Day 1: genetics, DNA
Day 2: proteins, signaling
Biology: the scientific study of living things ("organisms")

- composed of cell/s
- manipulate energy
- reproduce
- respond to environment
- adapt to environment
- grow and develop

Topics we will cover:

Today:
- Genetics
- DNA

Tomorrow:
- Proteins
- Signaling
Genetics
(Mendel, peas)

Inheritance
(chromosomes, mitosis/meiosis)

DNA
(definition, structure)

Central dogma
(replication, transcription, translation)

Replication
(DNA → DNA)

Transcription
(DNA → RNA)

Translation
(RNA → Protein)

Proteins
(amino acids, folding)

Signal Transduction
Gregor Mendel, “father of modern genetics”, 1822-1884

Laws of Mendelian inheritance:
Inheritance of traits in pea plants follow particular patterns.

Why peas?
Easy to grow, variety in shape/size/color, control of reproduction

seed shape  seed color  pod color  pod shape  flower color  flower position  stem length

Mendel’s first law: law of segregation

Each individual has two alleles for each characteristic, which segregate during gamete (sperm/egg) formation and unite during fertilization.
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DNA and inheritance

Contains the genetic instructions for all living organisms. Located in the nucleus of each cell.

In the nucleus, the DNA is arranged in chromosomes

23 \times 2 = 46 chromosomes

diploid: 2n
Haploid: n
Gametes

Meiosis

Mitosis
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DNA: in the beginning..

1928  Griffith’s experiment: transformation

1944  Avery, McCarty, MacLeod
DNA is the material transformed

1953  Watson and Crick, Rosalind Franklin
Discover the molecular structure of DNA
DNA structure

Double helix

A C G T nucleotides (4*10^9)

A - T
C - G

DNA = deoxyribonucleic acid
Each nucleotide is composed of a sugar, a phosphate and a base. The base determines the type of nucleotide
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Signal Transduction
Central dogma of molecular biology

The normal flow of biological information

**Replication**  DNA → DNA
during cell division

**Transcription**  DNA → RNA
copy specific segment
in DNA (=gene)

**Translation**  RNA → PROTEIN
translate information in
gene into a protein
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DNA replication

DNA is precisely replicated during cell division

Semi-conservative replication
DNA strands are complementary – each strand serves as a template for a new strand

DNA polymerase catalyzes polymerization of nucleotides into new DNA
Needs a primer
Accuracy: 1 pairing mistake per $10^9$ nucleotides, proofreading mechanisms
Additional players in replication process:

Helicase separates DNA strands to start replication
Primase catalyzes the synthesis of the primer
SSB (single strand binding proteins), protect the single strand DNA from premature annealing
Topoisomerase regulate DNA over/under winding

and more...

http://www.uic.edu/classes/phar/phar331/lecture4/
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   - Proteins
     (amino acids, folding)

   - Signal Transduction
Transcription

To copy a specific segment of the DNA (gene) to RNA

What is RNA (ribonucleic acid)?

*RNA differs from DNA in:*

(a) Slightly different structure

(b) Uracyl instead of Thymine  
(nucleotides A C U G)

(c) One strand

(d) Can fold and therefore perform catalytic functions
During transcription, the DNA opens up at a specific place (the gene)
One of the DNA strands serves as a template for RNA synthesis
mRNA is created

RNA polymerase performs transcription
Differs from DNA polymerase:
(a) Does not need a primer
(b) Uses U instead of T
(c) Accuracy: 1 mistake in $10^4$ nucleotides, proofreading by RNA polymerase itself
Alternative splicing

Discovered in 1977, only in eukaryotes
Number of genes in humans is less than expected - only ~25,000 genes

Gene includes:
Exons (expressed sequences) coding segments
Introns (intervening sequences) taken out of mRNA

Different combinations of exons create different mRNA
Thank you
Biology for Engineers (day 2)

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Transcription

**Gene**

DNA copying DNA in nucleus

**mRNA**

mRNA being translated

**Cytoplasm**

- Free amino acids
- tRNA bringing amino acid to Ribosome
- Ribosome incorporating amino acids into the growing protein chain

**Ribosome**
Translation

mRNA → protein
Translation of the information in mRNA (nucleotides) to protein (amino acids)

**Genetic code**: translation of nucleotides (A,C,G,U) to amino acids (X20) universal for all organisms

3 nucleotides (codon) = 1 amino acid
4 X 4 X 4 = 64 options,
Only 20 amino acids → redundancy

http://en.wikipedia.org/wiki/Genetic_code
http://www.nature.com/scitable/topicpage/the-information-in-dna-determines-cellular-function-6523228
**tRNA (transfer RNA)**

80bp long RNA molecule

Identification between codon and amino acid
Amino acid side – binds the amino acid
Anti codon side – binds the codon

Anti codon side is complementary to the codon in the mRNA

The wobble position (3rd nucleotide in codon) enables tRNA binding to more than one codon
Ribosome: translation “factory”, ensures the correct reading frame, 1 mistake in 1000 amino acids

3 steps in translation:
1) Initiation – start codon (AUG = Met)
2) Elongation – growing peptide chain
3) Termination – stop codon (UAA, UAG, UGA)
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Signal Transduction
Protein building blocks: amino acids

There are 20 amino acids
A protein is a chain of amino acid
(peptide: connected by peptide bonds)

Different amino acid properties:
**Peptide folding**

Peptides start folding as soon as they detach from the ribosome. Exposure of hydrophobic amino acids leads to aggregation and ultimately cell death.

A folded peptide is:
(a) Energetically stable
(b) Smaller volume, function
(c) Hydrophobic amino acids are protected

*Chaperones* assist with peptide folding by preventing peptide aggregation into non-functional structures.
Protein folding

- **Primary amino acid sequence**
- **Secondary sub structures**
  - Alpha helix
  - Beta sheets
- **Tertiary 3D structures**
- **Quaternary complex of proteins**

http://www.macalester.edu/psychology/whathap/UBNRPtse10/prionproteins.html
Example: Hemoglobin

Quaternary structure
Includes 4 globin molecules and 4 Heme groups
Heme group consists of an iron (Fe) atom in a porphyrin ring

Red blood cells contain many hemoglobins

Oxygen from lungs binds to Fe in hemoglobin \(\rightarrow\) Oxyhemoglobin

Oxygen released in tissue from Fe in hemoglobin \(\rightarrow\) Deoxy hemoglobin
Proteomics: study of proteins

What can be asked about proteins?

1) What is their function
   Where are they expressed and in what quantity? (microarray analysis)

2) Does protein structure reflect its function?
   Can secondary/tertiary/quaternary fold structures be predicted? (crystallography, models)
   Can our knowledge of protein structure be used to develop medicine? (CML cure)

3) Which proteins can interact together?
   How can this information be used to learn about different cellular mechanisms?
Microarrays

Measures of expressed genes (mRNA)
Example: microarray analysis of tumors


Cell cycle, invasion and metastasis, angiogenesis

→ Mammaprint, a diagnostic test to assess the risk of breast cancer metastasis
STI571: cure for chronic myeloid leukemia (CML)

In many CML patients, genes from chromosomes 9 and 22 undergo translocation, leading to an aberrant protein (bcr-abl).

STI571 inhibits bcr-abl activation, thus preventing tumor cell proliferation.
**Functions of proteins**

Carry out the processes in cells specified by information encoded in the genes.

**Enzymes:** catalyze chemical reactions (DNA polymerase)

**Structural proteins:** fibrous, provide shape to biological components (actin, tubulin)

**Signaling proteins:** involved in signal transduction (antibodies)
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Signal Transduction
Signal transduction
Example: insulin receptor pathway
A cell responds to outside signals through receptor proteins that bind ligands.

**Types of signaling:**

- **Contact-dependent** (immune cells)
- **paracrine** (growth signals)
- **endocrine** (insulin)
- **autocrine** (T cells)
- **synaptic** (neurons)
- **direct transfer** (gap junction)
Response to signals

A cell receives many signals and may respond to each signal differently.

The type of receptors on the cell determine the signals to which it responds. The same signal can have a different affect on different cell types.
Neuronal signaling

Synapse: signaling point between neurons pass information between the CNS and PNS

Forms at the axon of the signaling neuron and the dendrite of the receiving neuron
Membrane potential:
difference in electrical potential between the inside and outside of the cell,
Caused by concentration gradients and membrane permeability to ions
Neurons at resting state: -70 mV

Action potential:
event in which the electrical membrane potential of a cell rises and falls.

Neuron signaling:
Immune system signaling
The **immune system** is composed of different cell types that protect the body against foreign antigens

**Innate immune response:**
non-specific, first line of defense, activation of adaptive immune response
Adaptive immune response:
Highly specific, recognizes any antigen, capable of memory
Thank you