

## Molecular biology primer

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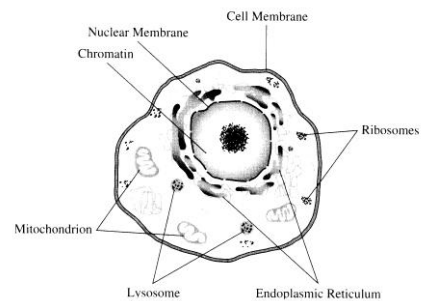
## Background biology

- A very brief introduction to cells, genes, DNA, RNA, and proteins, useful for understanding how the brain works.

## Life inside us: Cells

- The smallest unit considered to be alive
- A membrane-bound sack of proteins, DNA, and other chemicals

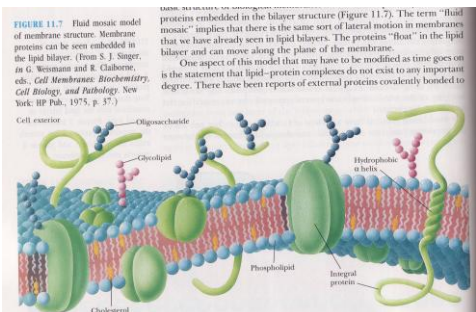
## Animal cell



## Mitochondria

- Convert energy from food into stored form (ATP)
- Sugar + oxygen => water + CO<sub>2</sub>
- Were once free-living organisms
  - Have their own DNA (mDNA)
  - Can duplicate themselves
- mDNA is passed from mother to child, not mixed with nuclear DNA
- Can trace ancestry through mDNA (mitochondrial Eve)

## Cell membrane is a mix of lipid, protein, and sugar molecules



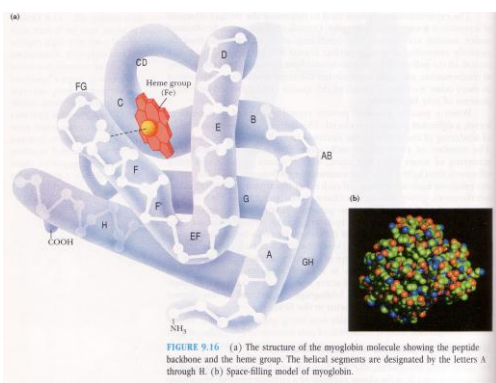
## Proteins

- Proteins are the building blocks of our bodies.
- They make up many of the components of our bodies (muscle, skin, brain), or direct the synthesis of components (bone).

- Some proteins are enzymes that catalyze reactions
  - breaking down the fat and sugar that we eat
  - synthesizing neurotransmitters
- Some proteins are hormones secreted by one cell to affect distant cells
  - the hormones estrogen, testosterone that affect brain development
  - the stress hormone cortisol

- Some proteins are receptors that sense the external environment
  - smell, taste, pain receptors.
- Some proteins are receptors that sense the body's internal environment
  - nerve growth signal receptors
- Some proteins are toxins
  - Neurotoxins in snake venom cause paralysis by blocking nerve transmission

- Proteins are made of different combinations of 20 amino acids.
- The 20 amino acids differ in their size, shape, and chemical properties.
- Think of the amino acids as 20 different shaped Lego pieces that can be put together to make different shaped proteins.
- The particular amino acids that comprise a protein determine its shape and what functions it can perform.

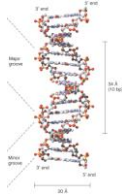


## Most drugs act by

- binding to protein receptors and altering their sensitivity, or
- binding to enzymes (proteins) and blocking their action.

## Genes, chromosomes & DNA

- Our genes are a set of instructions on how to make proteins (plus a few other things).



## Genes

- Genes are located on chromosomes, which are visible in a light microscope.



## Genes are made of DNA

- DNA has four chemical building blocks:
  - A, C, G, and T
- Each letter (A,C,G,T) is called a base or a nucleotide

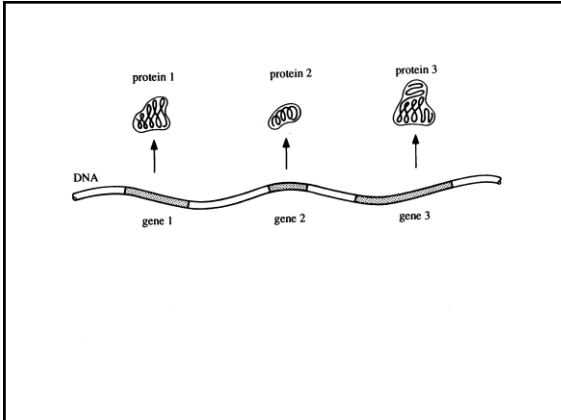
- Letters -> words -> book
- DNA (A,C,G,T) -> genes -> chromosomes

## SNP

- Single Nucleotide Polymorphism
- A single nucleotide difference between two DNA sequences
- One type of mutation

## From DNA to proteins

- A gene contains the code (DNA sequence) for the amino acids that make a protein

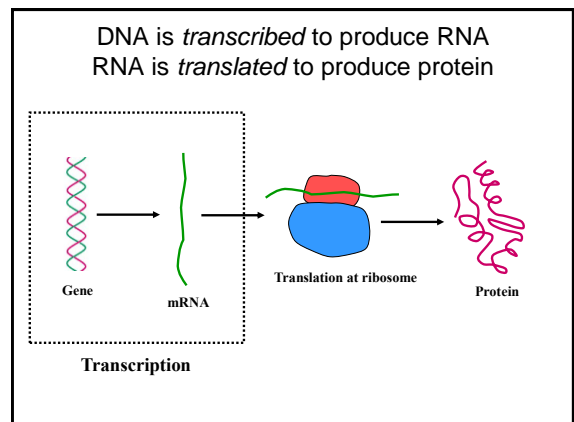


- DNA nucleotide sequences encode specific amino acids :
  - TTA encodes the amino acid Leucine
  - GTA encode the amino acid Valine
- Each amino acid is encoded by specific sequences of 3 nucleotides

- A mutation (such as a SNP) that changes one amino acid into another amino acid will make a small change in the shape of the protein.
- If that protein is a neurotransmitter receptor, it could become less sensitive, meaning that more stimulation is required before it responds.

- A mutation might also change the ability of a drug to bind to that protein, and may change how well the drug works.
- Mutations can cause differences in people's receptors, which in turn cause differences in their responses to drugs and signals from the environment.
- Differences in response to pain medication and anti-depressants may be caused by mutations.

- DNA is *transcribed* to produce RNA
- RNA is *translated* to produce protein
- DNA -> RNA -> protein
- DNA is stable and long-lived
- RNA is quickly degraded in the cell



## Gene expression

- Humans have 30,000 or more genes.
- Many genes encode proteins that perform functions only on a particular tissue, such as in brain, in kidney, or in muscle.
- Most genes are not turned on (expressed) in most tissues.

- A gene must be turned on (expressed) before it produces the corresponding protein.
- We can measure gene expression as a way to estimate how much protein is being produced.

## Measuring gene expression

- Quantitative PCR:
  - A method to measure the expression level (mRNA) of one or a few genes
- Microarrays:
  - A small device used to measure the expression of 10,000 or more genes simultaneously. Less accurate than PCR.



## Two copies of each gene

- Humans (and most other organisms) have two copies of each gene.
  - We get one copy from our mother and one copy from our father.
- Usually the two copies are different (SNPs).
- Sometimes both copies work, sometimes only one copy works, and sometimes neither copy works (leading to recessive diseases such as cystic fibrosis).
- Even when the two copies both work, they may have mutations that alter their relative efficiency.

## Genotype

- Genotype: the DNA sequence of a particular gene for a particular person
- This person's gene may differ from other people's genes because of mutations.
- Each different version of a gene is called an allele.

## Gene knockout

- An animal in which one or both of copies of a gene are deleted (by genetic engineering) is called a knock-out.
- Single knock-out: one copy of the gene
- Double knock-out: both copies deleted

## RNA interference

- The translation of RNA into protein can be prevented by the presence of a complementary (antisense) strand of RNA.
- This process is called RNA interference (RNAi).
- RNAi is similar in effect to a knock-out, but it is easier to control where and when it occurs, and sometimes easier to do.