Reading List

- Voet and Voet, “Biochemistry”, Wiley (~1000pp)
- Alberts et al, “Molecular Biology of the Cell”, Garland (> 1000pp)
- Howard, “Mechanics of Motor Proteins and the Cytoskeleton”, Sinauer (367 pp)

(The first two are classic textbooks used by biochemists and medics, and should be easily available. The third book is new, has a more physical perspective and may be harder to find.)

•Recent published articles for the second half of the course.

Short Option: Introduction to Biophysics.

12 lectures, of which two will cover problem sets.

First half – basics of molecular biology and biophysics

Second half – current experiments in biophysics.

Problem sets similar in style and content to exam questions

Hand-outs – most of the lecture slides plus notes, **BUT missing key equations and derviations**

Reading for lecture 1

1. **Introduction**
2. **Some basic chemistry**
3. **Building blocks of life**

- Voet and Voet, Chapters 1&2
- Alberts et al, Chapters 1&2

Life is Physics and Chemistry

"I must tell you that I can prepare urea without requiring a kidney or an animal…"

Wohler, 150 years ago, signalled the end of "vitalism"

We now know…

•Details of thousands of essential molecules of life, their structures and reactions

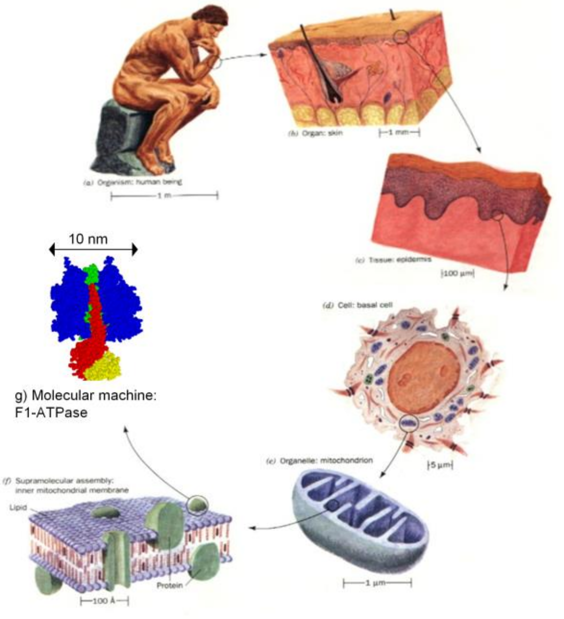
•Thermodynamic principles of the chemical and physical processes of life

•Mechanisms of operation of biological "machines" that perform living processes

The field has reached the stage where many of the current questions need to be answered using the concepts and techniques of physics.

This is just one example of a growing trend towards an INTER-DISCIPLINARY approach in modern research.

- But it's still extrememly complicated and much is left to learn.



The Structure of Living things

[Structural Heirarchy] (4)

This course will focus mostly on the Molecular Level.

Small molecules, macromolecules, molecular machines

Second section – experiments on the mechanism of single molecular machines.

The cell:

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Prokaryotes:

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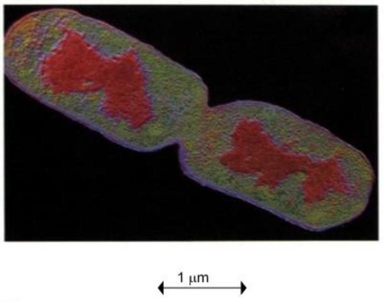
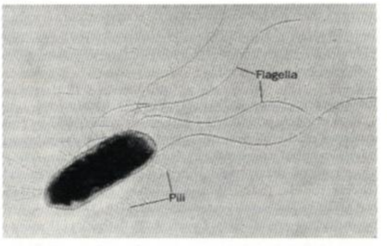
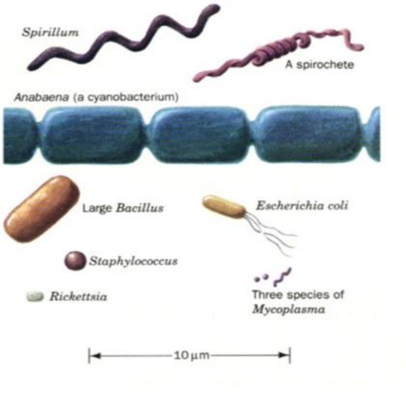




The Cell

[Prokaryotes. eg) *Escherichia coli*] (5)

A typical cell (*E. coli*) is: Water (70%), Protein (15%), RNA (6%), DNA (1%), polysacccharides etc (3%), Lipids etc (2%), inorganic ions (1%), other small molecules (1%).


Spirillum
A spirochete
Anabaena (a cyanobacterium)
Large Bacillus
Escherichia coli
Staphylococcus
Rickettsia
Three species of
Mycoplasma
10 µm

Eukaryotes:

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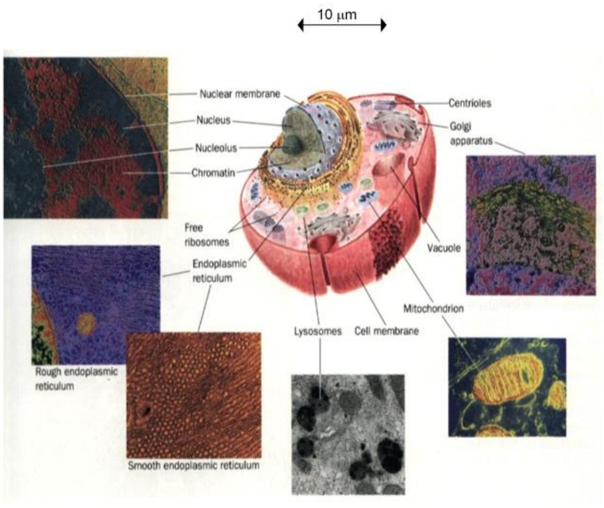
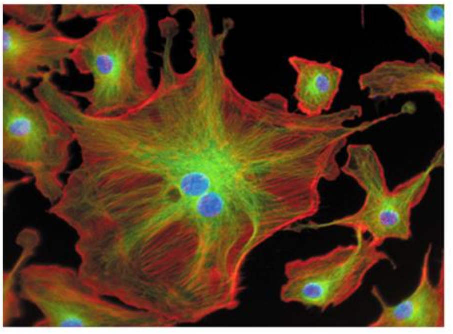
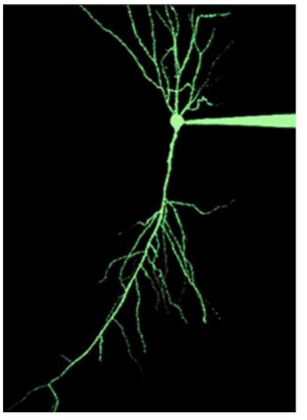


•Much more complex at every level (but NOT necessarily more “advanced”. Prokaryotes are specialized to grow fast, eukaryotes to do better in stable but limited environments).





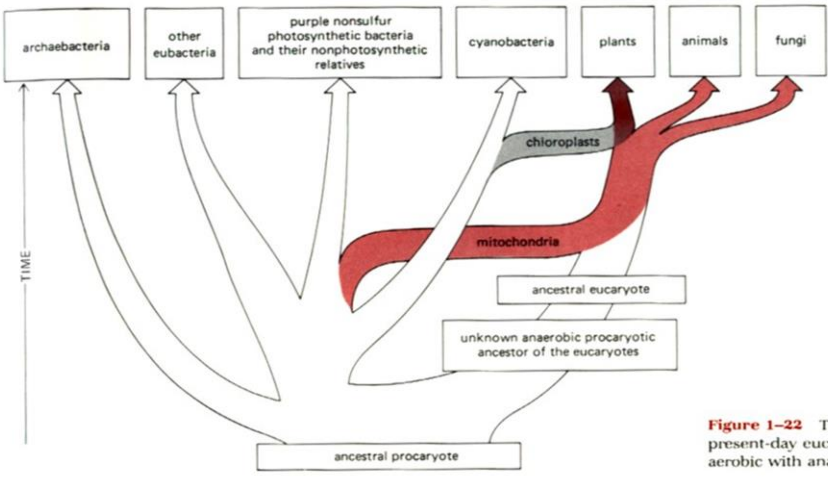
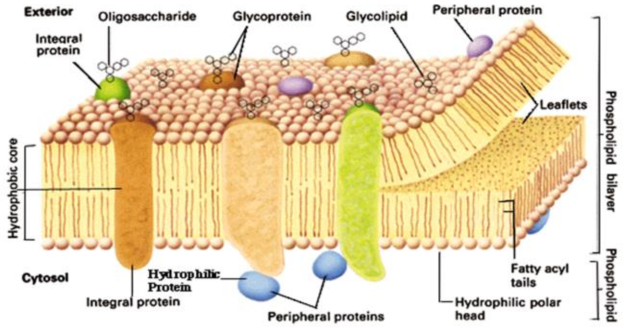


Figure 1–22 The postulated origin of present-day eucaryotes by symbiosis of aerobic with anaerobic procaryotes.

[Tree of life] (9)

Chloroplasts & mitochondria are captured prokayrotes.



Cell Membranes

[typical cell membrane] (10)

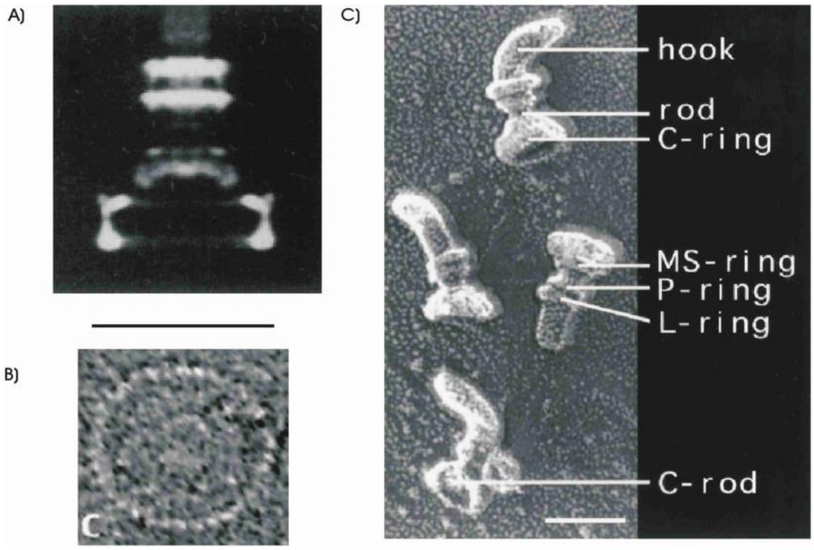
Defines the cell vs the rest of the world.

Concentrates the contents and prevents dissipation.

Stores energy by separating charges.

Allows comparments and provides a large surface area for reactions. (Particularly eukaryotic cells have complicated internal membrane structures.)

More details in lectures 6&7.



Macromolecules, and molecular Machines

[example 1: flagellar motor] (11)

An organism is a “society” of macromolecules and molecular machines. Each has its partiular set of functions, all are regulated, it can go wrong.

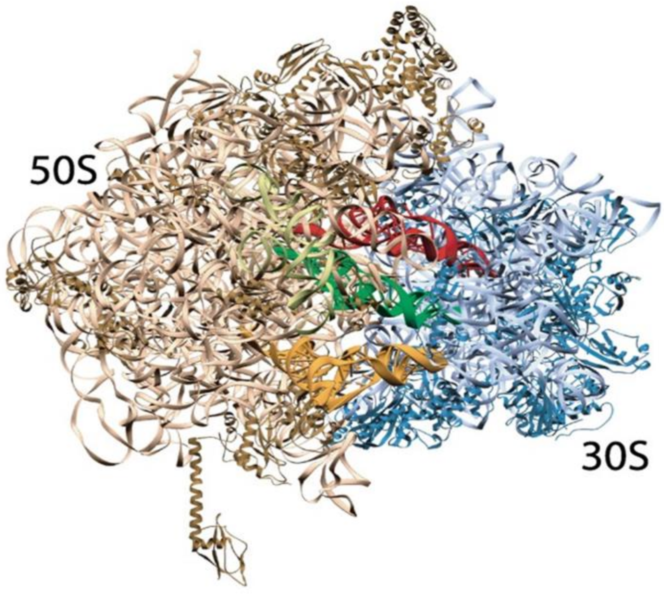
Level of complexity is very high – human brain contains 100 billion cells, each of which can connect to up to 10,000 others.

This course will study molecular machines, their structures and how they work

This is a new area which is expanding very rapidly.

Not just physics - “Interdisciplinary”.

Lots of info, course is only an introduction. **READ THE BOOKS!!!**



[example 2: the ribosome] (12)

Elemental composition of the human body

Element	Dry weight (%)
Carbon	62
Nitrogen	11
Oxygen	9.3
Hydrogen	5.7
*Calcium**	5.0
Phosphorus	3.3
Potassium	1.3
Sulphur	1.0
Chlorine	0.7
Sodium	0.7
Magnesium	0.3
~14 others	trace

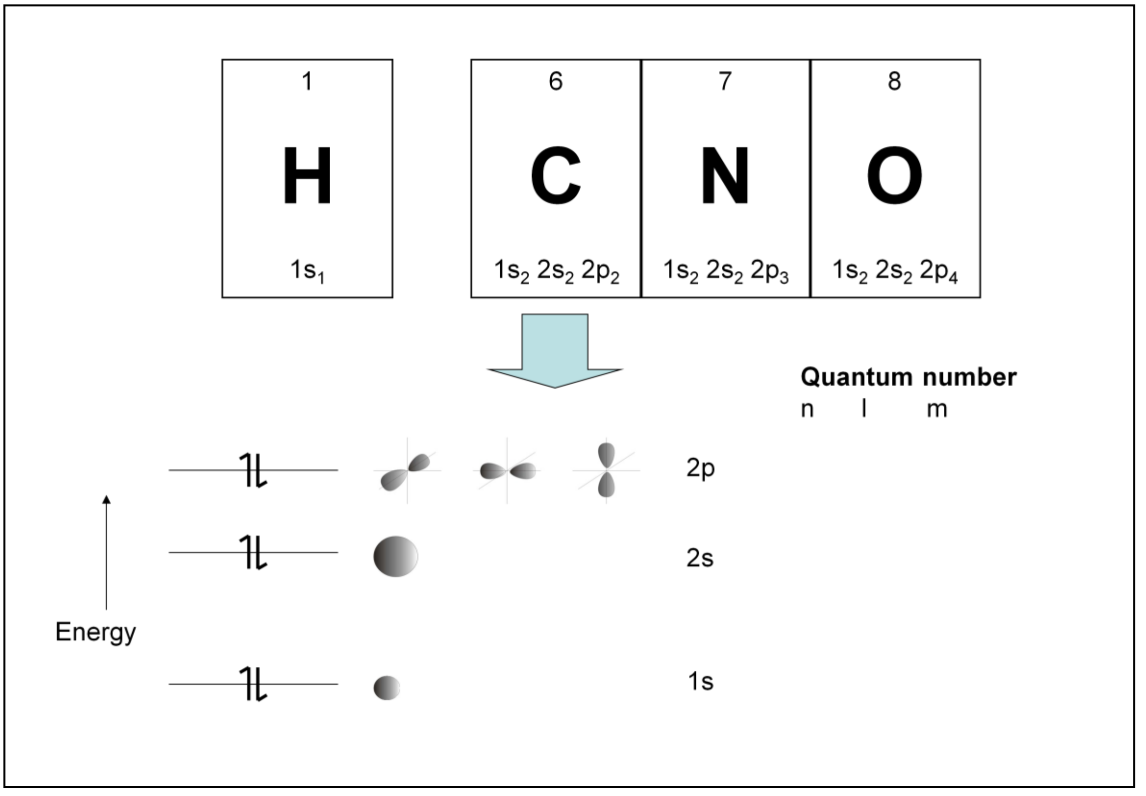
Some Basic Chemistry

[elements. Table of abundance] (13)

Italics – mostly as dissolve ions

Calcium – mostly in bone

Others form covalently bonded molecules

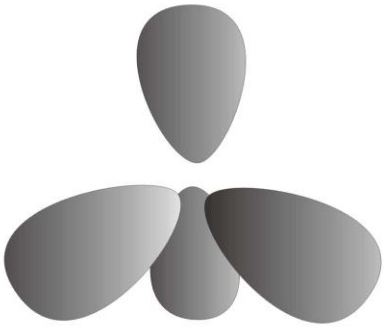


Covalent bonds

[periodic table, electrons in carbon] (14)

Quantum numbers from hydrogen atom eigenfunctions. n,l,m == radial, angular momentum, z-component

Pauli Exclusion Principle



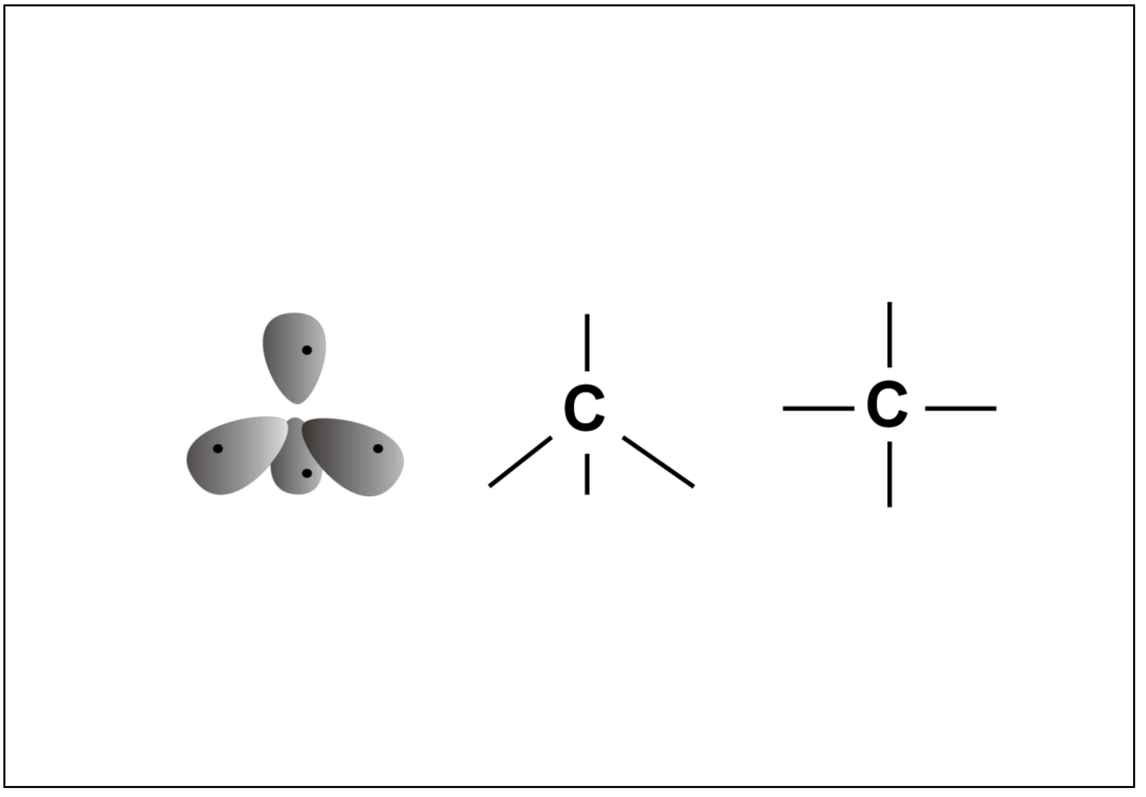
4 Hybrid 2s and 2p (sp) orbitals – Tetrahedral symmetry

[hybrid orbitals] (15)

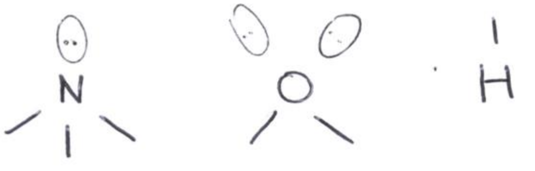
Linear superposition of s and p orbitals

Not lowest energy wavefunctions in isolated carbon atom.

But each orbital can contain TWO electrons, and if one is provided by another similar atom then these ARE lowest energy wavefunctions for the total system.

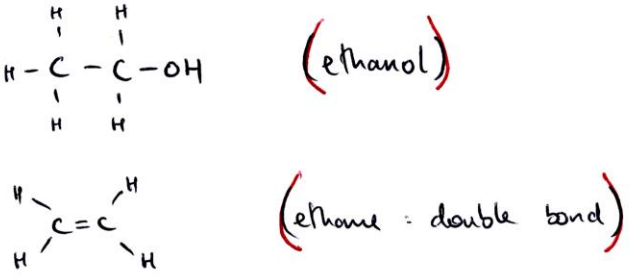


[representations of carbon] (16)



[nitrogen, oxygen, hydrogen] (17)

Filled orbitals contain electrons - negatively charged.



[some covalent bond structures] (18)

Carbon atoms can form chains

Double bonds

Bond energy = energy needed to separate into gaseous atoms

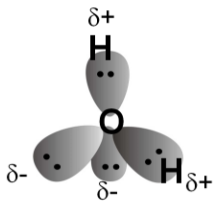
Typically 250-500 kJ / mole for covalent bonds (average c-c bond 348 kJ/mol)

1 mole = Avogadro’s number of molecules (6.02×10^{23})

348 kJ / mol = 5.7×10^{-19} J / molecule. Turns out this is a lot, covalent bonds are hard to break in a biological context, structures are stable

Water

- Large dipole moment



Consequences…

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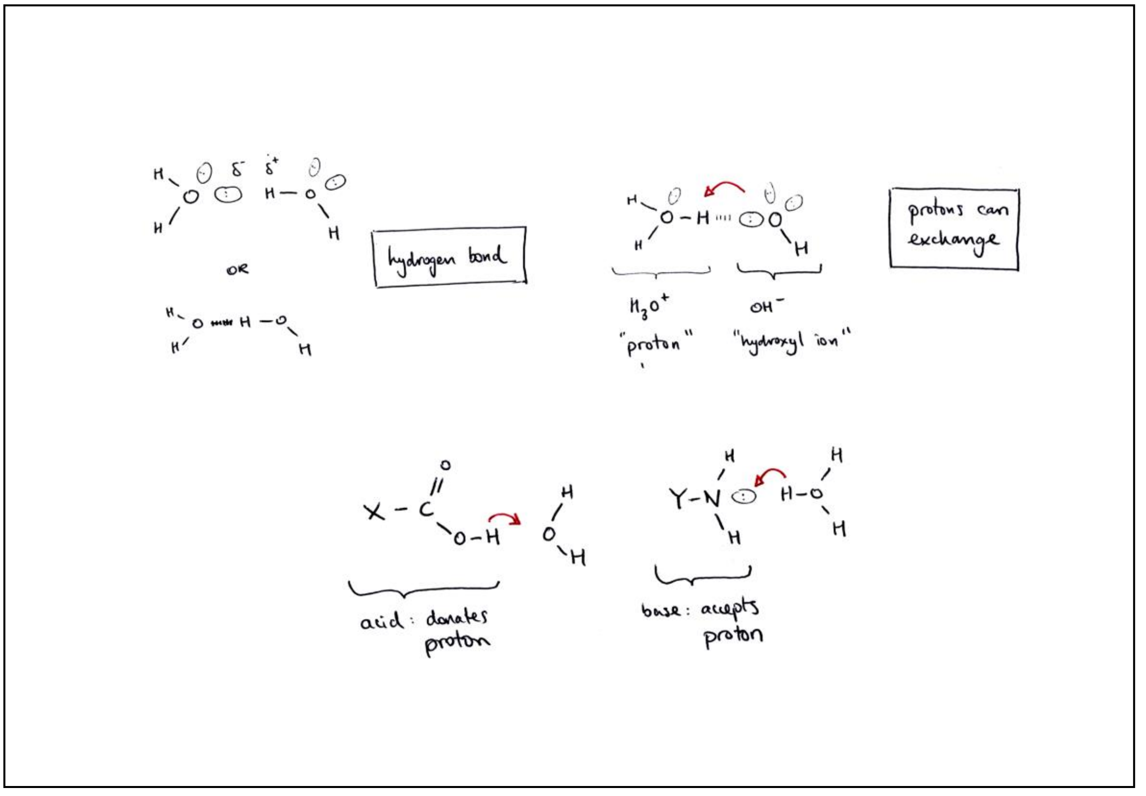
<u>Building Blocks of living molecules</u>

[water] (19)

Absolutely crucial. 70% of cell. Life depends upon its properties in many ways



[Hydrogen bonds, acids and bases] (20)

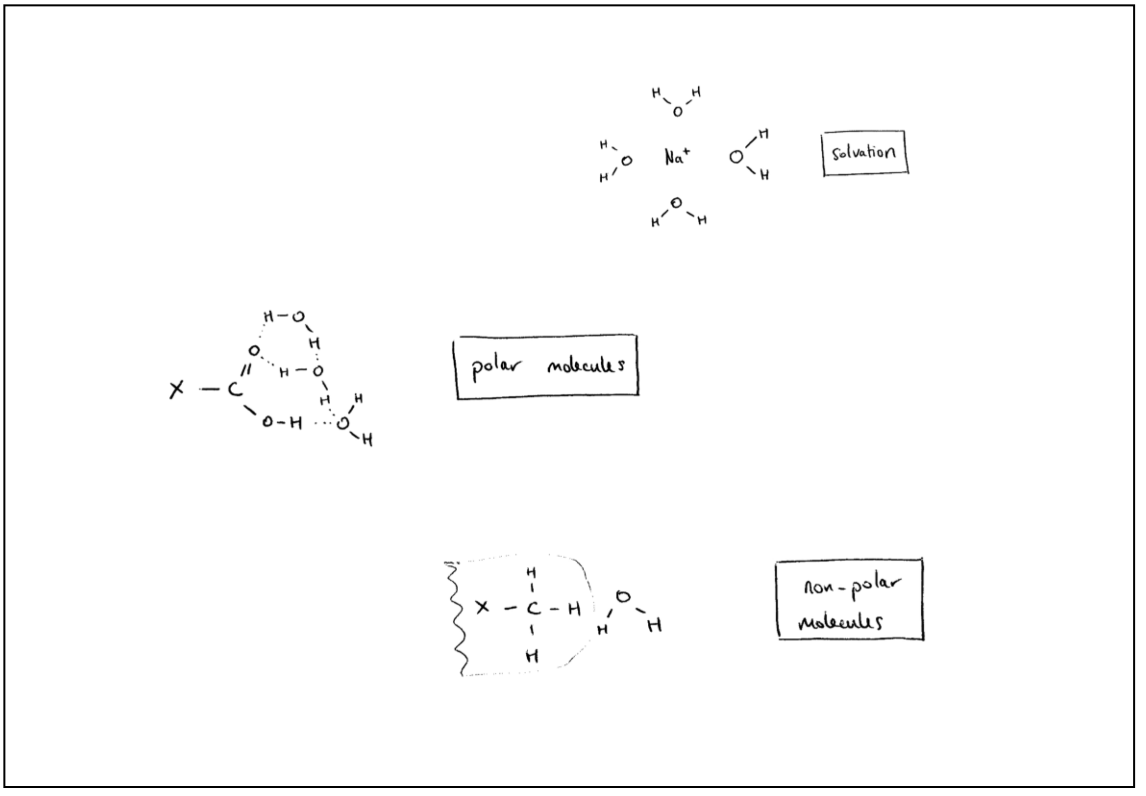
Hydrogen bond energy is ~20x less than covalent bond (~3 x 10^{-20} J)

Water has transient structure due to hydrogen bonds – high viscosity, specific heat

Ice, anomalous expansion (liquid oceans!)

Protons can hop – in pure water 10^{-7} moles per litre of H+, OH-

Protons can hop between other molecules too



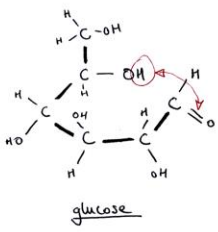
[ions and polar solvents, non-polar solvents] (21)

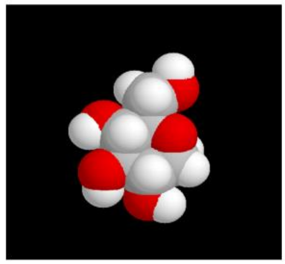
Water dipole means that **ions** dissolve easily – low energy

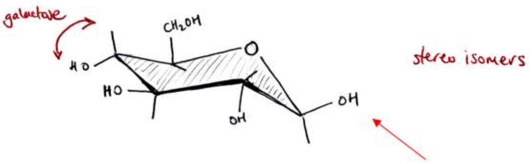
“polar” molecules form hydrogen bonds with water – also dissolve well

“non-polar” molecules do not, they disrupt water-water hydrogen bonds – high energy interface with water. “Hydrophobic” force.

(C-H bond is non-polar because C orbitals are larger than N, O, orbitals due to fewer protons in the nucleus)







[sugars] (22)

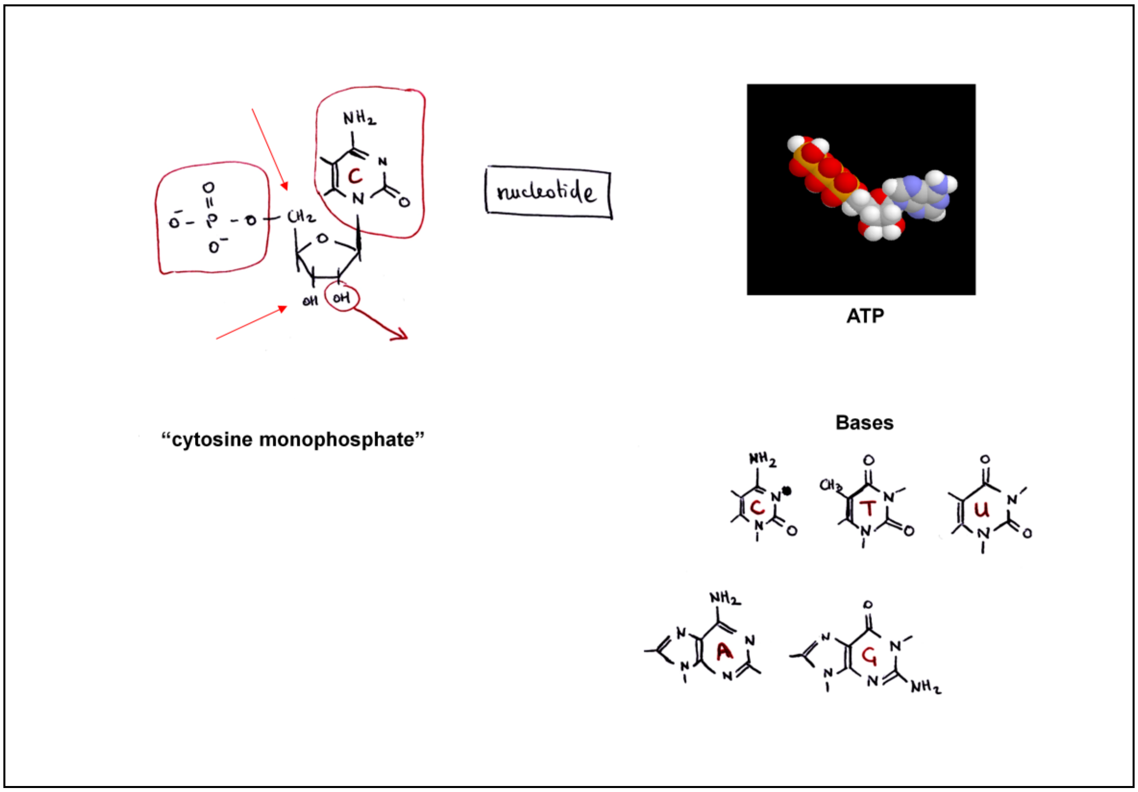
Many different forms are possible. In particular 6- and 5-carbon sugars

Sugars can link to each other (polysaccharides) or other things (eg nucleotides)

Cellulose, Glycogen

Glycoproteins, glycolipids

(space-filling model shows Van der Waals Radii – where V.d.W. force is zero.)



[Nucleotides] (23)

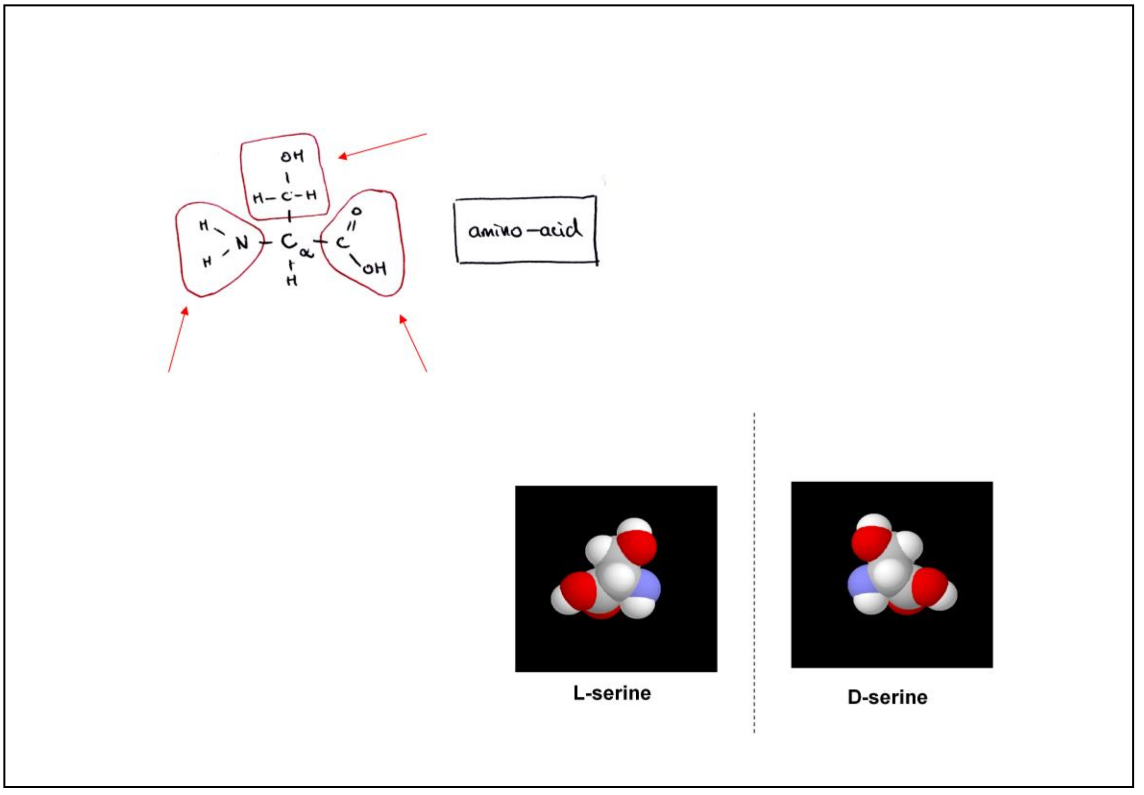
Base + sugar + phosphate = nucleotide

Posphorous – n=3 shell, has d-orbitals too (l=2), each electron (of 5) in outer shell can form a bond.

Two types of base: two purines, three pyrimidines

Can form chains – NUCLEIC ACIDS (DNA, RNA)

Also many other uses, eg ATP

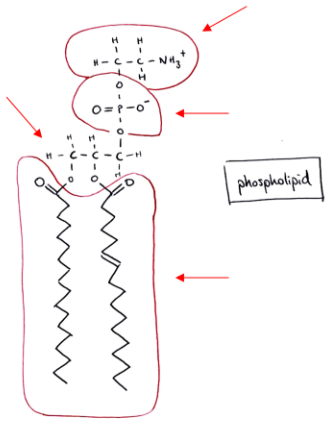


[amino acids] (24)

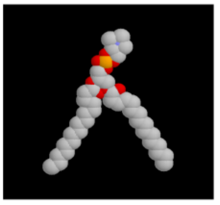
Twenty different side chains in living organisms

Polymerise to form PROTEINS

Steroisomers – mirror images. Proteins are all made of L-amino acids. Random ?



(prefix-) Phosphatidyl ethanolamine



[Phospholipids] (25)

Head groups are polar or charged ,tails are non-polar hydrocarbon chains. AMPHIPHILIC

Heads will partition into water, tails away from water – leads to spontaneous formation of “bilayer” membranes.

NB. Detergents are familiar amphiphilic molecules.

A soap film or bubble is like an inverted lipid bilayer.