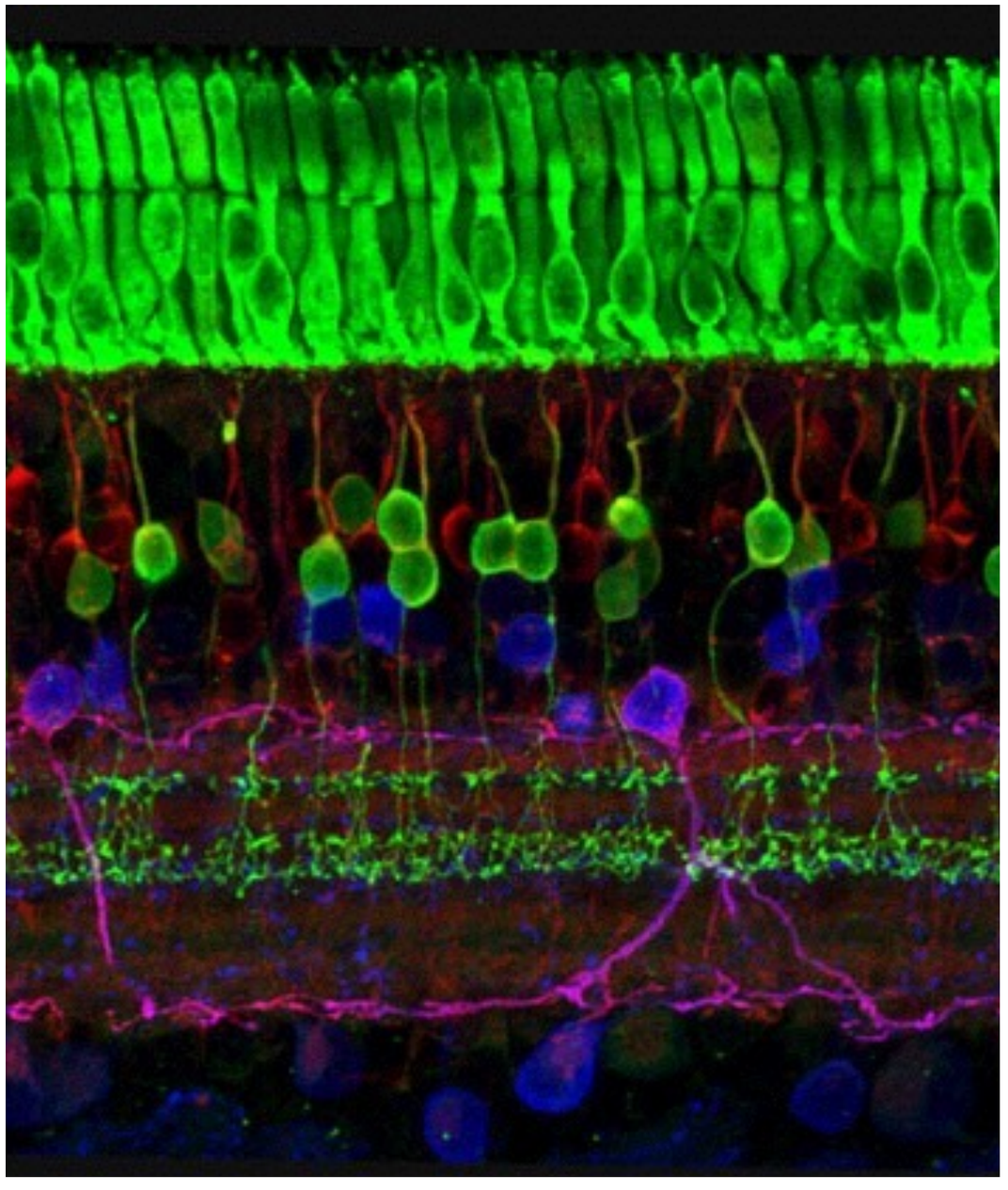
Molecular Biology

How do living things work?
Where are the instructions for making living things?
How do you build a living thing from the instructions?
Where do babies (animal, plant, bacterial, fungal, etc) come from?

Organisms Are Cell Bags

- Every organism is made up of cells
- Some one-celled organisms are just that: one cell
- Brain cells, skin cells, blood cells, heart cells, liver cells, etc.
- Different tissues in an organism have different cell types, but the cells all have common features



Nerve cells in the retina

Wei Li, National Eye Institute, NIH

Something Something, Cell Structure

Where Do Babies Come From?

- Asexual reproduction: in one-celled organisms, an (almost) identical copy of the organism splits off

- Sexual reproduction: two organisms exchange pleasantries and somehow a new baby organism comes about, distinct from either parent

Centre For Infections/Science Photo Library/Corbis

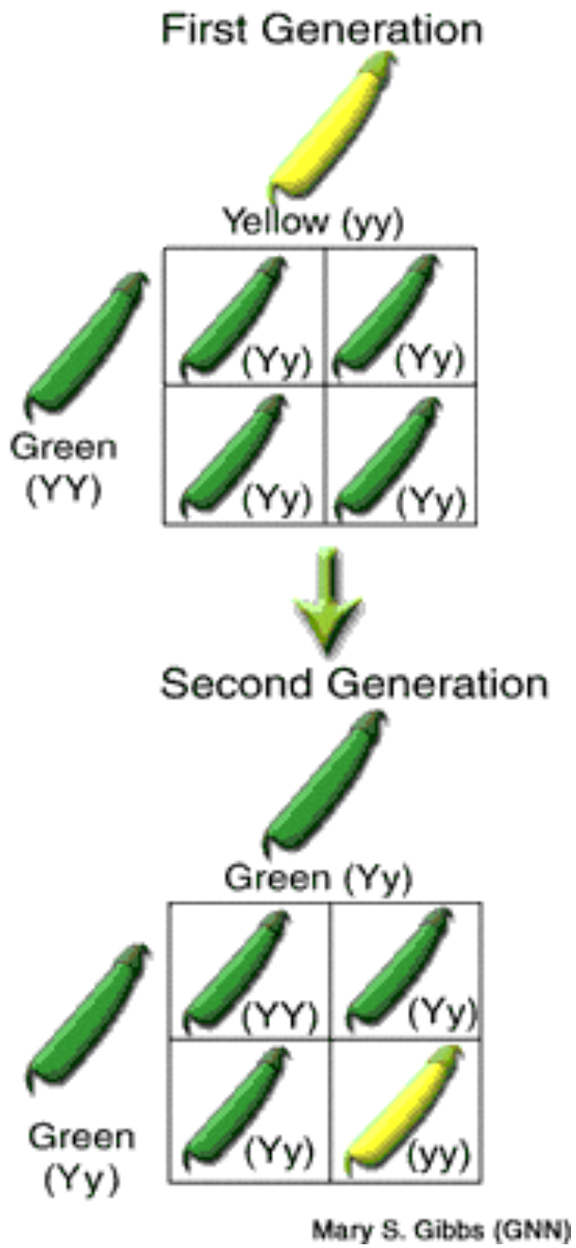
- In sexual reproduction, how do the characteristics of the parents get passed to the offspring?
- What determines which characteristics are chosen?

This Guy: Gregor Mendel

- Augustinian friar, German-speaking Moravian (Czech)
- Experimenting with peas, developed a theory of “genes”
- His theory: each physical attribute (“phenotype”) of the peas is determined by two copies of the gene (“alleles”)
- Dominant and recessive alleles for each gene

Mendelian Inheritance

- Each phenotype gets two alleles
- Dominant (Y) and recessive (y) alleles exist for each gene
- When a dominant and a recessive allele for a phenotype are both present (Yy), the dominant one determines the outcome
- World isn't quite this simple



Where And What Is Genetic Information?

- Each gene has two alleles per organism
- Where do these alleles live?
- What are the alleles made of?
- How do alleles store information? Binary? Analog (little record players)? Magnetic fields?

Pus To Nuclein

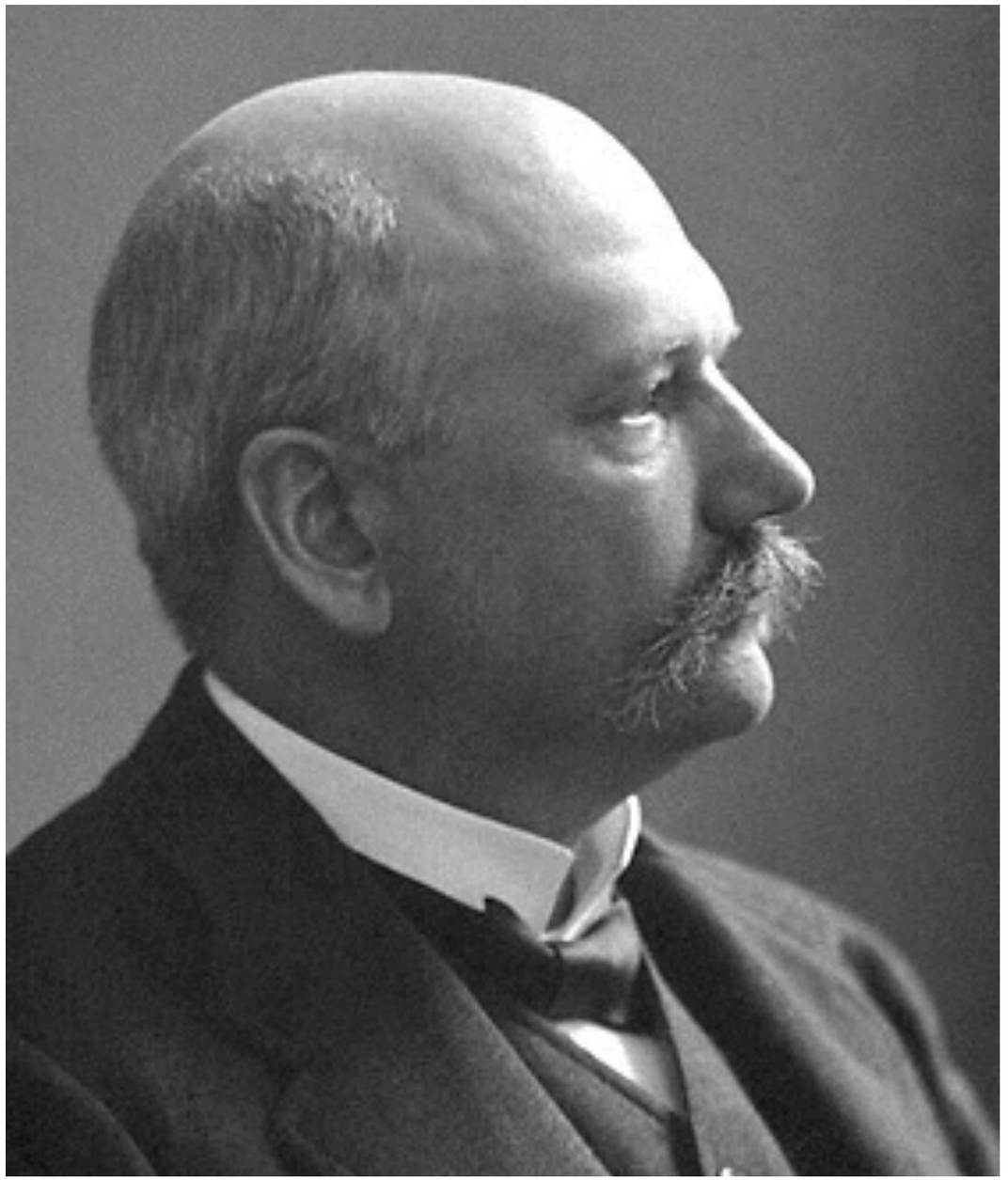
- 1869: Studying the chemistry of cell nuclei, Swiss chemist Friedrich Miescher discovered a phosphorous- and nitrogen-rich substance inside the nuclei of white blood cells (that he got from the pus off discarded surgical bandages). He named it “nuclein.”

Nuclein To Nucleobases

- 1885–1901: Studying nuclein (in the same lab where Miescher discovered it), Albrecht Kossel showed it consisted of a protein and non-protein component

- Isolated and named the five non-protein components: adenine, cytosine, guanine, thymine, and uracil

- Nobel Prize in 1910



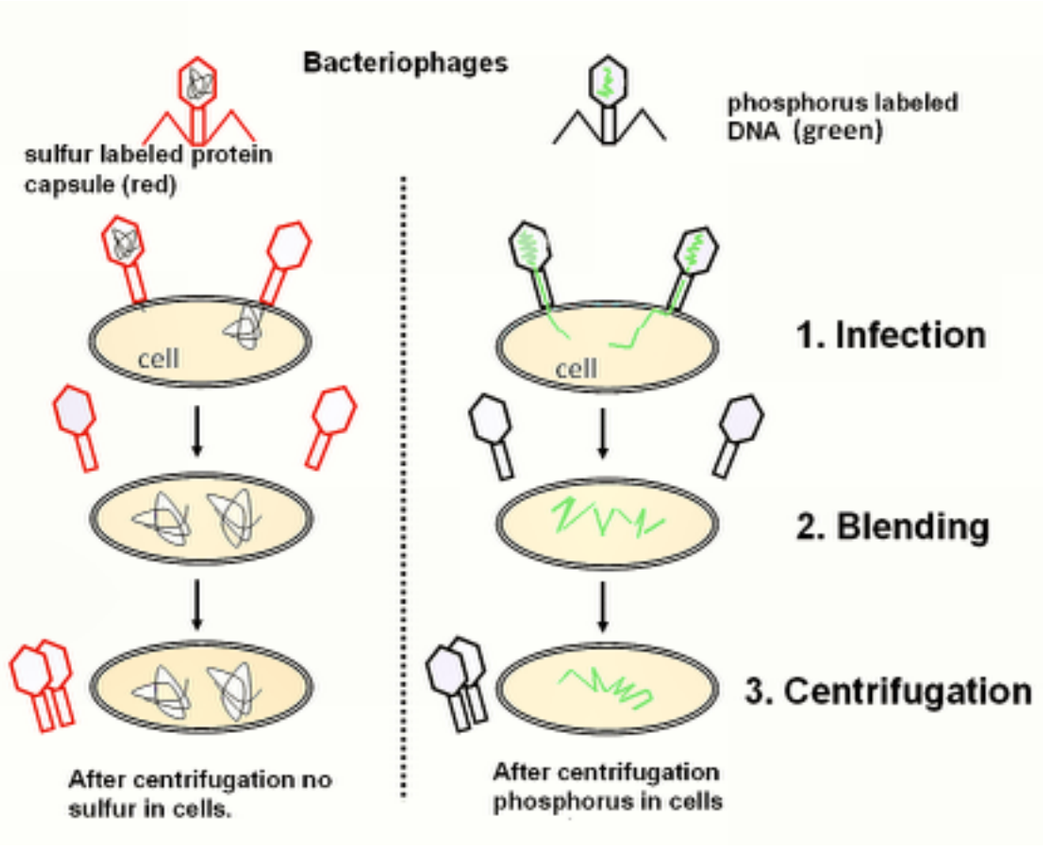
Hershey-Chase Experiment

- Early 20th century, most biologists thought genetic information was stored in proteins

- 1952: Alfred Hershey and Martha Chase confirmed that DNA carries genetic information

- Tagged protein shell and DNA of a bacteriophage with different radioisotopes

- The tagged DNA persisted across generations, the tagged protein didn't



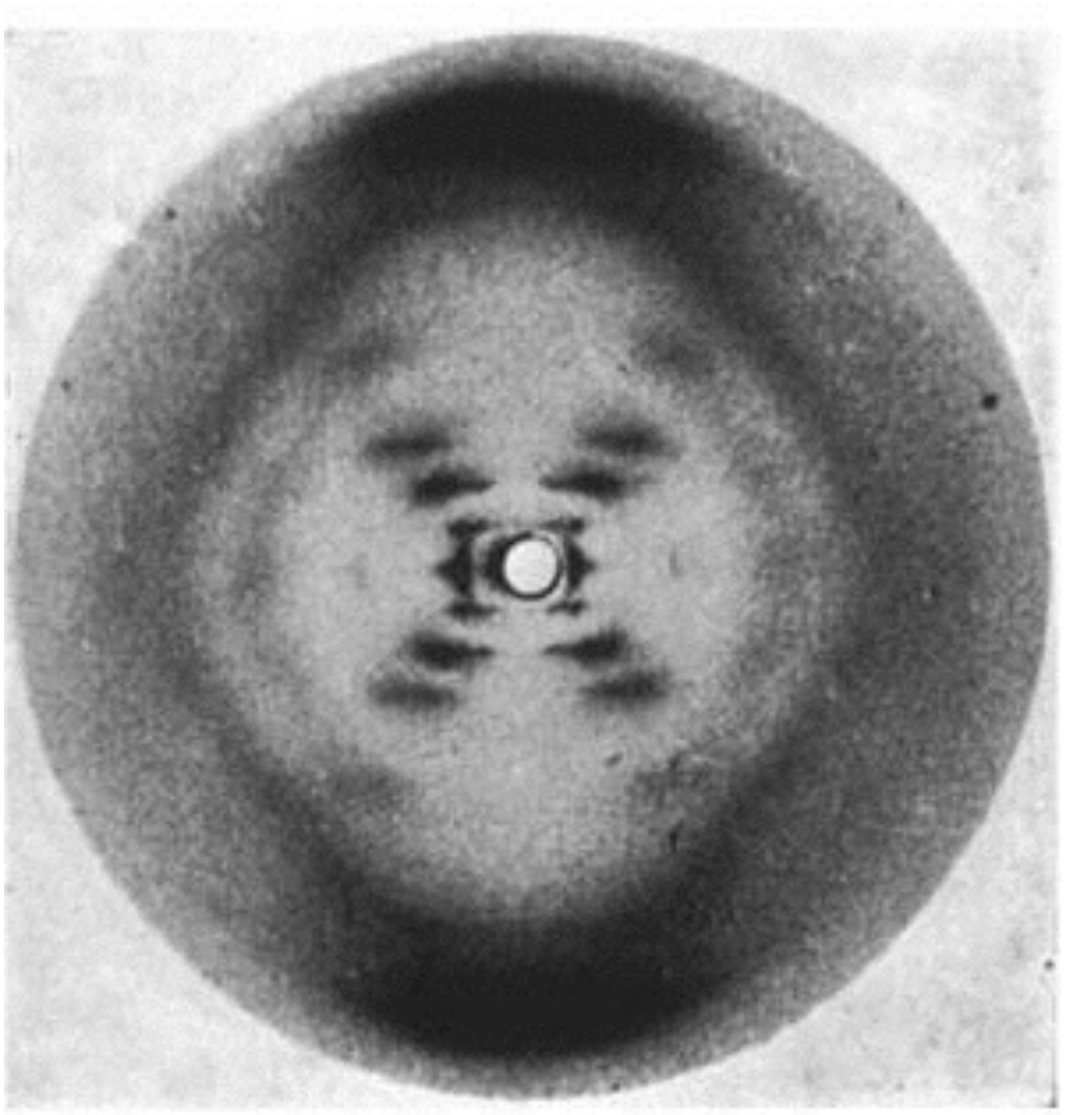
Genetic Information Is Stored In Some Chemical “DNA”

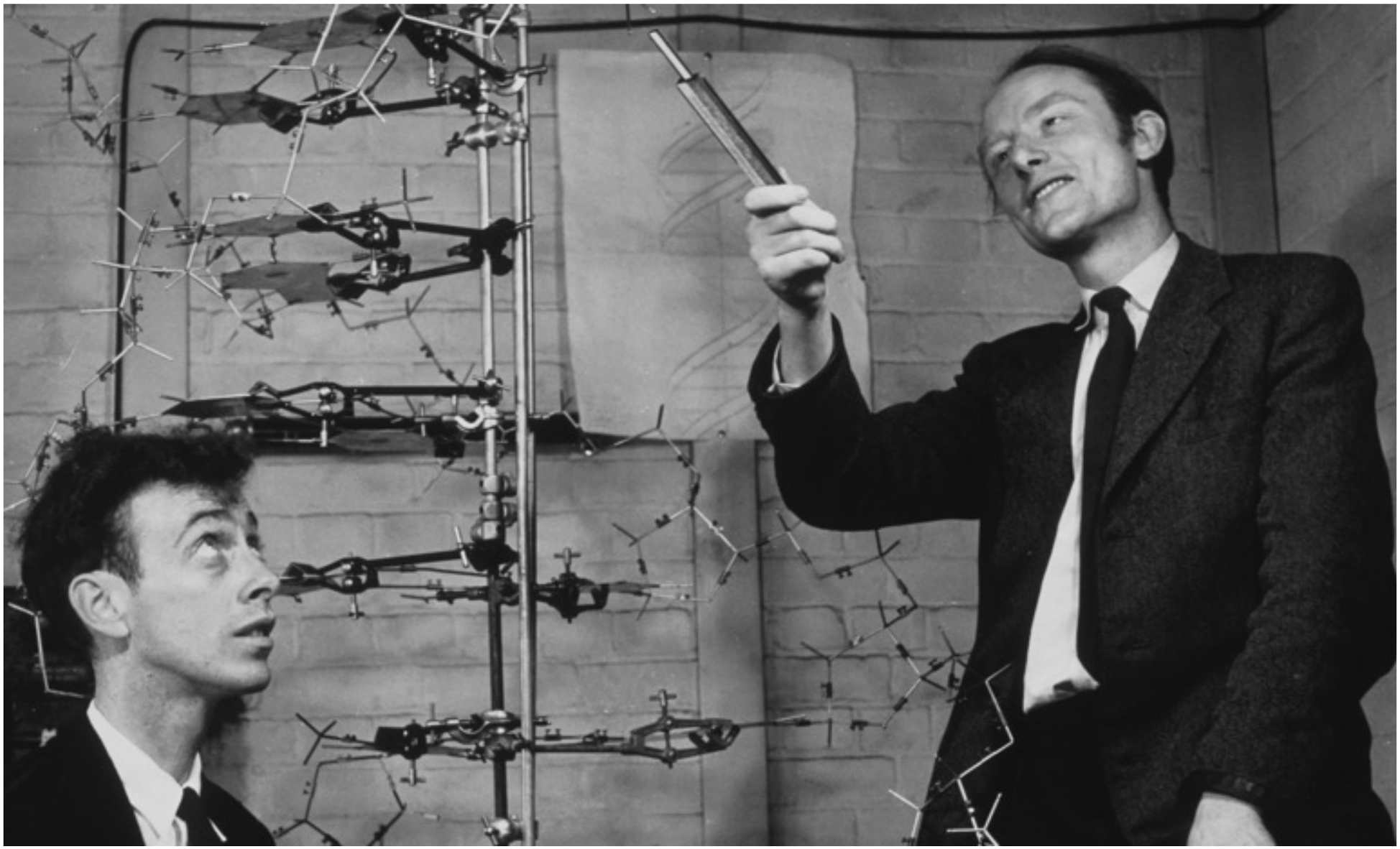
- How is information encoded in the chemical?
- How are the two alleles for each gene represented?

Photo 51

- 1952: Raymond Gosling, a student of Rosalind Franklin, took this X-ray diffraction image of crystalized DNA

- Maurice Wilkins showed this image to James Watson, providing crucial evidence for a double-helix model for DNA



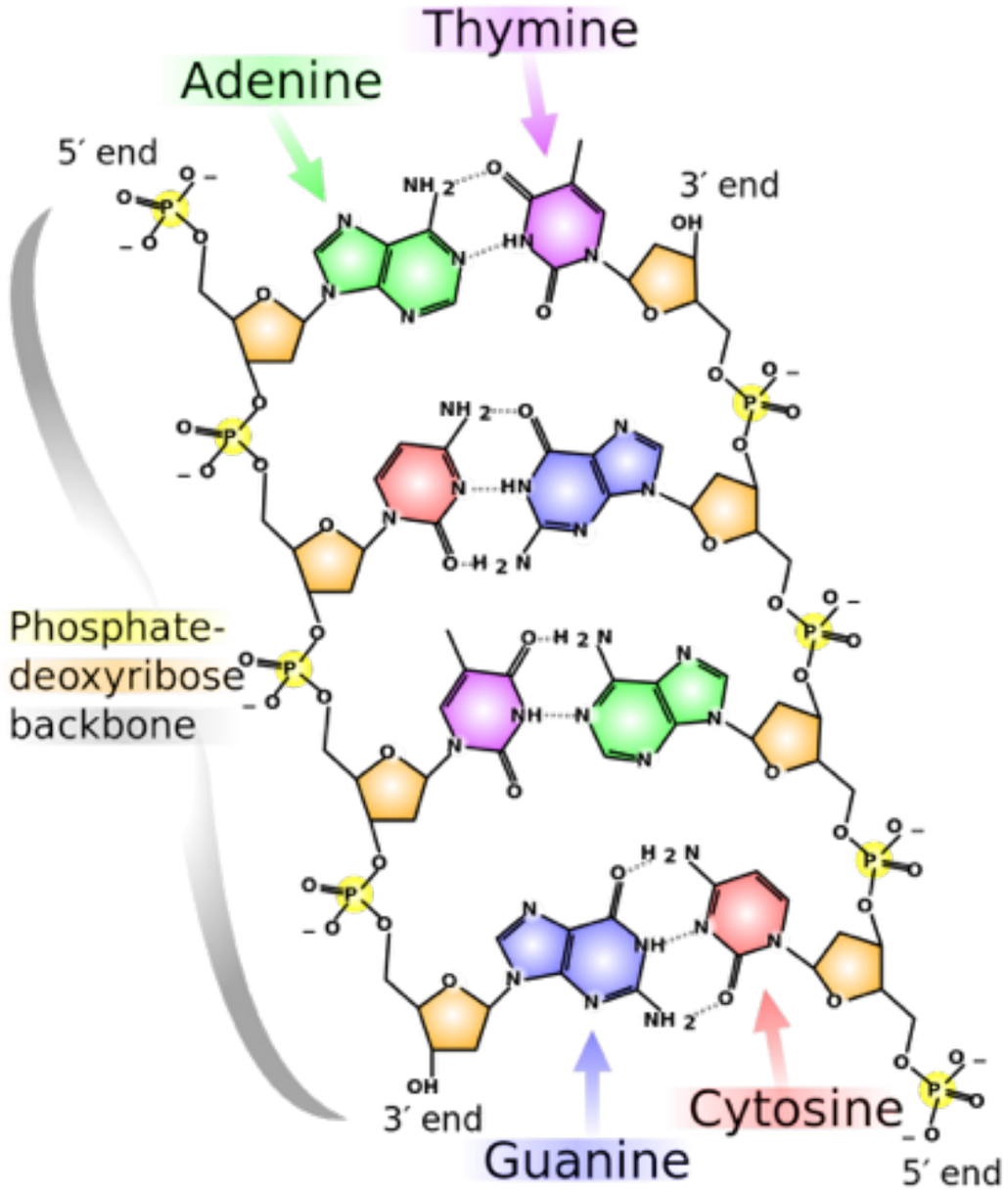


The Double Helix

1953: Based on Photo 51, Francis Crick and James Watson propose the first correct double-helix model for DNA

DNA Structure

- Sugar-phosphate backbone (The sugar is called “deoxyribose”)
- Adenine-Thymine pair
- Cytosine-Guanine pair
- The backbone bonds are covalent, which are strong
- The pair bonds are hydrogen bonds, which are weaker
- Each strand has a direction, and the two strands are anti-parallel



Something About Chromosomes

- Prokaryotic (circular) vs eukaryotic (linear)
- Humans are diploid, two copies
- Plants are weird
- (What about peas a la Mendel?)
- Mitochondria & plasmids?

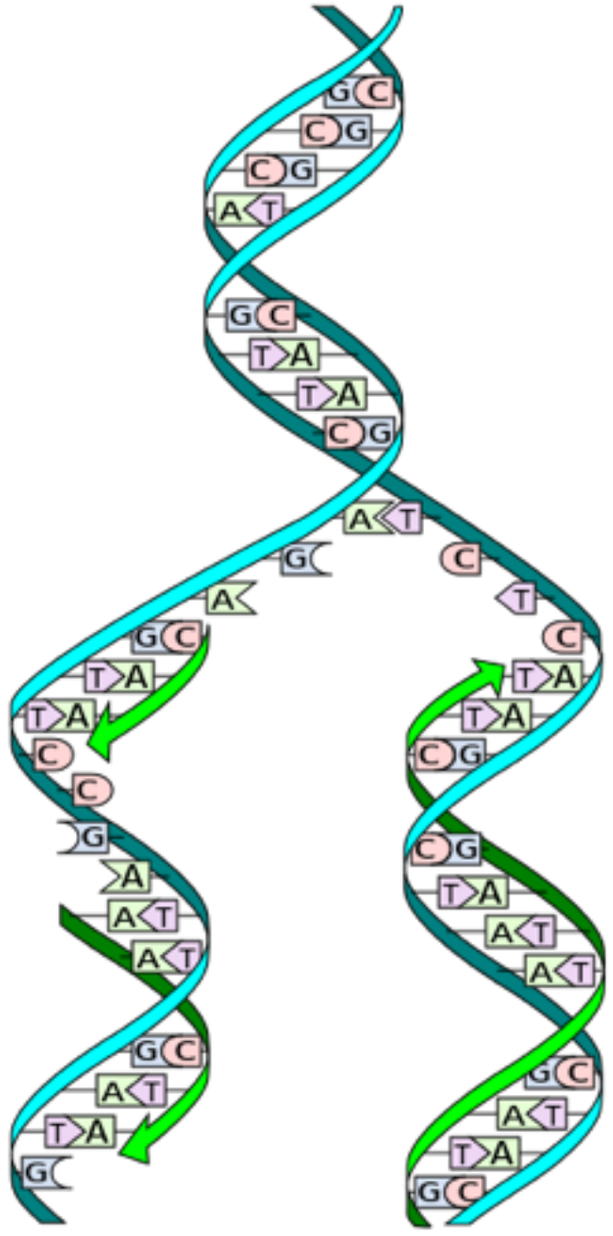
DNA Replication

- Cells divide in all living things: growth, repair, reproduction

- DNA contains specific “origins of replication”

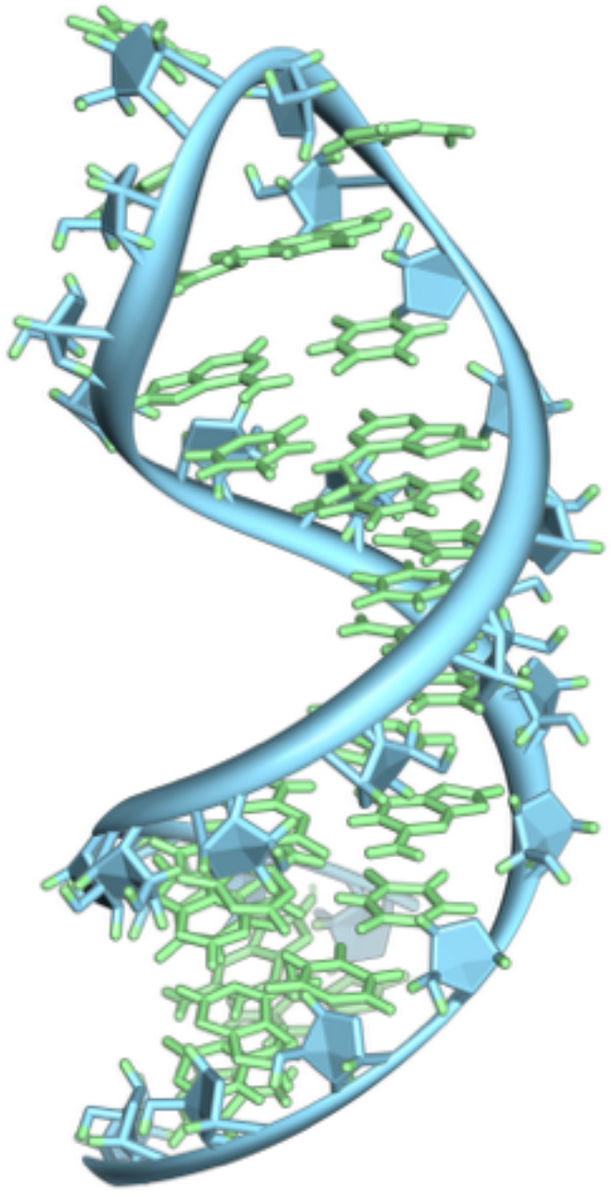
- DNA strands are separated at the origins; DNA polymerases (proteins) travel along each strand, attach complementary bases from 5’ to 3’ end

- Extremely accurate: 1 error every 10^9 bases



RNA: DNA's Single-Stranded Cousin

- Another nucleic acid, like DNA
- Ribose instead of deoxyribose in sugar-phosphate backbone
- Uracil rather than thymine
- Single-stranded
- Often has a secondary structure that's folded on itself
- Many types of RNA which perform many functions in cells



Messenger RNA

- DNA is valuable: protected in a wrapped-up, double-stranded configuration in the nucleus (in eurkaryotes)

- Somehow the genetic information needs to be transferred to protein-making complexes (ribosomes)

- mRNA is copied from DNA in the nucleus, takes the information to the ribosomes

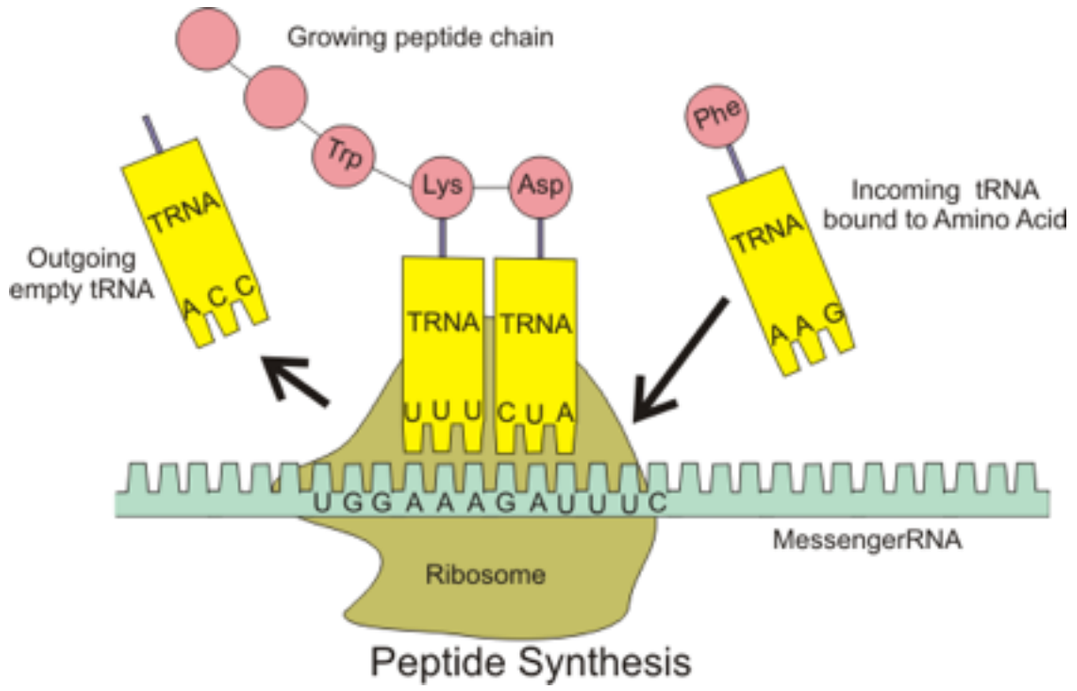
Transcription

- DNA and RNA can be transformed back and forth by the right enzymes, pairing bases

- RNA Polymerase copies DNA to RNA

Translation

- mRNA, copied from DNA, gets to ribosome
- Ribosome (made of protein and RNA components) is a protein-making factory
- mRNA template tells ribosome how to string together amino acids to create a protein



Maybe Ribosomes?

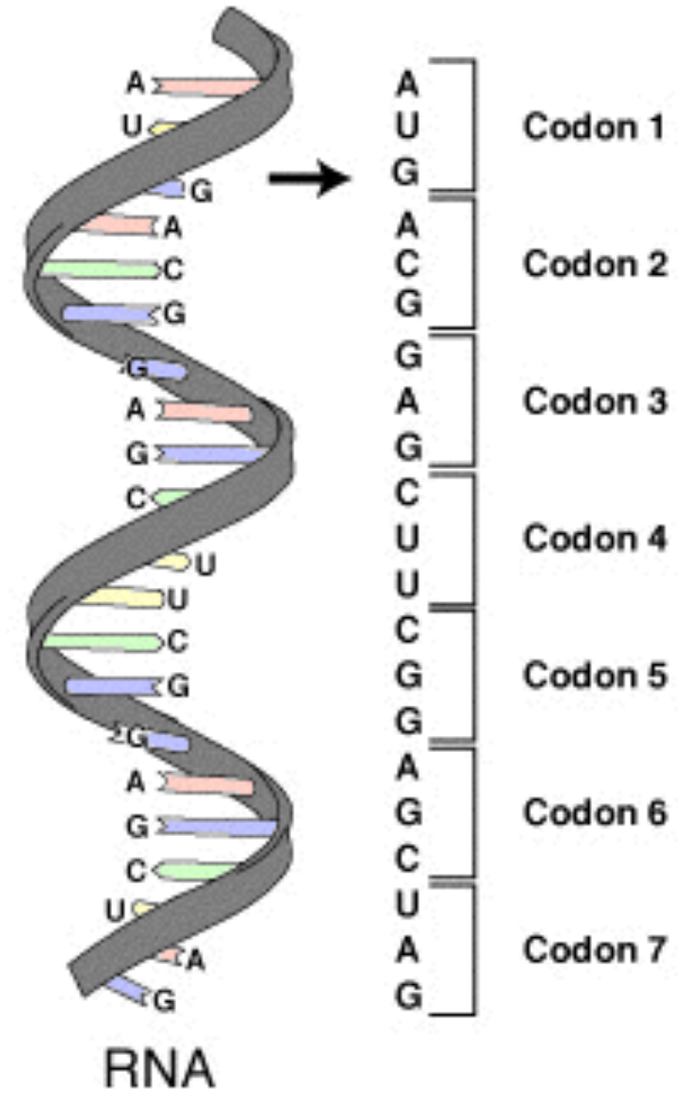
- Maybe something about rRNA, another type of RNA
- Another example or RNA as not just an information carrier, but a structure with function, works together with proteins
- Mention something about conserved ribosomal areas?

Wait…

- RNA is encoded with 4 bases
- Proteins are encoded with 20 amino acids
- How does a 4-letter alphabet get converted to a 20-letter alphabet?

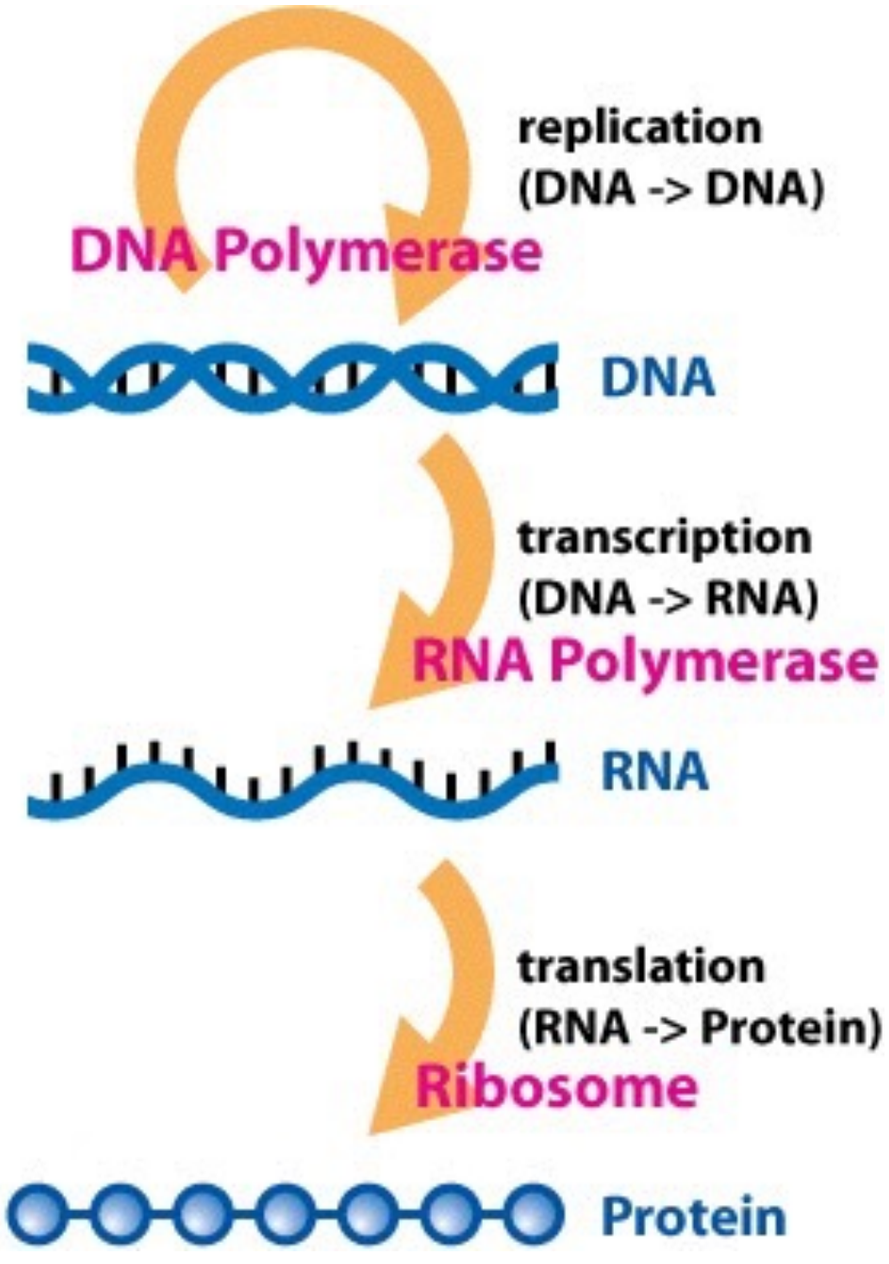
tRNA and Codons

- Amino acids are specified by 3-base codons in mRNA
- Transfer RNA (tRNA) is an RNA strand that folds in a way that one end matches a 3-base codon, and the other end attaches to the corresponding amino acid
- Some amino acids specified by more than one codon
- Some codons mean “stop”



Central Dogma Of Biology

- Genetic information is stored as DNA
- One gene per protein (more on this later)
- DNA is transcribed to RNA
- RNA is translated to protein
- Proteins are responsible for what's goin' on



This Is Biology

It Gets Weirder

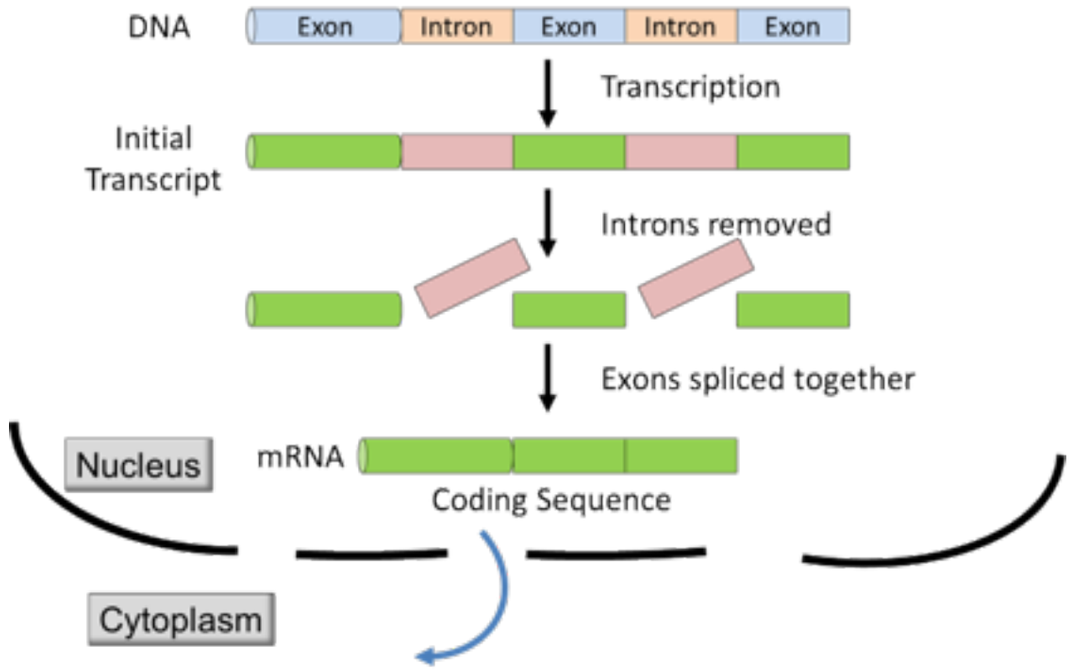
Exons and Introns

- One gene : one protein
  Of course it's not so simple

- Introns: regions of the genome that don't code for anything

- Exons: regions that code for stuff

- The initial transcription step produces pre-mRNA. Introns are removed to produce mRNA



Boston University School Of Public Health

Alternative Splicing

- Genes often contain multiple exons

- Different combinations of exons from the same gene can be spliced together to generate different protein *isoforms*

- How is splicing determined? Let me know—we'll share a Nobel Prize