C_{A2} and C_{A1} are any two concentrations, such as [A], (molarity), X_A (mole fraction), or p_A (partial pressure).
[Units don't matter here because its the **ratio** that matters.]
In other words: ***high concentration means high chem. potential!***

Consider the process A(high conc.) → A(low conc.)



$$\left(dG = \mu_{A_{Left}} dn_{A_{Left}} + \mu_{A_{Right}} dn_{A_{Right}} \right) ?$$

Spontaneous for $A_{Left} \rightarrow A_{Right}$.

$\mu_{A\,Left} > \mu_{A\,Right}$.

Natural for A to move from high to low conc.

i.e., high chemical potential → low chemical potential is spontaneous

Connecting with previous IDEAL GAS exercises:

ΔG for ideal gases & ideal solutions

Isothermal expansion of Ideal gas

$\Delta G = \Delta H - T\Delta S$ $= q_{rev} = -w_{rev}$ Real

$= \Delta H - T\left(nR \ln \frac{V_2}{V_1}\right)$

Causes Non ideal behavior Related to activity Coefficient

$= 0 - nRT \ln \frac{V_2}{V_1}$ Ideal

$= +nRT \ln \left(\frac{P_2}{P_1}\right)$ ← (partial pressu = Molarity x RT

General: $\Delta G = nRT \ln \left(\frac{C_2}{C_1}\right)$ **"Q"** for Quotient

Where C = Concentration in ANY units

General: $\Delta G = nRT \ln\left(\frac{C_2}{C_1}\right)$ ← What makes this negative?

Where C = Concentration in ANY units

SO Natural Spontaneous direction is To Lower concentration

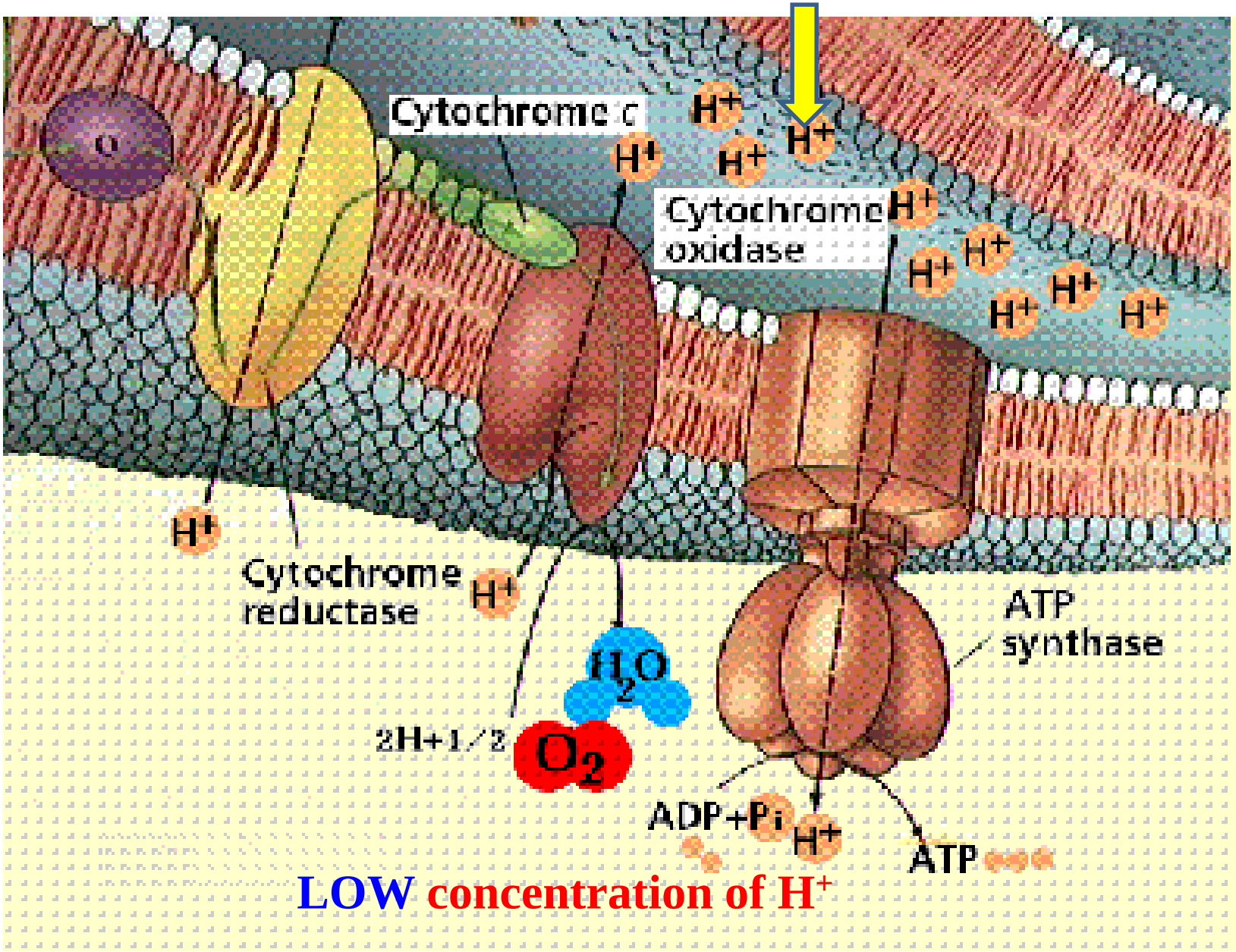
ΔG is NEGATIVE if $C_2 < C_1$

COMES FROM ΔS part !

only (if ideal)

ATP is made from the free energy stored in the H^+ concentration difference across the inner membrane of mitochondria

HIGH concentration of H^+



LOW concentration of H^+