Bil 255 - CMB

Chemical Makeup of Living Cells

Molecules of Living Systems chapter 2 pg 29-50

the chemical properties of the living state

The structure of biological molecules
how their shape determines the roles they play in the complex chemical processes of life.

Even the most complicated biological molecules can be divided into smaller and smaller functional groups

REDUCTIONISM

Some Web Resources that give 3-D shapes of Biomolecules

A Site of the Molecules of Life mwk

The chemicals of life…

ELEMENTS - substances composed of atoms all having an identical number of protons…

- can't be reduced to simpler substances by normal chemical means
- only 30 of 92 elements OCCUR IN LIVING SYSTEMS...
- 99% of LIVING MATTER is made of C H O N P S
  all have low atomic numbers
  & are easily reactive & form covalent bond

Molecular composition of cells...

Water (H_2O)……………………………………….	**70 %**
Inorganic ions (Na, K, Cl, PO_4)………………….	**1 %**
Small molecules (aa's, sugar, nucleotides)…..	**5 %**
Macromolecules (protein, n.a., etc)……………	**24 %**

Biomolecules, Weak Forces, & Design of Metabolism

1. BIOMOLECULES... (carbon skeletons)

mostly carbon compounds are found in living systems...

WHY Carbon ? - easily forms 4 covalent bonds...

thus makes many small biomolecules

- allows 3-D shapes that can evoke biological activity
- possesses great chemical reactivity…
- interacts with common chemical functional groups*

Functional Groups - groups of atoms, acts as a unit, give organic molecules their physical properties, chemical reactivity, & solubility in aqueous solutions. **common functional groups***

In bio-molecular chemistry, the concept of functional groups is useful, as a basis for classification of large numbers of compounds according to their chemical properties and reactivity.

most groups possess electronegative atoms [O, N, P, S]*

key bonds are : ester C-O-C* & amide -C-N-*

most are ionizable at physiological (pH 6.8 to 7.4) **read pages 40-50**

2. small Biomolecules [monomers]

Four majors groups of small biomolecules

a. SUGARS - compounds with formula $[CH_2O]_n$]

aldoses vs. ketoses*, rings*, α & ß-links*,
isomers: glucose vs. galactose*
glucose + glucose = mono-, disacc-*, tri-, poly- saccharides*
& long chain polymers of monosaccharides

b. FATTY ACIDS - long chain hydrocarbons*

saturated vs. unsaturated*
lipids* (triacylglycerols = animal fats*)
and phospholipids* of membranes.
easily self-assembly into aggregates*: soap micelles*
& bilayers.

steroid & cholesterols* (4-ring skeleton) are lipids because...
they're insoluble

c. **AMINO ACIDS*** pics Fig 2.21 peptide bond

hundreds known, but only 20 common in proteins of cell.

once established in the "primordial cell",
certain small biomolecules, as covalent themes,
seem to have been preserved throughout evolution
(i.e., they were favored energetically)

d. **NUCLEOTIDES*** parts

nitrogen containing "ring" compounds…

a nitrogenous-base linked to a 5-carbon sugar
(ribose & deoxyribose) & a phosphate

pyrimidines = **C, T, U** purines = **A, G**

nucleotides form the energy rich compounds
of cells (as ATP & GTP), as well as the nucleic acids.

Structural Chemistry: orientation of covalent bonds in space.

molecular configuration results in specific bond angles and molecular geometry

methane	CH_4	109.5o	- a tetrahedron	with free rotation
formaldehyde	$H_2C=O$	120o	- same plane	with no free rotation

one key to shape is the **ASSYMETRIC CARBON…**

a carbon atom bound to 4 dissimilar atoms

in a nonplanar configuration (tetrathedron)

results in 2 different spatial orientations producing **CHIRAL** molecules

ones that are mirror images of each other (optical or stereoisomers)

ENANTIOMERS*...

molecules **that are non-superimposable mirror images of one another**

called **Stereoisomers**... **two molecules are not equivalent or identical,**
and **have 2 molecular orientations or mirror images**

an optically active, CHIRAL*****, is not superimposable on its mirror image
chiral animation

stereoisomers may have mostly identical chemical properties,
but often rotate plane of polarized light via different angles.
LEVOROTARY* (L) - rotate light left (**- negative optical rotation**)
DEXTRORTATORY (D) - rotate light right (**+ positive optical rotation**)

and likely have different **BIOLOGICAL ACTIVITY...**
Parkinson's Disease & dihydroxyphenylalanine L-DOPA figure*****

Biological Activity & the Shapes of Biomolecules

Biological activity... is catalytic ability of molecules to do work
There are 2 properties of biomolecules, which gives them their unique FITNESS for Biological Activity & the Living State

A. CONFIGURATION: the spatial arrangement of atoms in molecules...
configuration can't be inter-converted w/o breaking bonds
based upon COVALENT BOND* - sharing of outer orbital e-'s between two atoms thereby forming a molecule

examples of Covalent Configurations:

isomers... based upon covalent bond configurations [glu v gal]*

BIOLOGICAL ACTIVITY & the Shape of Biomolecules

B. **CONFORMATION** [or shape] - surface outline or contour or 3-D orientation of chemical groups that are free to assume different positions in space without breaking any bonds

- do primarily to...
  FREE ROTATION of atoms about a single chemical bond
  WEAK NON-COVALENT FORCES hold atoms in spatial arrays-

- consequences of conformations...
  different isomeric shapes (forms) of molecules can exist, only one of which may be biologically active (others aren't)

  ENZYMES can distinguish between biologically active forms (isomers) based upon the "SHAPE" of that isomer

Weak Molecular Forces of Life

see **Panel 2.7 pg 78**

Non-covalent Electrostatic Interactions*... (in the 10-150 cal/mol)

IONIC bonds* - charged small ions (atoms which gained/lost e-'s) which attract (+/-); w/o water they are very strong (crystals of NaCl)
DIPOLES* - attractions via asymmetrical, internal distribution of charges in a molecule, which has no net charge (opposite poles +/- attract)
DISPERSION* (van der Waal's) Forces- electrostatic attraction based upon closeness of atoms; is important in macromolecular interactions for 3-D shapes
HYDROPHOBIC Interactions* - repulsion of electrostatic dipoles of water by non-polars- "fatty-hydrocarbon" groups self assembly
HYDROPHILIC Interactions* - substances that dissolve readily in water (ions & polar molecules) water, as a dipole, surrounds & solubilizes a solute molecule
HYDROGEN bonds [fig*]- electrostatic attraction between H of one atom and a pair of non-bonded e-'s on an acceptor group: O-H & N-H with O- & N-

Covalent Molecular Forces of Life

see table 2.1 pg 46

TYPE of BOND	ENERGY (Kc/mol)	TYPE of INTERACTIONS	ENERGY (Kc/mol)
SINGLE COVALENT BONDS		**NON-COVALENT BONDS**	
O - H	110	IONIC BONDS	1.0 - 5.0
H - H	104	HYDROGEN BONDS	1.0 - 2.0
C - H	99	VANDER WAALS	0.1 - 1.0
C - O	84	HYDROPHOBIC	0.1 - 1.0
C - C	83		
S - H	81		
C - N	70		
C - S	62		
DOUBLE BONDS			
C = O	170		
C = N	147		
C = C	146		

Biological Design
or How Weak Molecular Forces & Shape Build Form

Is there fundamental principle guides biological organization… in practice ?

some common-universal rules of molecular assembly must exist…
one sees recurring patterns of spirals, triangulated forms, & pentagons in **everything from crystals to proteins, viruses to plankton, paramecia to protozoa.**

Tensegrity – is an architectural principle of **biological shape & form**

How individual groups of molecules assemble themselves within whole living organisms is a fundamental question of the living condition (???)

...PRINCIPLE of SELF-ASSEMBLY...

molecules join to form larger & more stable structures, often with new & non-predicted properties or emergent properties...

macromolecules -> organelles -> cells -> tissues -> organs

The answer may lie in the principles of **tensegrity**...

the application of general architectural principles to biomolecules & living systems

TENSEGRITY defines the mechanical rules and how structures are stabilizedby balancing forces of internal tension and compression.

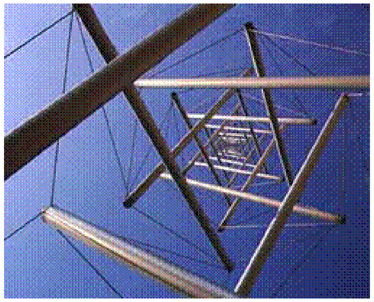
TENSEGRITY may be a fundamental aspect of SELF-ASSEMBLY -

an architectural system, mechanically stable, yet dynamic, where the forces of tension and compression balance.

"tension & compression are complementary elements in any structure"

- **Geodesic Domes (Buckminster Fuller)**

  entire structure distributes its mechanical stresses... frames of rigid struts connected into triangles, pentagons, or hexagons… each of which bears tension or compression



- Prestress Structures **(Snelson pic) -**

  struts that bear tension are distinct from ones that bear compression.

  Compression members can provide rigidity while remaining separate, not touching one another, held in stasis only by means of tensed wires. In both of these structures tension is continuously transmitted across all structural members.

Tensegrity in Biological Systems…

'Architecture of Life'   by Don Ingber

Organismal Level   (examples)

bones are the compression struts and
muscles, tendons, & ligaments are the tension bearing wires

Cell (1970's view)… membrane bound viscous *gel* **(molasses filled balloon)**
(today)… cytoskeletal awash in a viscous *gel*,
surrounded by membrane cytoskeletal elements as
microtubules…   act as compression "girders"
and microfilaments exert tension, pulling all a cell's parts
toward nucleus

Cytoskeleton is then a hard-wired molecular system that
stabilize cell form & shape.

Biological Tensegrity suggests -

that the structure of cell's cytoskeleton can be changed by altering the balance of physical forces transmitted across the cell's surfaces.

for example: cultured cells on glass [flat] vs a flexible surface [round]

Donald Ingber's Tensegrity Model of a Cell

Tensegrity further suggests –

Since many enzymes and other substances that control protein synthesis, energy conversion, & growth in the cell are physically immobilized upon the cytoskeleton, changing the cytoskeletal geometry & mechanics may affect biochemical reactions & even alter the genes which are activated and thus the proteins that may be made.

Binding a signal molecule (as a hormone) to a receptor, which traverses cell membrane into a cell, MAY CAUSE conformational changes at the opposite end of the receptor, which in turn may trigger a cascade of molecular restructuring inside a cell, including reorientation of the cytoskeleton.

SELF-ASSEMBLY…

of molecules into organelles and/or cells into tissue is not much different from self-assembly of atoms into compounds.

The shape a molecules assumes is characteristic of the way the structure as a whole will behave in 3-D space, and maybe cells respond in a similar way according to rules of Tensegrity

Fully triangulated tensegrity structures, once self assembled, may have been selected for through evolution, because of their structural efficiency, their high mechanical strength, & minimal use of materials.

Tensegrity may be the most economical and efficient way to build cell structure.

SUMMARY:

a few fundamental principles of chemistry are essential for understanding cellular processes at the molecular level:

1. covalent and non-covalente lectrostatic forces control molecular shape & form forces of configuration and conformation result in biologically active molecules
   figure 2.1a
2. small molecules are the building blocks of larger molecules
   monomer make polymers, make supramolecular complexes, make organelles...
   fig 2.1b

3 and 4 are to be covered under metabolism.

3. chemical reaction are reversible depending on rate constants and the [P] & [R]
   fig 2.1c
4. source of cellular chemical energy is the hydrolysis of ATP, when high energy phosphoanhydride bonds are broken by addition of water (hydrolysis).
   fig 2.1d