Chem 352 - Lecture 1
Introduction to Biochemistry

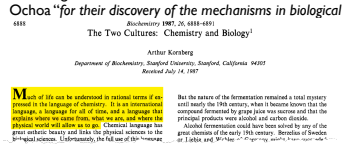
Question for the Day: *What characteristics distinguishes a living systems, such as yourself, from a non-living system?*

1

Introduction

"*Much of life [bio] can be understood in rational terms if expressed in the language of chemistry. It is an international language, a language for all time, and a language that explains where we came from, what we are, and where the physical world will allow us to go.*" Arthur Kornberg, 1987.

- Kornberg shared the 1959 Nobel Prize with Severo Ochoa "*for their discovery of the mechanisms in biological*


6888 *Biochemistry* **1987**, *26*, 6888–6891

The Two Cultures: Chemistry and Biology[1]

Arthur Kornberg

Department of Biochemistry, Stanford University, Stanford, California 94305
Received July 14, 1987

Much of life can be understood in rational terms if expressed in the language of chemistry. It is an international language, a language for all of time, and a language that explains where we came from, what we are, and where the physical world will allow us to go. Chemical language has great esthetic beauty and links the physical sciences to the [illegible] sciences. Unfortunately, the full use of this language

But the nature of the fermentation remained a total mystery until nearly the 19th century, when it became known that the compound fermented by grape juice was sucrose and that the principal products were alcohol and carbon dioxide.

Alcohol fermentation could have been solved by any of the great chemists of the early 19th century. Berzelius of Sweden or Liebig and Wöhler of [illegible]

2

Introduction

The language of biochemistry

- ***Words***: Chemical names and structures
- ***Sentences***: Chemical reactions
  - ***Subjects***: Reactants
  - ***Predicate***: Products
  - ***Verbs***: Enzymes (the biological catalysts)
- ***Paragraphs***: Metabolic Pathways

Interactive Metabolic Map

- http://www.metabolic-pathway.com/fullMap.html

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The Origins of Biochemistry

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The Science of Biochemistry

The Origins of Biochemistry

- For over 8,000 years humans have made use of fermentation as a way of preserving dietary calories.
  - When fermentation is carried out by the fungus yeast, sugar is converted to CO_2 and ethanol (bread, beer, wine)
  - When fermentation is carried out by certain bacteria, sugar is converted to lactic acid (yogurt), or acetic acid (vinegar).

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The Science of Biochemistry

The Origins of Biochemistry

- ***Concept:*** *Early biochemists had to confront the doctrine of* ***vitalism****, which claimed that living matter and nonliving matter were fundamentally different.*
- Vitalism posited that only *living organisms* can make *organic molecules*.
  - It argued the living organisms were able to do this because they possessed a special "life force".
- It was Friedrich Wöhler who demonstrated that a special "life force" was not necessary to the organic molecule urea.

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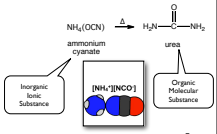
The Science of Biochemistry

The Origins of Biochemistry

- Friedrich Wöhler (1800-1882) is credited with challenging this doctrine in 1828 when he carried out a simple experiment showing that the *organic* molecule, **urea**, could be synthesized from an *inorganic* salt, **ammonium cyanate**



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The Science of Biochemistry

The Origins of Biochemistry

- Additional evidence was provided by the brothers, Eduard and Hans Buchner.
- They studied yeasts ability to ferment sugar into CO_2 and ethanol.
- Eduard (1860-1917) and Hans (1850-1902) Buchner were able to show that living yeast cells were not required for alcohol fermentation.
  - Extracts from dead yeast cells could also carry out fermentation of sugars.

Nobel Prize 1907

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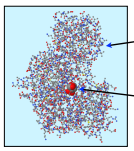
The Science of Biochemistry

The Origins of Biochemistry

- In the late 1800's it was recognized that catalysts were responsible for fermentation.
  - These catalysts were named ***enzymes***
  - In the early 1900's it was shown that enzymes were large protein molecules.



Hexokinase
the enzyme that catalyzes the first reaction in glycolysis and fermentation pathways.
Molecular weight = 49,600 g/mol

Glucose
a sugar that is the reactant for the reaction catalyzed by hexokinase
Molecular weight = 180 g/mol

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The Science of Biochemistry

The Origins of Biochemistry

- Also in the late 1800's Gregor Mendel demonstrated that the different traits displayed by organisms were due to inheritable elements.
  - These elements became known as ***genes***
- In the early 1900's, genes were discover to be associated with cellular structures called ***chromosomes***, which are composed of both proteins and nucleic acids.
  - At first it was believed that the genetic information of genes was stored in the protein portion of the chromosome.

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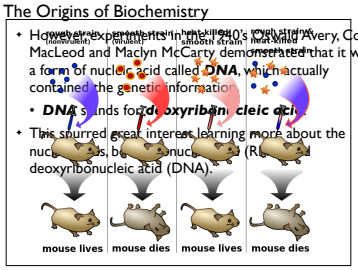
The Science of Biochemistry

The Origins of Biochemistry

- However experiments in the 1940's by Oswald Avery, Colin MacLeod and Maclyn McCarty demonstrated that it was a form of nucleic acid called ***DNA***, which actually contained the genetic information.
  - ***DNA*** stands for ***deoxyribonucleic acid***
- This spurred great interest in learning more about the nucleic acids, both ribonucleic acid (RNA) and deoxyribonucleic acid (DNA).



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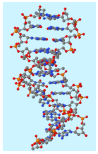
The Science of Biochemistry

The Origins of Biochemistry

- ***Concept:*** *Biology was transformed in 1953, when James Watson and Francis Crick proposed the double-helical model for DNA structure.*

James Watson (1928-)
Francis Crick (1916-2004)

Nobel Prize 1962



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The Science of Biochemistry

The Origins of Biochemistry

- Watson and Crick's model gained almost immediate acceptance because of its ability to explain how genetics information could be replicated and passed down to the next generation.

MOLECULAR STRUCTURE OF NUCLEIC ACIDS

A Structure for Deoxyribose Nucleic Acid

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The Science of Biochemistry

The Origins of Biochemistry

- Since 1953
  - The role of RNA in gene expression
  - Deciphering the genetic code
  - Recombinant DNA technology and gene splicing
  - Control and modification of gene expression
  - The sequencing of the entire human genome
  - Discovery of additional roles for RNA
  - CRISPR technology and gene editing

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The Science of Biochemistry

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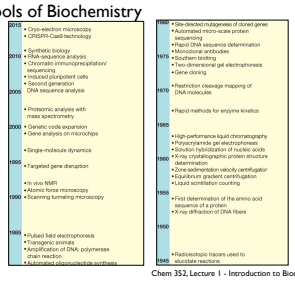
The Science of Biochemistry

The Tools of Biochemistry



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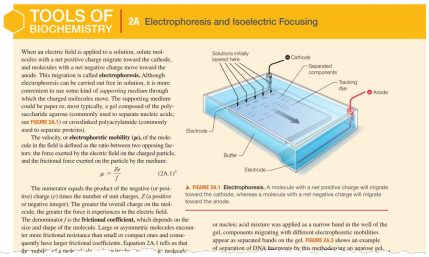
The Science of Biochemistry

The Tools of Biochemistry



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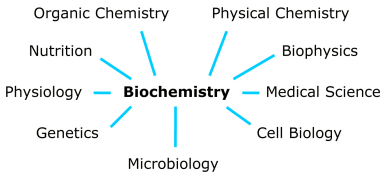
The Science of Biochemistry

Biochemistry as a discipline relies on a number of other disciplines, which makes it very interdisciplinary.



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The Elements and Molecules of Living Systems

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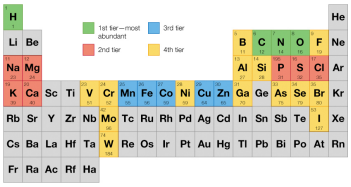
Elements and Molecules of Living Systems

The Chemical Elements of Cells and Organisms

- ***Concept:*** *Life depends primarily on a few elements (C, H, O, N, S and P), although many others have essential functions as well.*



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Elements and Molecules of Living Systems

The Origin of Biomolecules and Cells

- Before life was formed on earth the atmosphere was likely a reducing one that containing little oxygen.
- Stanley Miller demonstrated in 1953 that certain building blocks of complex biomolecules, such as amino acids, could have been produced under these conditions
  - He combined methane, ammonia, hydrogen, water in a closed container and exposed it to electrical discharges.

Video:
- The Miller-Urey Experiment Explained

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Elements and Molecules of Living Systems

The Origin of Biomolecules and Cells

- Even though the theory of evolution can explain how more complex life forms evolved from simpler ones, it does not explain how cells, as the basic unit of living systems, first formed.
- Many biochemists, however, believe that ancient cells used ribonucleic acid (RNA) to carry out the roles that both DNA and proteins now play in living cells.
  - That time in our history is often referred to as the"RNA World"

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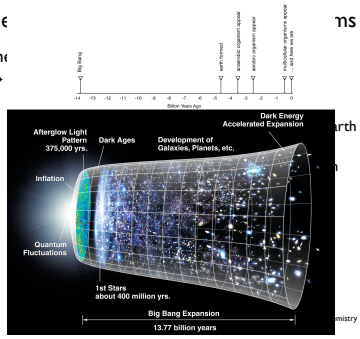

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Elements and Molecules of Living Systems

The Complexity and Size of Biological Molecules

- The complexity and size of biological molecules is very wide-ranging.
- When referencing the size of a single biological molecule we will use the unit of mass called a Dalton (Da)
  - If a mole (6.02×10^{23}) of carbon-12 atoms weighs 12 g, then one carbon atom weighs 12 Da.
  - If a mole of a particular protein weighs 49,212 g, then one molecule of that protein weighs 49,212 Da

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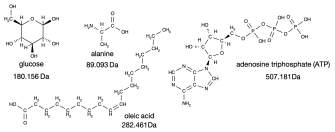
Elements and Molecules of Living Systems

The Complexity and Size of Biological Molecules

- The smaller sized molecules, often referred to as ***metabolites***, include sugars, amino acids, fatty acids and nucleotides.



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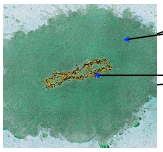
Elements and Molecules of Living Systems

The Complexity and Size of Biological Molecules

- At the other end of the spectrum are the biological ***macromolecules***.
  - Proteins (7,000 Da → 1million Da)
  - Nucleic acids (→ 20 billion Da)



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Elements and Molecules of Living Systems

The Biopolymers: Proteins, Nucleic Acids, and Carbohydrates

- ***Concept:*** *Cells use a modular approach for constructing large molecules*
- The good news is that the biological macromolecules are ***polymers***.
  - This means that they are made by joining small molecules called ***monomers*** together, much like beads on a string.
  - When all of the monomers are the same, the result is called a ***homopolymers***.
  - When different monomers are used, the result is called a ***heteropolymer***.
  - Polymers can be either ***linear*** or ***branched***.

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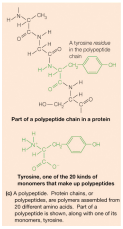
Elements and Molecules of Living

The Biopolymers: Proteins, Nucleic Acids, and Carbohydrates

- **Proteins** are ***linear heteropolymers*** of amino acid monomers.



(a) A polypeptide. Protein chains, or polypeptides, are polymers assembled from 20 different amino acids. Part of a polypeptide is shown, along with one of its monomers, tyrosine.

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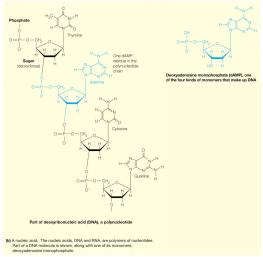
Elements and Molecules of Living

The Biopolymers: Proteins, Nucleic Acids, and Carbohydrates

- **Nucleic** acids are ***linear heteropolymers*** of nucleotide monomers.



(b) A nucleic acid. The nucleic acids, DNA and RNA, are polymers of nucleotides. Part of a DNA molecule is shown, along with one of its monomers, deoxyadenosine monophosphate.

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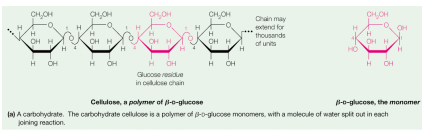
Elements and Molecules of Living

The Biopolymers: Proteins, Nucleic Acids, and Carbohydrates

- **Polysaccharides**, which are a form of carbohydrate, and they can be either ***linear*** or ***branched homopolymers*** or ***heteropolymers*** of monosaccharide monomers



(a) A carbohydrate. The carbohydrate cellulose is a polymer of β-D-glucose monomers, with a molecule of water split out in each joining reaction.

Cellulose is a linear homopolymer of glucose monomers

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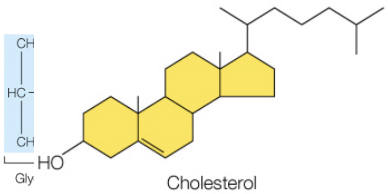
Elements and Molecules of Living Systems

Lipids



(a) A ... rated

fa**(c)** *Cholesterol*, a sterol

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Elements and Molecules of Living Systems

Lipids and Membranes

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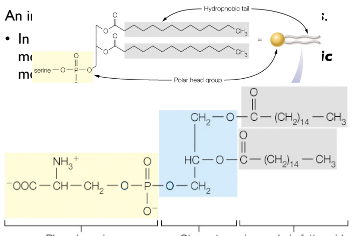

(b) A phospholipid *(phosphatidylserine)*

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Distinguishing Characteristics of Living System

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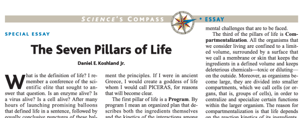
Characteristics of Living Systems

Concept: *Life depends on creating and duplicating order in a chaotic environment. This ordering requires energy.*

- In 2002, the American biochemist Daniel Koshland summarized the essential attributes that distinguish living systems from nonliving things.


SCIENCE'S COMPASS • ESSAY

SPECIAL ESSAY

The Seven Pillars of Life

Daniel E. Koshland Jr.

What is the definition of life? I remember a conference of the scientific elite that sought to answer that question. Is an enzyme alive? Is a virus alive? Is a cell alive? After many hours of launching promising balloons that defined life in a sentence, followed by equally conclusive punctures of these bal-

ment the principles. If I were in ancient Greece, I would create a goddess of life whom I would call PICERAS, for reasons that will become clear.

The first pillar of life is a **Program**. By program I mean an organized plan that describes both the ingredients themselves and the kinetics of the interactions among

mental challenges that are to be faced.

The third of the pillars of life is **Compartmentalization**. All the organisms that we consider living are confined to a limited volume, surrounded by a surface that we call a membrane or skin that keeps the ingredients in a defined volume and keeps deleterious chemicals—toxic or diluting—on the outside. Moreover, as organisms become large, they are divided into smaller compartments, which we call cells (or organs, that is, groups of cells), in order to centralize and specialize certain functions within the larger organism. The reason for compartmentalization is that life depends on the reaction kinetics of its ingredients,

(Koshland, D.E. **2002**, "The Seven Pillars of Life", Science 295, 2215-2216)

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Characteristics of Living Systems

1. ***A program*** (organized plan for constitution and regeneration; DNA)
2. ***Improvisation*** (changing the program as surroundings change; evolution)
3. ***Compartmentation*** (ability to be separate from environment; membranes)
4. ***Energy*** (ability to maintain order despite overall positive entropy)
5. ***Regeneration*** (compensation for environmental wear and tear; repair)
6. ***Adaptability*** (ability to respond to environmental changes)
7. ***Seclusion*** (operation of processes and pathways in isolation)

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The Cell

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The Cell

Concept:

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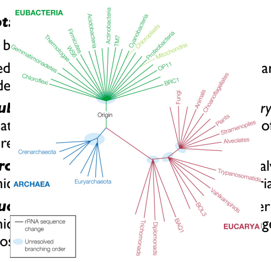

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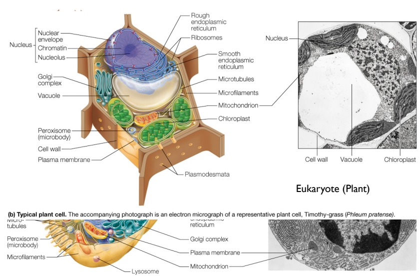
The Cell



Eukaryote (Plant)

(b) Typical plant cell. The accompanying photograph is an electron micrograph of a representative plant cell, Timothy-grass (*Phleum pratense*).

(a) Typical animal cell. The accompanying photograph is an electron micrograph of a representative animal cell, a white blood cell.

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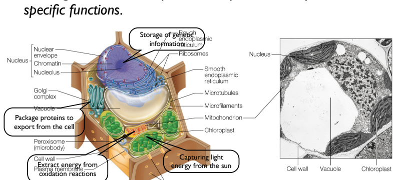
The Cell

- ***Concept:*** *A Eukaryote cell can are thought of as a factory, with organelles and compartments specialized to perform specific functions.*



Eukaryote (Plant)

(b) Typical plant cell. The accompanying photograph is an electron micrograph of a representative plant cell, Timothy-grass (*Phleum pratense*).

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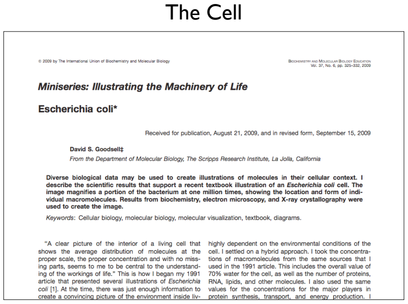
The Cell



BIOCHEMISTRY AND MOLECULAR BIOLOGY EDUCATION
Vol. 37, No. 6, pp. 325–332, 2009

Miniseries: Illustrating the Machinery of Life

Escherichia coli*

Received for publication, August 21, 2009, and in revised form, September 15, 2009

David S. Goodsell‡
From the Department of Molecular Biology, The Scripps Research Institute, La Jolla, California

Diverse biological data may be used to create illustrations of molecules in their cellular context. I describe the scientific results that support a recent textbook illustration of an *Escherichia coli* cell. The image magnifies a portion of the bacterium at one million times, showing the location and form of individual macromolecules. Results from biochemistry, electron microscopy, and X-ray crystallography were used to create the image.

Keywords: Cellular biology, molecular biology, molecular visualization, textbook, diagrams.

"A clear picture of the interior of a living cell that shows the average distribution of molecules at the proper scale, the proper concentration and with no missing parts, seems to me to be central to the understanding of the workings of life." This is how I began my 1991 article that presented several illustrations of *Escherichia coli* [1]. At the time, there was just enough information to create a convincing picture of the environment inside liv-

highly dependent on the environmental conditions of the cell. I settled on a hybrid approach. I took the concentrations of macromolecules from the same sources that I used in the 1991 article. This includes the overall value of 70% water for the cell, as well as the number of proteins, RNA, lipids, and other molecules. I also used the same values for the concentrations for the major players in protein synthesis, transport, and energy production. I

The Information Explosion

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The Information Explosion

Concept: *Much of today's biochemistry looks at the cell globally, attempting to understand its functions in terms of the cooperative expression of genes.*

- New scientific tools and techniques are being developed and used to generate and analyze increasing amount of biochemical and molecular biological information.
- ***Bioinformatics*** is the discipline that applies the tools of information science to biology.
  - Examples include,
    - Mathematical analyses of DNA sequence data
    - Computer simulations of metabolic pathways
    - Structure-based drug design through the structural analysis of potential drug targets (enzymes or receptors)

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The Information Explosion

- ***Omics*** are novel, comprehensive approaches for analysis of complete genetic and molecular profiles of humans and other organisms.
  - For example
    - *genetics*, an approach that focuses on studying ls single genes, whereas,
    - *gen**omics*** focuses on all genes (genomes) and their inter-relationships.

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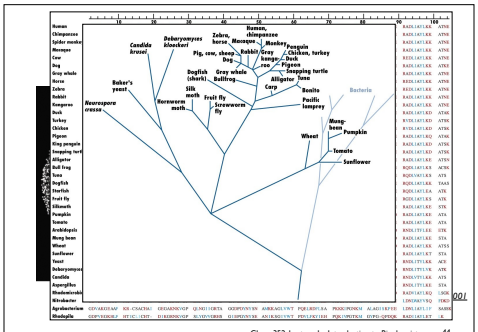

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The Information Explosion

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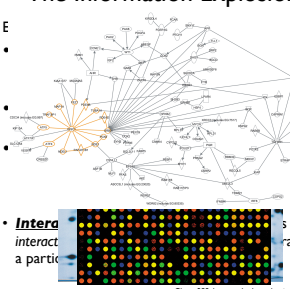

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Chapter 1 Summary

- The aim of biochemistry is to understand and explain living systems in molecular terms.
- Biochemistry bridges biological and chemical sciences by focusing at the molecular level on what happens in living systems.
- Living systems are composed of cells, which can be divided into three major types: bacterial, archaeal, and eukaryotic.
- Biochemistry is an experimental science and uses a variety of different tools and techniques, some of which generate large amount of information.

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Up Next

Lecture 2 - Weak interactions in an aqueous environment

- Noncovalent interactions
- Role of water in biological processes
- Acid-Base Equilibrium
- Interactions between macro-ions in solution

Reading

- Chapter 2 of Appling *et al.*

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