CMB311

Fall 2017

Lecture 1 Notes

For the record, here is the practical information:

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This lecture introduced the course, providing a context in which all subsequent topics will be discussed.

I. What is Biochemistry?

Definition: Biochemistry is the study of the chemical processes that occur inside the cell, as well as the structure, function and biosynthesis of the macromolecules responsible for these processes.

The chemical processes inside the cell include:

- metabolism
- transport of materials into (ions, nutrients) and out of (ions, waste products) the cell
- energy production
- information processing; biosynthesis of DNA, RNA and Proteins

The structure and function of macromolecules

- Nucleic Acids (DNA and RNA)
- Proteins
- Membranes (technically, these are not macromolecules, but large associations of lipids that serve to compartmentalize cells and provide a barrier between the cytoplasm (inside) and the outside of the cell)
- Polysaccharides (polymers of sugars, used primarily as energy stores)

Only a handful of chemical elements found in the periodic table are central to Biochemistry. These are C (carbon), N (nitrogen), O (oxygen), P (phosphorus), S (sulfur) and H (hydrogen). There are of course other elements found in trace amounts, including Fe (iron), Na (sodium), K (potassium), Se (selenium) and so on, but macromolecules and other important biomolecules (carbohydrates, lipids, amino acids, etc.,) are composed of C, N, O, P, S and H. C is especially central; biochemistry is organic chemistry.

Biochemistry uses organic molecules because of carbon's special chemical properties.

- forms stable C-C single bonds

- forms stable bonds with other elements
- forms C=C double bonds, C=N double bonds
- has tetrahedral bonding geometry
- forms long chains and branched molecules; non-biological examples include diamond, graphite, fullerenes

Biomolecules combine carbon with other elements, including oxygen, nitrogen, phosphorus, sulfur and hydrogen to form a wide range of complex molecules. These are then combined in various arrangements to produce extremely large and incredibly complex polymers called macromolecules. Some of these polymers then combine in various arrangements to produce enormous multi-component complexes with molecular weights in the millions (vs. the mass of a hydrogen atom of 1). Some macromolecules then go on to carry out a vast array of biochemical reactions, otherwise known as metabolism. At first glance, making sense of all this seems a hopeless task...

II. The Logic of Biochemistry

Fortunately, there is actually logic to biochemistry. Macromolecules are actually polymers (from the ancient Greek πολυς+ μερος, or many + parts) built up from smaller units called monomers (μονος + μερος, or single + part). Thus, becoming familiar with a relatively limited number of molecules allows one to understand the principles that determine the structure of all macromolecules.

- amino acids are linked together to form proteins
- nucleotides are linked together to form nucleic acids (DNA and RNA)
- monosaccharides are linked together to form polysaccharides (starch, glycogen)
- lipids associate (non-covalently) to form membrane structures

As we will see later on in the course, there is a limited set of organic reactions that comprise metabolic pathways. We will focus on both the principles and the particular details of these pathways.

III. Life is unified by a common Biochemistry

All life is related, meaning all living things share a common ancestry. Based on gene sequences, we now know that all life can be classified into three Domains.

- Bacteria: Single-celled microbes. Represent the majority of Earth's biomass. Very diverse metabolically.
- Archaea: Once thought to be bacteria, these single-celled microbes superficially resemble bacteria, but phylogenetically are actually more closely related to Eukaryotes.
- Eukaryotes: Characterized by complex cellular structures with a membrane-bound nucleus, distinct mitochondria, chloroplasts (plants). Some are multicellular (like us).

At first glance, it's hard to see any similarity among animals, protists, plants and bacteria, but these differences begin to disappear as we dig deeper towards the cellular and molecular level. At the cellular level, plants and animals don't look nearly so distinct. At the molecular level, all life looks pretty much the same. That's because the molecular processes common to all life have not dramatically changed since the divergence from our last common ancestor. One advantage for us is that it allows us to draw broad conclusions based on studying a few species. Bacteria are especially useful in this regard.

Inside a typical bacterial cell (*E. coli*) macromolecules are found in the following proportions:

- Protein 55.0%
- RNA 20.5%
- DNA 3.1%
- Lipid 9.1%
- Glycogen 2.5%

Proteins are by far the most abundant macromolecules. They are responsible for providing the cell with its structure, for carrying out metabolism as enzymes, for binding to DNA to control gene expression, for transporting material into and out of the cell, and for cell motility (movement). Nucleic Acids (DNA and RNA) are involved in gene expression and heredity. Note that RNA is far more abundant than DNA, and most of this is in ribosomes, which are the factories for making proteins.

How are these macromolecules produced? This is illustrated in the 'Central Dogma of Molecular Biology'.

- DNA serves as the template for its own synthesis (Replication)
- DNA serves as the template for RNA synthesis (Transcription)
- RNA serves as the template for Protein synthesis (Translation)

Also...

- RNA can serve as the template for DNA synthesis (Reverse Transcription)
- RNA can serve as the template for its own synthesis (RNA Replication)

But...

- There is no known way for protein to act as a template for macromolecular synthesis

It is worth expanding this framework to include metabolism (the second section of the course). Metabolism provides the cell with energy, and makes the precursors (monomers) used to build the macromolecules. So, to reiterate, all life is unified by a common biochemistry, and this is evident in the similarity in all organisms of macromolecules and the biochemical pathways used for energy and biosynthesis...

IV. How did all this biochemistry stuff evolve?

Obviously, we can look at fossils of animals and reconstruct some evolutionary history, but as we go back in time, there are not traces to tell us what happened at the very earliest stages in the evolution of life.

First of all, can we even ask this question, or is there something fundamentally impenetrable about this most fundamental aspect of biology? In 1828 Friedrich Wöhler succeeded in synthesizing urea, which had at that time only been known to occur as a result of biological processes. This synthesis ruled out the idea of some 'vital force' in biology, George Lucas notwithstanding. This meant that understanding biology in terms of physics and chemistry should be possible.

In 1953, Stanley Miller combined gases that were expected to be present in the primitive Earth atmosphere (methane, ammonia, and hydrogen) and added energy in the form of an electric discharge (simulating lightning). This produced many precursors to macromolecules. This suggested that life could arise by natural processes. However, making *macro*molecules in a laboratory is a big challenge.