SISG 2022 - Module 2

Introduction to Genetics and Genomics

Molecular Biology

4pm EDT, Monday, July 11th

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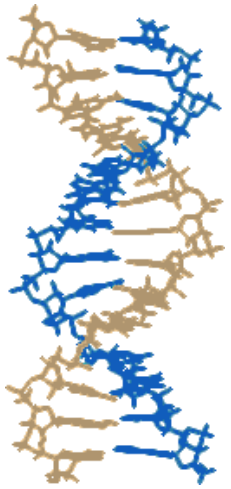
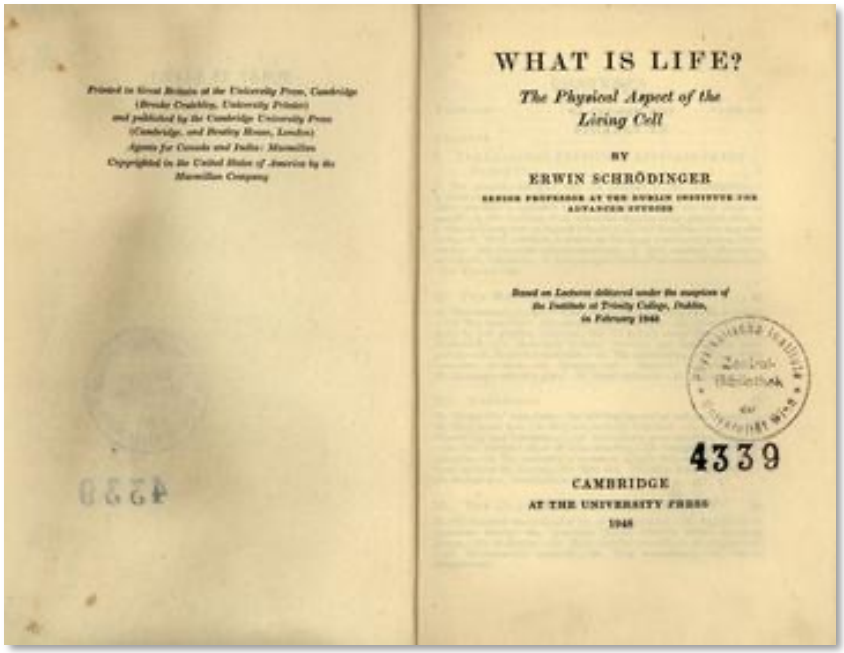


What are genes made of?



WHAT IS LIFE?

The Physical Aspect of the Living Cell

BY

ERWIN SCHRÖDINGER

CAMBRIDGE

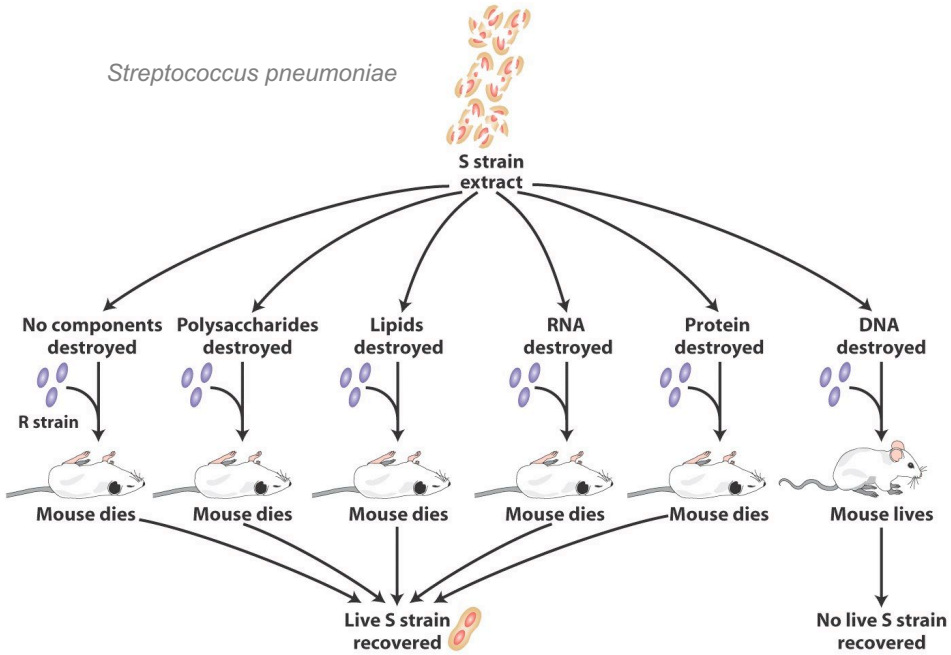
AT THE UNIVERSITY PRESS

1945

- What is the hereditary molecule?

- Schrödinger incorrectly suggested that genetic information is contained in the form of aperiodic crystals

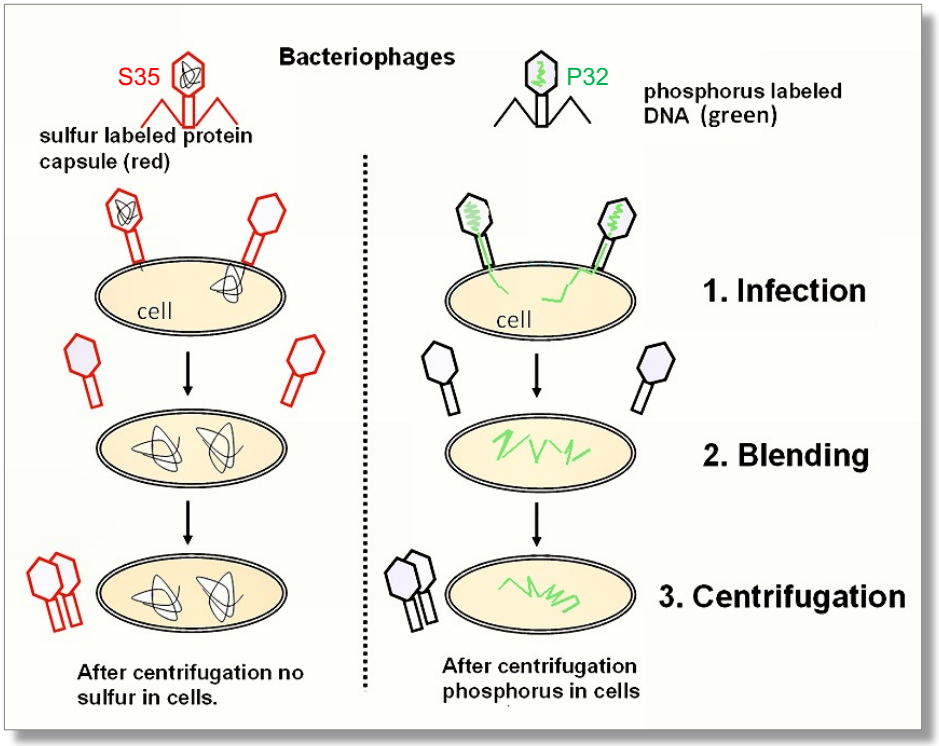
DNA is the transforming factor



- Avery, MacLeod, and McCarty (1944)
- DNA from virulent type S bacteria is able to transform nonvirulent type R bacteria

DNA is the hereditary material

T2 phage infects *E. coli*



Hershey and Chase (1952)

Watson and Crick: double helix structure of DNA

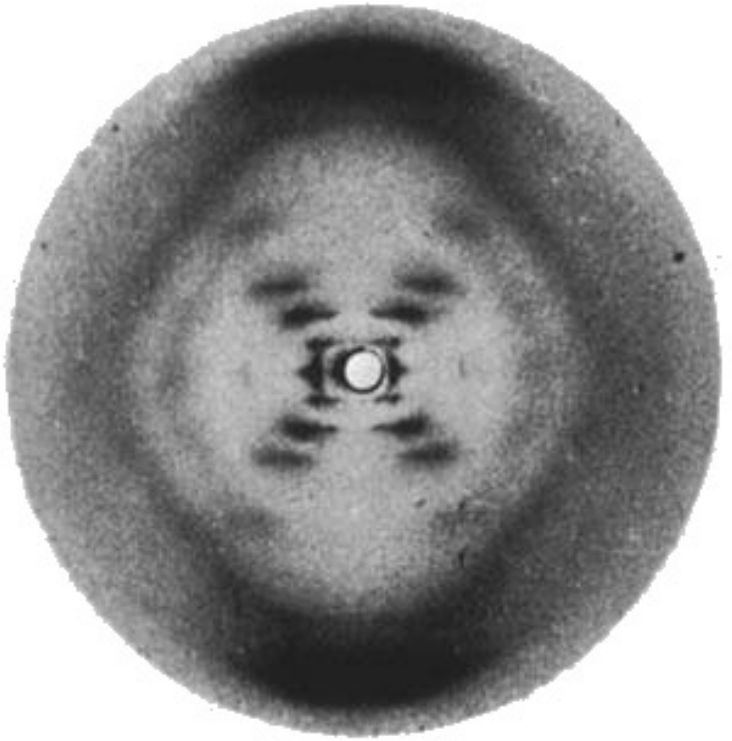


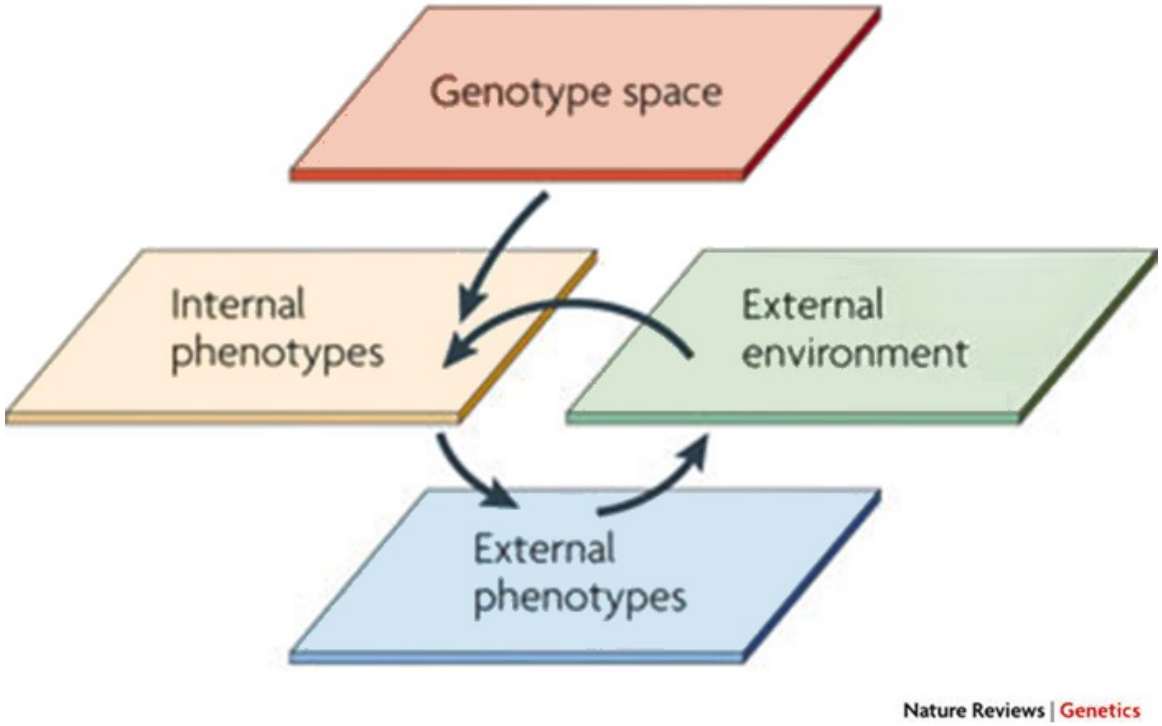
Photo 51: X-ray diffraction of DNA
(Gosling and Franklin)

Information and genetics

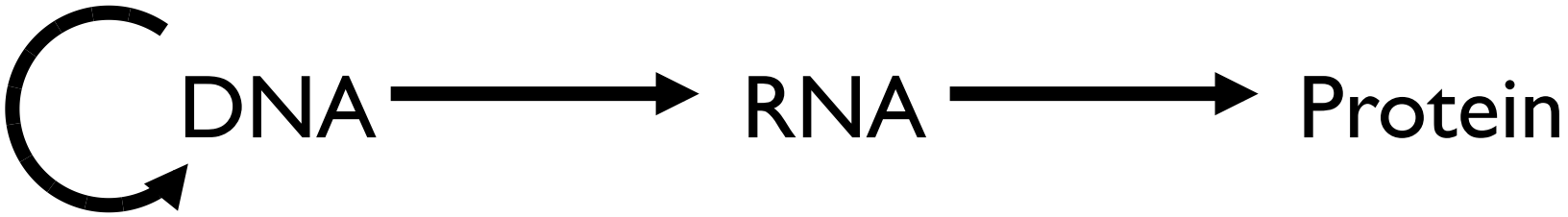
- How much information is contained in DNA?
  - 133 base pairs → 4^{133} possibilities
  - $4^{133} = 10^{80}$ (the number of atoms in the universe)

- Information flow in genetics: genotype → phenotype

Genotype-phenotype map



Central Dogma of Molecular Biology*



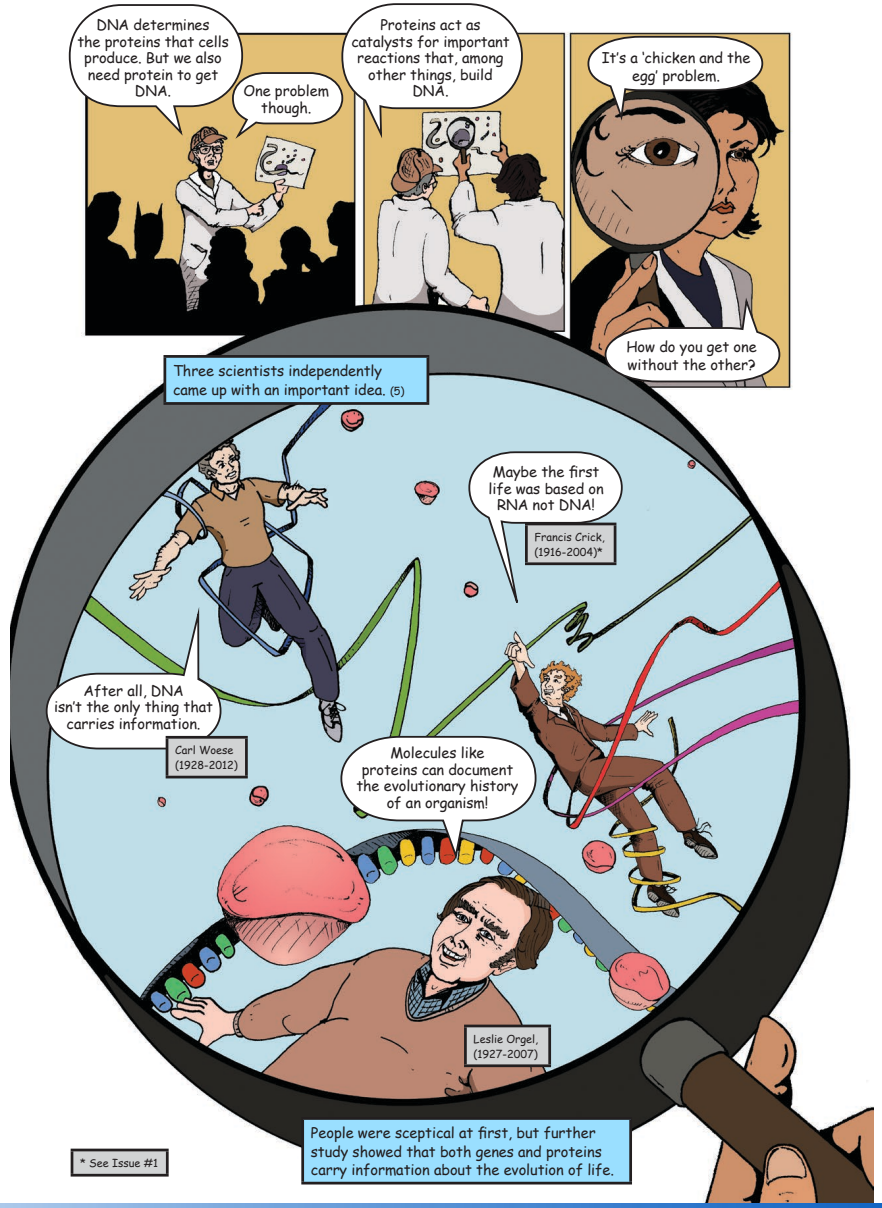
*Things are not quite this simple!

What are some exceptions to the Central Dogma?

Central Dogma: implications

- Mendelism vs. Lamarckism (acquired characteristics)
- Germline vs. soma (Weismann)
- Genes as information - decoupling of structure and function
- Biological “laws” are full of exceptions

RNA world



DNA

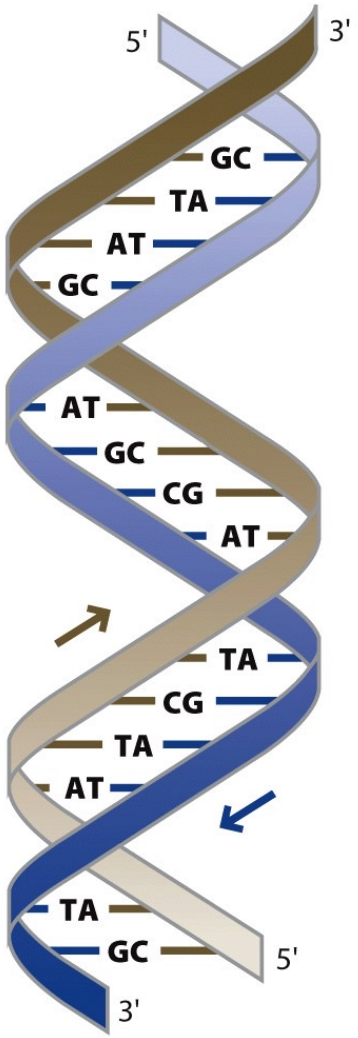


Figure 2.4b Human Evolutionary Genetics, 2nd ed. (© Garland Science 2014)

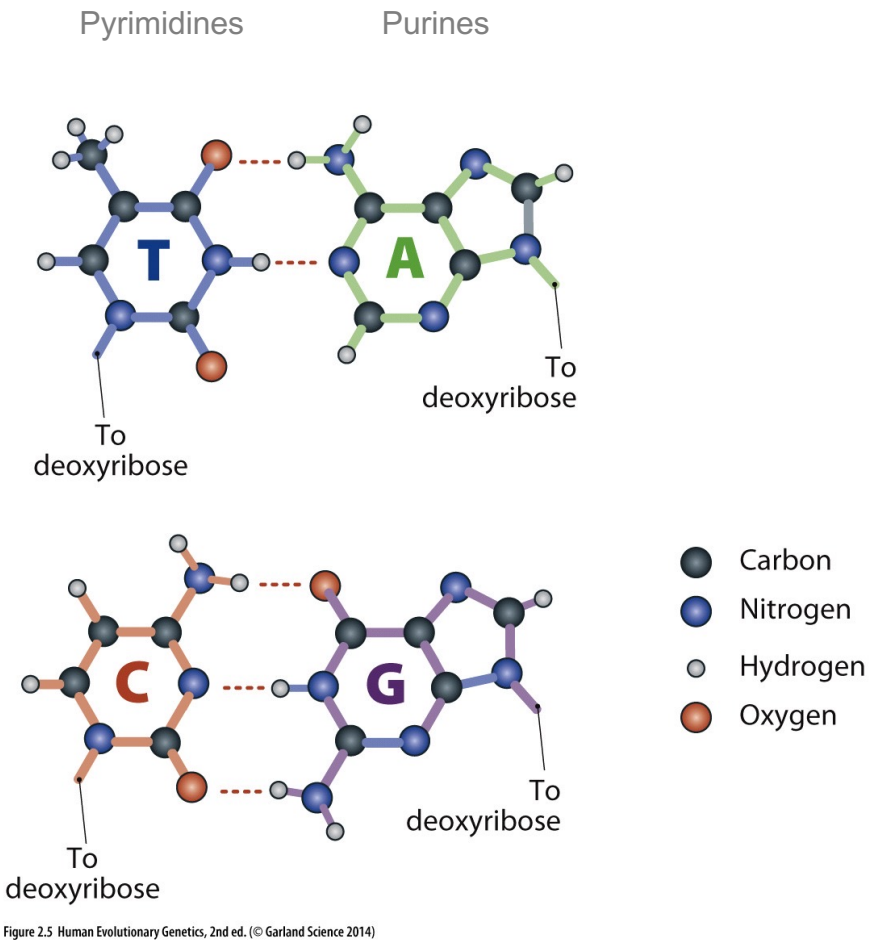
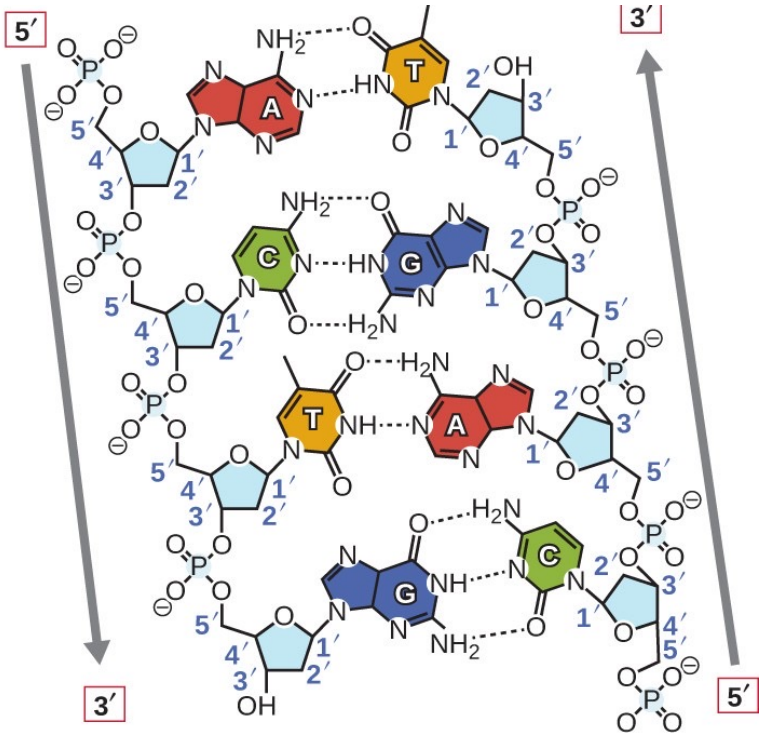


Figure 2.5 Human Evolutionary Genetics, 2nd ed. (© Garland Science 2014)

5' to 3 '



- The structure of DNA is a double helix that looks like a twisted ladder
- The sides of the ladder are made of alternating sugar (deoxyribose) and phosphate molecules, while the steps of the ladder are made of nucleobases
- The two DNA strands are antiparallel to each other

DNA packaging

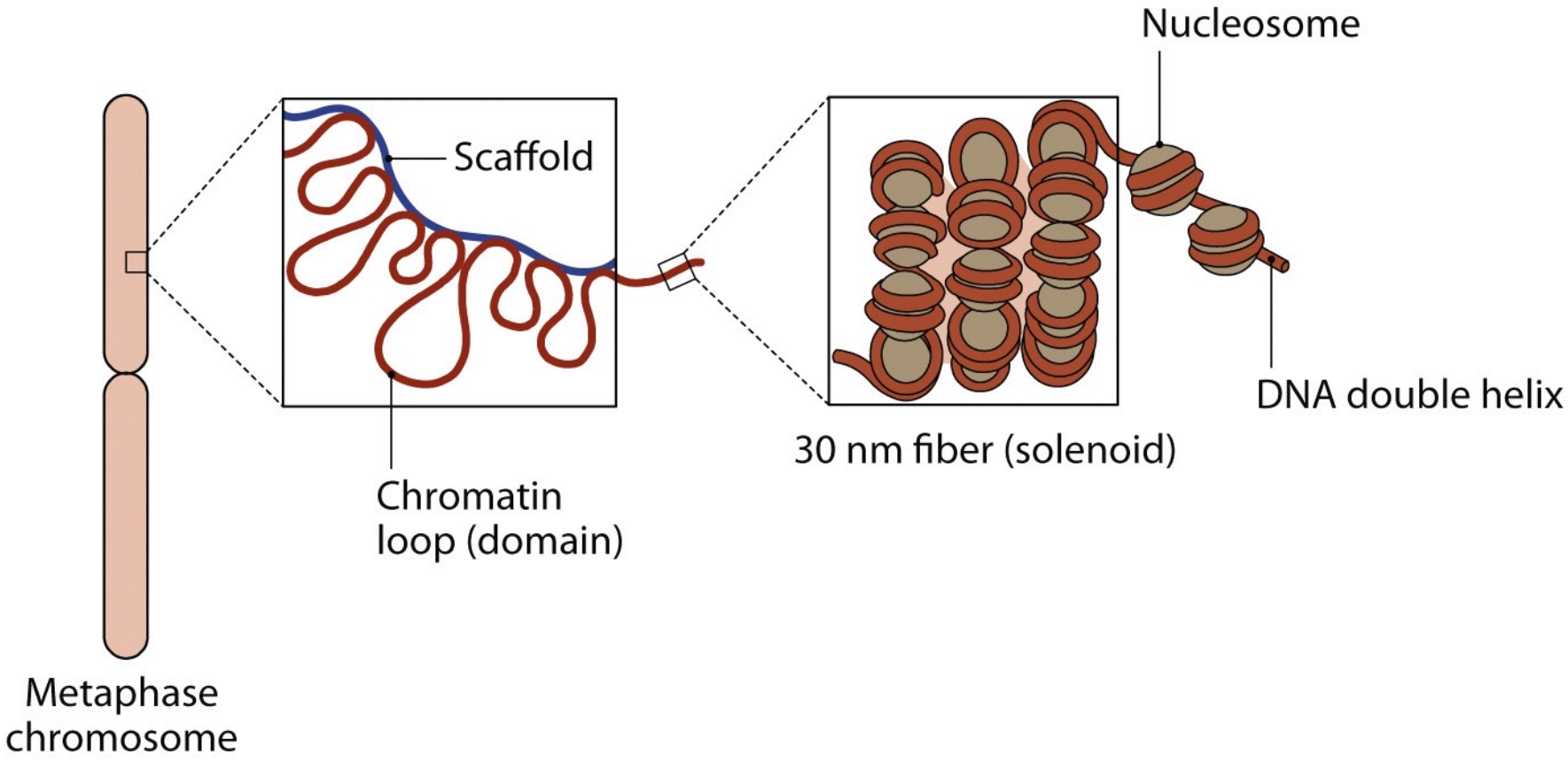
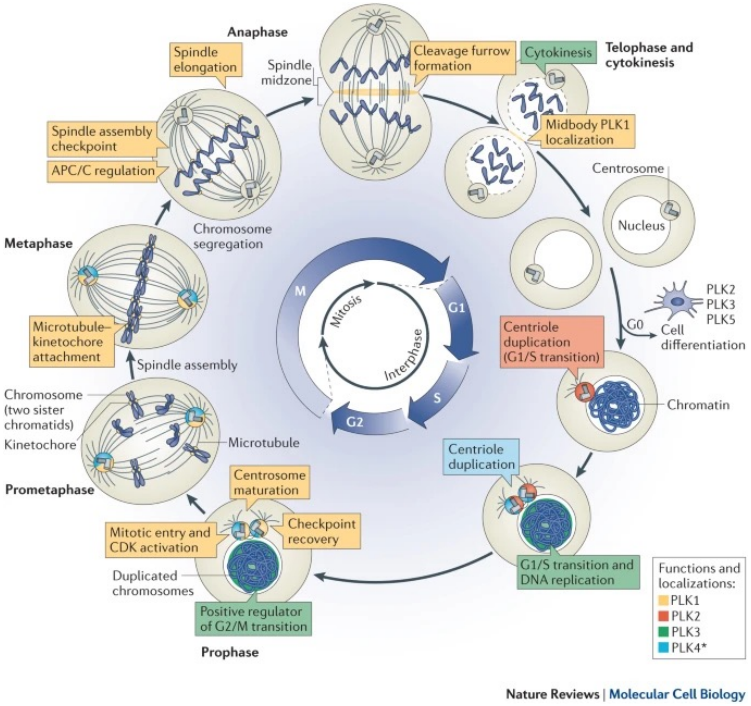
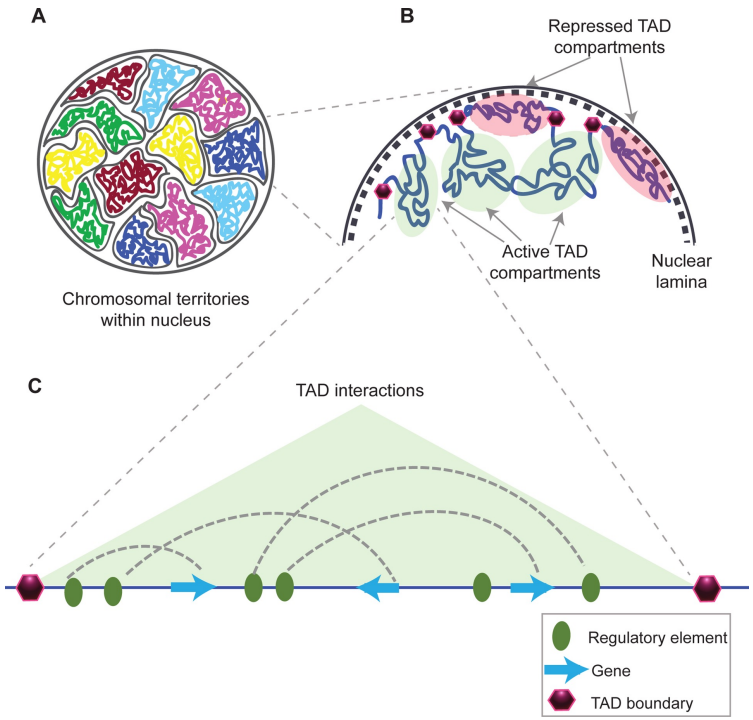


Figure 2.11 Human Evolutionary Genetics, 2nd ed. (© Garland Science 2014)

Chromatin and TADs

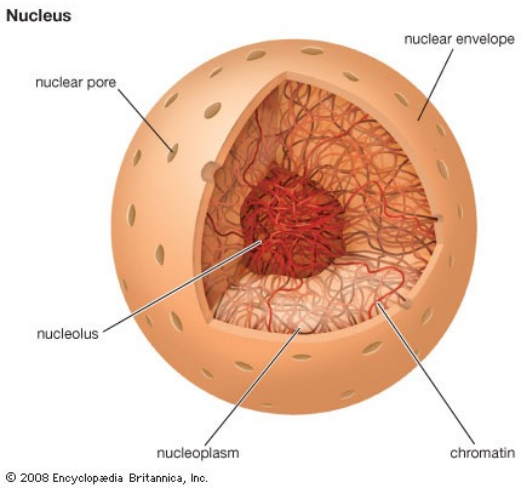




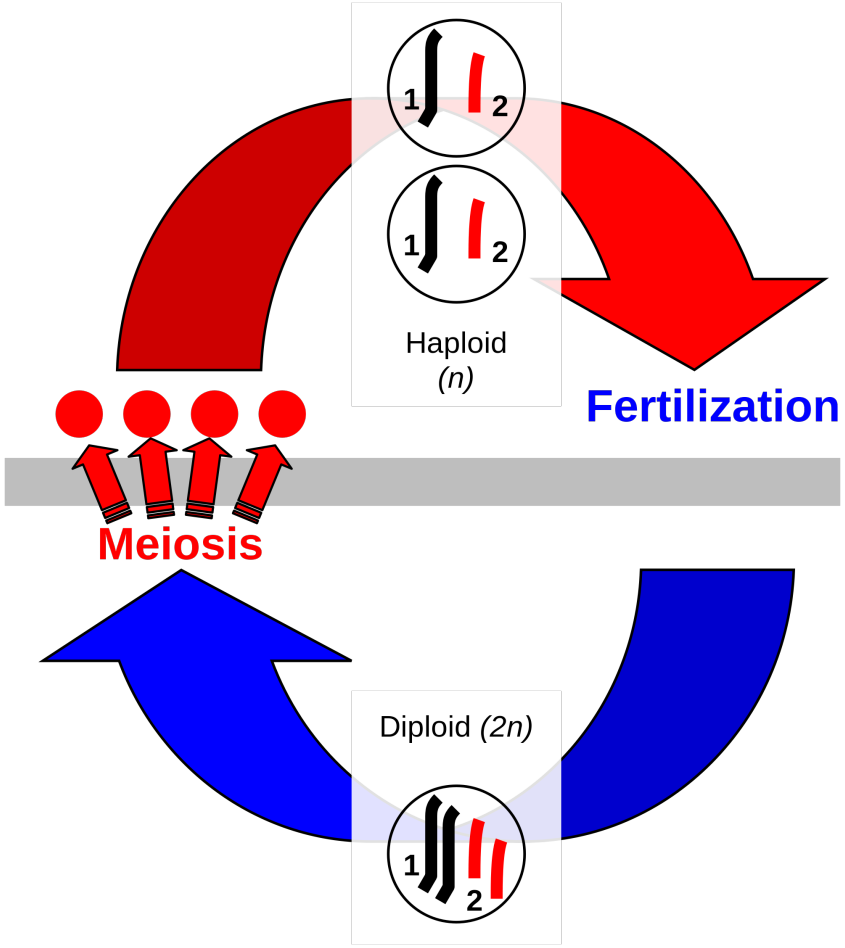
- Chromomes are not visible during most of the cell cycle
- Chromatin is in its least condenced state during interphase
- TAD: topologically associating domains

DNA packaging: implications

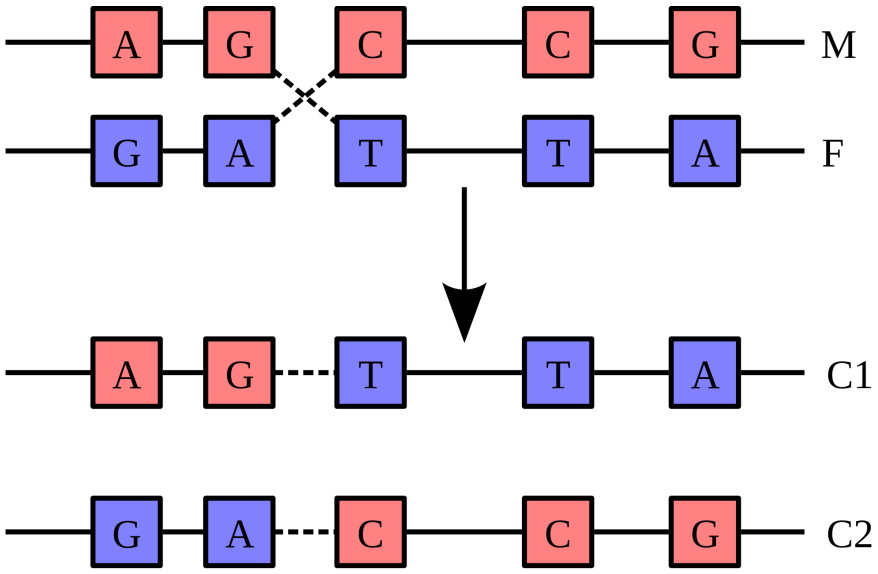
- Exposed DNA is more likely to be functional
- Proximity in 3D space matters
- Histone code



Ploidy



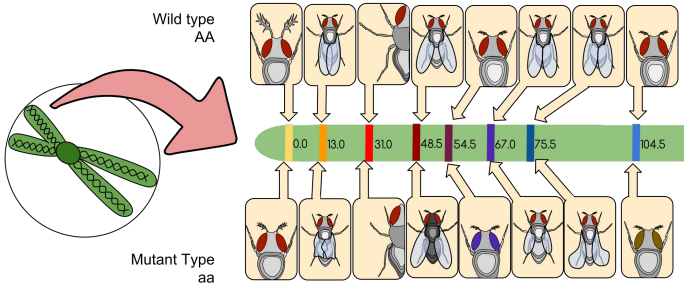
Recombination



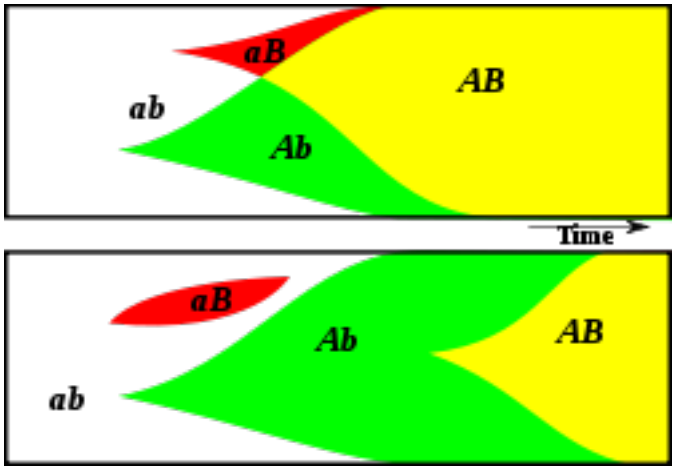
- Recombination occurs in meiosis
- It is a byproduct of the need to pair homologous chromosomes

Recombination: implications

- Genetic maps and linkage disequilibrium



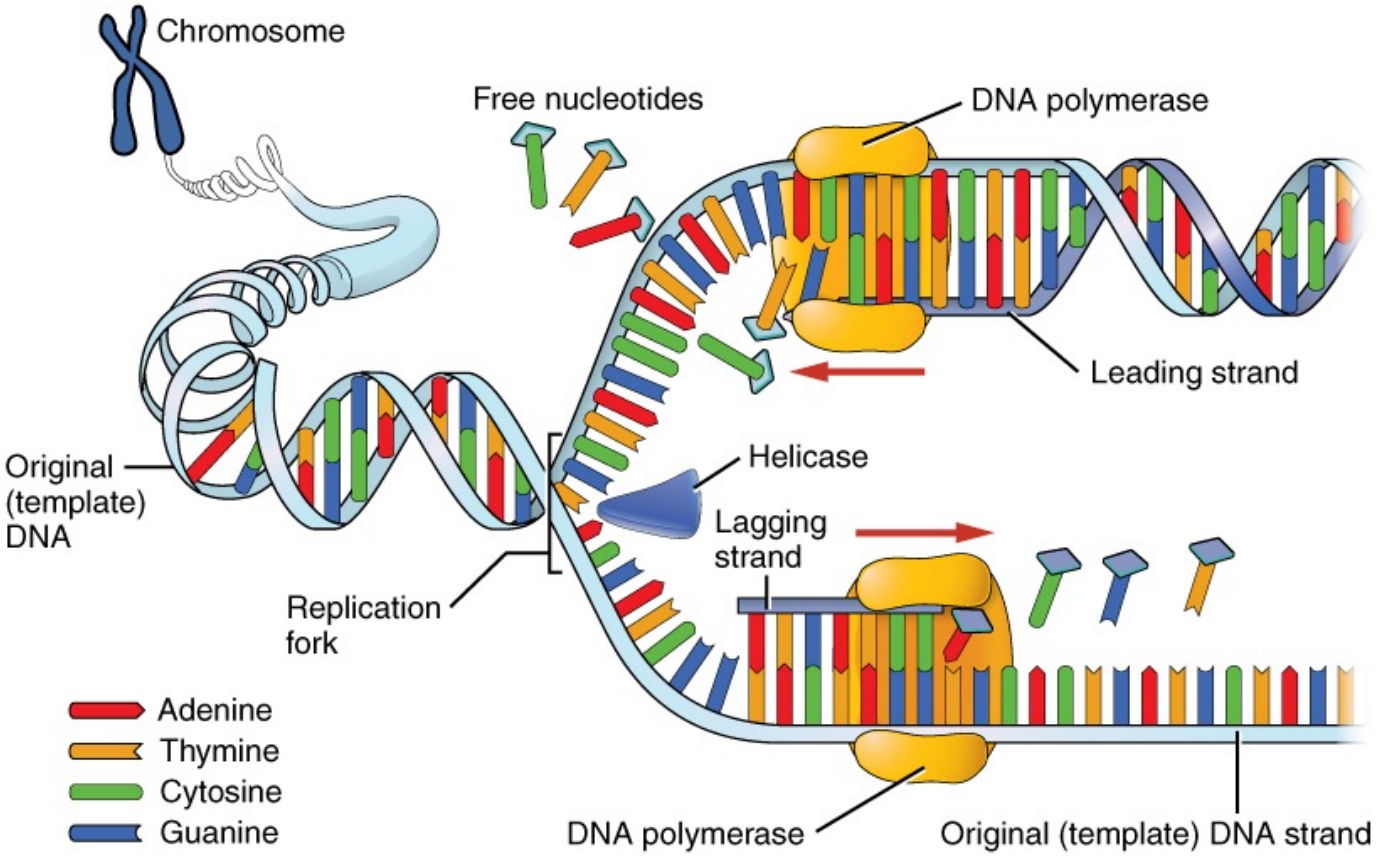
- Benefits of sex



Sexual reproduction (recombination)

Asexual reproduction

DNA replication

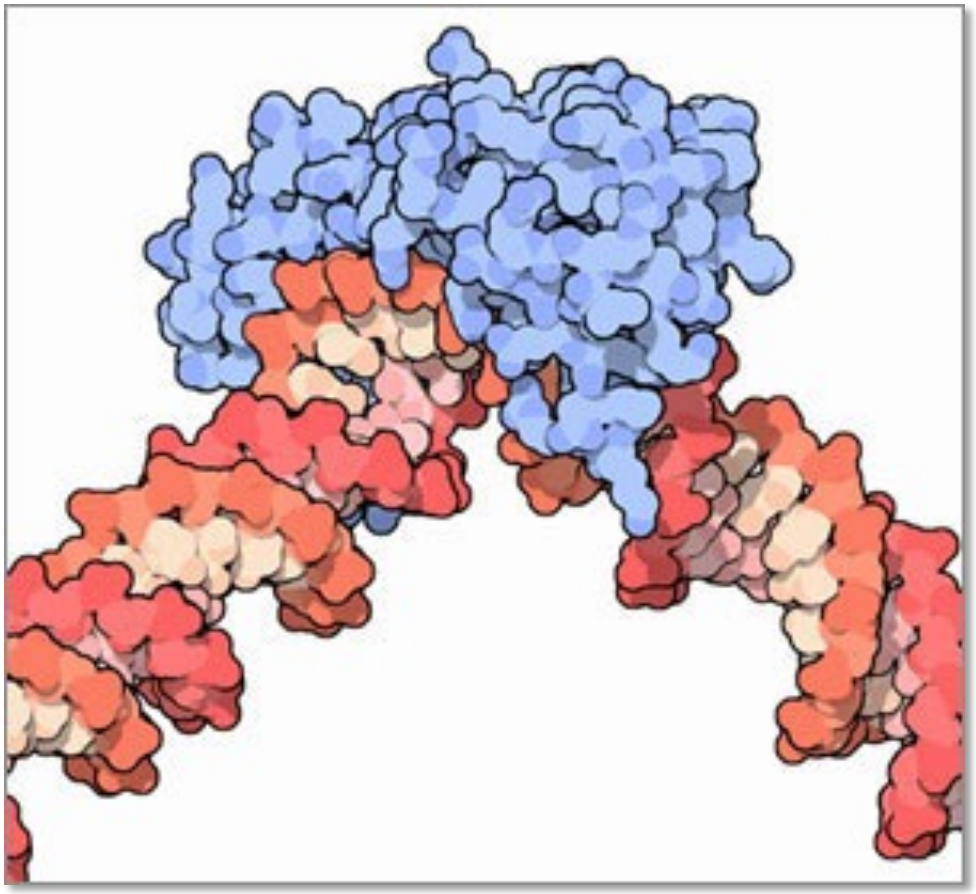


- Stages: initiation, elongation, and termination

DNA replication: implications

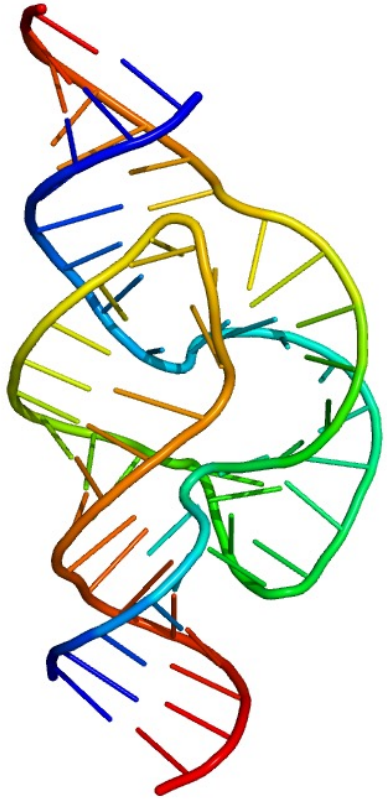
- Semi-conservative replication
- 5′ → 3′ directionality causes problems (solved by evolution)
- Potential for miscopying → **mutations**
- Comparative genomics

Transcription factors and gene regulation



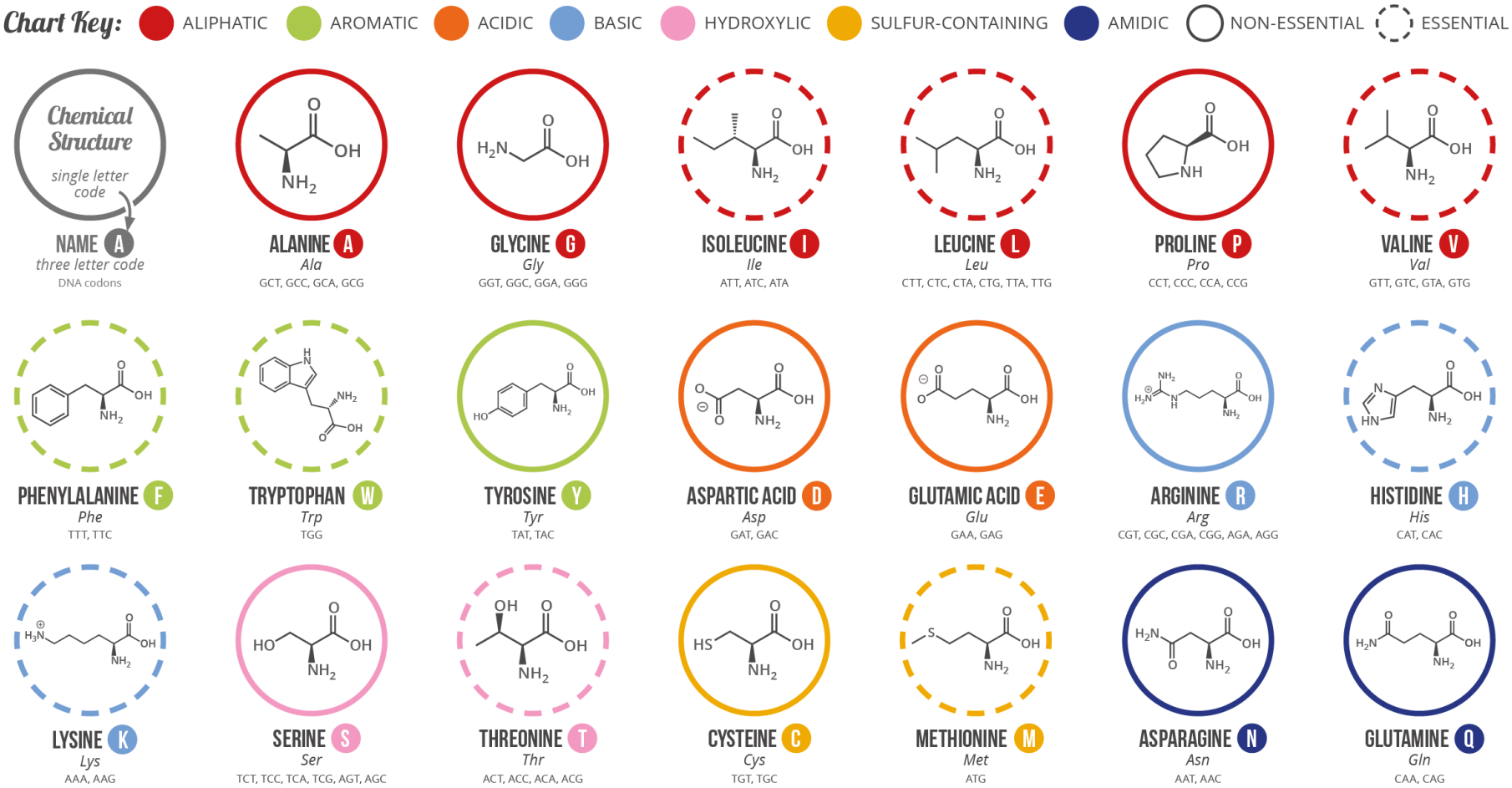
RNA comes in many different flavors

- mRNA: messenger RNA
- tRNA: transfer RNA
- rRNA: ribosomal RNA
- Regulatory RNAs (miRNA, siRNA, piRNA)



Ribozyme image: Wikimedia Commons

Proteins are made of amino acids



Note: This chart only shows those amino acids for which the human genetic code directly codes for. Selenocysteine is often referred to as the 21st amino acid, but is encoded in a special manner. In some cases, distinguishing between asparagine/aspartic acid and glutamine/glutamic acid is difficult. In these cases, the codes asx (B) and glx (Z) are respectively used.

From DNA to RNA to protein

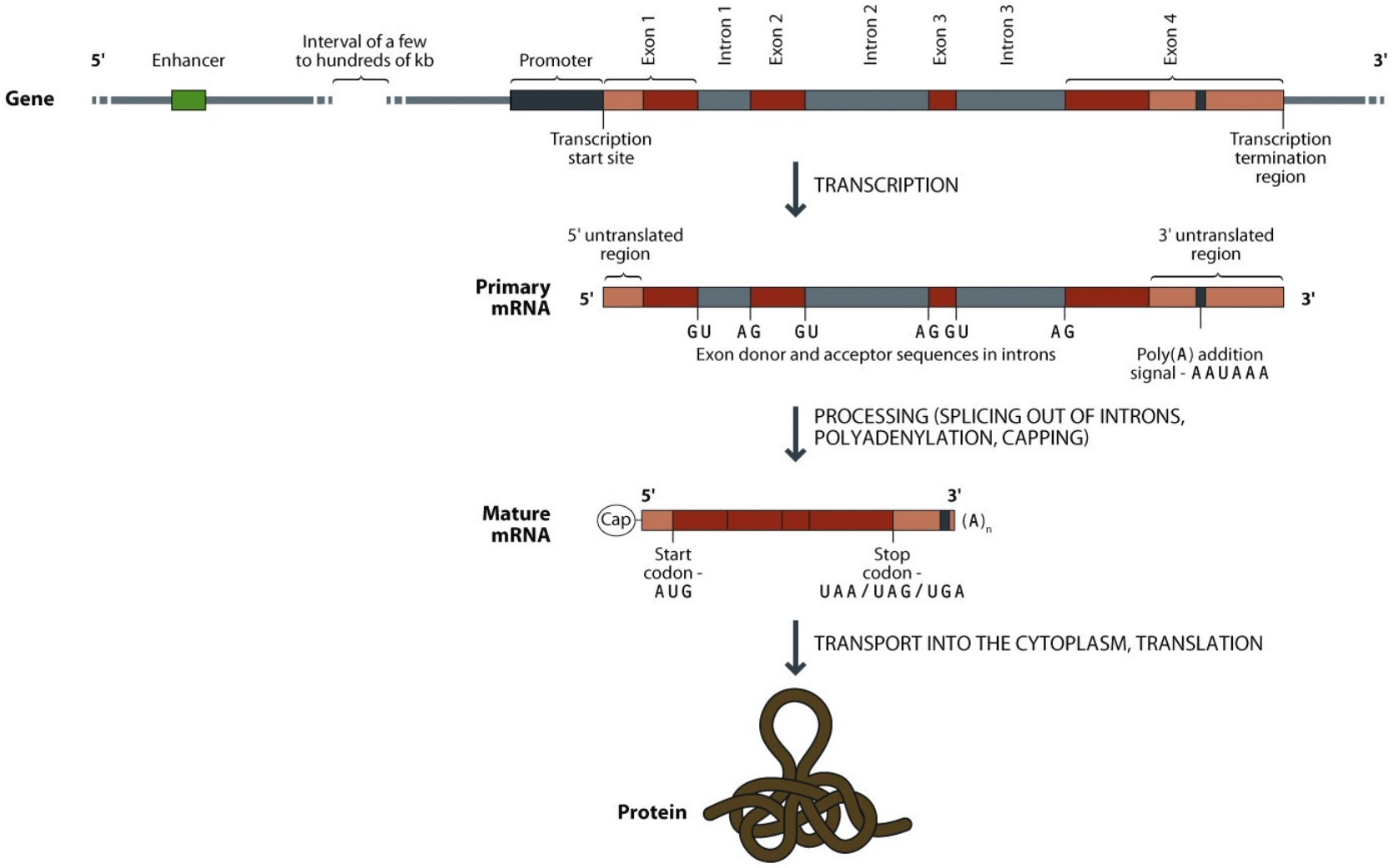


Figure 2.6 Human Evolutionary Genetics, 2nd ed. (© Garland Science 2014)

Transcription: DNA serves as a template

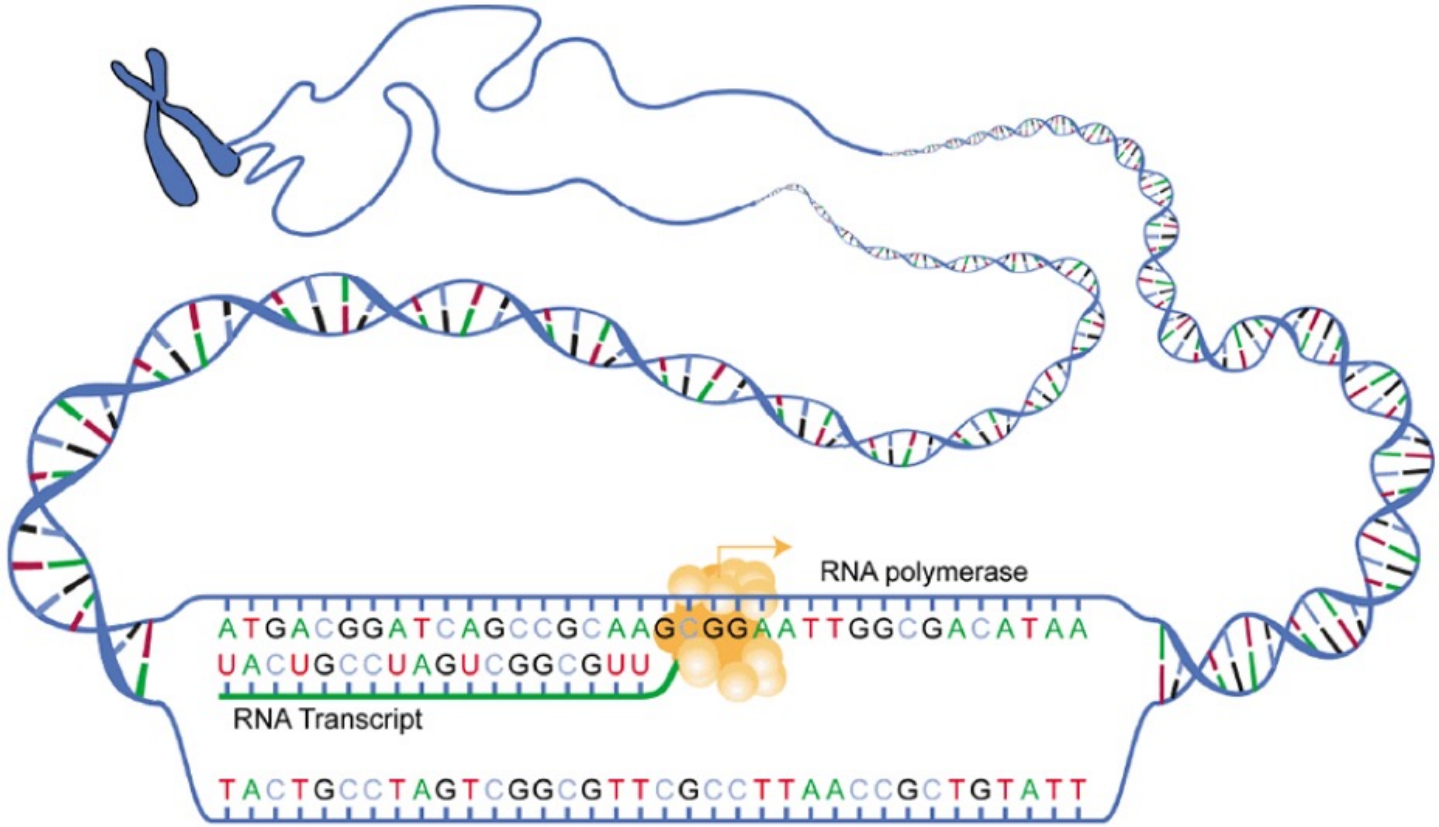
5′ … CGATCGGACTACGGACTAGCGACTACGA … 3′ **Sense strand of DNA**

3′ … GCTAGCCTGATGCCTGATCGCTGATGCT … 5′ **Antisense strand of DNA**

Transcription of antisense strand

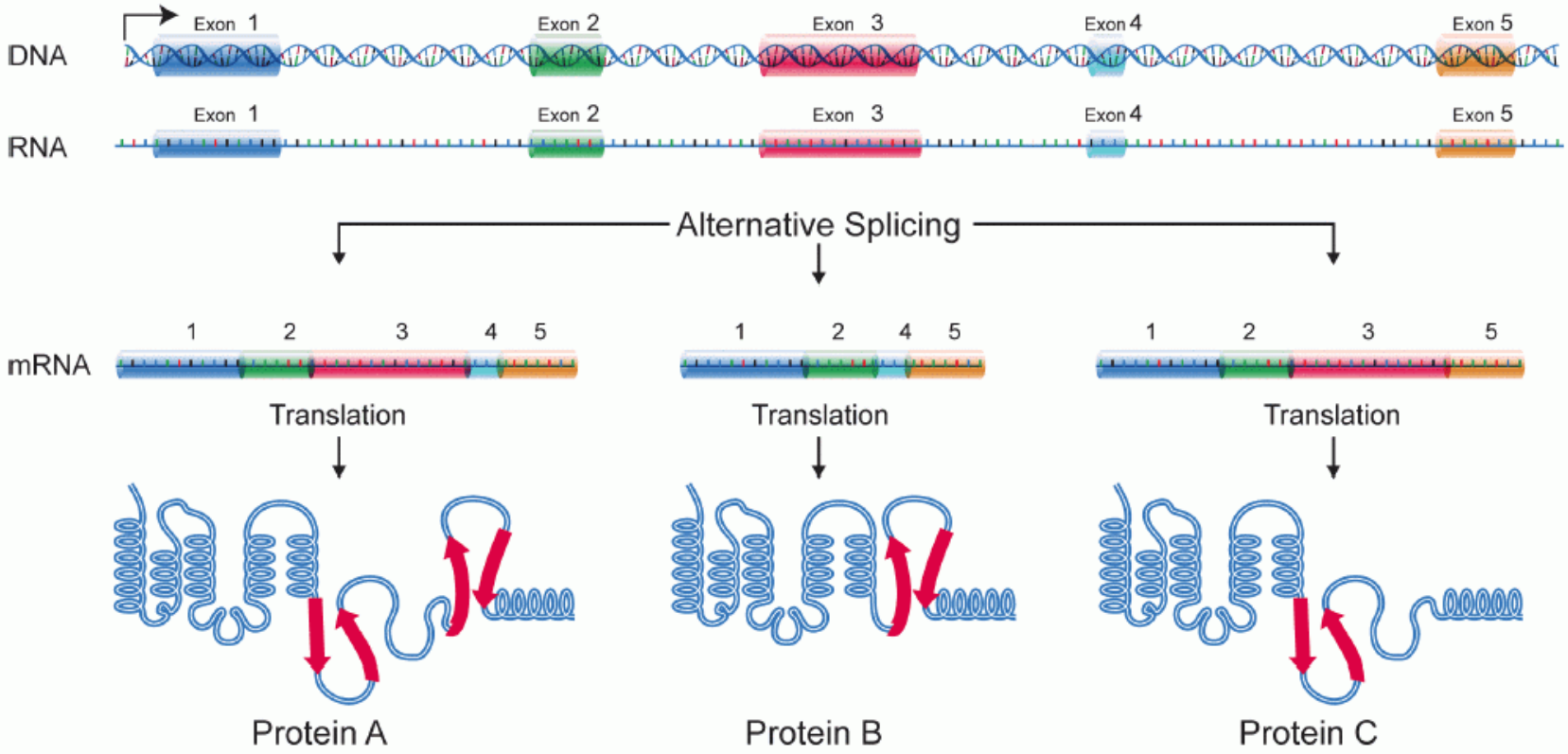
5′ … CGAUCGGACUACGGACUAGCGACUACGA … 3′ **RNA**

Transcription (DNA to RNA)



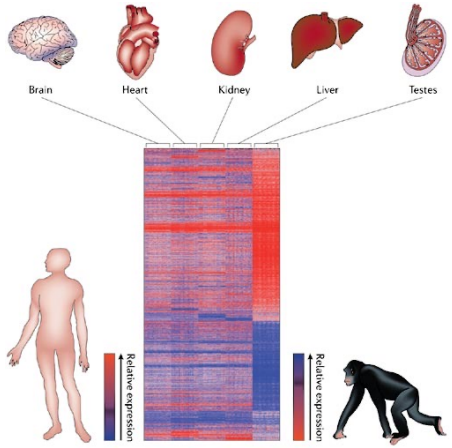
- Major steps: initiation, promoter escape, elongation, and termination

Splicing

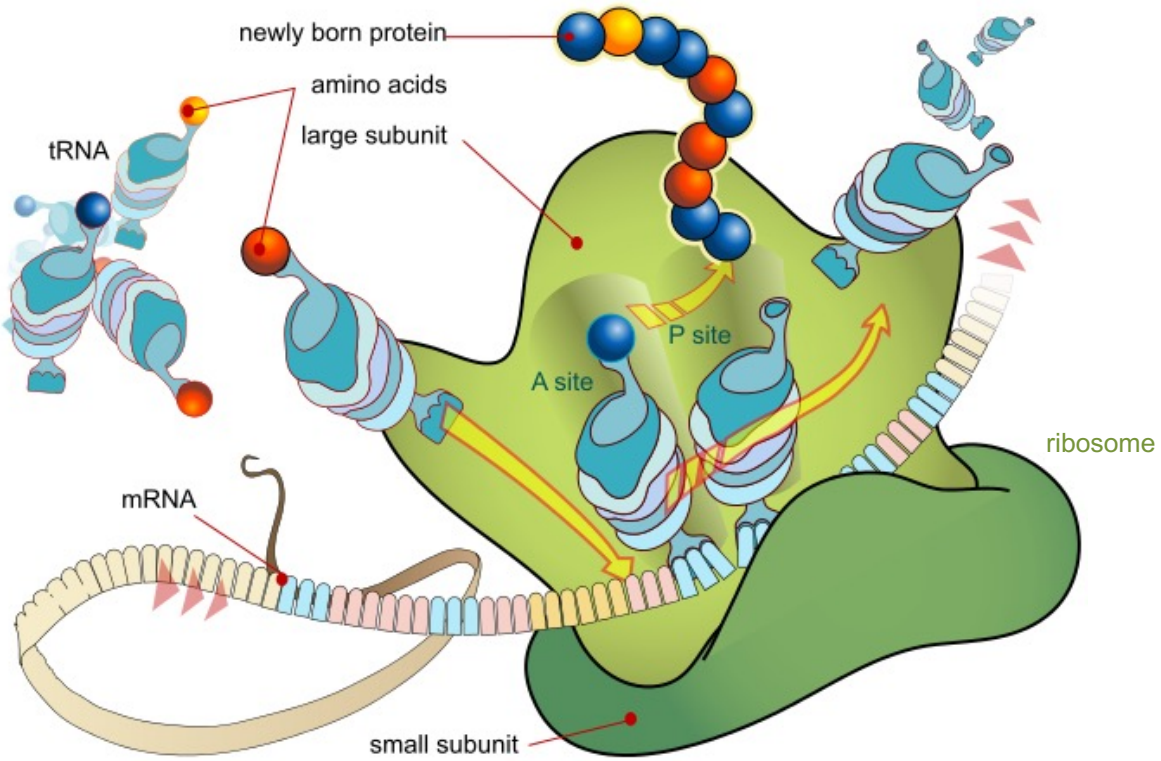


Transcription: implications

- **Gene expression**: transcriptional activity of a gene that results in RNA
- Inducible system that allows organisms to respond to environments
- Helps explain how different cell types can share same DNA

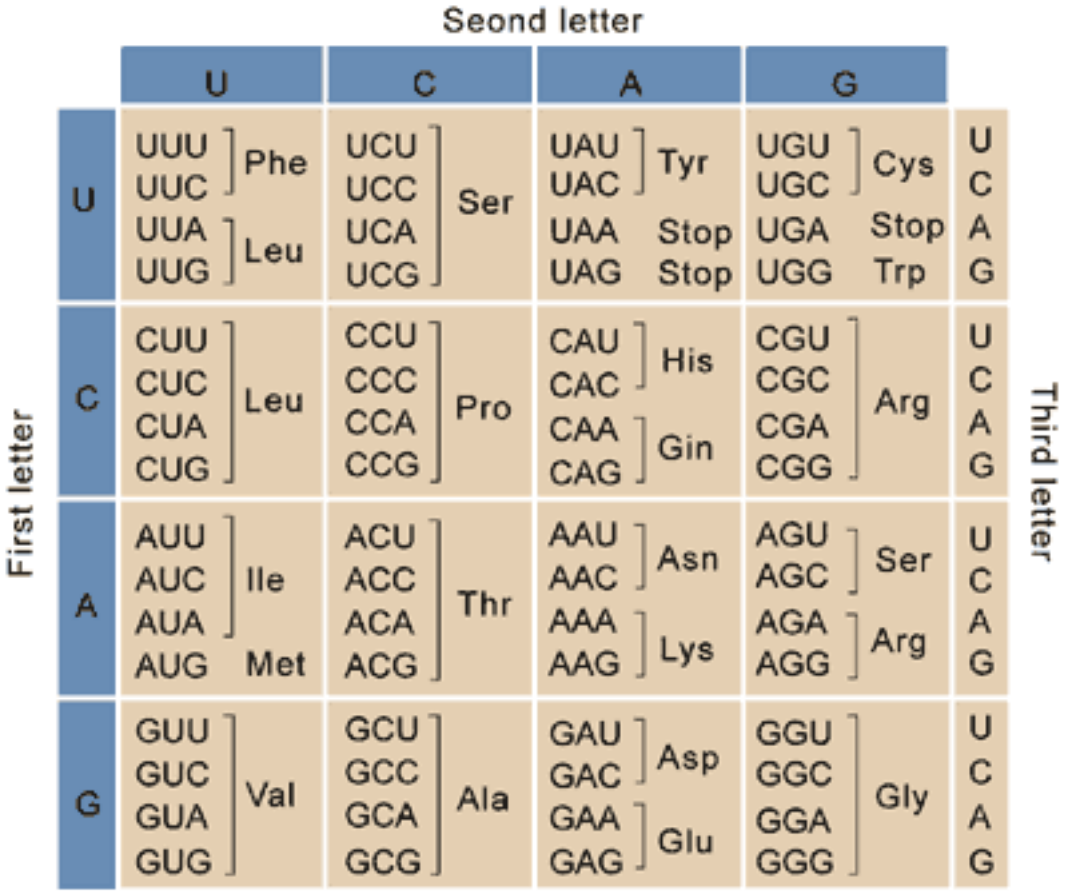


Translation (RNA to protein)



- Stages: initiation, elongation, and termination

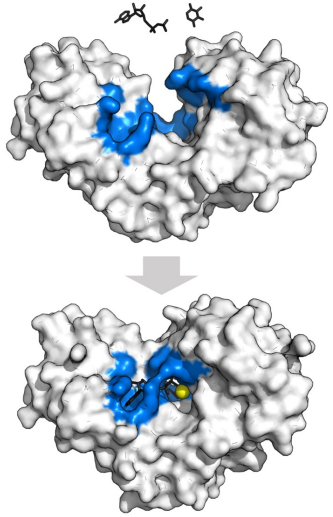
The genetic code



Does the codon table look random?

Translation: implications

- The genetic code is (relatively) arbitrary... frozen accident?
- Phase and frameshift mutations
- Post-translational modifications (e.g., glycosylation)
- **Enzymes**: a substance produced by a living organism that catalyzes a specific biochemical reaction. Enzymes are made of proteins

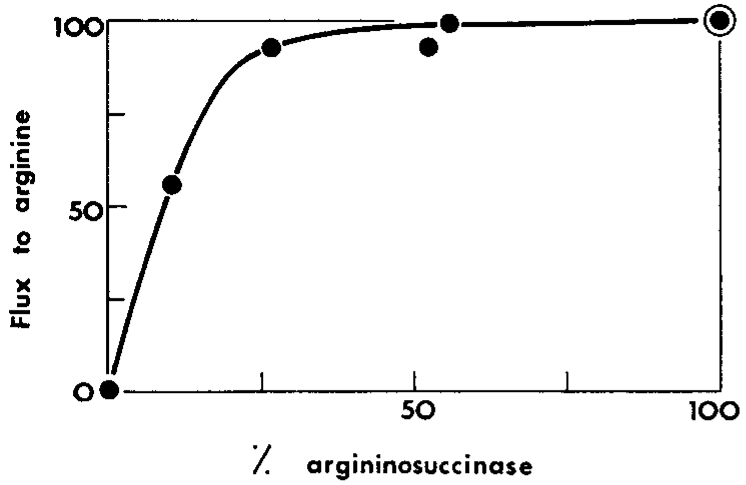


Building blocks of life

- Carbohydrates
- Proteins
- Lipids
- Nucleic acids

From biochemistry to dominance and recessivity

- Kacser and Burns (*Genetics*, 1981)
- Dominance can arise as an emergent property of metabolic flux



- Having half as much of an enzyme is much better than having none

Movie clips

hhmi | BioInteractive

- DNA packaging: https://www.youtube.com/watch?v=ttu3sCFpp-M
- Transcription: https://www.youtube.com/watc...v=-AnsJILjbz8
- Translation: https://www.youtube.com/watch?v=tTlZQQtoq5Q