Genetics 101

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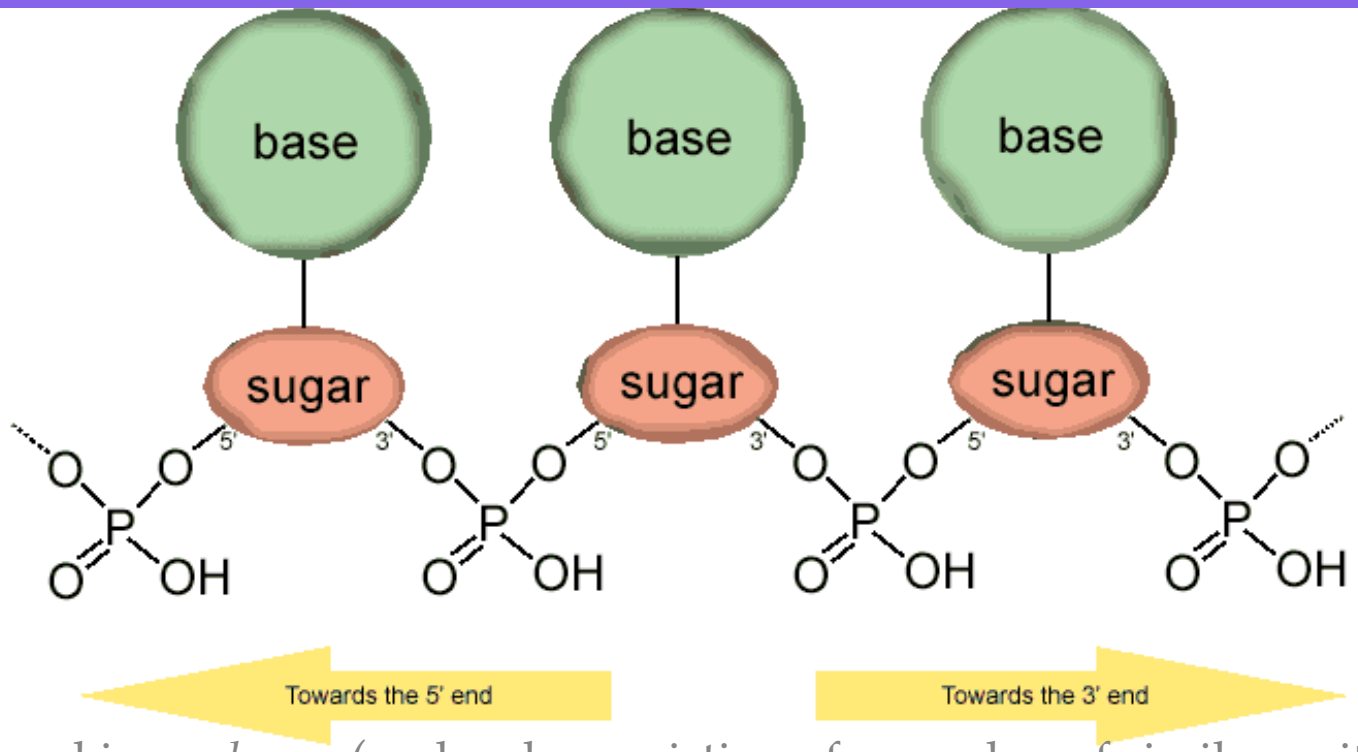
Universal Rules of Biology

- All cells store genetic (hereditary) information in *DeoxyriboNucleic Acid* (*DNA*)
- All cells replicate their genetic information by using the original DNA as a template and *enzymes* (biological catalysts that speed the process)
- All cells transcribe DNA into *RiboNucleic Acid* (*RNA*) and translate RNA into proteins in the same way
- There are exceptions to every rule in biology, including this one

Other Rules (and Exceptions)

- Mammals bear live young
- Human cells have *mitochondria* (small organs that produce energy for the cell)
- Cells contain DNA
- Sex of an individual is determined at fertilization by presence or absence of X and Y *chromosomes* (DNA structures)

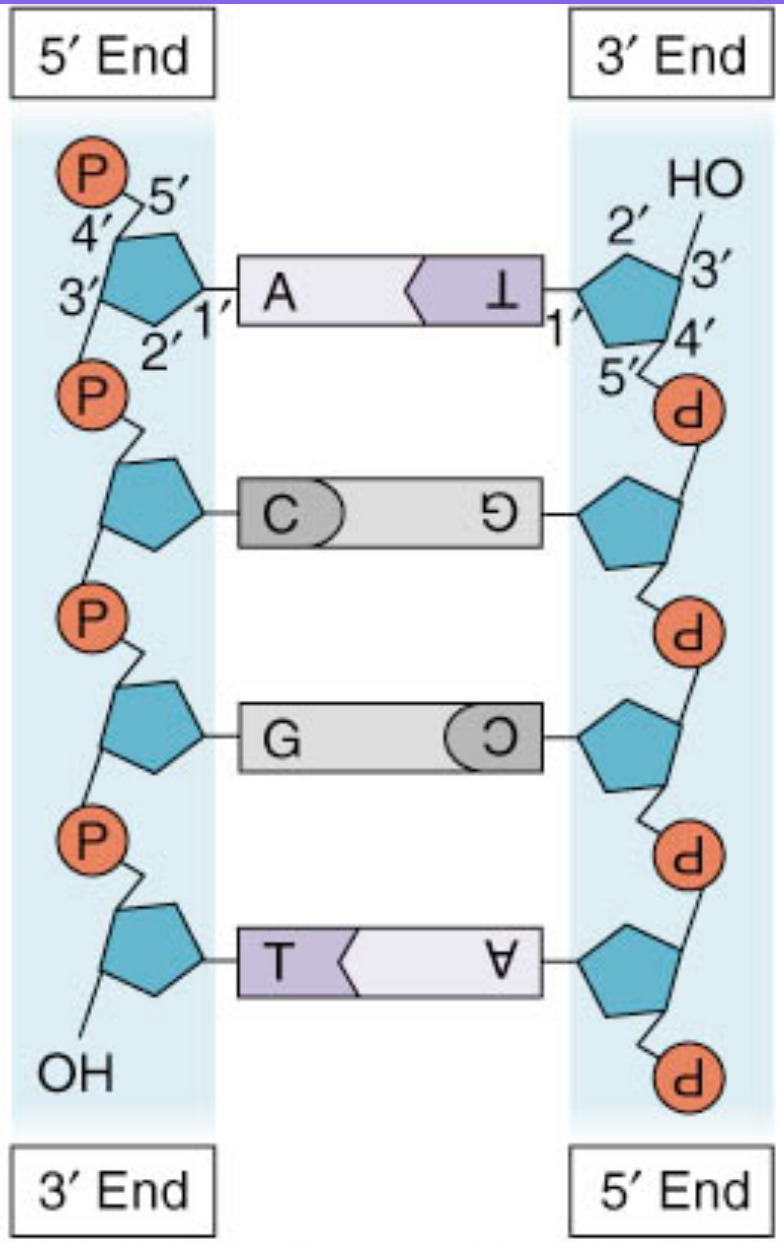
DNA Molecular Structure



- DNA strand is a *polymer* (molecule consisting of a number of similar units bonded together) of *nucleotides* held together by strong, *covalent* (shared electron pair) bonds
- Each nucleotide consists a sugar (*deoxyribose*), a *phosphate* (phosphorus+oxygen combination), and a *base* (molecule that can donate an electron pair)
- The sugars are not symmetrical -- at one end they are joined to the phosphate by the 5th carbon (the *5′* end) and at the other by the 3rd carbon (*3′*); thus, DNA strands are directional

DNA Bases

- Four bases encode information in DNA: *adenine* (A), *guanine* (G), *cytosine* (C), and *thymine* (T)
- A and T are complementary, link via weak hydrogen bonds; same with G and C
- Double-stranded DNA links complementary bases; exactly complementary strands have opposite directions
- The two strands twist into a double helix

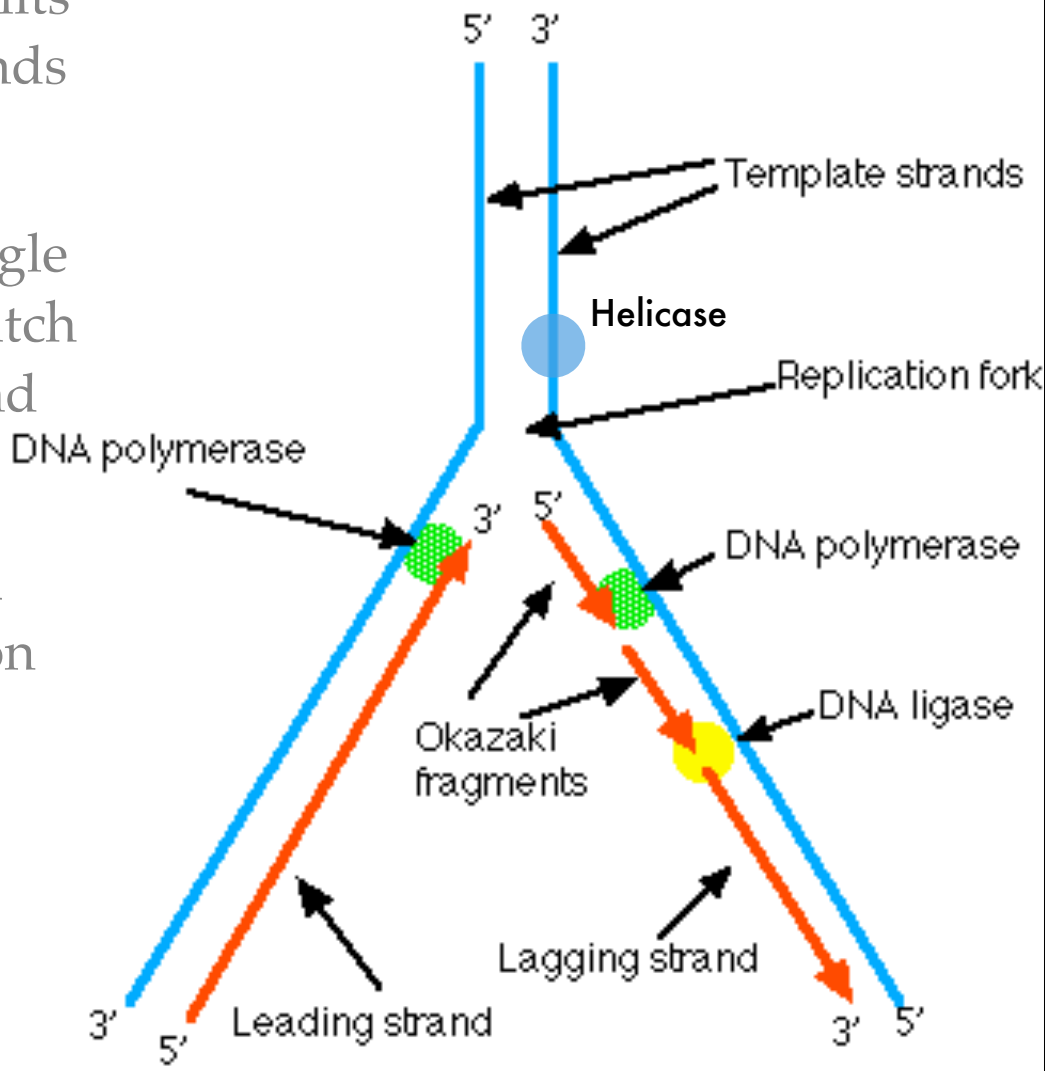


DNA Replication

Process 1: a DNA *helicase* (enzyme) splits the double strand into two single strands

Processes 2,3 (one for each strand): a DNA *polymerase* (enzyme) uses the single strand nucleotides as a template to match up complementary free nucleotides and build the other strand

- Strands replicated differently as DNA polymerases only work in one direction
- DNAReplication.flv - http://www.youtube.com/watch?v=5VefaI0LrgE&feature=grec_index



Replication Errors

- Low error rate (10^-9) due to error correcting processes
- *Dissociation during conformation* -- for new nucleotide to be covalently bound to growing polymer, DNA polymerase must undergo conformational change -- incorrect nucleotide more likely to dissociate
- *Exonucleolytic proofreading* -- a mismatched nucleotide at the extension end of the new strand prevents further extension -- it will be clipped off by an exonucleolytic enzyme
- *Strand-directed mismatch repair* -- on the new strand, mismatches are recognized, excised, and resynthesized
- Yet, replication a significant source of mutations

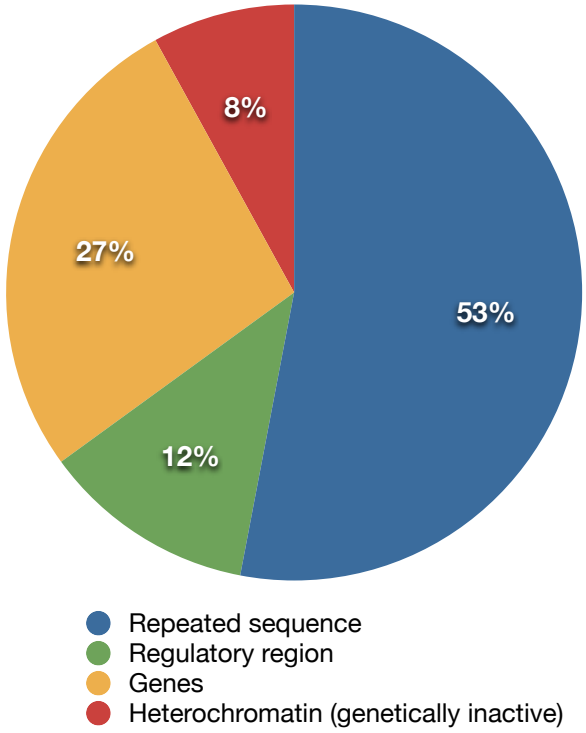
Genome Sizes

Species	*Common name*	*Million bases*
Protopterus aethiopicus	lungfish	139000
Fritillaria assyriaca	butterfly	124900
Triticum aestivum	wheat	16000
Nicotiana tabacum	tobacco	4400
Homo sapiens	**human**	**3200**
Mus musculus	mouse	2400
Drosophila melanogaster	fruit fly	120
Arabidopsis thaliana	mouse-ear cress	100
Caenorhabditis elegans	roundworm	78
Saccharomyces cerevisiae	yeast	12
Escherichia coli	bacteria	5

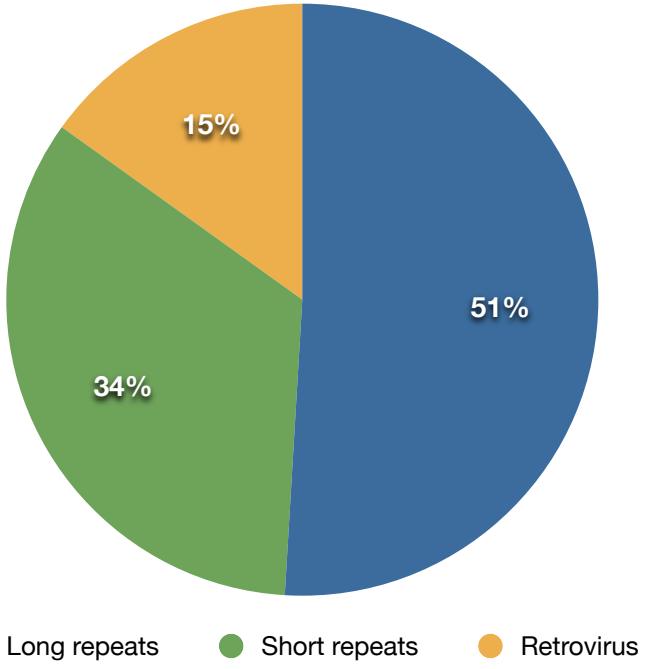
- Lungfish genome would need a 38 bit address
- Data requires challenging Computer Science

Human Genome Composition

Complete Composition

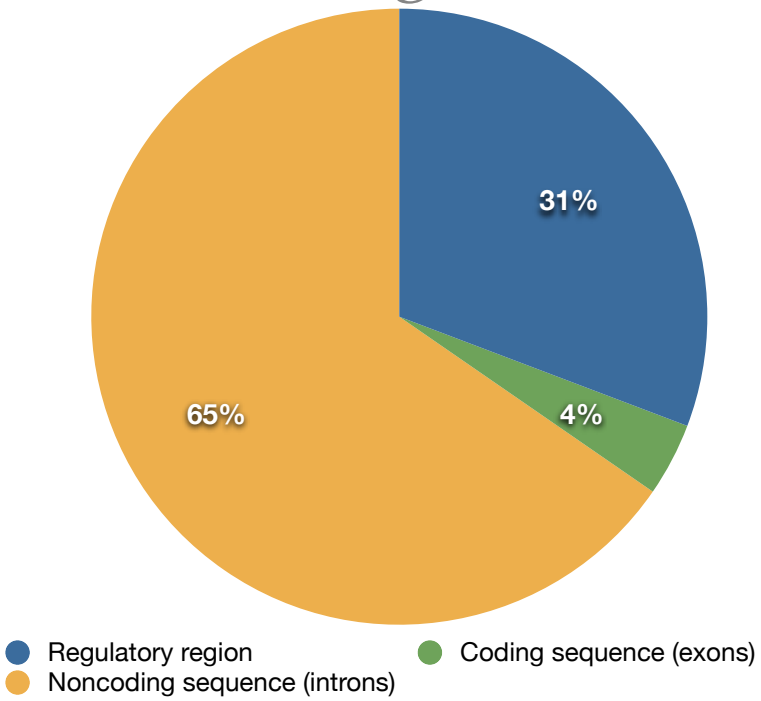


Repeated Sequence



Genes

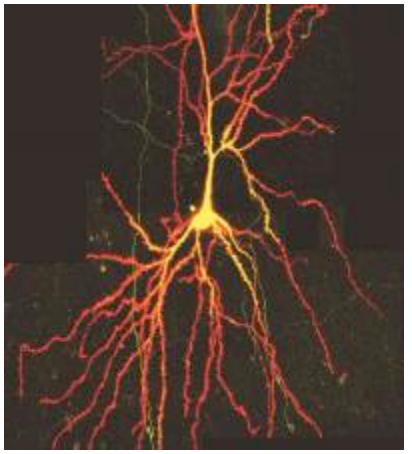
- A *gene* is a DNA segment corresponding to a protein
- Human genes made up of regulatory region, *exons* (coding DNA), and *introns* (noncoding DNA)



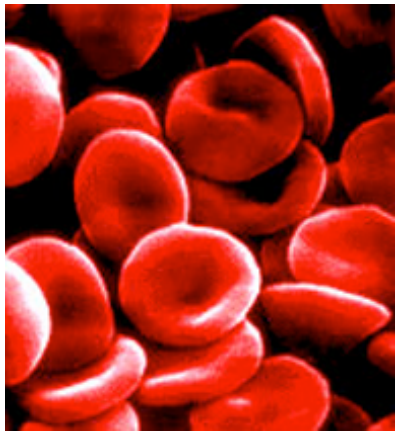
Species	***Common name***	***Genes***
Triticum aestivum	wheat	107K-334K
Homo sapiens	**human**	**22K-30K**
Mus musculus	mouse	20K
Drosophila melanogaster	fruit fly	14K
Arabidopsis thaliana	mouse-ear cress	21K
Caenorhabditis elegans	roundworm	20K
Saccharomyces cerevisiae	yeast	6K
Escherichia coli	bacteria	4K

Gene Regulation

- All cells in an individual have same genome
- Differences due to gene regulation -- activating or deactivating gene(s) under various conditions
- Development during gestation also due to gene regulation
- Gene regulation made complex, multicellular organisms possible
- An *operon* is a group of genes controlled by a single, regulatory region



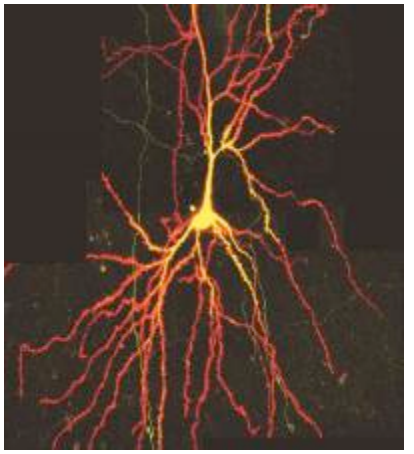
neuron



red blood cell

Gene Regulation

- Gene regulatory proteins switch genes on (*activators*) or off (*repressors*) by binding to an area of the DNA regulatory region for the gene
- Genes similar to content addressable memory, with activator similar to tag
- Gene regulatory region also contains a *promoter* at the start of the gene's coding DNA
- Regulatory region for a Drosophila gene is 20K bases long and has sites for > 20 regulatory proteins



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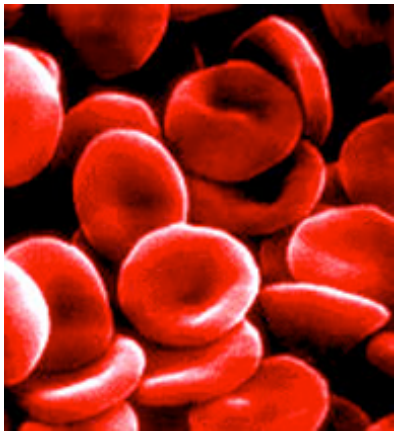
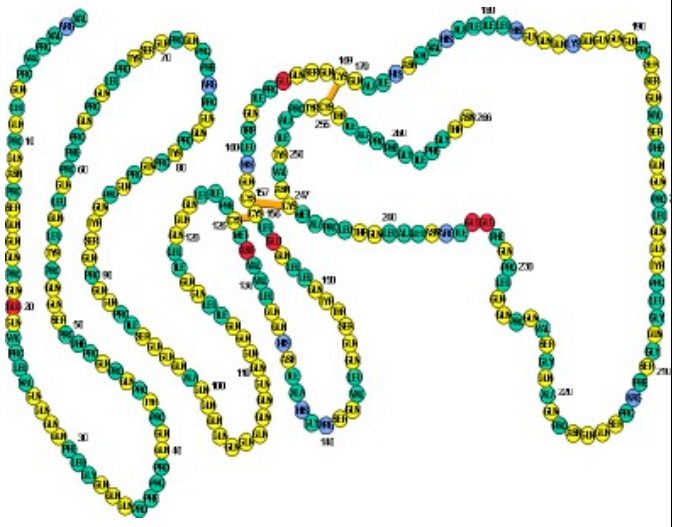


red blood cell

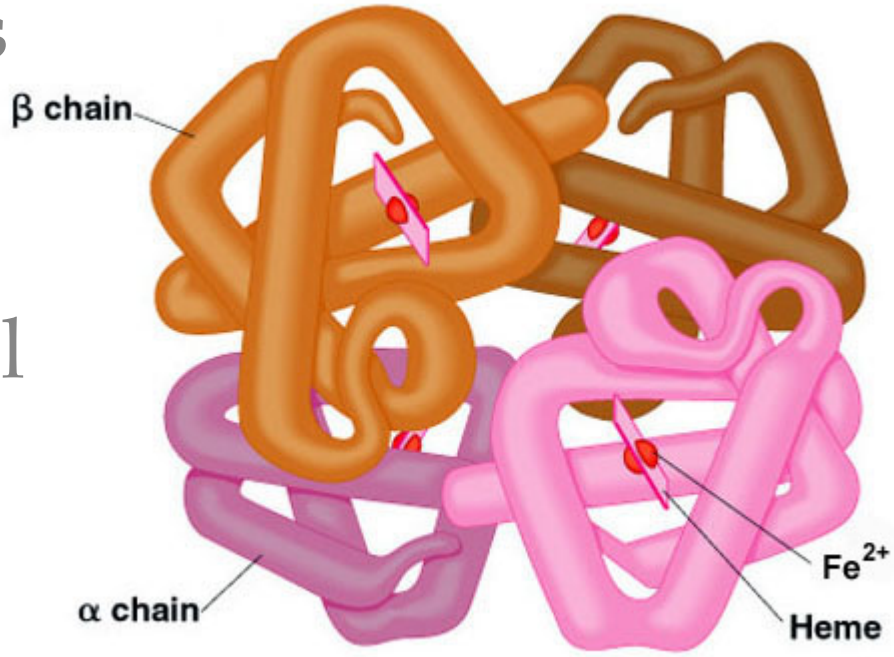
Proteins

- An *amino acid* is a molecule that contains an acid group, an *amine* (nitrogen+hydrogen) group, and a side chain that varies with the specific acid
- A *protein* is an amino acid polymer
- 20 different amino acids are used to make proteins
- Proteins typically fold into complex, 3D shapes
- Proteins typically have reactive sites on their surface
- Structural proteins make up a cell's structure -- e.g. keratins for skin, hair, nails
- *Enzymes* catalyze (increase the speed of) chemical reactions -- e.g. lactase converts lactose to glucose
- Nucleic acid binding -- e.g. gene regulation
- Signal transduction -- extracellular stimuli causing intracellular change; e.g. photon hitting retina cell



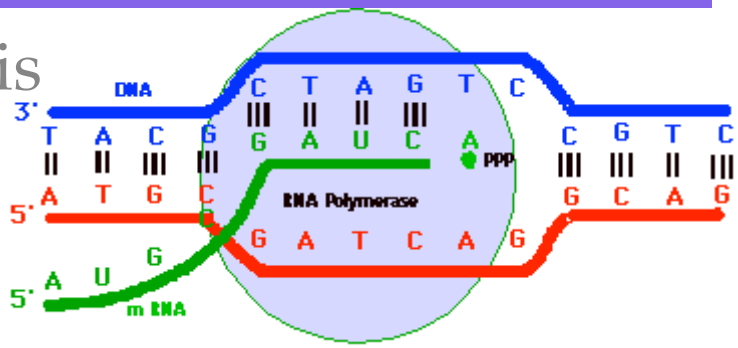
Hemoglobin

- Protein complex of 2 alpha globins and 2 beta globins
- Carries oxygen to tissues
- Releases oxygen where cell metabolism is high
- Highly conserved



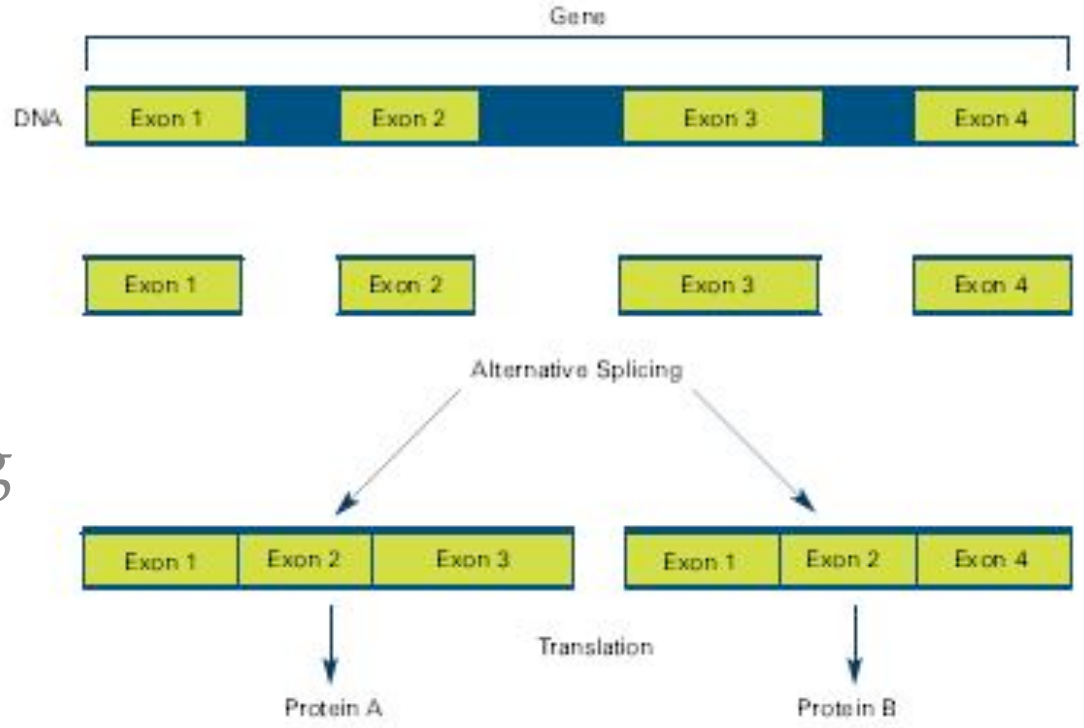
Protein Synthesis - Transcription

- Gene activation begins protein synthesis
- *Transcription*:
  - RNA polymerase (also called transcriptase) binds to DNA at promoter
  - RNA polymerase reads single strand of DNA and synthesizes corresponding single-stranded messenger RNA (*mRNA*)
- RNA is similar to DNA
  - uses *ribose* sugar instead of deoxyribose
  - uses *uracil* (U) base instead of thymine (T) base



Protein Synthesis - RNA Processing

- *RNA processing*:
  - introns spliced out of RNA
  - allows alternate splicing (more than one protein from a given gene)
- Code reuse / hacking new function

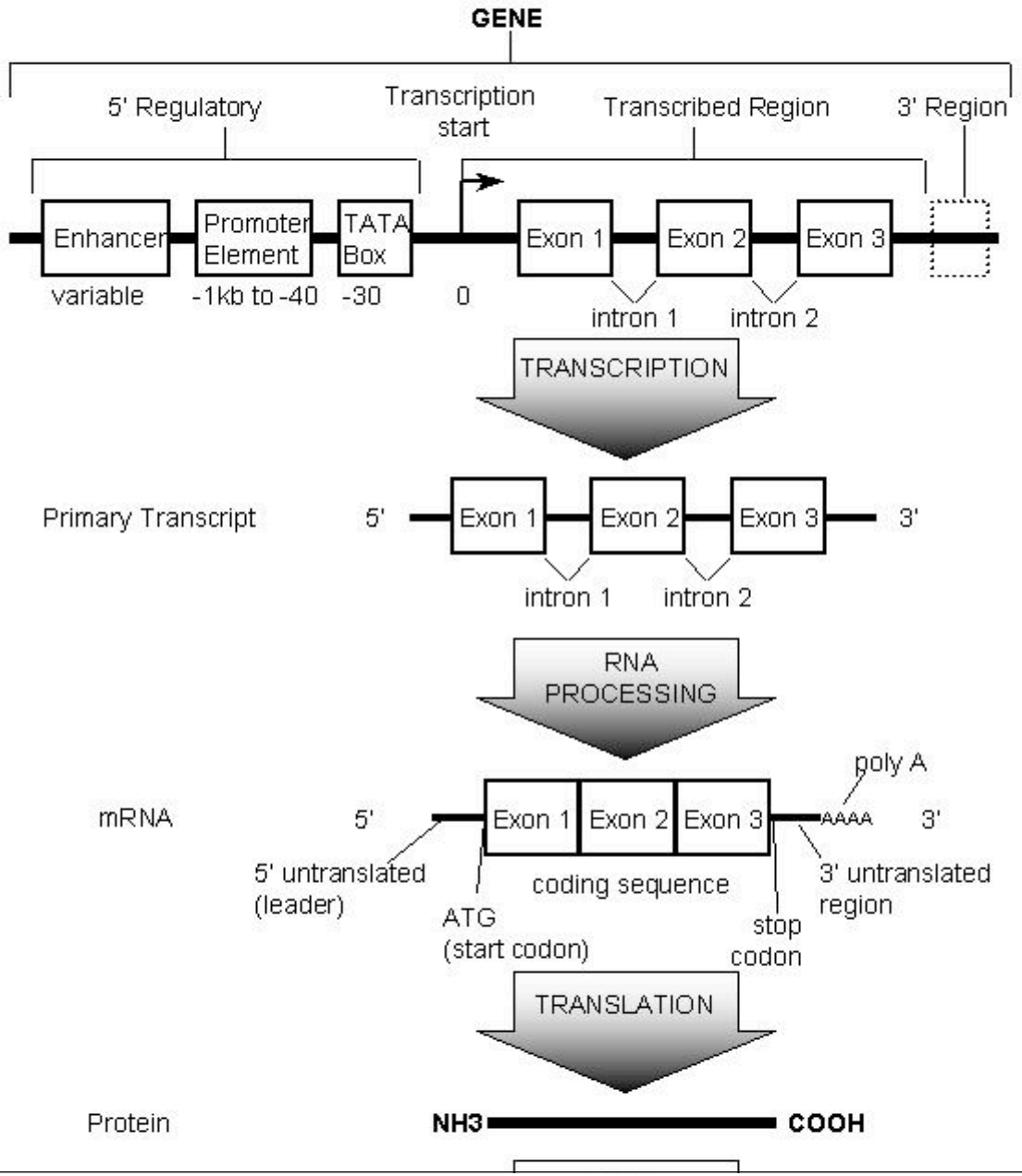


Protein Synthesis - Translation

- *Translation*:
  - *Ribosome* (RNA/protein complex) reads mRNA
  - mRNA bases are read in triples known as *codons*
  - Each codon corresponds to one of the 20 amino acids or the stop code which halts translation
  - 4^3 codons map to 20 amino acids + stop => code is redundant, robust
  - Ribosome synthesizes corresponding protein by polymerizing appropriate amino acids

1st letter	Second Letter: U	Second Letter: C	Second Letter: A	Second Letter: G	3rd letter
U	UUU Phe UUC UUA Leu UUG	UCU UCC UCA UCG Ser	UAU Tyr UAC UAA Stop UAG Stop	UGU Cys UGC UGA Stop UGG Trp	U C A G
C	CUU CUC CUA CUG Leu	CCU CCC CCA CCG Pro	CAU His CAC CAA Gln CAG	CGU CGC CGA CGG Arg	U C A G
A	AUU AUC AUA Ile AUG Met	ACU ACC ACA ACG Thr	AAU Asn AAC AAA Lys AAG	AGU Ser AGC AGA Arg AGG	U C A G
G	GUU GUC GUA Val GUG	GCU GCC GCA Ala GCG	GAU Asp GAC GAA Glu GAG	GGU GGC GGA Gly GGG	U C A G

Protein Synthesis



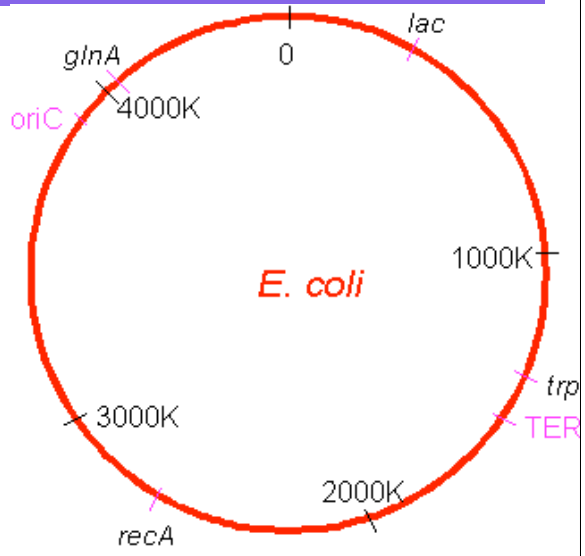
- ProteinSynthesis.flv
- http://www.youtube.com/watch?v=D3fOXt4MrOM

Ribosome ≠ Turing Machine

- Protein synthesis within a cell highly parallel -- many ribosomes / cell
- Ribosome only moves 1 direction on mRNA
- Ribosome doesn't write mRNA

Cell Division

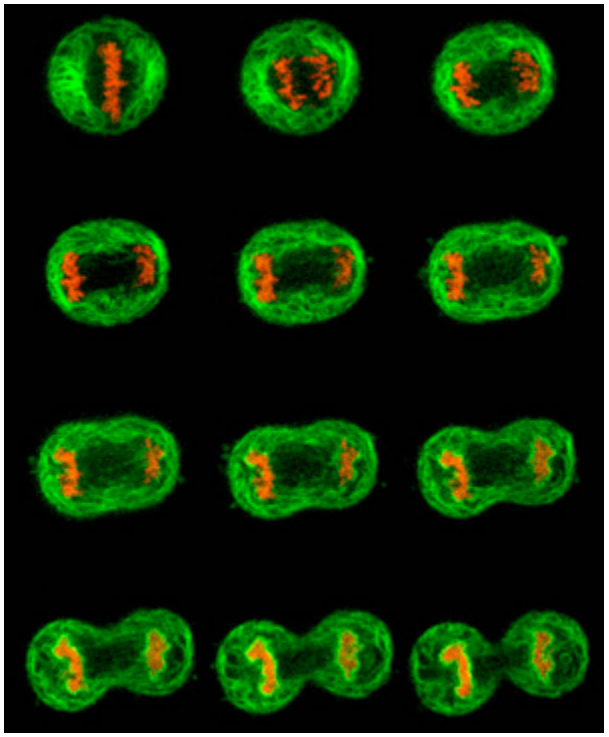
- Asexually reproducing organisms
  - unpaired chromosomes
  - mitosis cell division only
- Sexually reproducing organisms
  - *diploid* genome -- chromosomes are paired, one in each pair from each parent
  - mitosis cell division
  - meiosis cell division -- producing *gametes* (egg and sperm cells) with *haploid* (unpaired) genomes
  - haploid egg and haploid sperm combine during fertilization to produce new, diploid cell



chromosome pair

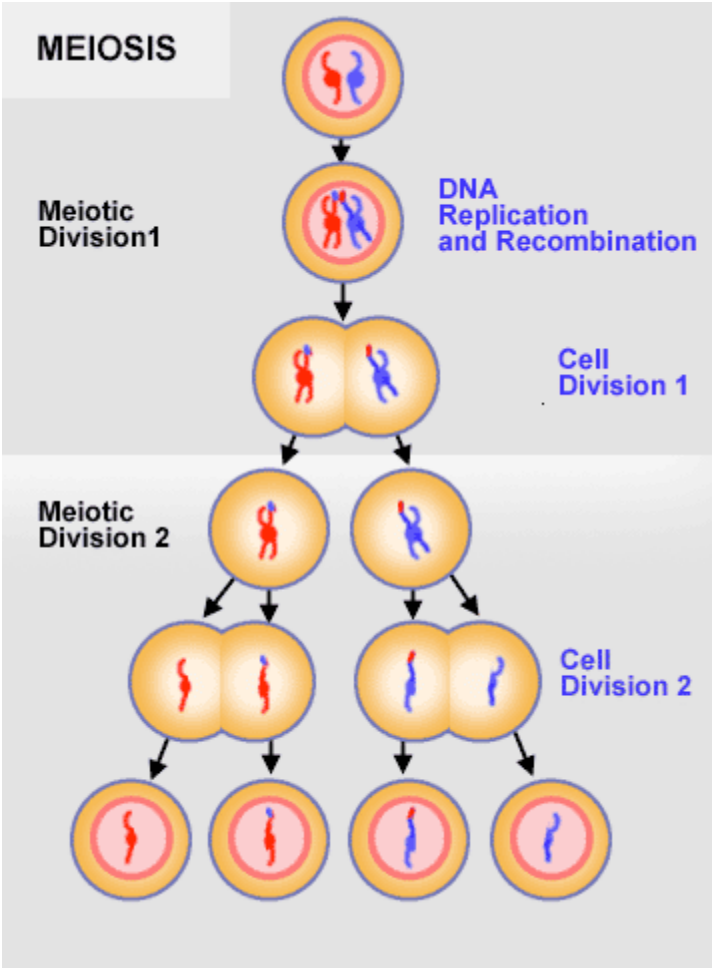
Mitosis

1. DNA replicated
2. Chromosome(s) created from replicated DNA
3. Nucleus divides to produce daughter nuclei, each with a complete genome
4. Cell divides to produce daughter cells



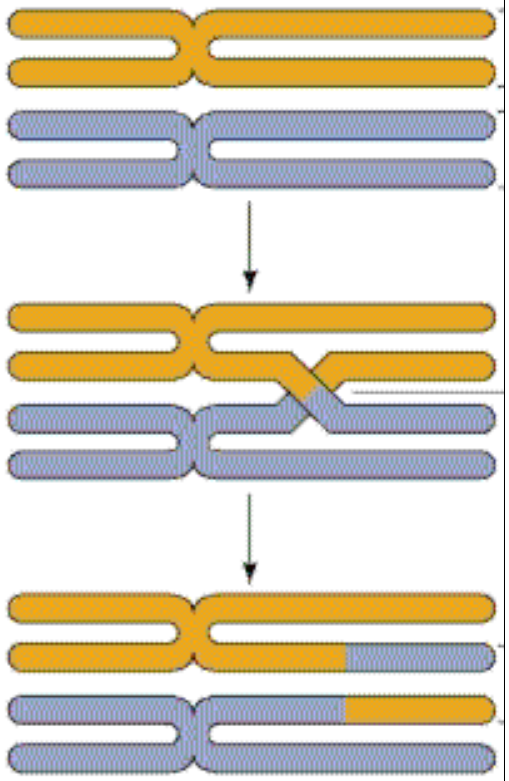
Meiosis

1. DNA replicated in diploid cells
2. Chromosomes created -- *crossover*, if any, occurs during this phase
3. Nucleus divides to produce daughter nuclei, each with a diploid genome
4. Cell divides to produce daughter cells
5. 2 nuclei divide again to produce 4 daughter nuclei, each with a haploid genome
6. 2 cells divide to produce 4 daughter cells



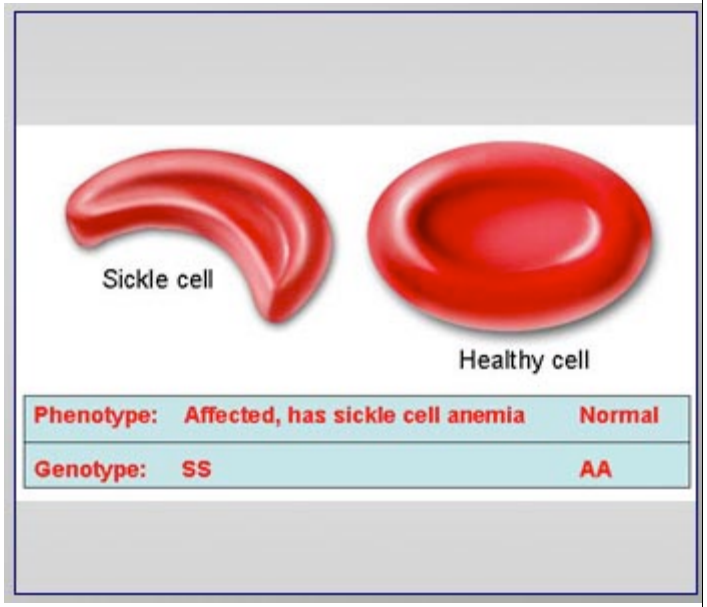
Crossover in Meiosis

- *Crossover* occurs sometimes during meiosis chromosome duplication
- New chromosomes are produced that consist of the corresponding part of each parents' chromosome
- Adaptability produced is significant advantage to sexual reproduction
- Analogous to two different coders dividing up methods for a class



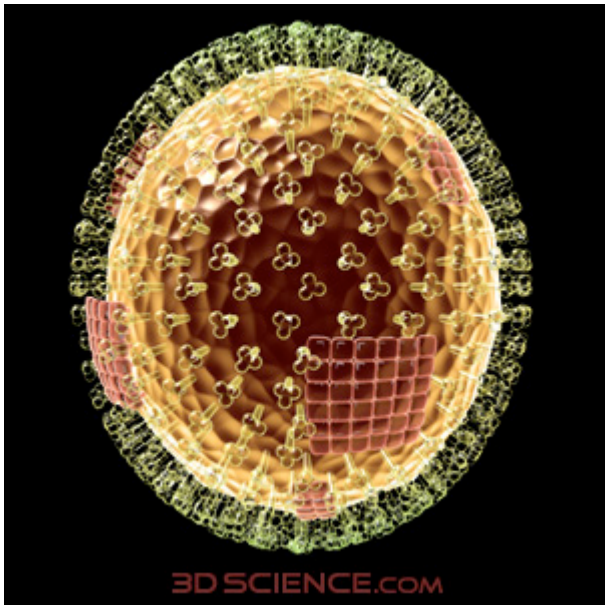
Gene Variations

- A given gene may have variations known as *alleles*
- The specific allele (or pair of alleles in diploid genomes) an individual has is its *genotype*
- The appearance or behavior it has due to its genotype is its *phenotype*
- If the two alleles in a pair are identical, the individual *homozygous*; otherwise, it is *heterozygous*
- Heterozygous sickle cell genotype (AS) helps prevent malaria



Viruses

- *Viruses* are non-living parasitic complexes that depend on the mechanisms of their hosts, e.g. ribosomes, to reproduce
- Viruses consist of genetic material (DNA or RNA) and an enclosing protein coating
- *Retroviruses* use a reverse transcriptase to put their genes into their host's genome
  - Can be deadly, e.g. HIV
  - Can be useful for gene therapy
- Some viruses, called *oncoviruses*, can cause cancer



Influenza virus

References

- Larry Gonick, & Mark Wheelis. (2005). *The Cartoon Guide to Genetics*. New York: Collins Reference.
- Bruce Alberts, Alexander Johnson, Julian Lewis, Martin Raff, Keith Roberts, & Peter Walter. (2002). *Molecular Biology of the Cell*. New York, NY: Garland Science.