Lecture 1

Introduction to the origins of biochemistry. Chemistry of biochemistry. Water. Acid Base chemistry and biomolecules

Origins of biochemistry

- Where does biochemistry begin?
- In his book "On the Generation of Animals, 1651" **William Harvey said"*Omne vivum esx ovo*"** translates into essentially meaning that a complete living organism arises from the simple egg.
- But long before this man questions life's origins

Origins of biochemsitry

- What is the origin of life. Greek philosophers asked this question.
- **Anaximander** life originated from the moisture that covered the earth before it was dried up by the sun. The first animals were a kind of fish, with a thorny skin (the Greek word is the same that was used for the metaphor 'the bark of a tree' in Anaximander's cosmology). Originally, men were generated from fishes and were fed in the manner of a viviparous shark. The reason for this is said to be that the human child needs long protection in order to survive. Some authors have, rather anachronistically, seen in these scattered statements a proto-evolutionist theory.

Geologists made the first discoveries that questioned the biblical teachings of god as creator

- **Leonardo Da Vinci** (1452-1519) was a self made geologist. He realized the notion of sedimentation representing a time line with the older fossils lying beneath those that were newer. The presence of fossilized creatures atop mountains that clearly came from the sea suggested to Da Vinci that the earth had undergone great geological changes, such that mountains now stood where the sea had once been.

Geology

- **Nicolaus Steno** one of the great scientist of his age formalized da Vinci's notions of sedimentation in his treatise the Prodromus, set forth the principle; written in 1668,, "The law of superposition". Superposition argues that sedimentary rock provides a history of ancient times as the upper layers are younger and the lower layers are older. He also noted that although many sedimentary rock formations were found vertical that they were deposited horizontally, the law of original horizontality. However, like most of the great scientific minds of Europe he was greatly influence by Biblical teachings and interpreted his conclusion that in Tuscany, where he carried out his studies, there had been two great floods, one occurring during the second day of creation and the other during the Great Flood

Geology

- **Georgius Agricola,** considered the father of geology, described fossils in great detail, beginning a systematic catalogue of them. His observations were published in "On the Nature of Fossils" in 1564. He speculated little on fossils being the possible remains of ancient organisms a point that was much debated in his time.

Geology

- **William Smith** born in1769, had little formal education but as a surveyor made many inspired fossil observations, an interest that he began at an early age. He is known for his description of the specific fossils in each stratum layer, and that successive layers contained related but different species. This principle of faunal succession, showed that the same fossil types (species) could be found in the same sedimentary layers in any location and that the species found in other layers followed the same succession. Clearly, these observations mark the beginnings of evolutionary thought.

Geology

- **Mary Anning Georges** Her discoveries of *Ichthyosaurus* and the first plesiosaur gained her recognition and respect among paleontologist of her day despite her limited education and lack of social status. She is credited in finding many of the best fossil examples of her time.
- **Georges Cuvier** who used Georges' fossils to help advance his theories of fossils being the remains of extinct species. Cuvier believed that the earth was very old and that mass extinction of species had occurred on various occasions, a phenomenon he referred to as "revolutions".

Geology

- **Adam Sedgwick**, was one of a group of scientist that defined the geological time periods that we are familiar with today. His work in collaboration with **Roderick Impey Murchison**, carried out in England, Scotland and Wales, described the upper Cambrian (Latin for Wales) and the lower Silurian (named for a Celtic tribe). Sedgwick shared a mutual respect for **Charles Darwin**.

Geology

- Charles LyleHe thought it would be more practical to exclude sudden geological catastrophes to vouch for fossil remains of extinct species and believed it was necessary to create a vast time scale for Earth's history. This concept was called Uniformitarianism.
- Charles Darwin was a close friend and corresponded regularly with Lyle. He credited Lyle for influencing his thinking that eventually lead to his theories on evolution.

Geology;Age of the earth

- In parallel with the field observations that these scientist made the question of the age of the earth was long considered.
- Many novel methods were employed to determine the age of the earth including studies on the rate of cooling of an iron ball and extrapolating to a ball the size of earth, Mathematical approaches such as that of the great scientist **William Thomson** (better known as Lord Kelvin) estimated the age of the earth, based on loss of heat, to be less than 500 million years old.

Geology; age of the earth

- **Henri Becquerel** discovered radioactivity. It was soon realized that the energy from radioactive decay was enough to keep the planet hot. But more than that, it could be used for dating rocks.
- Used mother/daughter isotopes as way to measure earth's age. Assume that one no daughter to start with and there is only one way to make daughter and no mother element is added over time.
- Using radioactive dating techniques, the age of the Earth has been shown to be (again and again) 4.65 billion years.

Evolution

- From 1831 to 1836 Darwin served as naturalist aboard the H.M.S. Beagle on a British science expedition around the world. In South America Darwin found fossils of extinct animals that were similar to modern species. On the Galapagos Islands in the Pacific Ocean he noticed many variations among plants and animals of the same general type as those in South America. The expedition visited places around the world, and Darwin studied plants and animals everywhere he went, collecting specimens for further study.

Evolution

- Darwin's theory of evolutionary selection holds that variation within species occurs randomly and that the survival or extinction of each organism is determined by that organism's ability to adapt to its environment. He set these theories forth in his book called, "On the Origin of Species by Means of Natural Selection, or the Preservation of Favoured Races in the Struggle for Life" (1859).

Evolution is an essential part of biochemistry

- Evolution is at the heart of modern biological thought. One tenant of evolution is that all species evolved from some other species and all life evolved from some common ancestors. This means that all organisms are related and therefore similar. In general our goal as scientists is to understand better the human condition. However, for the most part our study of humans is rather limited. The study of other organisms is generally carried out and our findings extrapolated to humans. Almost everything that we know about biochemistry was first discovered in bacteria and yeast. At the same time we can't know everything from these simple organisms. It is important to pick the right **model system**; the choice being dependent on the question asked.

Darwin cont.

- Darwin's theory of evolution ignited scientist of the late 19^{th} century. Research institutes and field labs abounded as there was a huge movement to further study and add proof to Darwin's theory. Thousands of plants and animals were collected and studied. Observations of unusual adaptations of animals to their environment were continually being reported. The question that went unanswered or at least unrecognized for nearly 50 years was how did animals change over time and once change how was that change maintained?

The answer came from Mendel

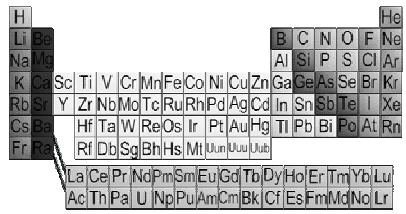
- Of course we all know it was Gregor Mendel who provided the answer. A contemporary of Darwin, Mendel showed that traits were carried from generation to generation in a predictable manner and that the information is carried by "factors" (the term genes was not coined until the 1900's by Columbia University professor Walter Sutton). Mendel's studies provided the means by which new traits could be acquired by an organism as it evolved. But what determines the actual traits? What material makes our eyes brown, determines where we eat meat, plants or both, mammal or insect? The answer is proteins. Genes determine traits and they carry the information about the properties of every protein. That information is a blue print on how to make each protein. So what are proteins? This is where biochemistry begins.

How did life begin and why are living things composed of particular molecules

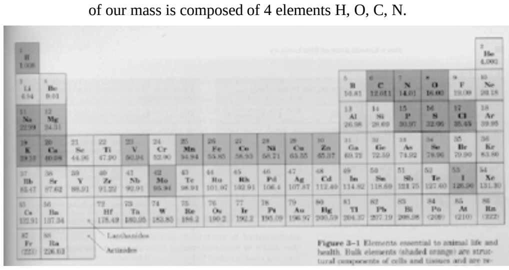
- We don't have the answer to this question but we can speculate. It seems likely that simple organic molecules formed from the earths primordial soup. The atmosphere may have been reducing (as opposed to oxidizing as it is today). Experiments carried out in the 1950s demonstrated that when simple compounds, H2O NH3 CH4 and H2 were exposed to electric discharge for about a week many more complex molecules formed, including some amino acids (aspartic, glutamic, alanine and glycine). The theory continues that somehow these molecules polymerized making more complex molecules which eventually were enclosed in a membrane. The critical step is the formation of molecules that could use complementation to form copies of themselves, thus allowing for inheritance.

Biochemistry is complex but it all makes sense

Periodic table



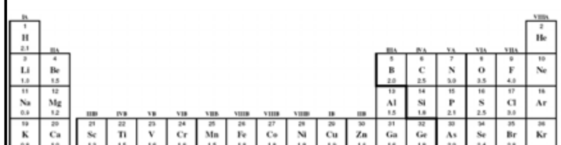
Why are all organisms compose of a handful of different elements. 99% of our mass is composed of 4 elements H, O, C, N.



Pink are the most common elements with minor elements shown I light orange.

These Elements readily form covalent bonds.

Covalent bonds form when unpaired electrons in outer orbits of an element combine with an electron from another element that also has an unpaired electron. By sharing electrons these molecules become stable.



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Lewis Dot Structure

H•							He:
Li•	Be•	•B•	•C•	•N:	:O:	•F:	:Ne:
Na•	Mg•	...etc.					

Remember organic chemistry? Ionic bond


sodium metal

+


chlorine gas

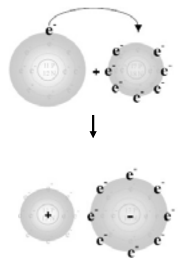
→


table salt

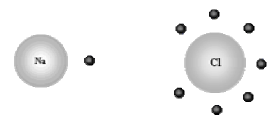
- While there are only 118 or so elements listed on the periodic table, there are obviously more substances in nature than 118 pure elements. This is because atoms can react with one another to form new substances called compounds. Formed when two or more atoms chemically bond together, the resulting compound is unique both chemically and physically from its parent atoms.

Formation of an ionic bond

- In ionic bonding, electrons are completely transferred from one atom to another. In the process of either losing or gaining negatively charged electrons, the reacting atoms form ions. The oppositely charged ions are attracted to each other by electrostatic forces which are the basis of the ionic bond
- For example, during the reaction of sodium with chlorine:

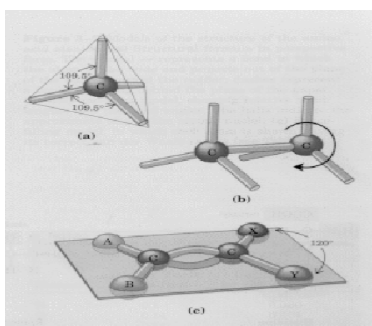


Ionization in motion



In general, reactions between metals and nonmetals tend to be ionic in nature.

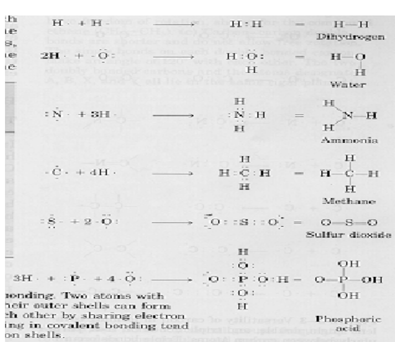
Central to biomolecules is Carbon. Carbon-carbon single bonds show free rotation, while carbon=carbon double bonds are rigid. Carbon can form a multitude of bonds unlike any other element.



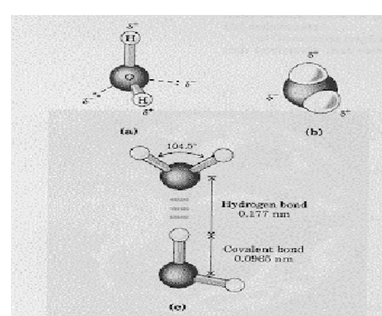
Covalent bonds

- What about reactions between 2 nonmetals? Many nonmetals do bond together. Hydrogen atoms, for example, often react with other hydrogen atoms. Which will become positively charged and which negative? Actually neither. Neither atom has any stronger pull (or affinity) for electrons than the other, so these reactions do not form ions. In fact, the 2 atoms share each others' electrons in what is called a **covalent bond**.

Examples of some common covalent bonds, found in living organisms



Most of the cell is water and so water greatly influences the character of biomolecules. As see in the picture below water is a polar molecule.

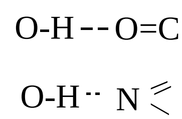


Polar vs nonpolar covalent bonds

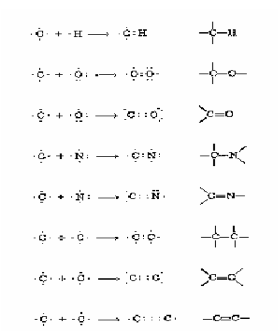
- So, if one atom has a much greater affinity for electrons than another, the two may form an ionic bond. If two atoms have equal electron affinities they form covalent bonds. What if two atoms are slightly unequal? In a molecule of water for example, oxygen has a greater affinity for electrons than hydrogen, but not enough to pull the electrons away completely and form ionic bonds. This is possible because there are 2 types of covalent bonds. **Non-polar covalent bonds** are formed when atoms share electrons equally, such as in the examples above. But when one atom has a greater affinity for electrons in a molecule, the shared electrons will spend more time around that atom and the bond formed will be a **polar covalent bond**.

Water

- Water forms hydrogen bonds with itself and molecules dissolved in it.When salts are dissolved in water the ionic interactions are disrupted NaCl in water becomes Na+ Cl-.
- Water can have a power effect on molecules that are not soluble in it. These are nonpolar molecules such as hydrocarbons. Fats float on water. Some amino acids are polar and other nonpolar. Proteins are made of both and when dissolved in water there 3D shape is partially determined by this interaction.

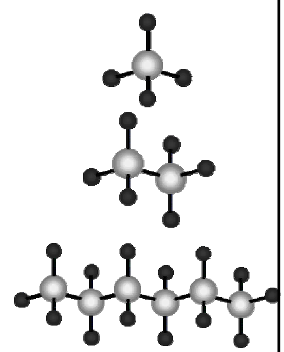


Some of the properties of carbon bonding are shown below.



Nomenclature of Organic Molecules

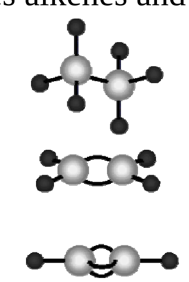
- a carbon atom in a molecule forms 4 bonds to other atoms. In this family of compounds all bonds are single (2 electron) bonds and each carbon is bonded 4 times to either other carbons or to hydrogens. Since atoms with 4 bonds and no lone pairs have a tetrahedral geometry, each carbon atom in an alkane is tetrahedrally substituted.
- The simplest member of the alkane family has one carbon bonded to four hydrogens. The name of this compound (CH_4) is obtained by putting together the root name for one carbon (meth) and the family name (-ane) to give *methane*.



alkanes

Number of Carbon Atoms	Root Name
1	meth
2	eth
3	prop
4	but
5	pent
6	hex
7	hept
8	oct
9	non
10	dec
11	undec
12	dodec
13	tridec
14	tetradec
15	pentadec
20	icos
21	henicos
22	docos
30	triacont
40	tetracont

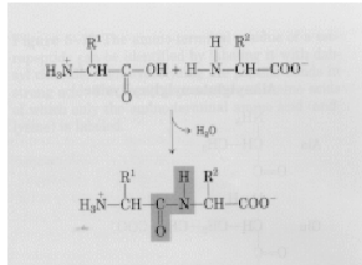
Alkanes alkenes and alkynes



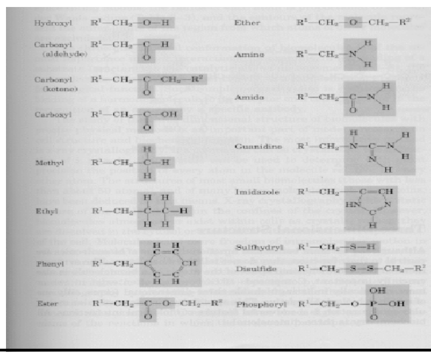
Hydrocarbons are the building block of organic molecules found in living things. Replacement of hydrogen with other functional groups give organic molecules their unique properties.

- Alcohols have one or more hydroxyl groups   -OH
- Amines have amino groups - NH_2
- Aldehydes have carbonyl groups like this-   C-H (with ∥ O below the C)
-
- Ketones look like this   C-C (with ∥ O below the first C)
-
- Carboxyl groups look like this   C-OH (with ∥ O below the C)

We find that many biomolecules have two functional groups such as amino acids which have a carboxyl and amino group. It is the joining of these two functional groups that leads to the polymerization of amino acids into proteins.



Some common chemical bonds formed with carbon.



Bond strength of some common biomolecules

Strength of bonds common in biomolecules			
Type of bond	Bond dissociation energy (cal/mol)	Type of bond	Bond dissociation energy (cal/mole)
O-H	**451**	**Double bonds**	
H-H	**435**	**C=O**	**712**
P-O	**419**	**C=N**	**815**
C-H	**414**	**C=C**	**611**
N-H	**388**	**P=O**	**502**
C-O	**352**		
CC	**348**	**C/C**	**815**
S-H	**338**	**N/N**	**930**
C-N	**223**		
N-O	**222**		

Dissociation constants and Acid-Base chemistry

The place to start is with water, H_2O. Water undergoes a small amount of ionization forming H^+ and OH^- ions. This is shown by the expression below:

H_2O <=====> $H^+ + OH^-$

This equation holds for not only water but for all solutions. The concentrations of reactants and products:

A+B<=====> C+D

The values for A, B, C, and D are fixed at a particular temperature and so they can be defined by a constant referred to as the equilibrium constant K_{eq}. Returning to water we can define its equilibrium constant as:

$$K_{eq} = \frac{[H^+][OH^-]}{[H_2O]}$$

Water exists primarily as H_2O and only 1 molecule in 10,000,000 (1 x 10^7) dissociate into its corresponding ions $[H^+] + [OH^-]$ at 25°C. If we calculate the molarity of water we find that it is 1000/18 i.e. a liter of water weighs 1000g/lit and the molecular weight of water is 18g/m. So if we divide 1000g/lit by 18g/m we get 55.8 moles/lit, usually written as 55.8M were M (molar) means moles per liter. The K_{eq} can be determined experimentally by measuring the current in pure water where we assume that all of the electro-conductivity results from the presence of H+ and OH- ions. This number is 1.8 x 10^{-16}. Now we can calculate the concentrations of H+ and OH- in pure water at 25°C:

$$(55.8\ M)(1.8 \times 10^{-16}\ M) = [H^+][OH^-]$$

$$1 \times 10^{-14}\ M^2 = [H^+][OH^-]$$

So the product of $[H^+][OH^-]$ is 1×10^{-14} M. This is referred to as neutral pH. Furthermore the concentrations of H^+ and OH^- ions are equal. This means that we can rewrite this as:

$$[H^+][OH^-] = [H^+]^2$$

in other words.

$$[H^+] = \sqrt{1.0 \times 10^{-14}\ M^2}$$

$$[H^+] = [OH^-] = 1 \times 10^{-7}\ M = K_w$$

This is also referred to as K_w or the ionization constant of water. From this we can go on to determine the concentration of H^+ in any aqueous solution. For this we use pH. This term is just a simplified way of expressing the hydrogen ion concentration as:

$$pH = \log \frac{1}{[H^+]} = -\log [H^+]$$

From this equation we substitute 1×10^{-7} for $[H^+]$ and we get

$$pH = \log \frac{1}{1 \times 10^{-7}} = \log [1 \times 10^7] = \log 1 + \log 7 = \mathbf{7}$$

Thus, the pH of water is 7.

Now let's consider the case of weak acids and bases or the dissociation of biological molecules into there ionic forms (e.g. amino acids). An acid is any substance that can donate a hydrogen ion. A base is any substance that can accept a hydrogen ion. A weak acid or base is defined as an acid which does not completely dissociate in solution. In any acid base reaction the there is a proton donor and a proton acceptor. Making the **conjugate acid-base pair**. This is written as

$$HA + H_2O \Longleftarrow\!\!=\!\!=\!\!\Longrightarrow H_3O^+ + A^-$$

For a weak acid the level of H^+ in solution is defined by the equilibrium constant, K_{eq} which is also called the dissociation constant when referring to acids and bases K_a. As with water we can refer to this as pK_a. The dissociation constants of several weak acids and there pK_a values are listed in the table on the next slide.

$$Ka = \frac{[H_3O^{+}][A^-]}{[HA][H_2O]} \qquad Ka[H_2O] = \frac{[H_3O^{+}][A^-]}{[HA]} \qquad pK = -\log K$$

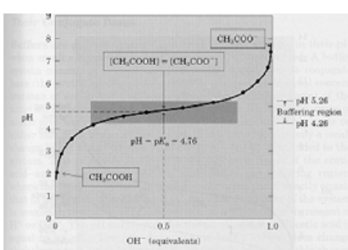
Table of weak acids

Table 4–7 Dissociation constant and pK_a of some common weak acids (proton donors) at 25 °C

Acid	K_a (M)	pK_a
HCOOH (formic acid)	1.78×10^{-4}	3.75
CH_3COOH (acetic acid)	1.74×10^{-5}	4.76
CH_3CH_2COOH (propionic acid)	1.35×10^{-5}	4.87
$CH_3CH(OH)COOH$ (lactic acid)	1.38×10^{-4}	3.86
H_3PO_4 (phosphoric acid)	7.25×10^{-3}	2.14
$H_2PO_4^-$ (dihydrogen phosphate)	1.38×10^{-7}	6.86
HPO_4^{2-} (monohydrogen phosphate)	3.98×10^{-13}	12.4
H_2CO_3 (carbonic acid)	1.70×10^{-4}	3.77
HCO_3^- (bicarbonate)	6.31×10^{-11}	10.2
NH_4^+ (ammonium)	5.62×10^{-10}	9.25

Titration of weak acids and bases

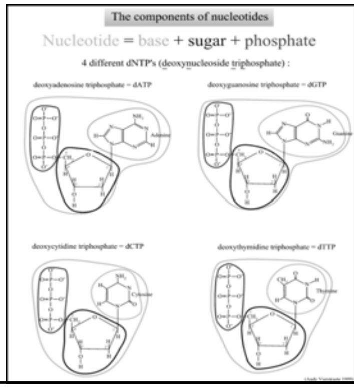
To determine the concentration of acid $[H^+]$ in a weak acid such as acetic acid CH_3COOH, we can do a titration. This is done by adding a strong base (e.g. NaOH) of a known concentration to a weak acid also of a known concentration and measuring when the pH reaches neutral, that is when all of the H^+ have been associated with the OH^- ions of the NaOH forming water H_2O and the only H^+ are from water so the pH is 7.



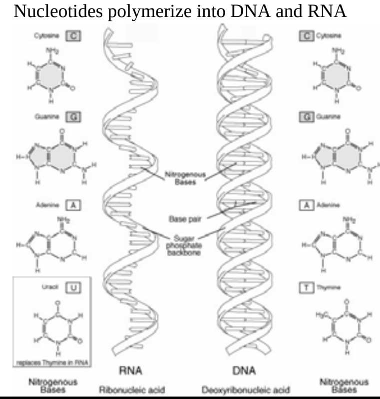
Biomolecules

- Many biomolecules are synthesized from smaller molecules. Such molecules are called polymers. They include:
- DNA and RNA both polymers or nucleotides
- Proteins are polymers of amino acids
- Lipids are polymers of fatty acids
- Polysaccharides are polymers of sugars.

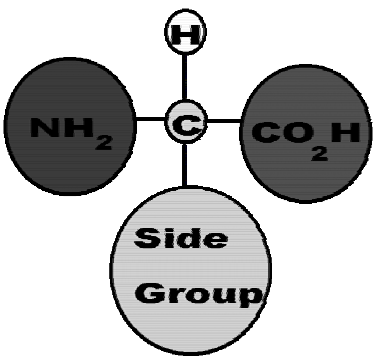
DNA and RNA



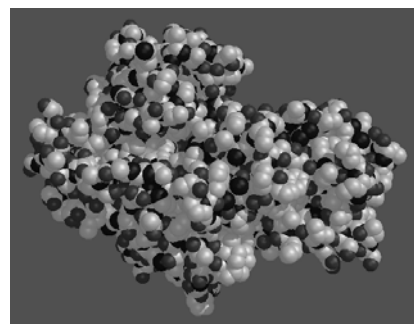
Nucleotides polymerize into DNA and RNA



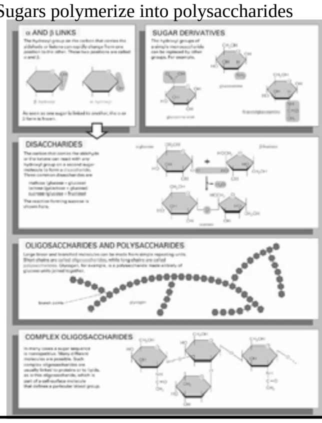
Amino acids



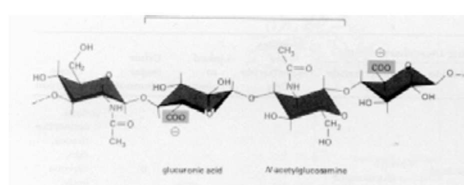
Amino acids polymerize into proteins



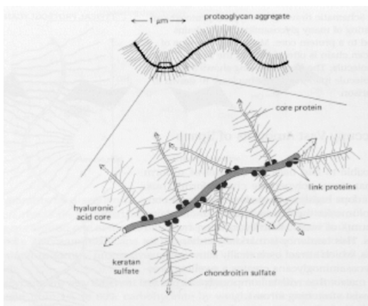
Sugars polymerize into polysaccharides



A major form of polysaccharide found in the extracellular matrix is hyaluronic acid shown below



This glycosaminoglycan can contain hundreds of repeating units. They can further combine with proteins to form proteoglycans where a multiple glycosaminoglycans attach to a core protein. These structures can be massive. One called aggrecan is found in cartilage can be on the order of 3 million molecular weight and be the size of a bacteria.



Chemical bonds are of three basic types. Covalent bonds made between two identical molecules such as C-C then both hold onto the electrons equally and the bond is nonpolar. If a bond forms between molecules of different electronegativity then one molecule has a greater affinity for the electrons and polarized and thus more reactive. When a bond forms between atoms of greatly different electronegativities then the bond is easily lost as one atom readily gives up the shared electrons to the other such as in a salt.

Table 3–4 The electronegativities of some elements

Element	Electronegativity*
F	4.0
O	3.5
Cl	3.0
N	3.0
Br	2.8
S	2.5
C	2.5
I	2.5
Se	2.4
P	2.1
H	2.1
Cu	1.9
Fe	1.8
Co	1.8
Ni	1.8
Mo	1.8
Zn	1.6
Mn	1.5
Mg	1.2
Ca	1.0
Li	1.0
Na	0.9
K	0.8

* The higher the number, the more electronegative is the element.