# CS262

## A Zero-Knowledge Based Introduction to Biology

# Biology

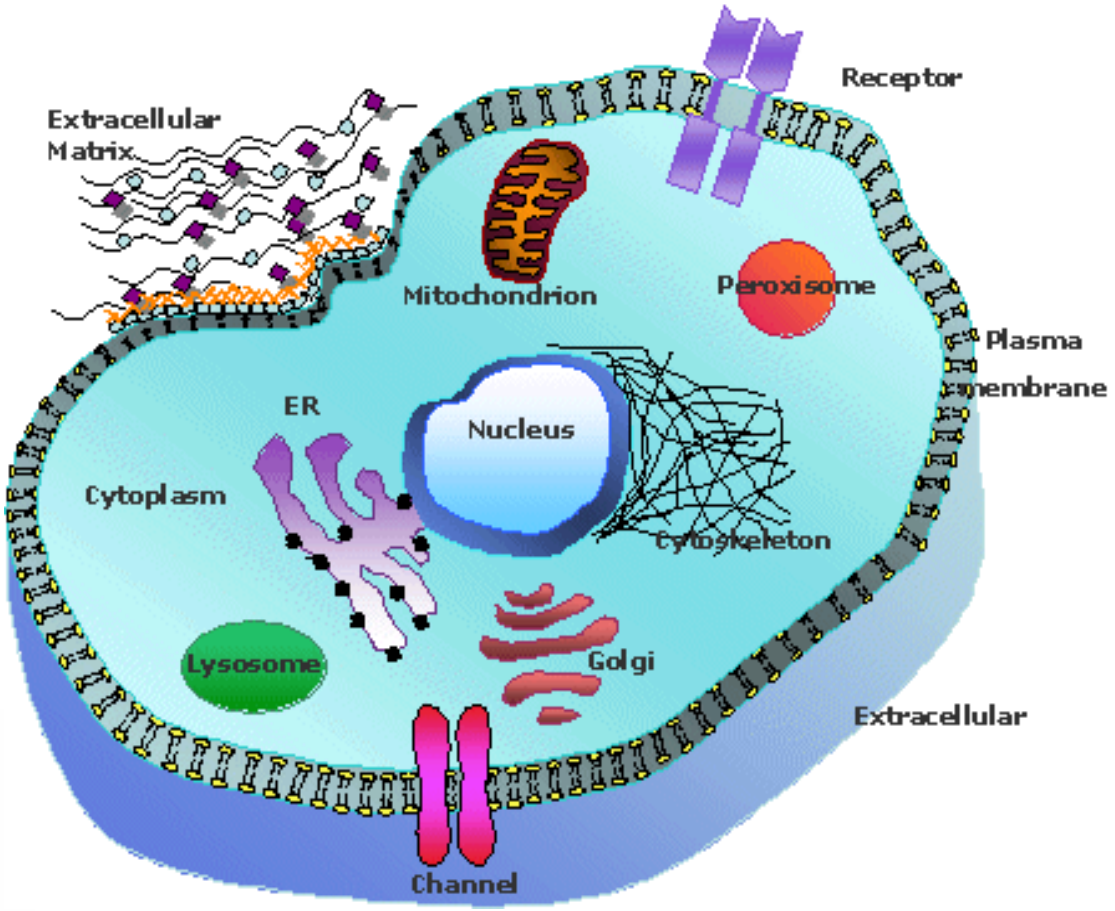
- From the greek word *βίος* = life
- Timeline:
  - 1683 – discovery of **bacteria**
  - 1858 – **Darwin**'s natural selection
  - 1865 – **Mendel**'s laws
  - 1953 – **double helix** suggested by Watson-Crick
  - 1955 – discovery of DNA and RNA **polymerase**
  - 1978 – sequencing of first genome (5kb virus)
  - 1983 – invention of **PCR**
  - 1990 – discovery of **RNAi**
  - 2000 – human genome (draft)

# How to learn some?

- Online sources
  - Wikipedia
    - http://www.wikipedia.org/
  - John Kimball's Biology Pages
    - http://biology-pages.info/
- Cold Spring Harbor Meetings
  - CSHL Biology of Genomes
  - CSHL Genome Informatics
- Hang out with biologists

# The Cell

**cell, nucleus, cytoplasm, mitochondrion**



# How many?

- Cells in the human body:

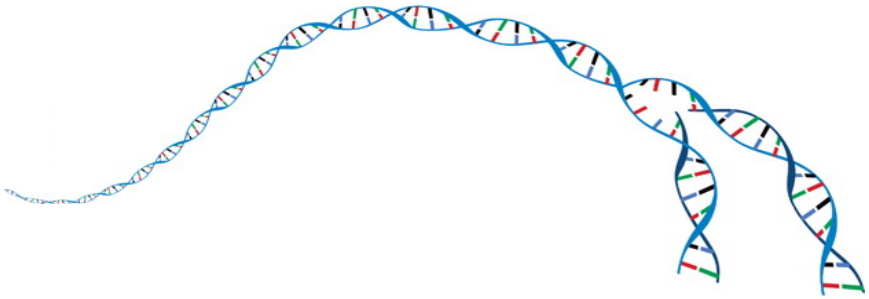
  $\sim 10^{14}$ (100 trillion)

  $\sim 10^{15}$ bacterial cells!

# Chromosomes

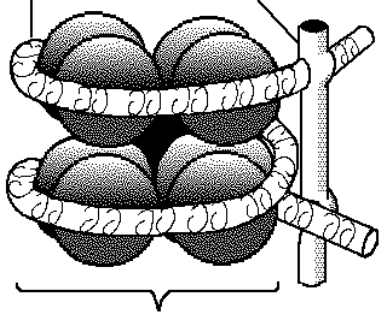
**histone, nucleosome, chromatin, chromosome, centromere, telomere**

ome



DNA H1

chromatin



~146bp

H2A, H2B, H3, H4

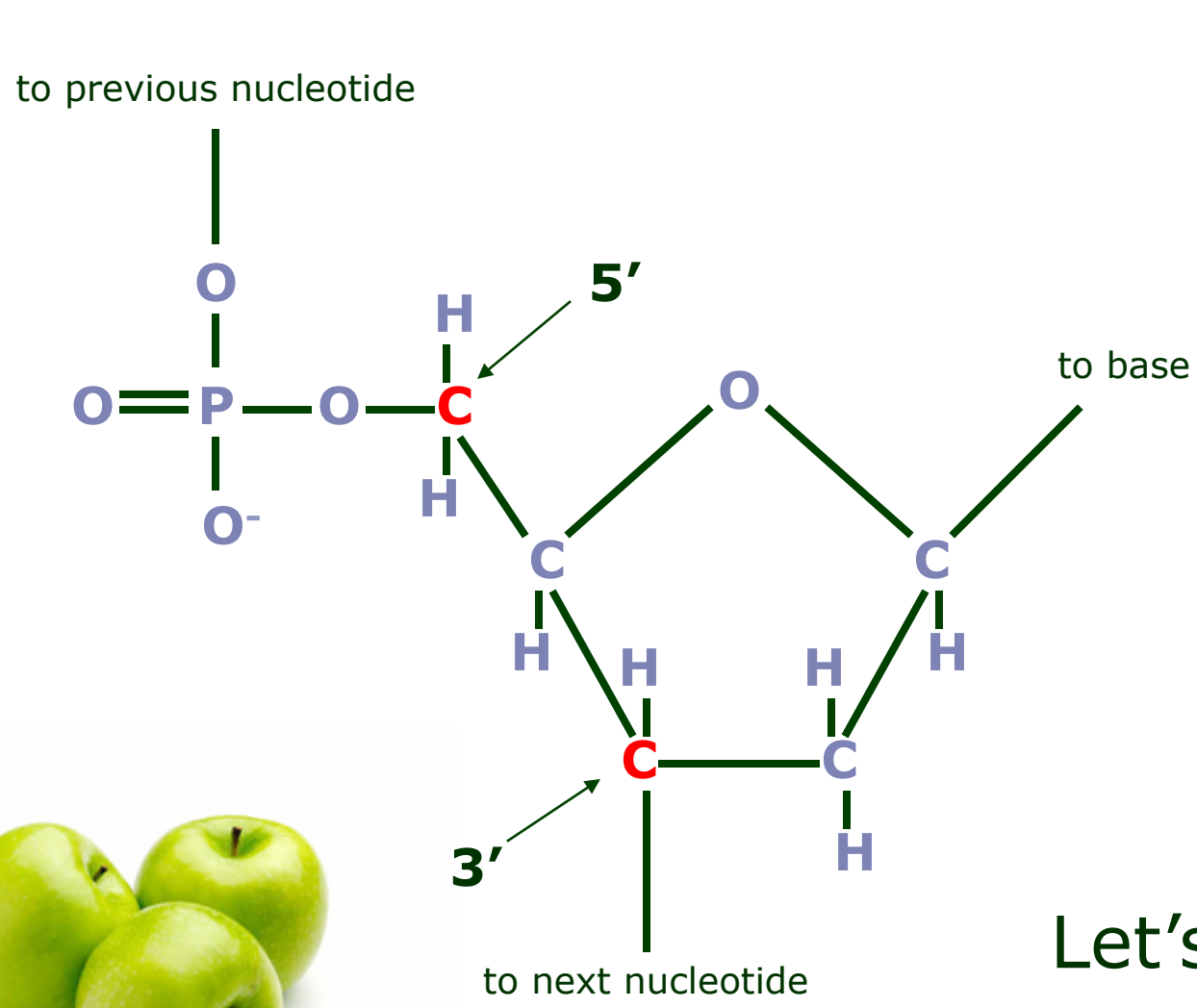
# How many?

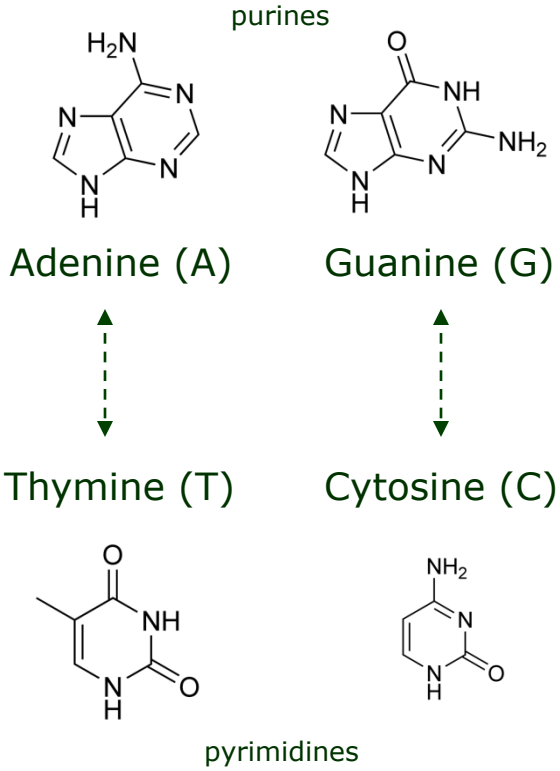
- Chromosomes in a human cell:

  46 (2x22 + X/Y)

# Nucleotide

**deoxyribose, nucleotide, base, A, C, G, T, purine, pyrimidine, 3’, 5’**

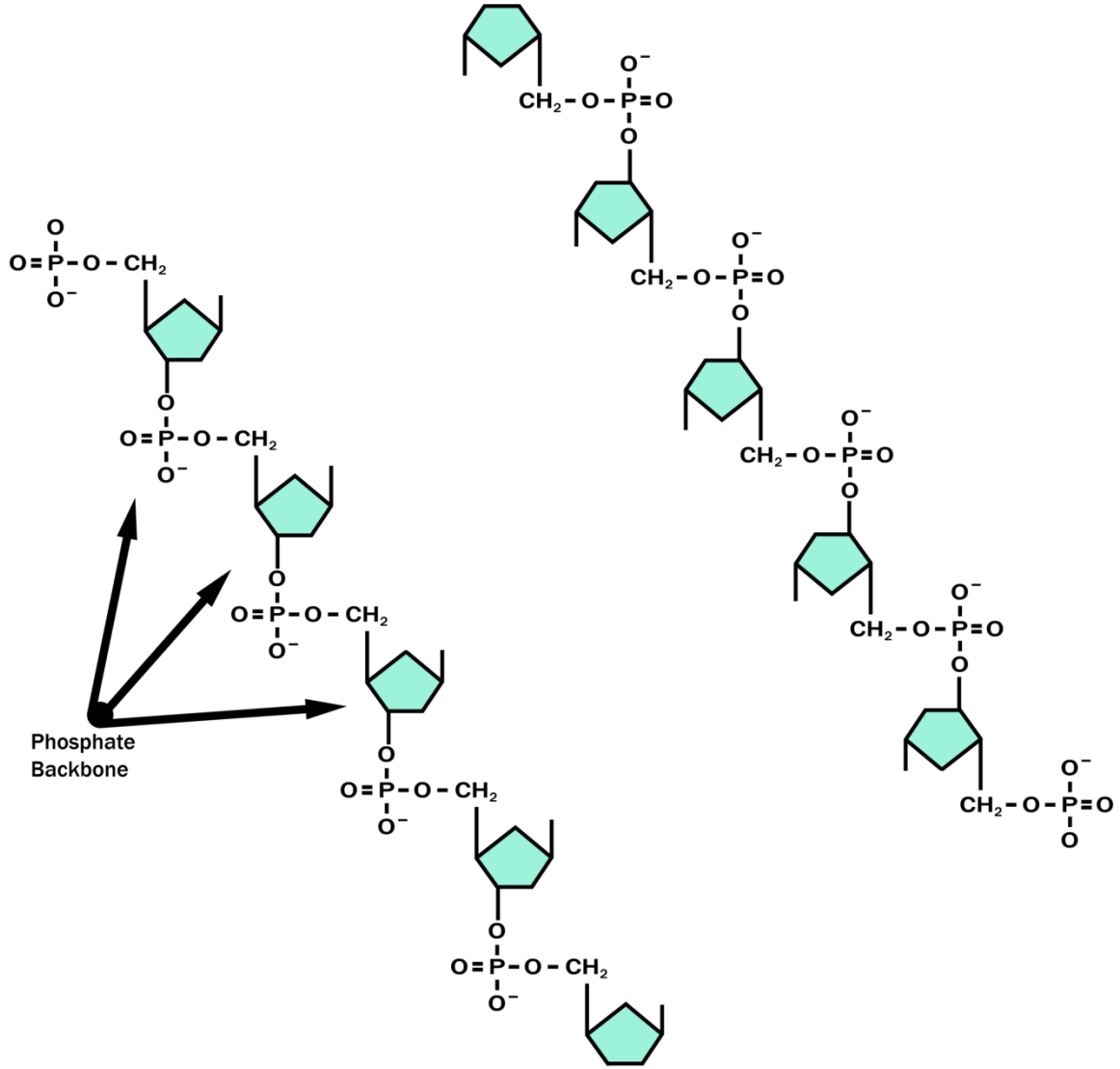




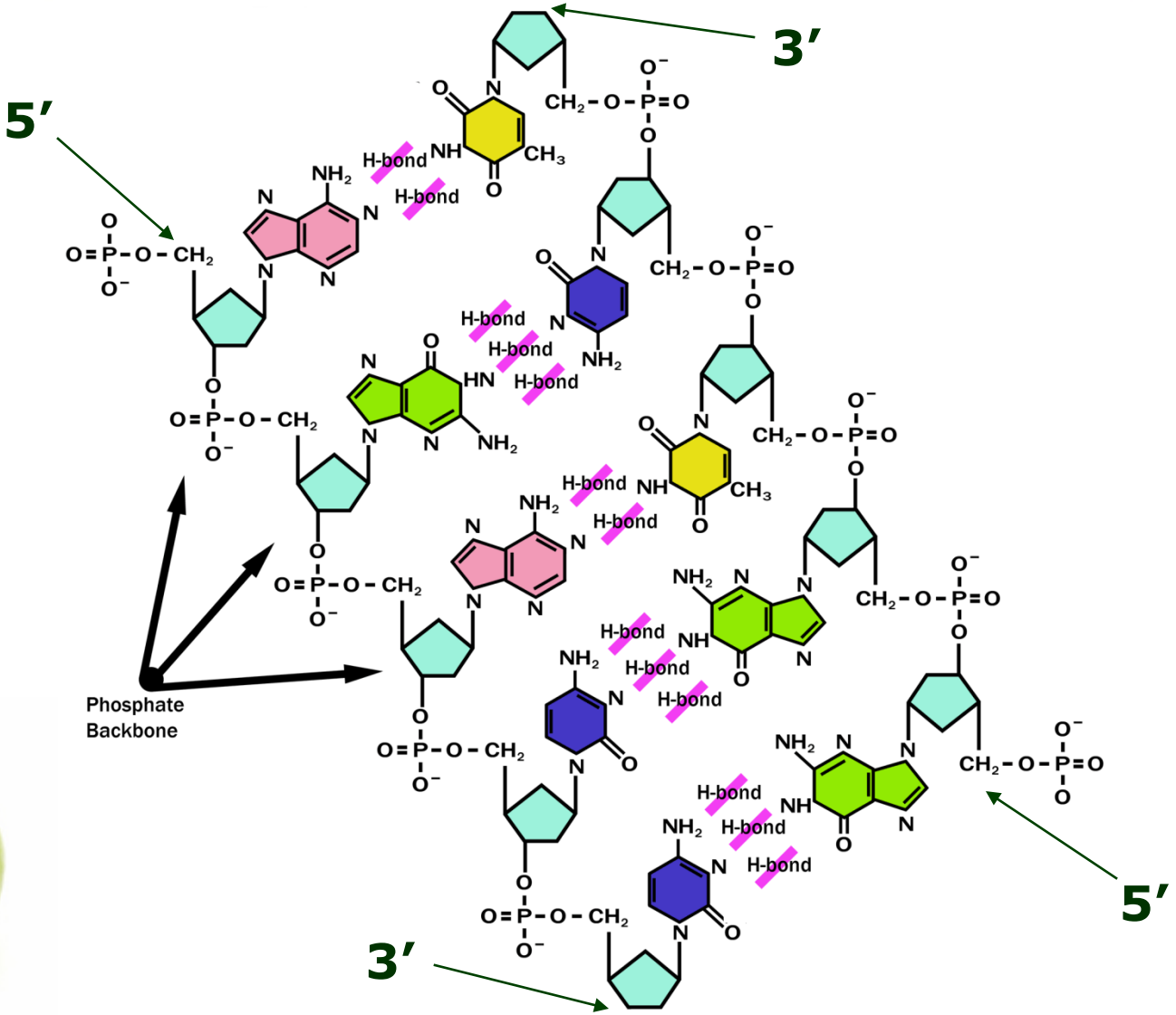

Let’s write “AGACC”!

# “AGACC” (backbone)




# “AGACC” (DNA)

**deoxyribonucleic acid (DNA)**

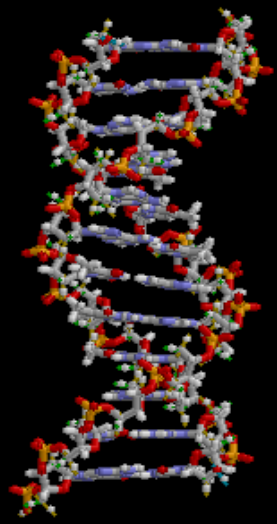



# DNA is double stranded

**strand, reverse complement**

5’ — AGACC — 3’

3’ — TCTGG — 5’

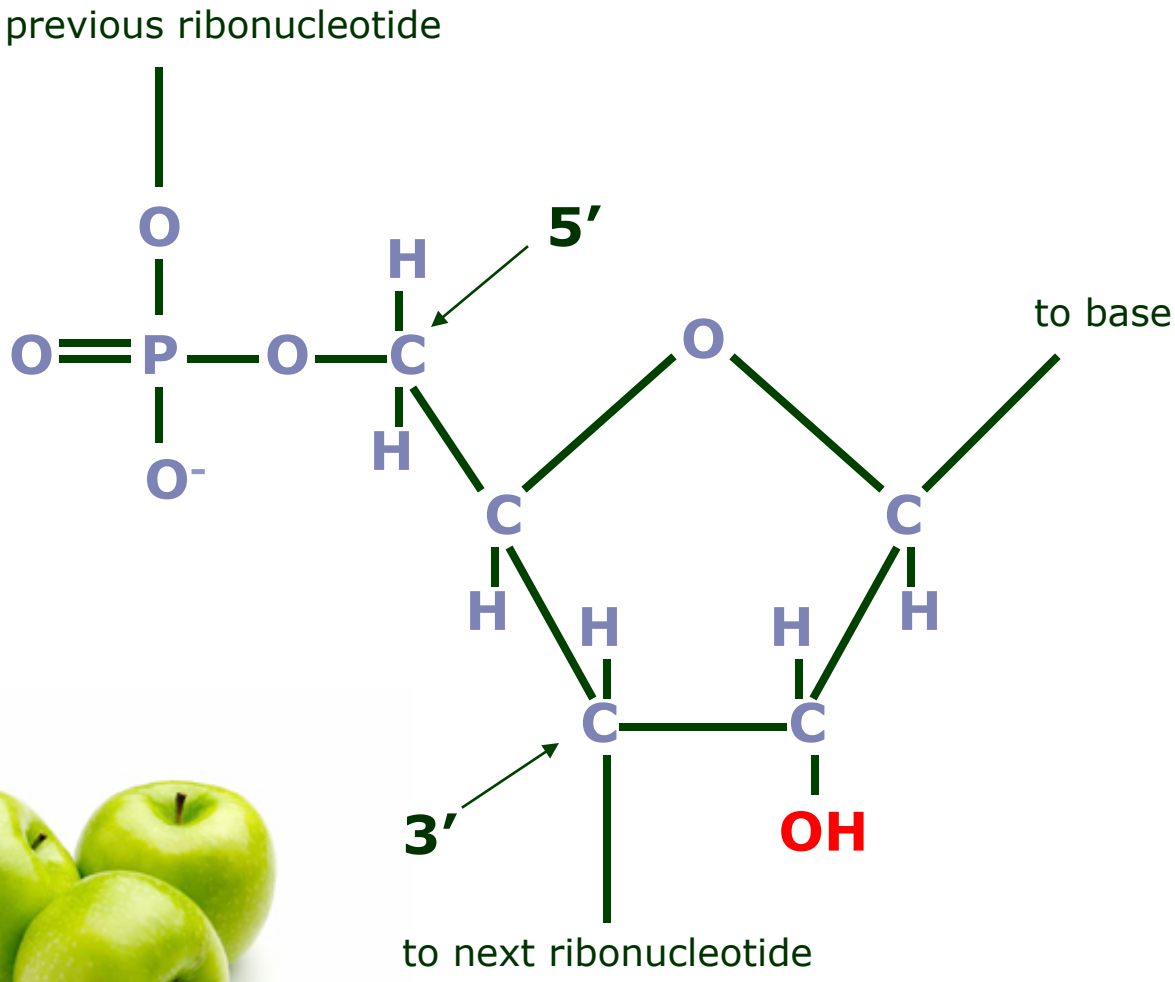


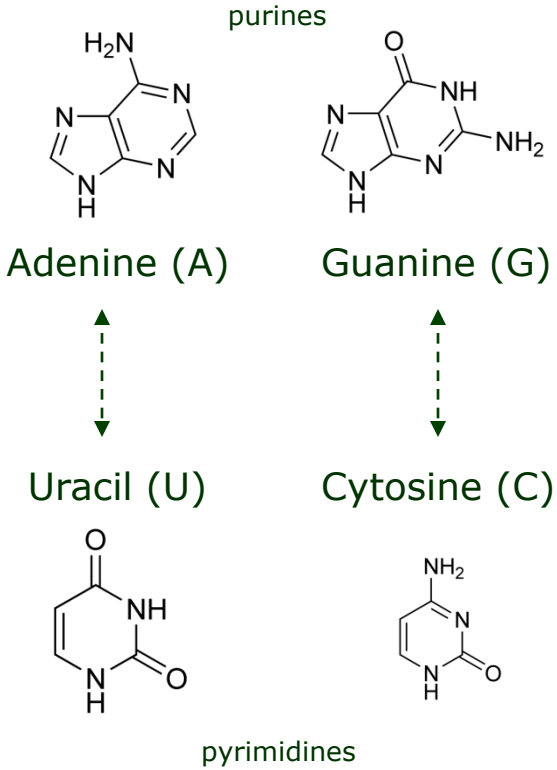
DNA is always written 5’ to 3’

AGACC or GGTCT

# RNA

**ribose, ribonucleotide, U**



# How many?

- Nucleotides in the human genome:

  ~ 3 billion

# Genes & Proteins

**gene, transcription, translation, protein**

Double-stranded DNA

5′ TAGGATCGACTATATGGGATTACAAAGCATTTAGGGA...TCACCCTCTCTAGACTAGCATCTATATAAAACAGAA 3′

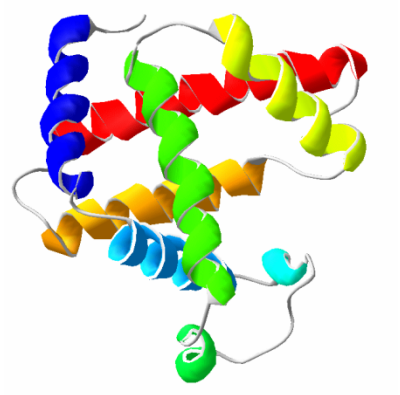
3′ ATCCTAGCTGATATACCCTAATGTTTCGTAAATCCCT...AGTGGGAGAGATCTGATCGTAGATATATTTTGTCTT 5′

(transcription)

Single-stranded RNA AUGGGAUUACAAAGCAUUUAGGGA...UCACCCUCUCUAGACUAGCAUCUAUAUAA

(translation)

protein



# How many?

- Genes in the human genome:

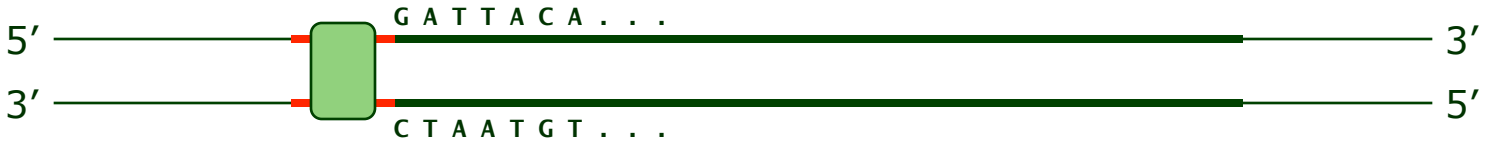
  ~ 20,000 – 25,000

# Gene Transcription

**promoter**


# Gene Transcription

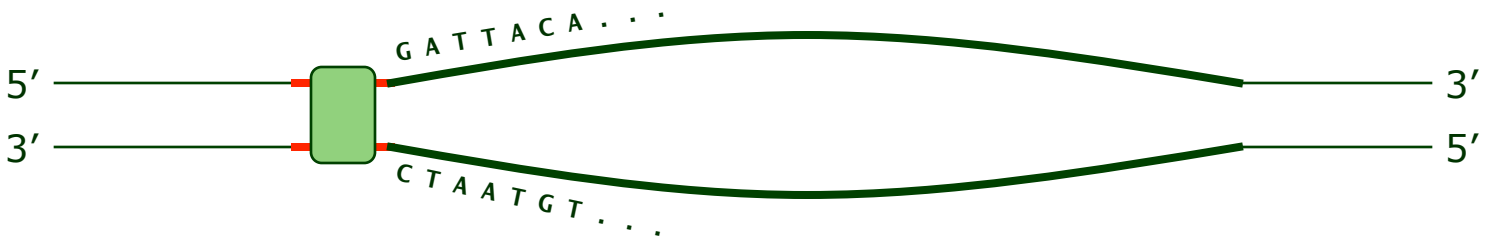
**transcription factor, binding site, RNA polymerase**




**Transcription factors** recognize **transcription factor binding sites** and bind to them, forming a complex.

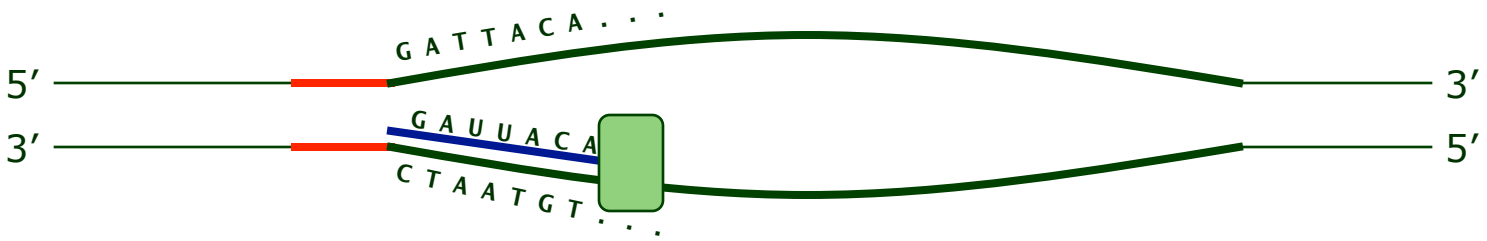
RNA polymerase binds the complex.

# Gene Transcription




The two strands are separated

# Gene Transcription



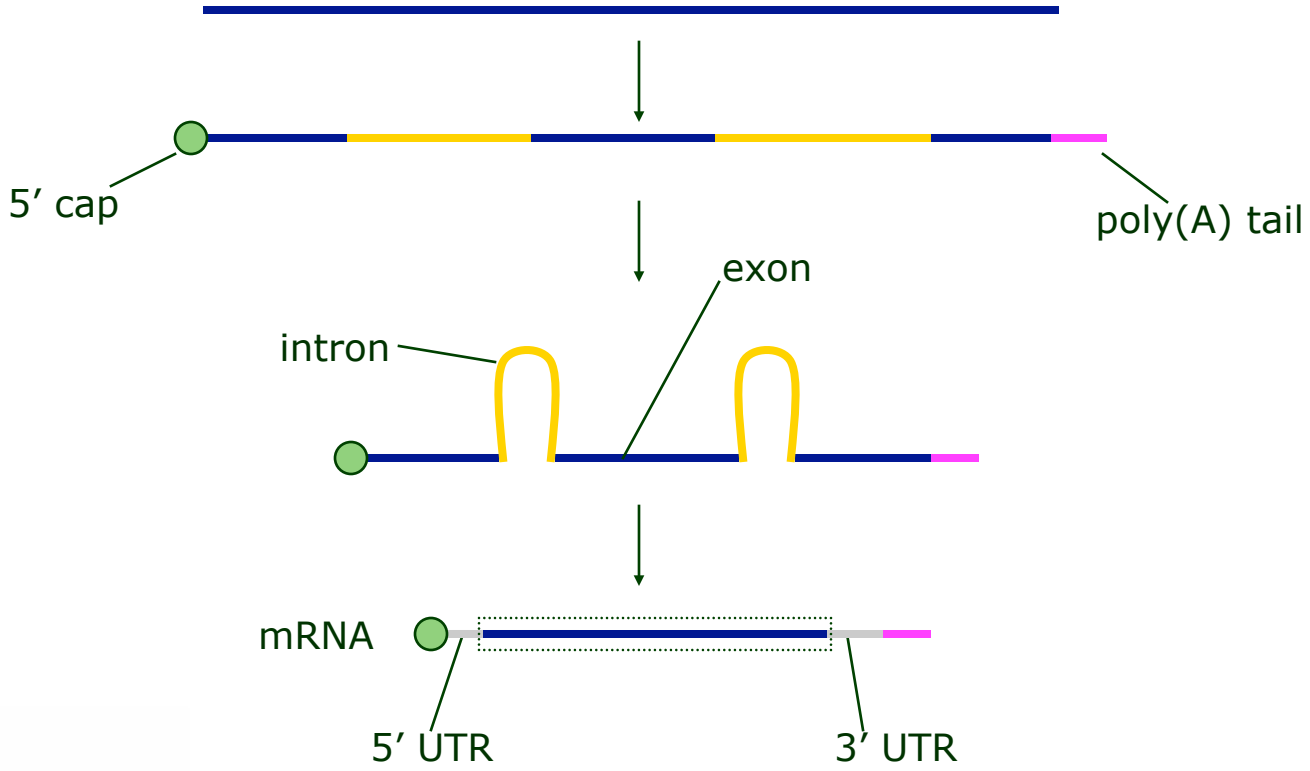

An RNA copy of the 5′→3′ sequence is created from the 3′→5′ template

# Gene Transcription

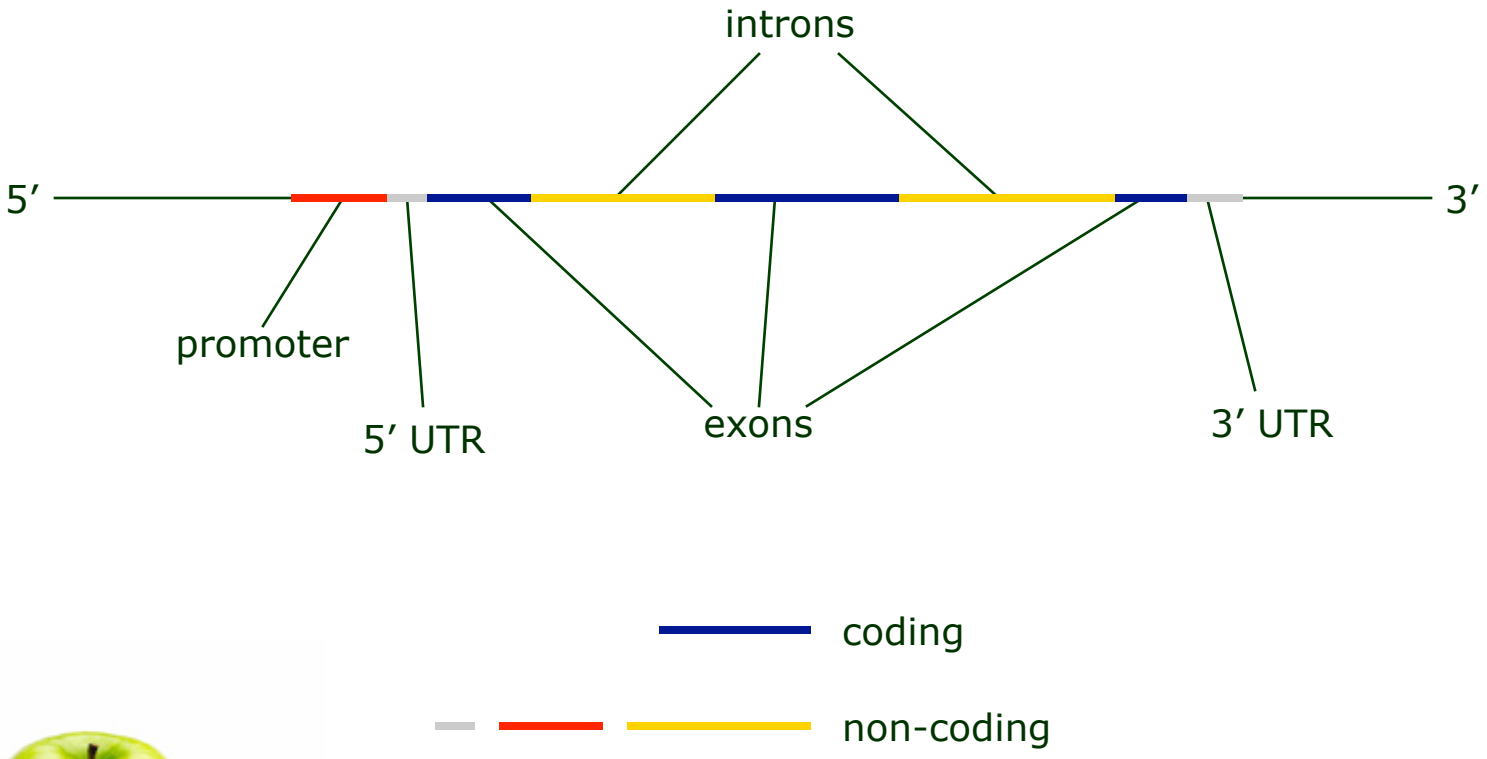


# RNA Processing

**5’ cap, polyadenylation, exon, intron, splicing, UTR, mRNA**




# Gene Structure

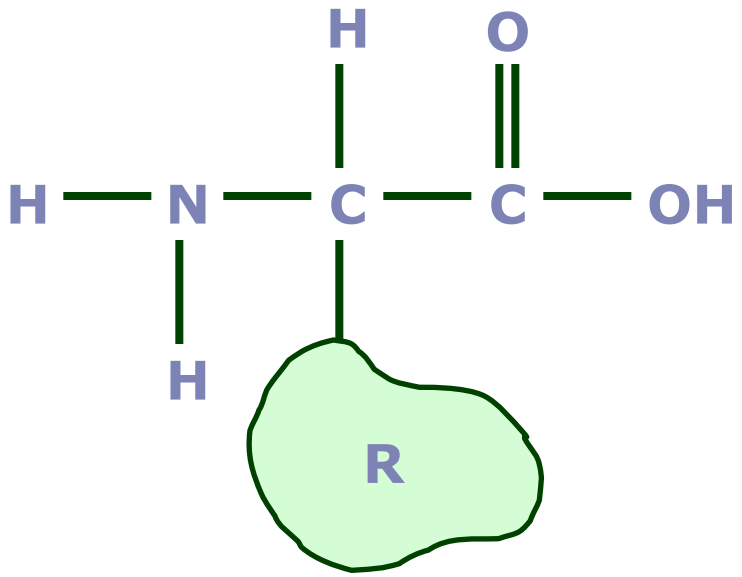



# How many?

- Exons per gene:
  ~ 8 on average (max: 148)
- Nucleotides per exon:
  170 on average (max: 12k)
- Nucleotides per intron:
  5,500 on average (max: 500k)
- Nucleotides per gene:
  45k on average (max: 2,2M)

# Amino acid

**amino acid**

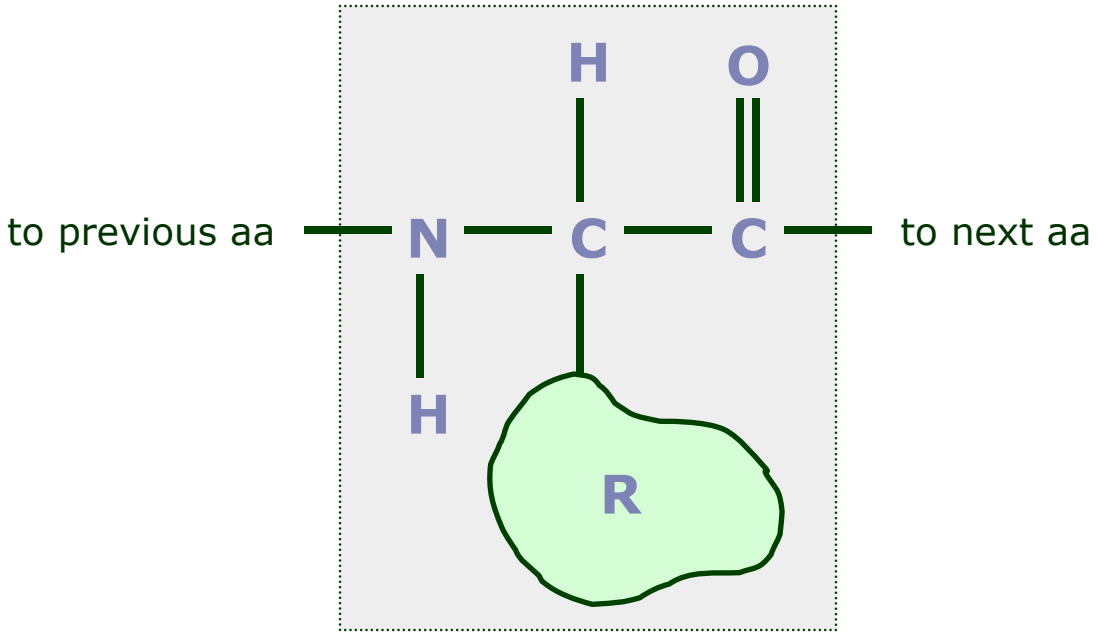


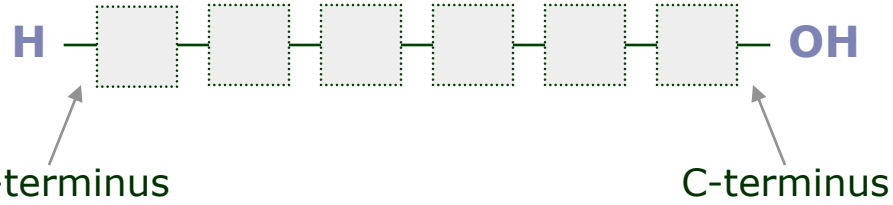

Alanine
Arginine
Asparagine
Aspartate
Cysteine
Glutamate
Glutamine
Glycine
Histidine
Isoleucine
Leucine
Lysine
Methionine
Phenylalanine
Proline
Serine
Threonine
Tryptophan
Tyrosine
Valine

There are 20 standard amino acids

# Proteins

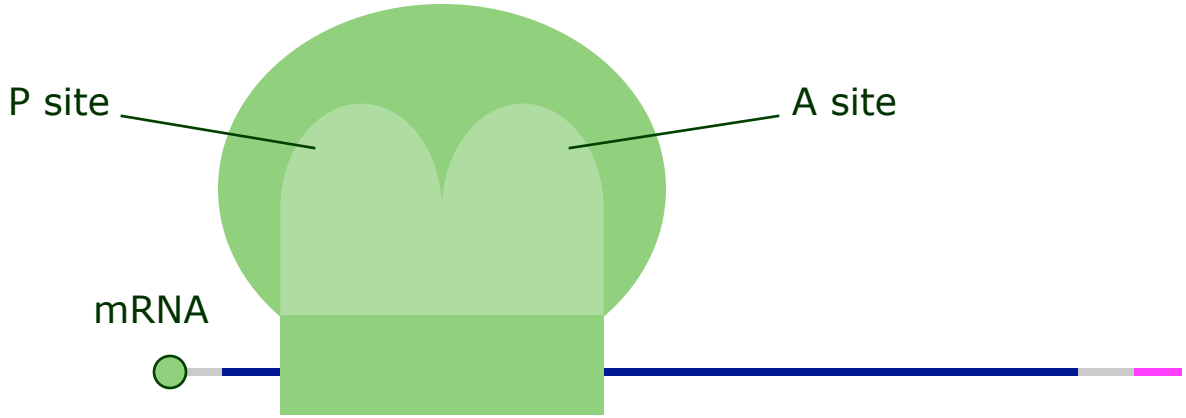
## N-terminus, C-terminus



# Translation

**ribosome, codon**



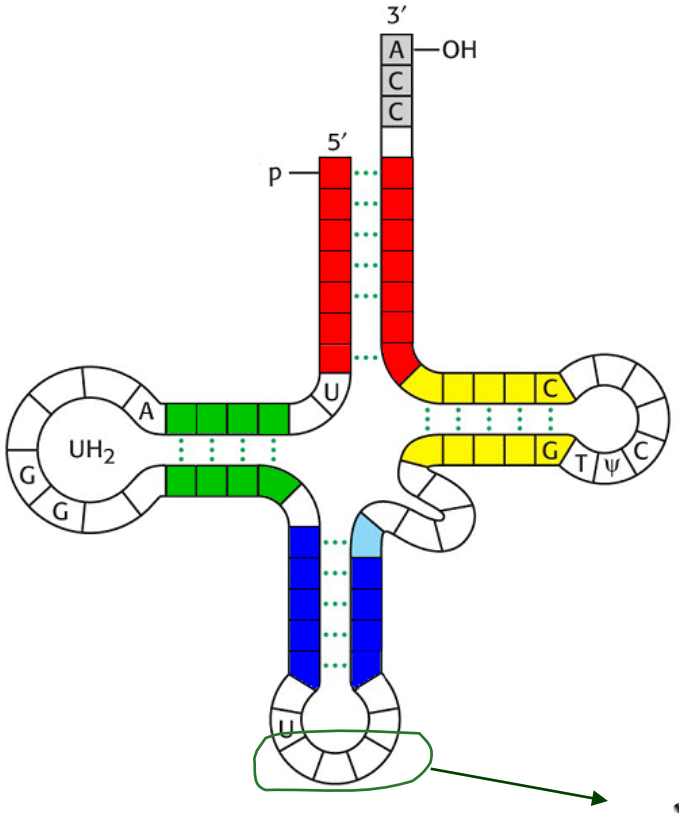

The ribosome synthesizes a protein by reading the mRNA in triplets (codons). Each codon is *translated* to an amino acid.

# The Genetic Code

| | U | C | A | G | |
|---|---|---|---|---|---|
| **U** | UUU **Phenylalanine** (Phe) | UCU **Serine** (Ser) | UAU **Tyrosine** (Tyr) | UGU **Cysteine** (Cys) | **U** |
| | UUC Phe | UCC Ser | UAC Tyr | UGC Cys | **C** |
| | UUA **Leucine** (Leu) | UCA Ser | UAA **STOP** | UGA **STOP** | **A** |
| | UUG Leu | UCG Ser | UAG **STOP** | UGG **Tryptophan** (Trp) | **G** |
| **C** | CUU **Leucine** (Leu) | CCU **Proline** (Pro) | CAU **Histidine** (His) | CGU **Arginine** (Arg) | **U** |
| | CUC Leu | CCC Pro | CAC His | CGC Arg | **C** |
| | CUA Leu | CCA Pro | CAA **Glutamine** (Gln) | CGA Arg | **A** |
| | CUG Leu | CCG Pro | CAG Gln | CGG Arg | **G** |
| **A** | AUU **Isoleucine** (Ile) | ACU **Threonine** (Thr) | AAU **Asparagine** (Asn) | AGU **Serine** (Ser) | **U** |
| | AUC Ile | ACC Thr | AAC Asn | AGC Ser | **C** |
| | AUA Ile | ACA Thr | AAA **Lysine** (Lys) | AGA **Arginine** (Arg) | **A** |
| | AUG **Methionine** (Met) or **START** | ACG Thr | AAG Lys | AGG Arg | **G** |
| **G** | GUU **Valine** (Val) | GCU **Alanine** (Ala) | GAU **Aspartic acid** (Asp) | GGU **Glycine** (Gly) | **U** |
| | GUC Val | GCC Ala | GAC Asp | GGC Gly | **C** |
| | GUA Val | GCA Ala | GAA **Glutamic acid** (Glu) | GGA Gly | **A** |
| | GUG Val | GCG Ala | GAG Glu | GGG Gly | **G** |

# Translation (tRNA)

**tRNA, anticodon**

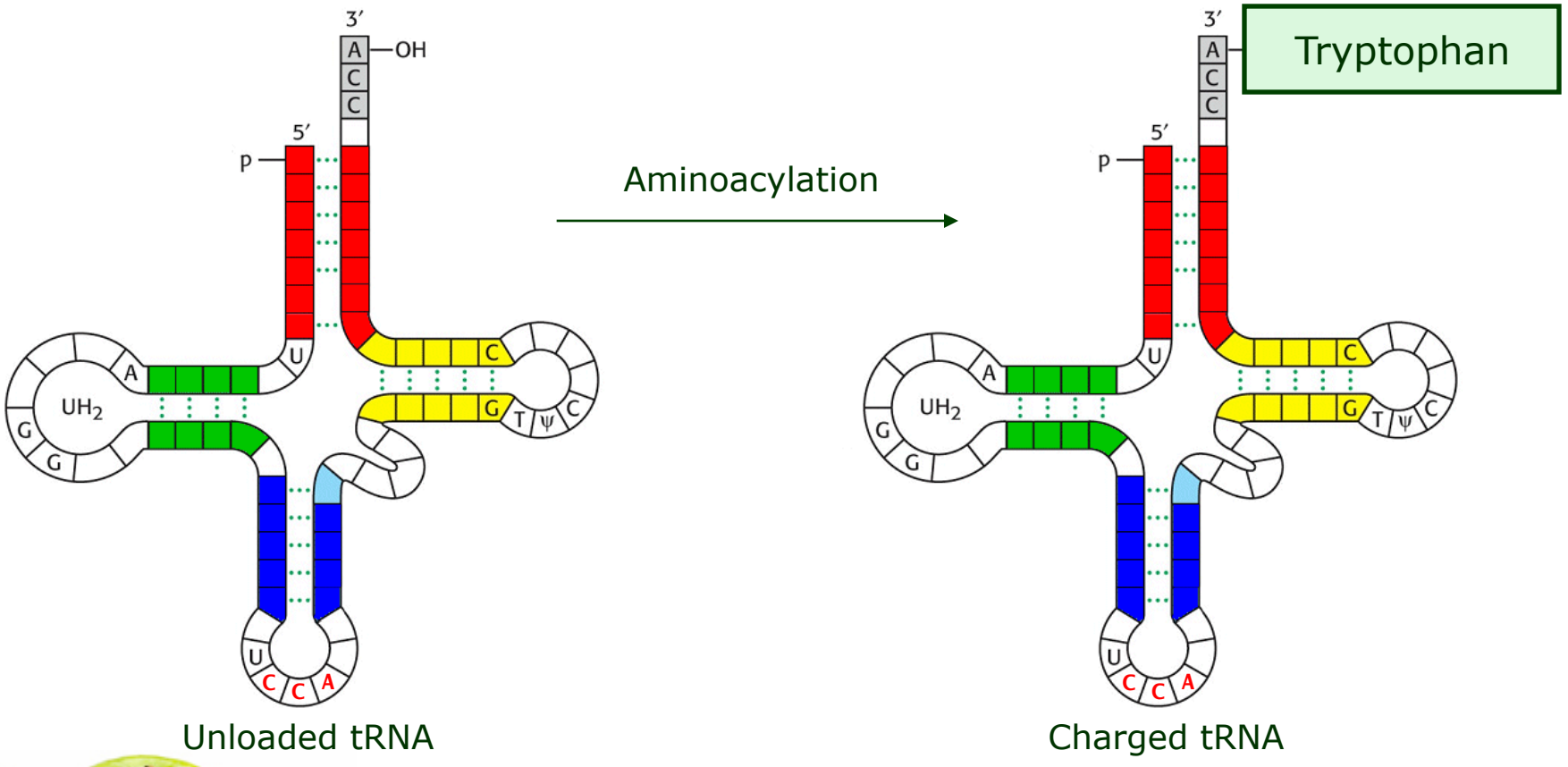



(Tryptophan codon: UGG)


Tryptophan anticodon

# Translation (tRNA)

**aminoacylation**




Unloaded tRNA

Charged tRNA

# Translation

5′ . . . A U U A U G G C C U G G A C U U G A . . . 3′

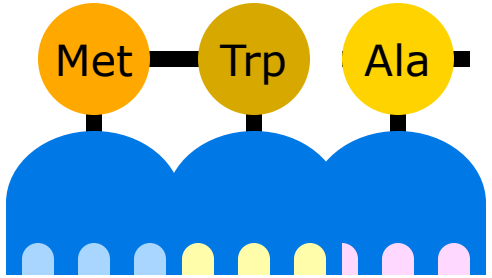
UTR | Met | Ala | Trp | Thr

Start Codon

# Translation

5′ . . . A U U A U G G C C U G G A C U U G A . . . 3′

# Translation




5′ . . . A U U A U G G C C U G G A C U U G A . . . 3′

# Errors?

**mutation**

- What if the transcription / translation machinery makes mistakes?
- What is the effect of **mutations** in coding regions?

# Reading Frames

**reading frame**

G C U U G U U U A C G A A U U A G

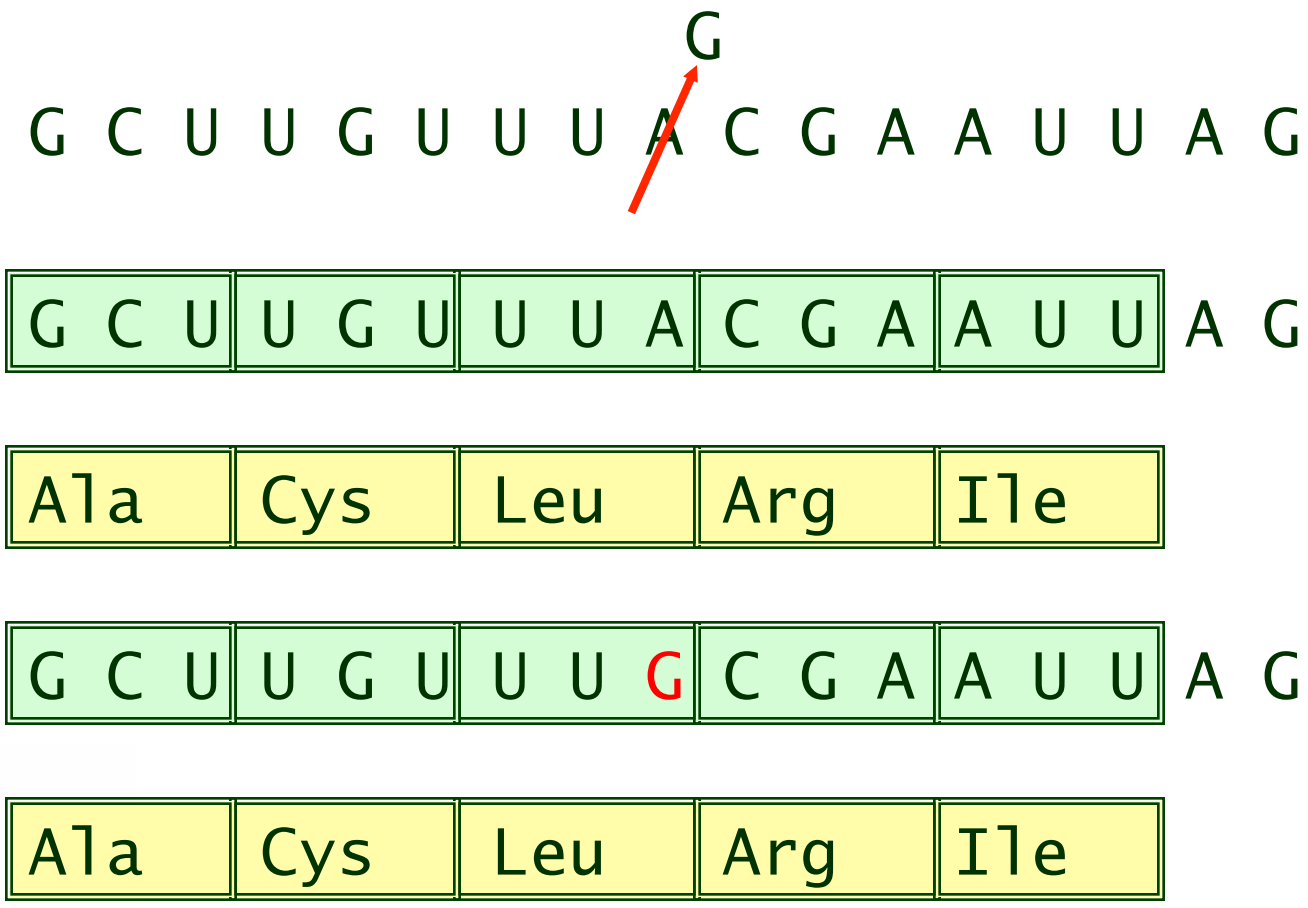
G C U U G U U U A C G A A U U A G

G C U U G U U U A C G A A U U A G

G C U U G U U U A C G A A U U A G

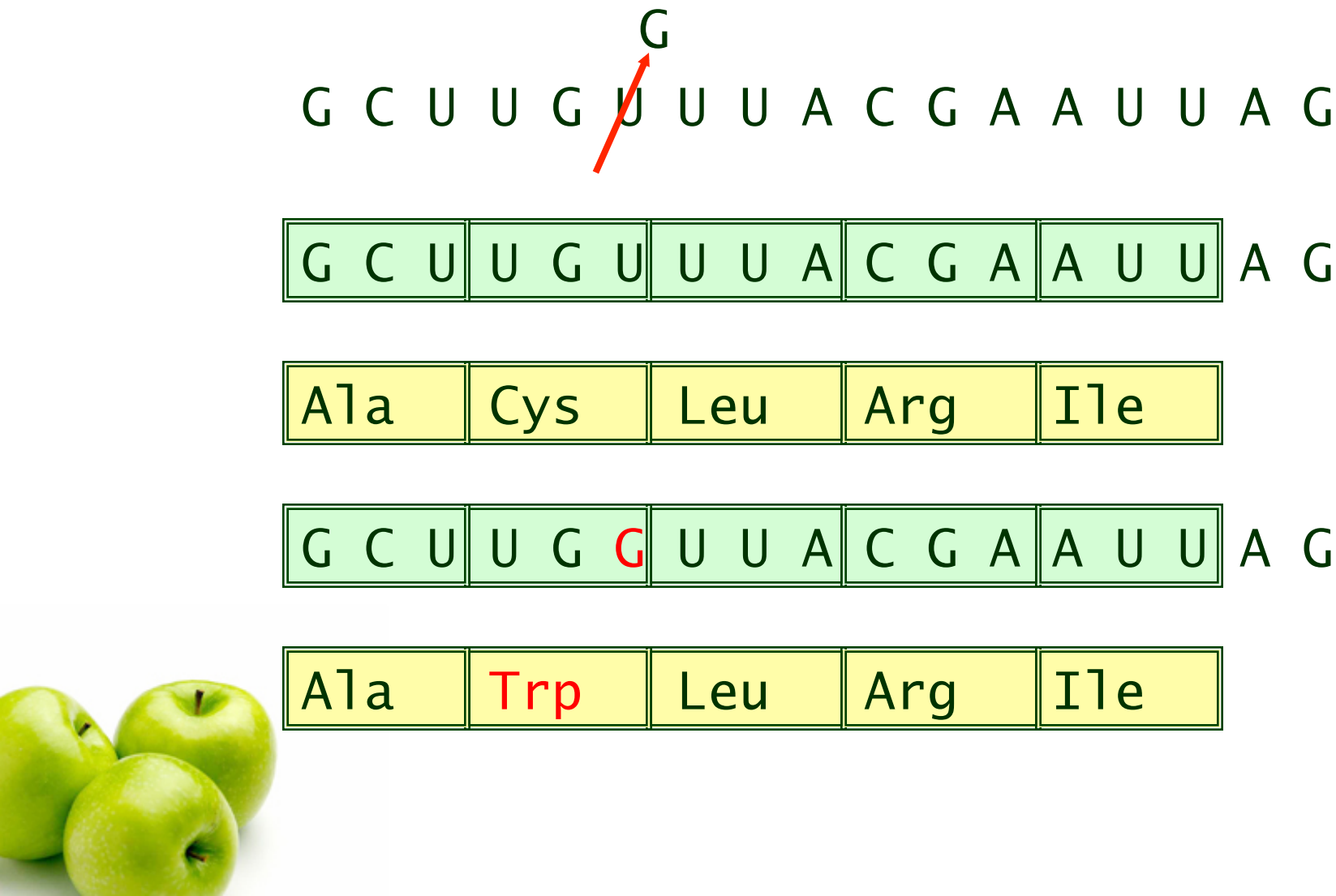
# Synonymous Mutation

**synonymous (silent) mutation, fourfold site**



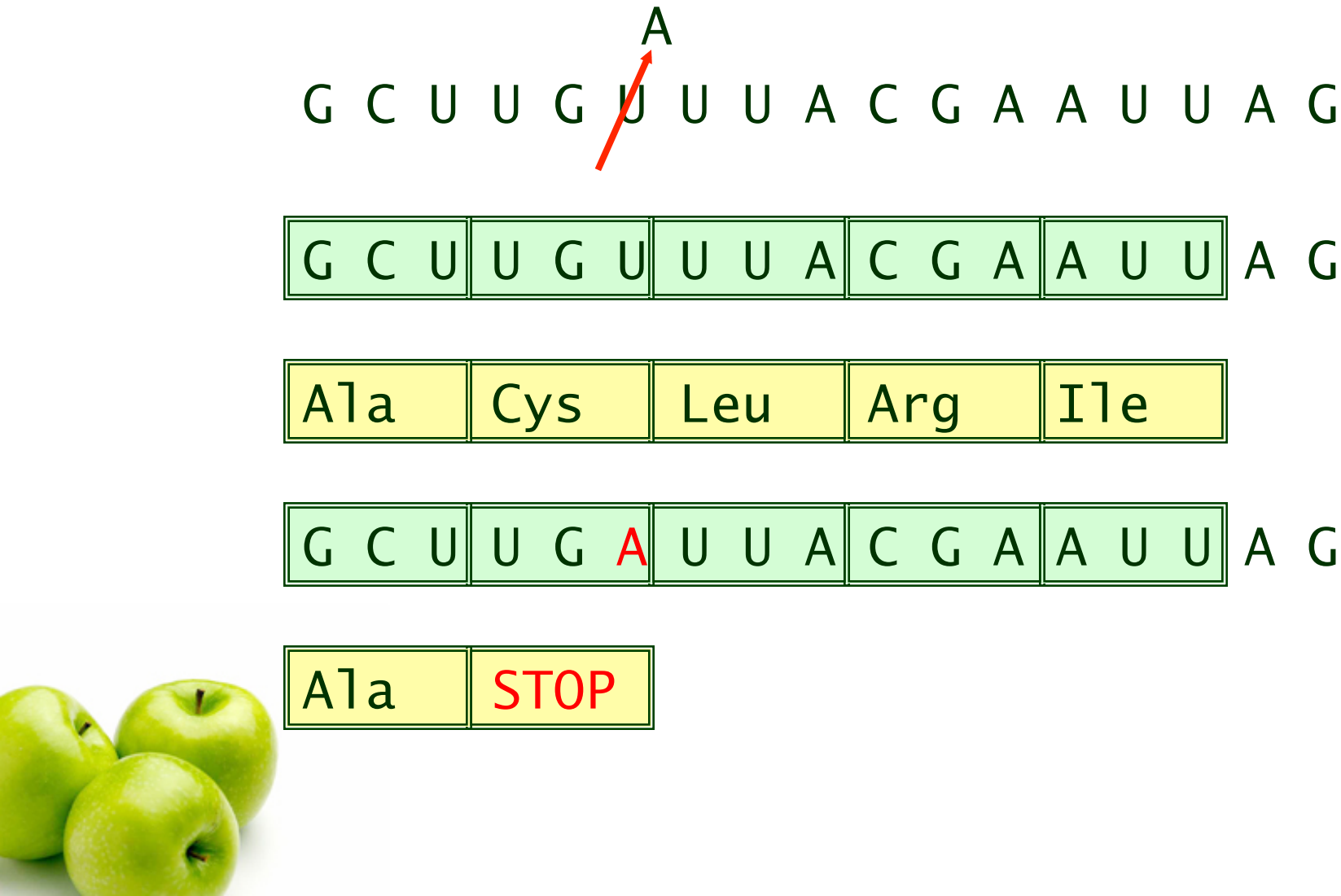
# Missense Mutation

**missense mutation**



# Nonsense Mutation

**nonsense mutation**



# Frameshift

**frameshift**

G C U U G U U U A C G A A U U A G

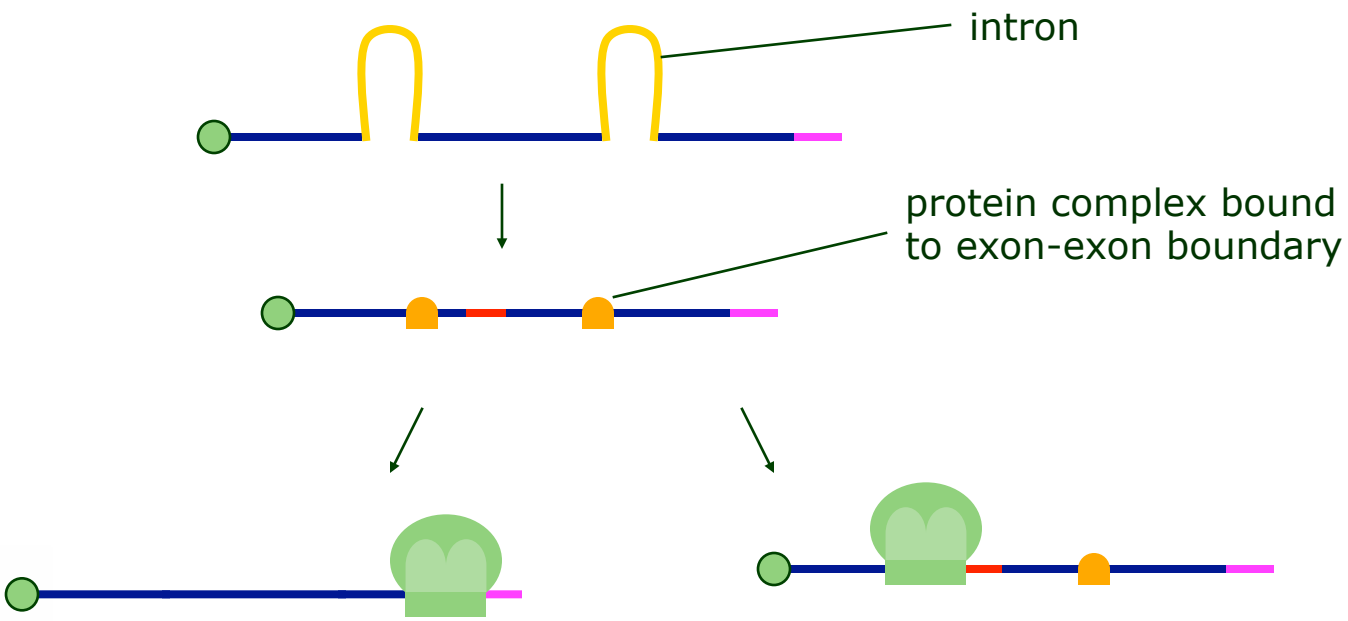
| | | | | | |
|---|---|---|---|---|---|
| G C U | U G U | U U A | C G A | A U U | A G |
| Ala | Cys | Leu | Arg | Ile | |

| | | | | | |
|---|---|---|---|---|---|
| G C U | U G U | U A C | G A A | U U A | G |
| Ala | Cys | Tyr | Glu | Leu | |

# Quality Control

**nonsense-mediated decay**

- Nonsense-Mediated mRNA Decay (NMD)
  (Destroy mRNA with premature STOP codon)




# Gene Expression Regulation

**regulation**

- When should each gene be expressed?
- **Regulate** gene expression

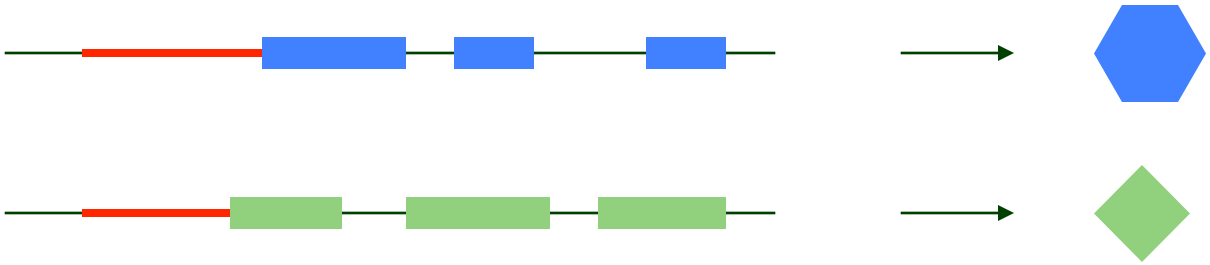
Examples:

- Make more of gene A when substance X is present
- Stop making gene B once you have enough
- Make genes $C_1$, $C_2$, $C_3$ simultaneously

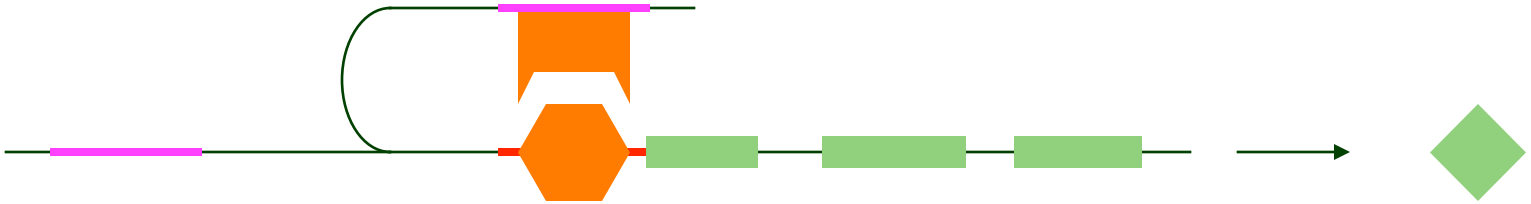
# Regulatory Mechanisms

**enhancer, silencer**

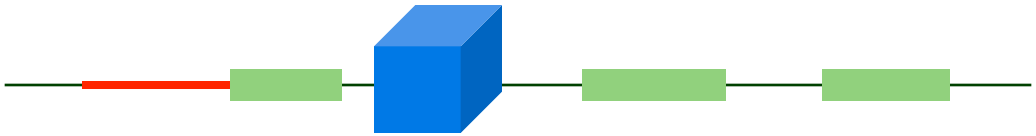
Transcription Factor Specificity:



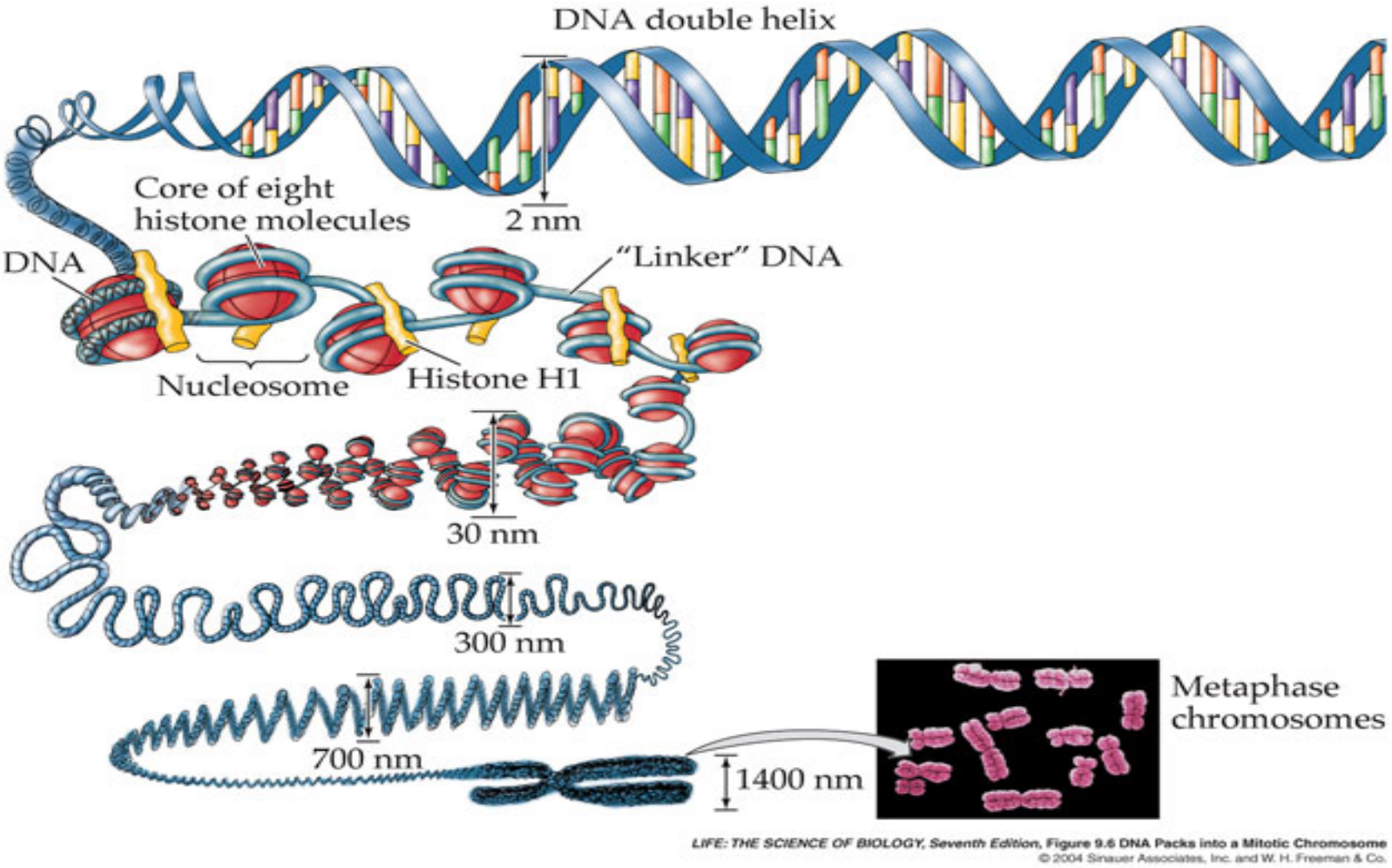
Enhancer:



Silencer:



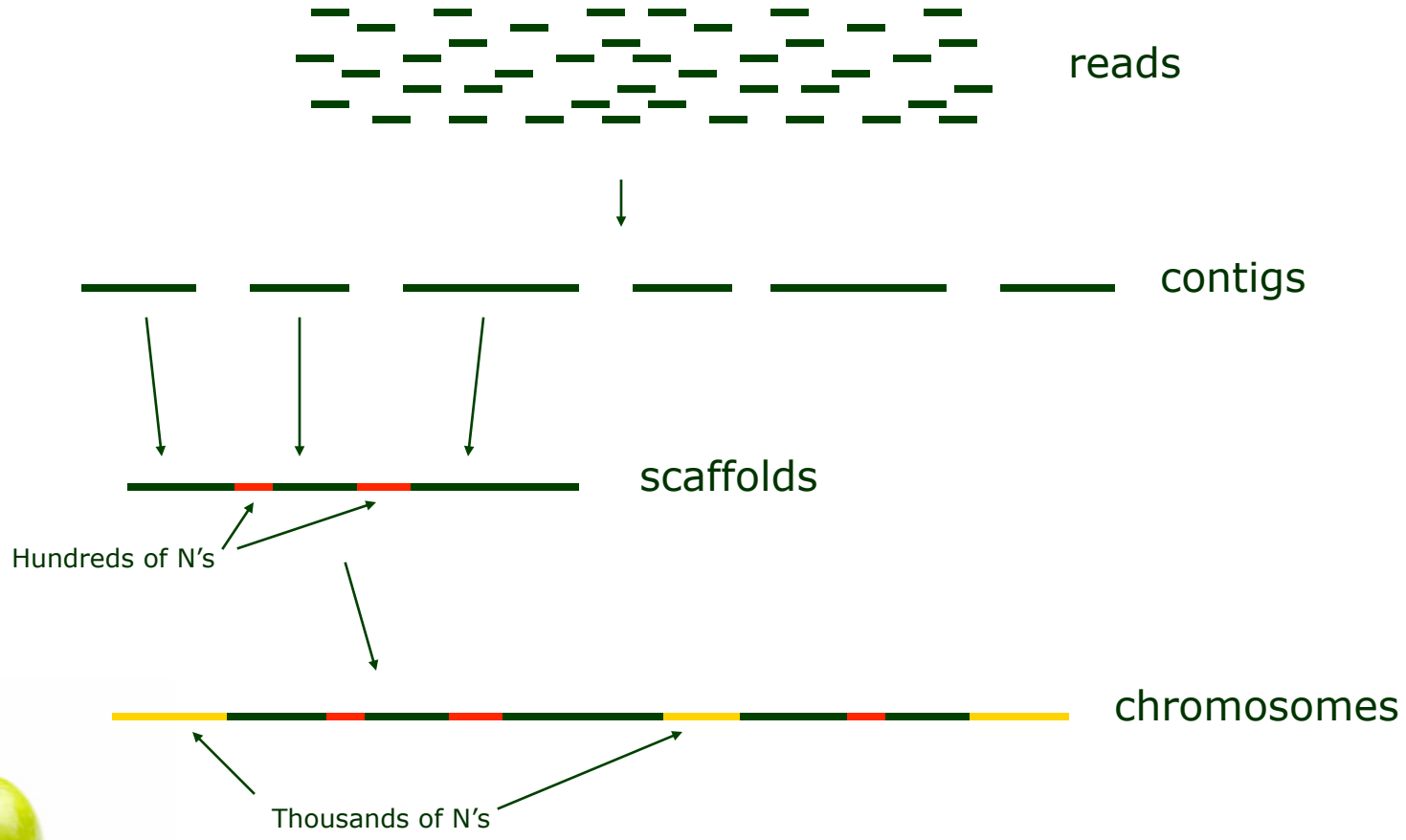
# Chromatin




*LIFE: THE SCIENCE OF BIOLOGY, Seventh Edition*, Figure 9.6 DNA Packs into a Mitotic Chromosome

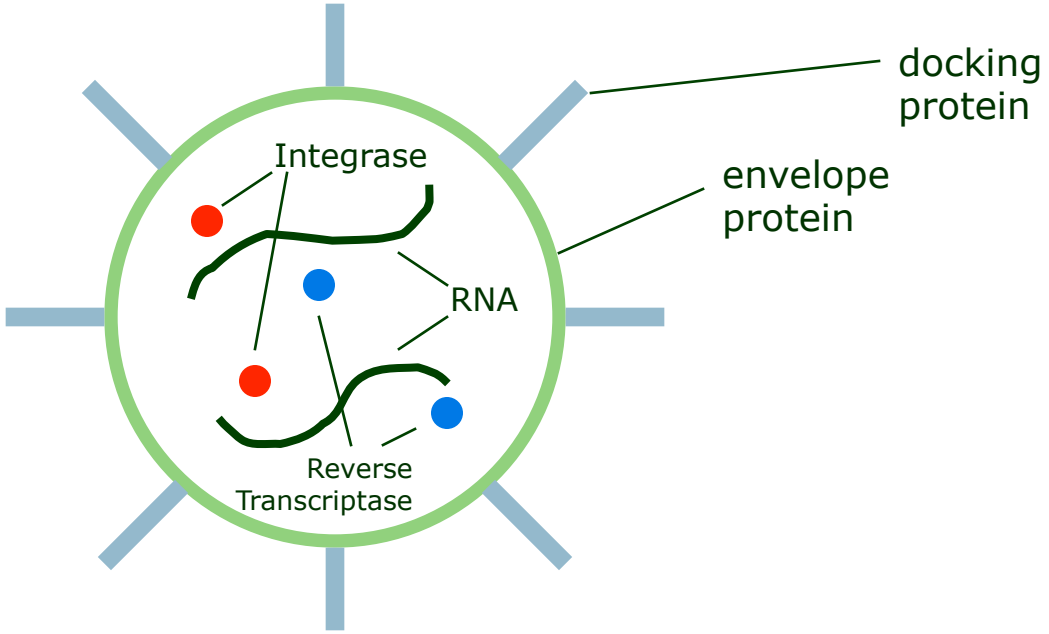
# Assemblies

**read, contig, scaffold, sequencing gaps, assembly**

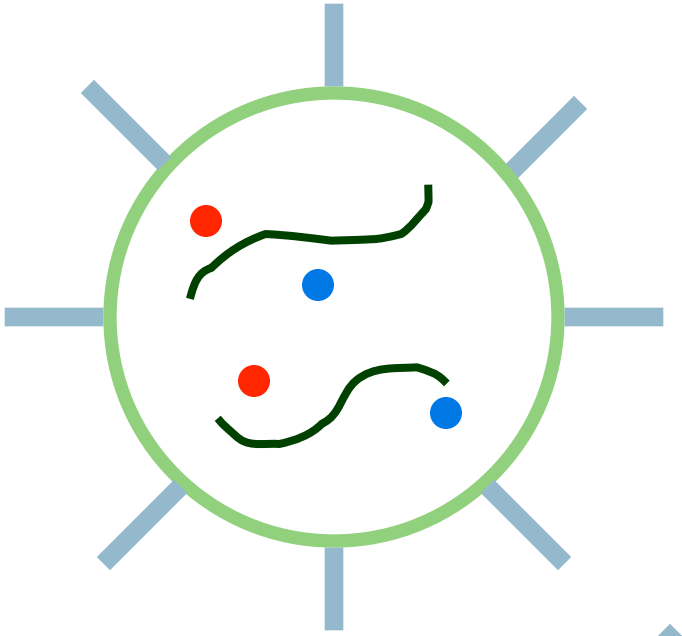



# Retrovirus

**virus, reverse transcriptase, integrase**

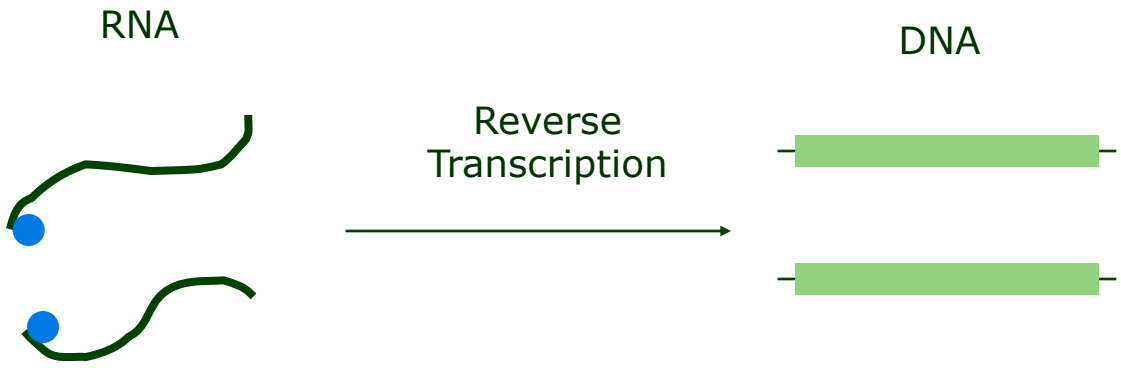



# Infection

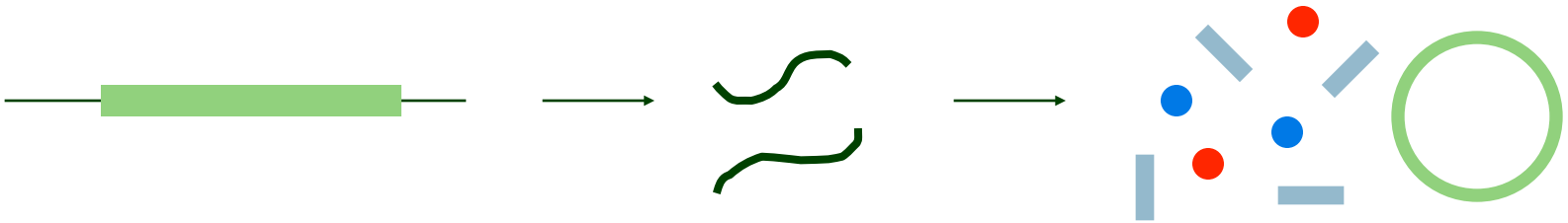


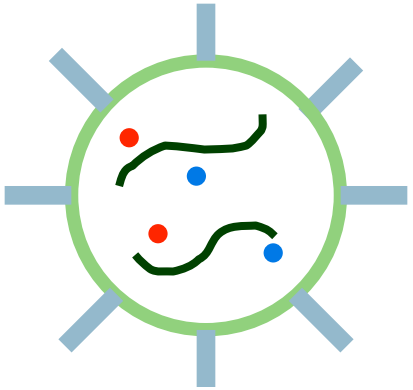
# Infection

# Replication cycle




# Replication cycle





# Are they alive?

- Polio virus made from scratch ($300,000 DARPA project – 2002)

> “ The first part of the sequence was painstakingly pieced together by hand and took over a year. The researchers then hired a commercial laboratory, Integrated DNA Technologies, to synthesise the remaining two thirds of the sequence mechanically. This took an additional two months.”

# Are they alive?

- Polio virus made from scratch ($300,000 DARPA project – 2002)

> “ Once the entire sequence was replicated, it was reconverted into RNA by enzymatic means. Viral propagation and replication were accomplished by throwing the virus into a predesigned protein soup that contained all the polymerases and other enzymatic ingredients necessary for RNA transcription and translation. The synthetic virus was able to successfully replicate itself from this mixture.”

# Are they alive?

- Polio virus made from scratch ($300,000 DARPA project – 2002)

> “ The viral copies were then injected into the brains of mice, which subsequently developed paralysis indistinguishable from polio. ”

# The end?


READING THE ENTIRE GENOME CODE...
Listen to this part: 'AGGCTAATC CGCATAACTG'
Wow!

# Keywords

cell, nucleus, cytoplasm, mitochondrion, histone, nucleosome, chromatin, chromosome, centromere, telomere, deoxyribose, nucleotide, base, A, C, G, T, purine, pyrimidine, 3′, 5′, deoxyribonucleic acid (DNA), strand, reverse complement, ribose, ribonucleotide, U, gene, transcription, translation, protein, promoter, transcription factor, binding site, RNA polymerase, 5′ cap, polyadenylation, exon, intron, splicing, UTR, mRNA, amino acid, N terminus, C terminus, ribosome, codon, tRNA, anticodon, aminoacylation, mutation, reading frame, synonymous (silent) mutation, fourfold site, missense mutation, nonsense mutation, frameshift, nonsense-mediated decay, regulation, enhancer, silencer, read, contig, scaffold, sequencing gaps, assembly, virus, reverse transcriptase, integrase