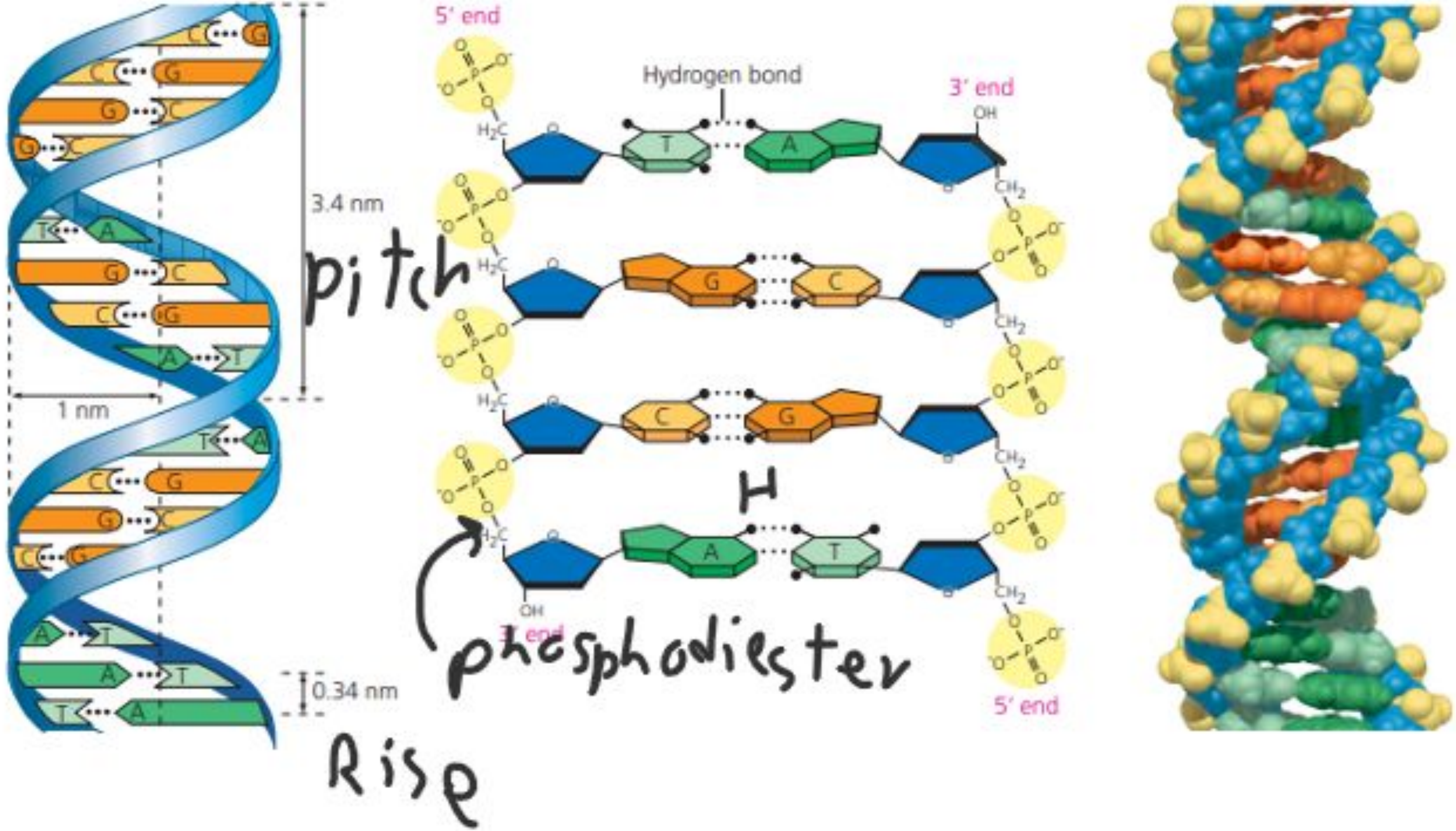
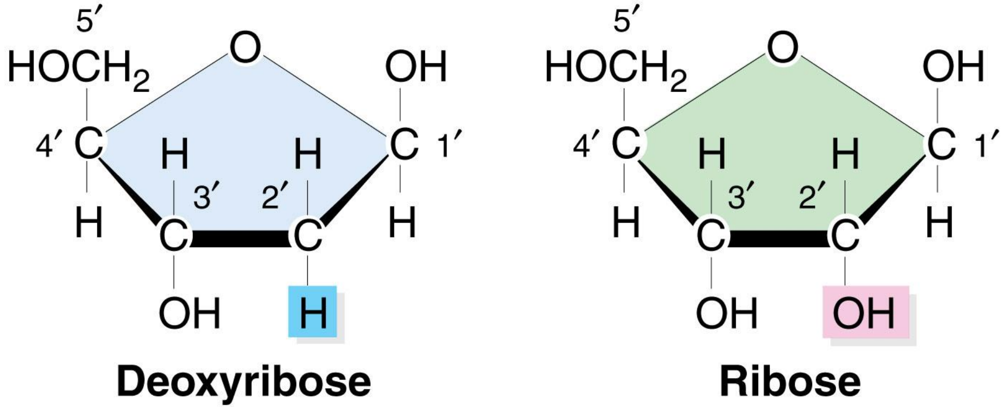
Genetics Review

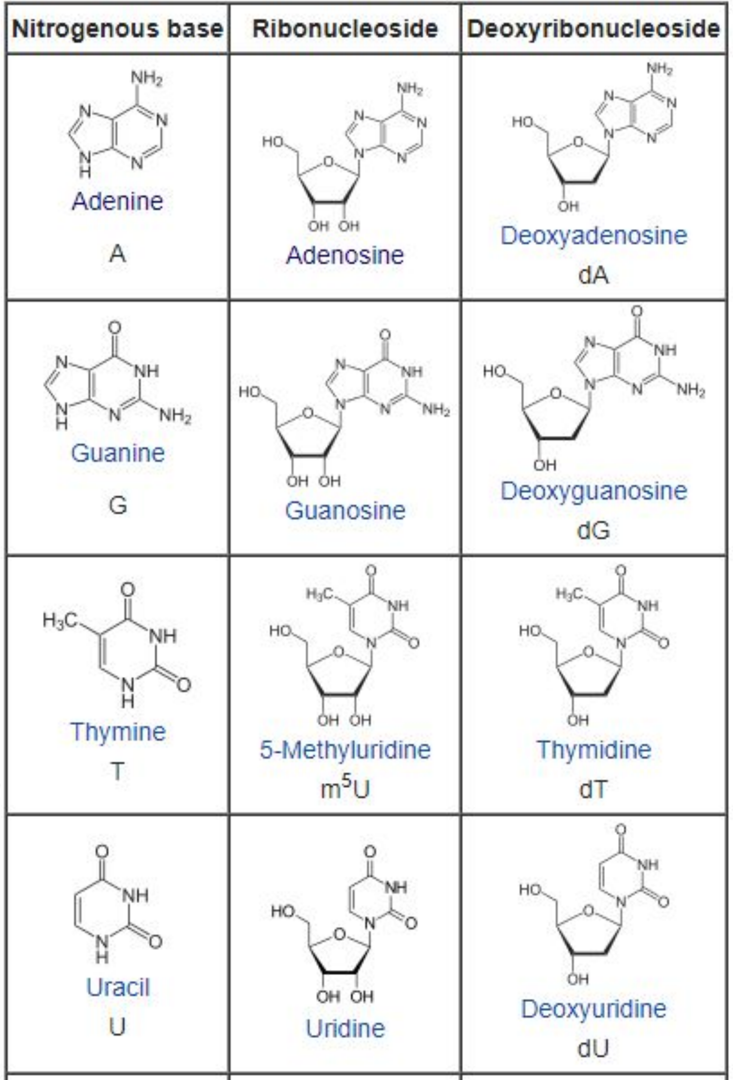
Presentation by Andrey and Laurie, Slides by Slidego

DNA Structure

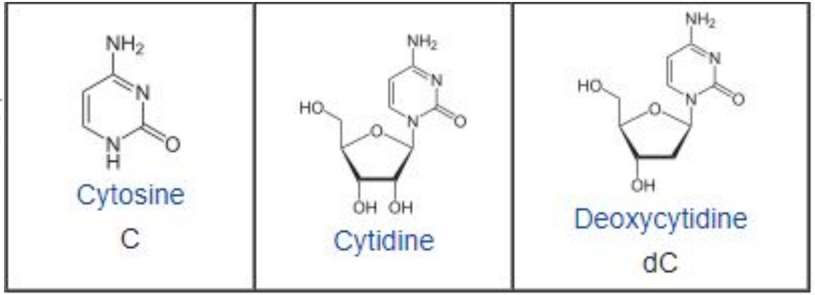


DNA Structure





Nitrogenous base	Ribonucleoside	Deoxyribonucleoside
Adenine A	Adenosine	Deoxyadenosine dA
Guanine G	Guanosine	Deoxyguanosine dG
Thymine T	5-Methyluridine m^5U	Thymidine dT
Uracil U	Uridine	Deoxyuridine dU



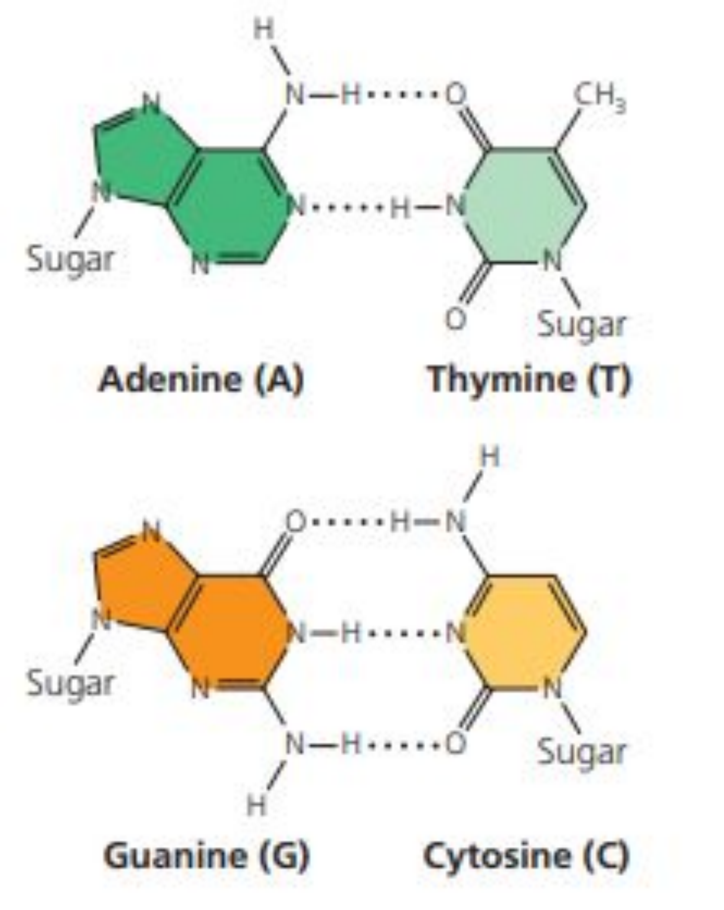
Cytosine C	Cytidine	Deoxycytidine dC

Chargaff's rules

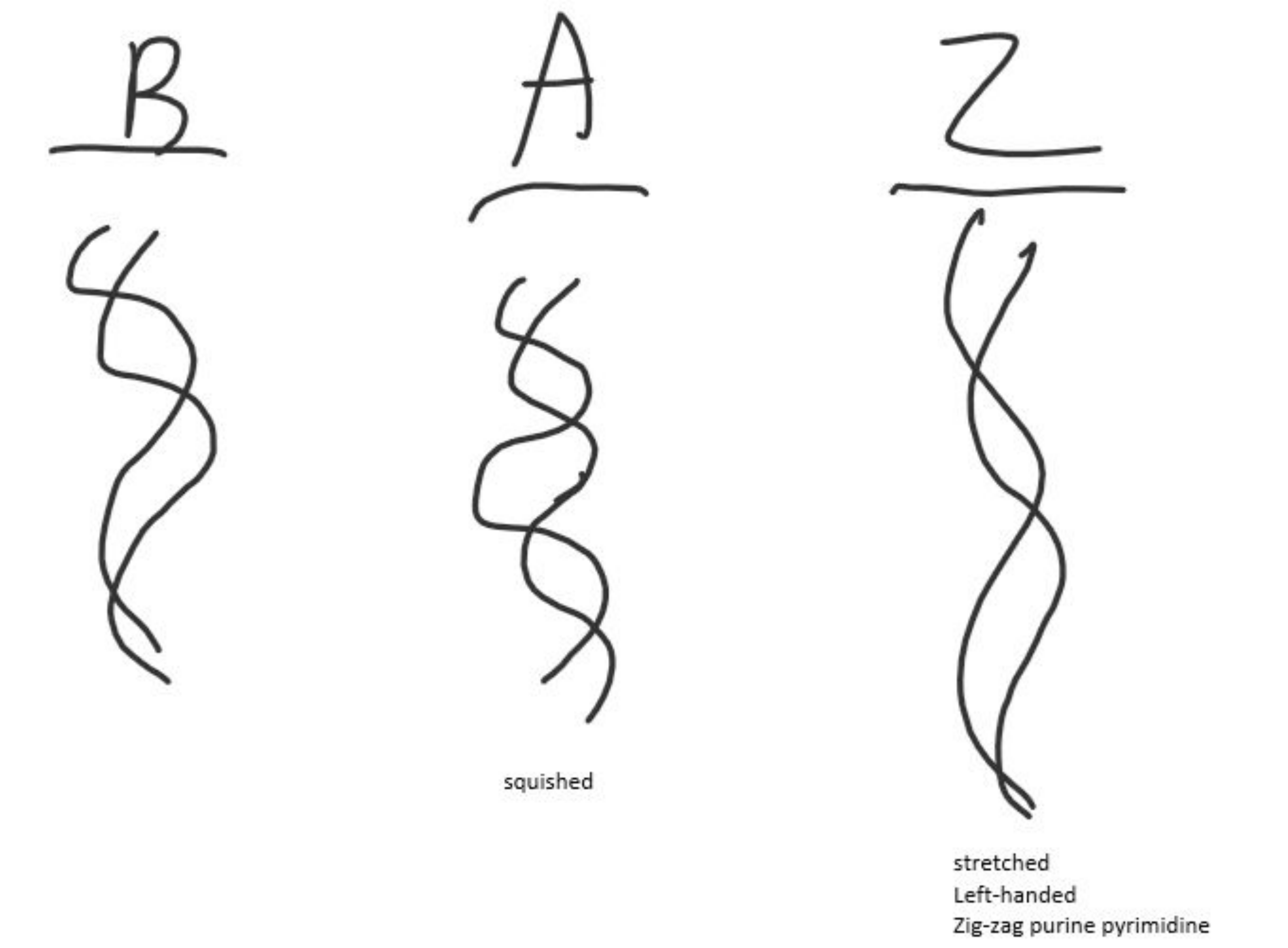
1. Base composition of DNA varies between species
2. A=T and C=G

Watson & Crick/ Maurice Wilkins/ Rosalind Franklin

1. Double helix structure of DNA
2. **Purine**: A & G
3. **Pyrimidine**: C & T
4. Strands are antiparallel



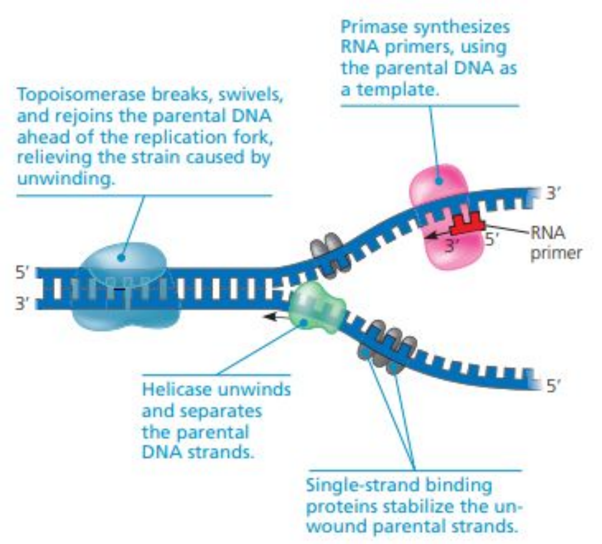
Types of DNA

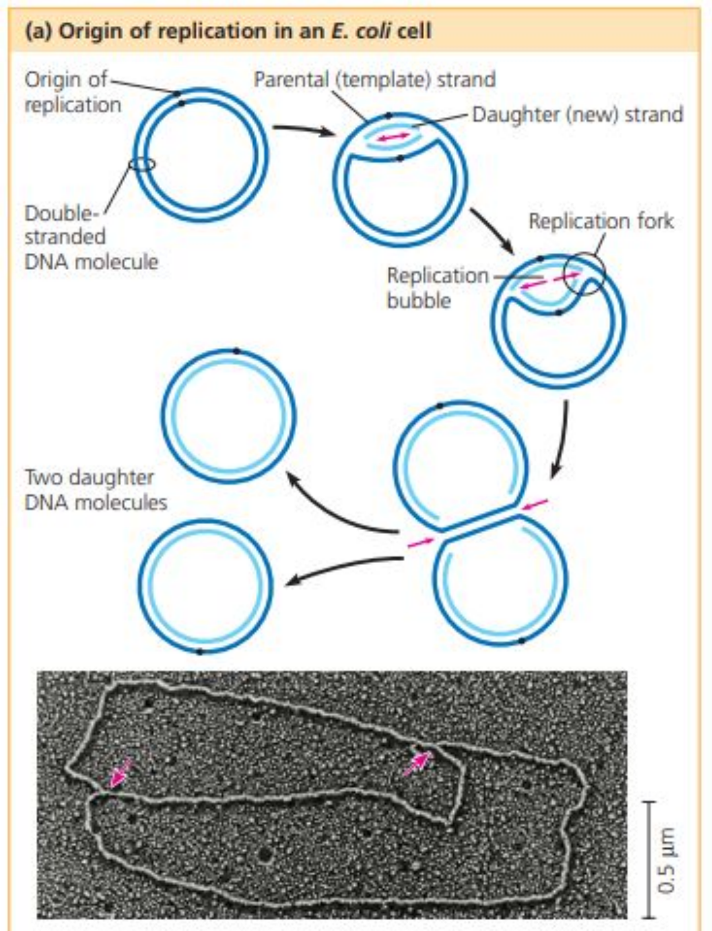

B
A
Z
squished
stretched
Left-handed
Zig-zag purine pyrimidine

Prokaryotes

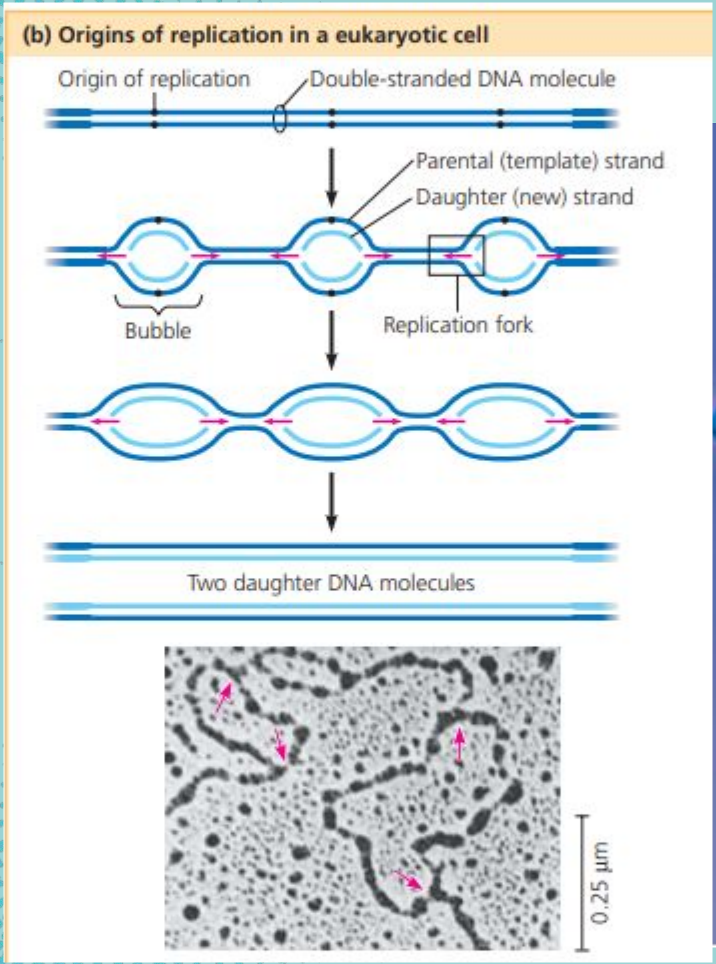
DNA Replication

- Has 1 circular chromosome
- Has only 1 **origin of replication**
- Uses **DNA Polymerase I** & **III**

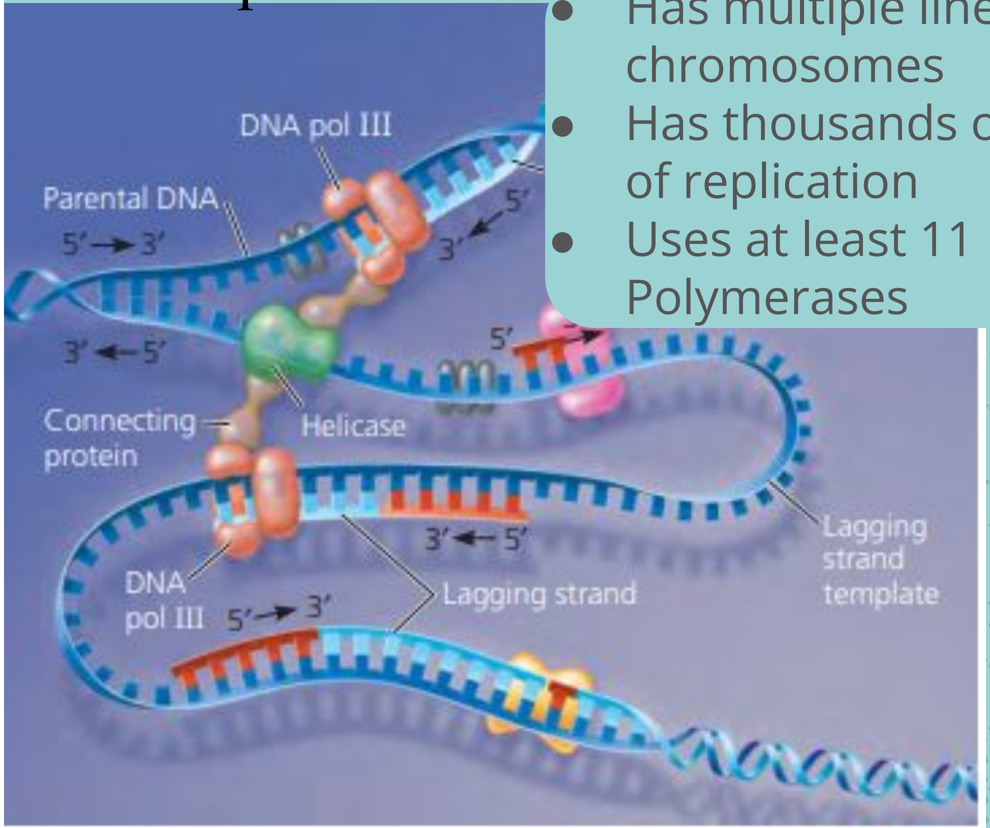




Eukaryotes



DNA Replication

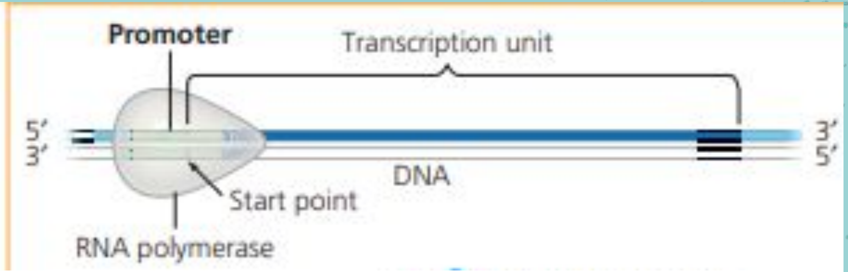


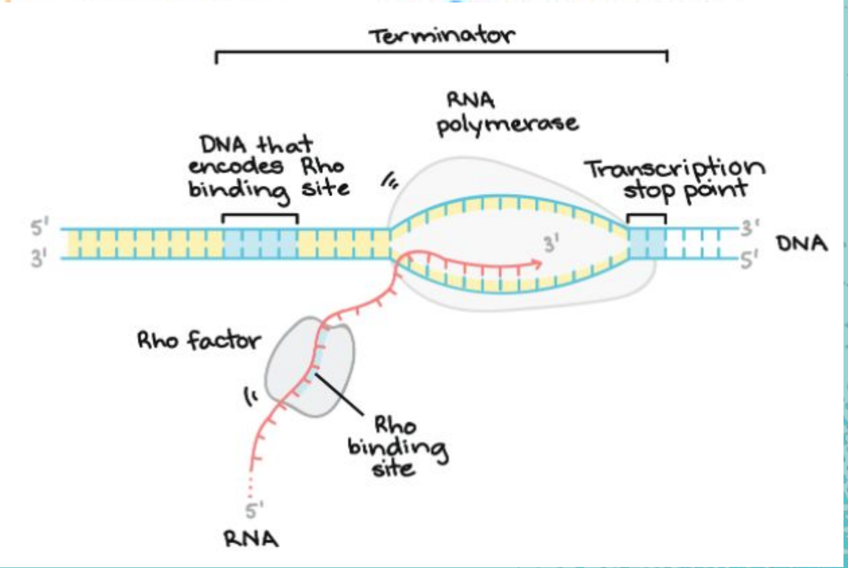
- Has multiple linear chromosomes
- Has thousands of origins of replication
- Uses at least 11 DNA Polymerases

Prokaryotes

Transcription

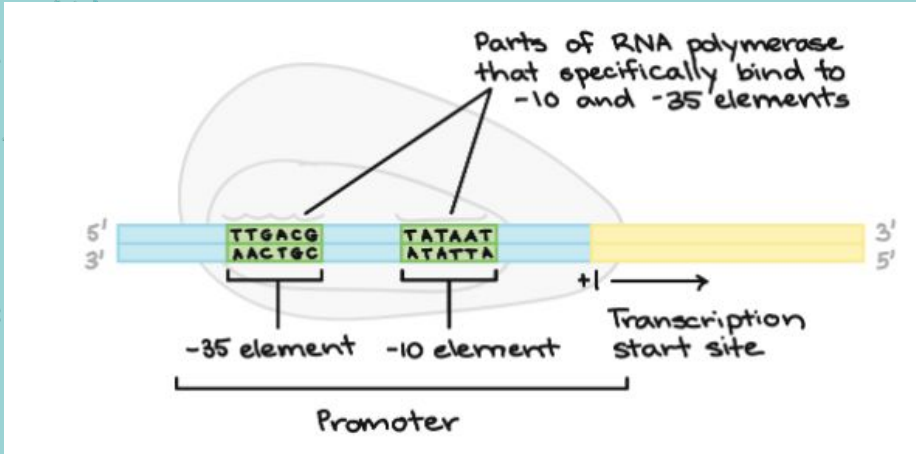
- RNA Polymerase
- RNA Polymerase binds to **promoter**
    a. **Start point** - the part in the promoter where RNA Polymerase binds
- **Terminator sequence** stops transcription
    a. **Rho-dependent**: Rho binding site in RNA causes Rho factor to bind and wiggle up the RNA. When it reaches polymerase, the RNA detaches
    b. **Rho-independent**: CG region causes hairpin in RNA, which makes polymerase stop

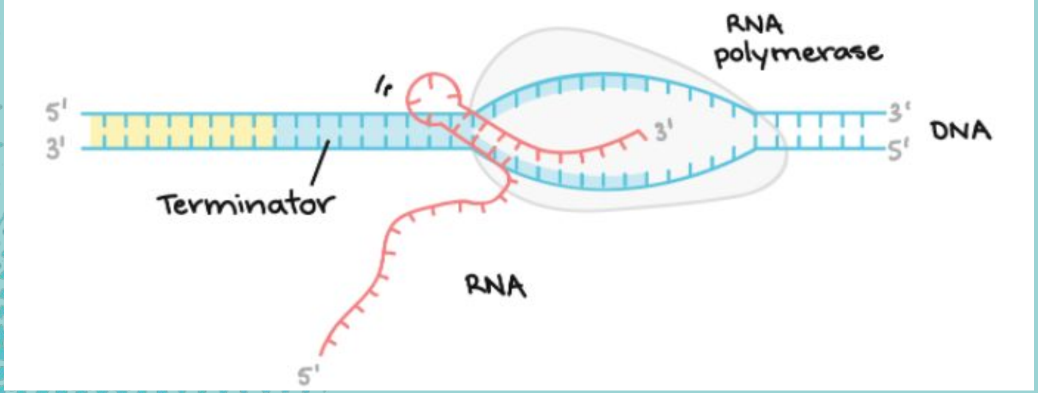




Eukaryotes

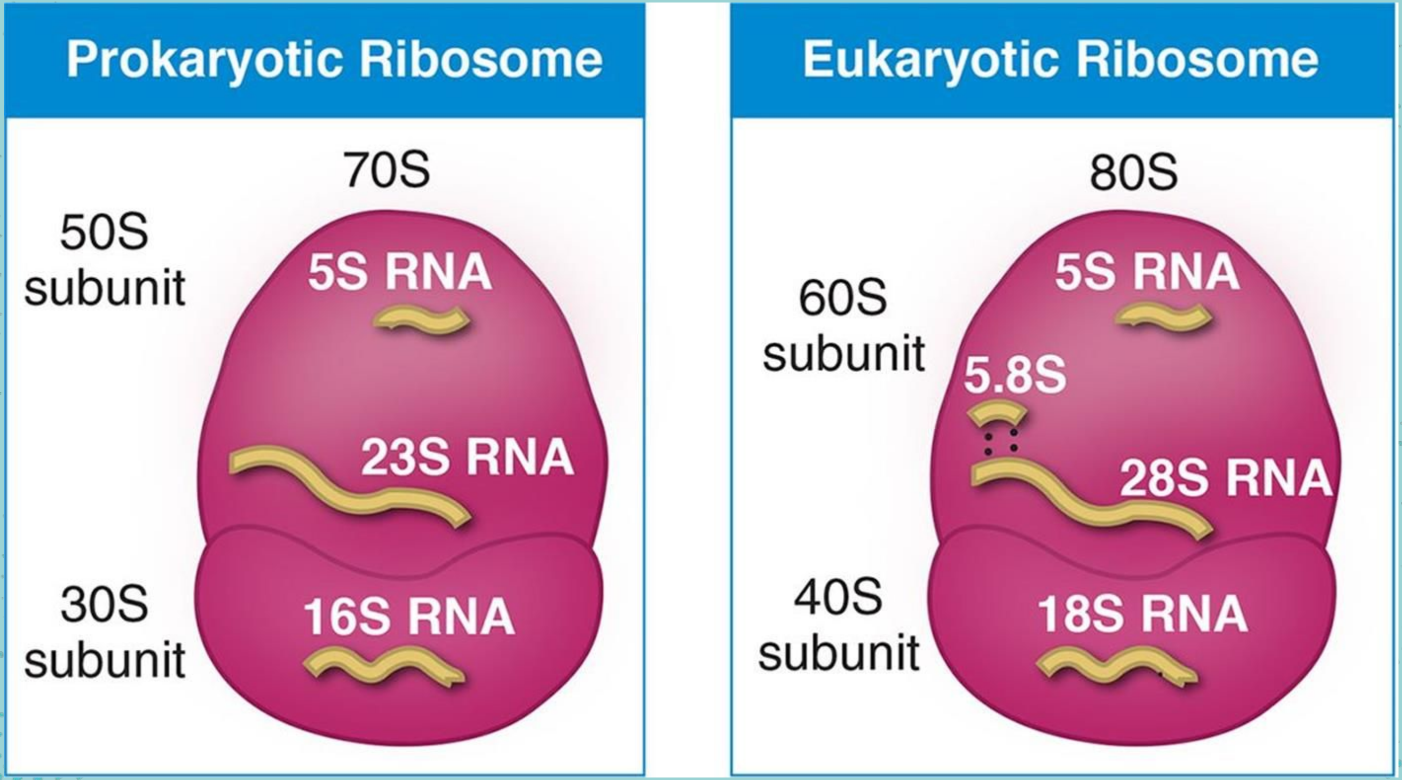
Transcription

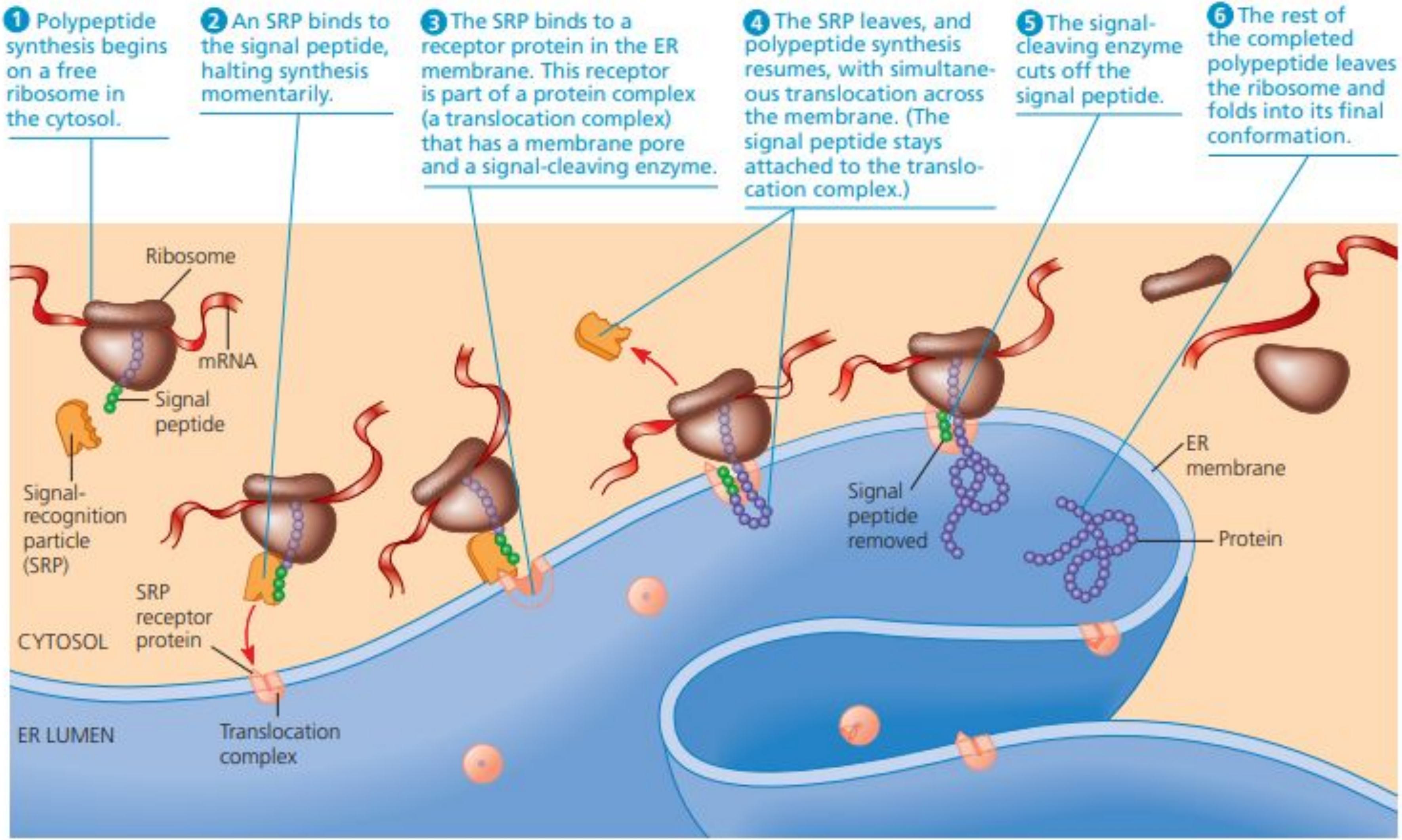




- Has at least 3 RNA Polymerases; **RNA Polymerase II** is the one used
- RNA Polymerase requires **transcription factors**
- RNA transcript is cut free 10-35 bp downstream of polyadenylation sequence (AAUAAA)

Translation





1 Polypeptide synthesis begins on a free ribosome in the cytosol.
2 An SRP binds to the signal peptide, halting synthesis momentarily.
3 The SRP binds to a receptor protein in the ER membrane. This receptor is part of a protein complex (a translocation complex) that has a membrane pore and a signal-cleaving enzyme.
4 The SRP leaves, and polypeptide synthesis resumes, with simultaneous translocation across the membrane. (The signal peptide stays attached to the translocation complex.)
5 The signal-cleaving enzyme cuts off the signal peptide.
6 The rest of the completed polypeptide leaves the ribosome and folds into its final conformation.
Ribosome
mRNA
Signal peptide
Signal-recognition particle (SRP)
SRP receptor protein
CYTOSOL
ER LUMEN
Translocation complex
Signal peptide removed
ER membrane
Protein

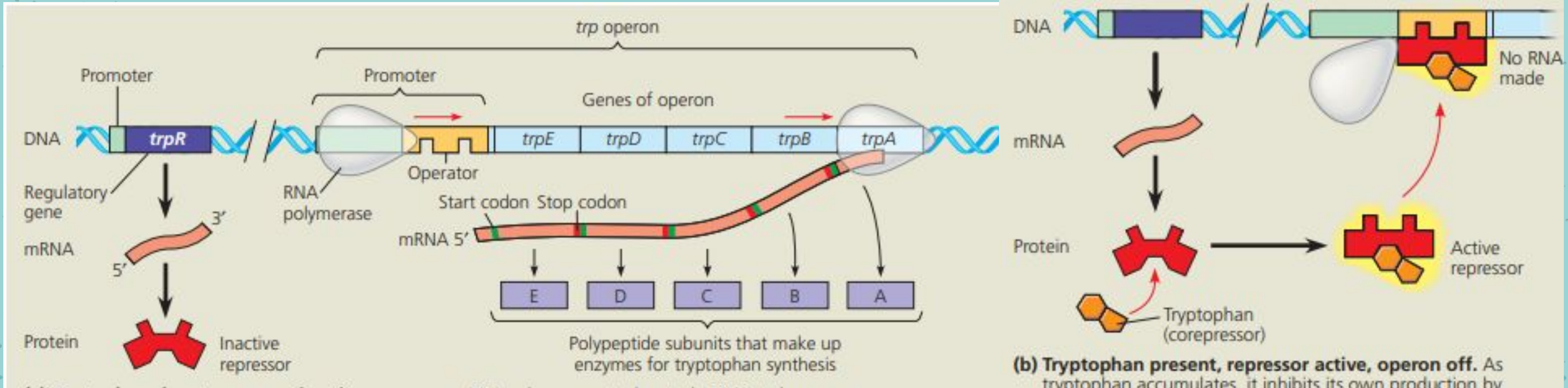
Prokaryotes

Gene Regulation

Eukaryotes

- Operons

- Control elements
- RNA splicing



(a) Tryptophan absent, repressor inactive, operon on. RNA polymerase attaches to the DNA at the promoter and transcribes the operon's genes.

(b) Tryptophan present, repressor active, operon off. As tryptophan accumulates, it inhibits its own production by activating the repressor protein, which binds to the operator, blocking transcription.

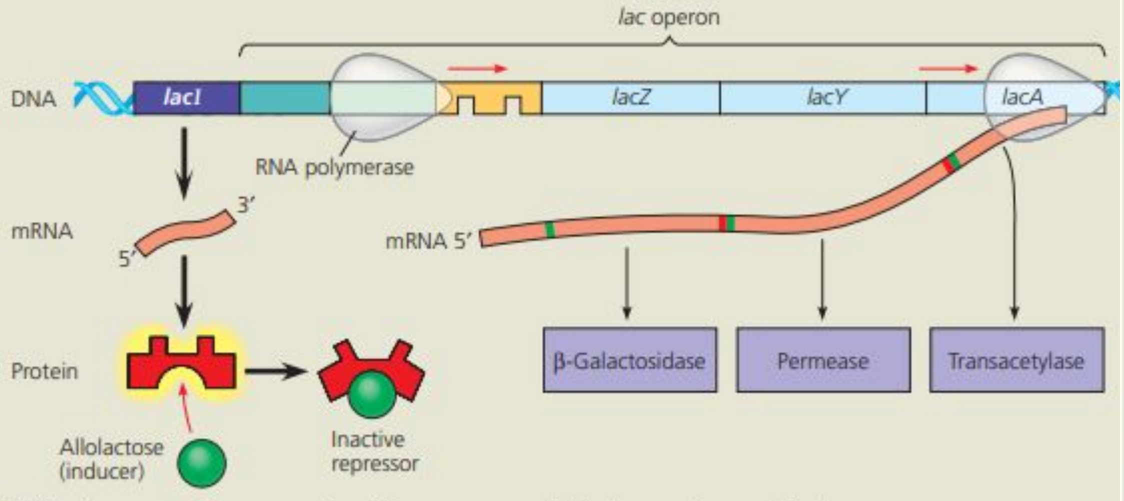
Prokaryotes

Gene Regulation

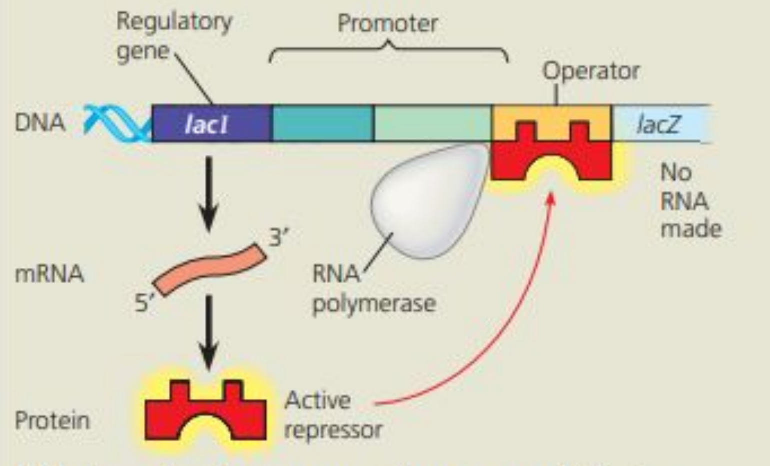
Eukaryotes

- Operons

- Control elements
- RNA splicing



(b) Lactose present, repressor inactive, operon on. Allolactose, an isomer of lactose, derepresses the operon by inactivating the repressor. In this way, the enzymes for lactose utilization are induced.



(a) Lactose absent, repressor active, operon off. The *lac* repressor is innately active, and in the absence of lactose it switches off the operon by binding to the operator.

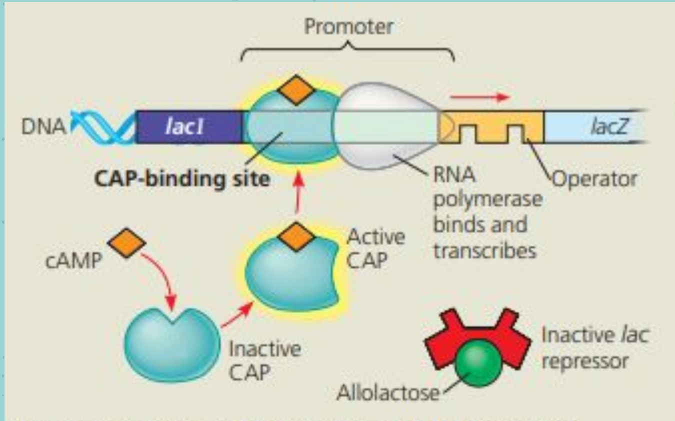
Prokaryotes

- Operons

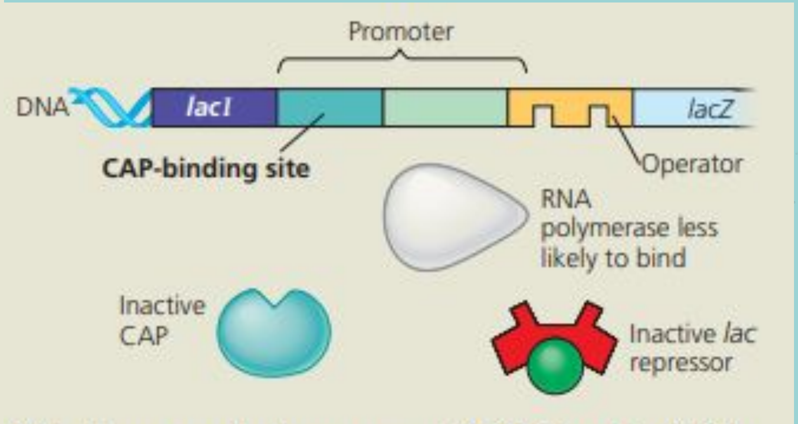
Gene Regulation

Eukaryotes

- Control elements
- RNA splicing



(a) Lactose present, glucose scarce (cAMP level high): abundant *lac* mRNA synthesized. If glucose is scarce, the high level of cAMP activates CAP, and the *lac* operon produces large amounts of mRNA coding for the enzymes in the lactose pathway.



(b) Lactose present, glucose present (cAMP level low): little *lac* mRNA synthesized. When glucose is present, cAMP is scarce, and CAP is unable to stimulate transcription at a significant rate, even though no repressor is bound.

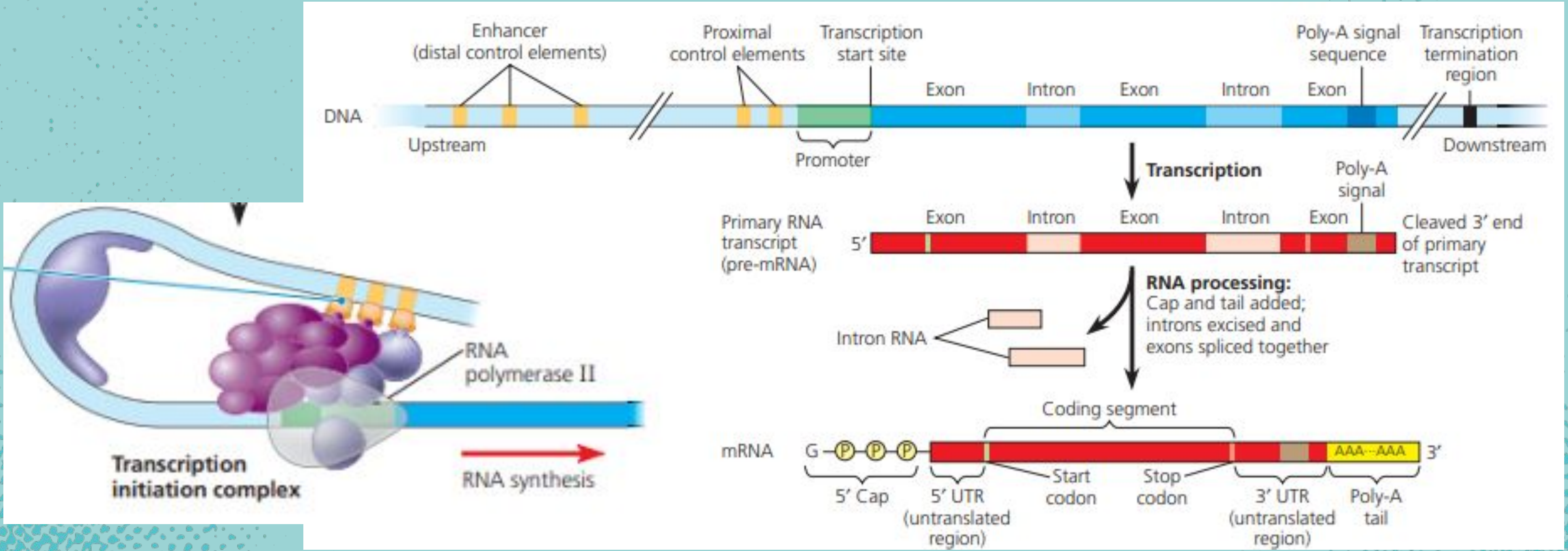
Prokaryotes

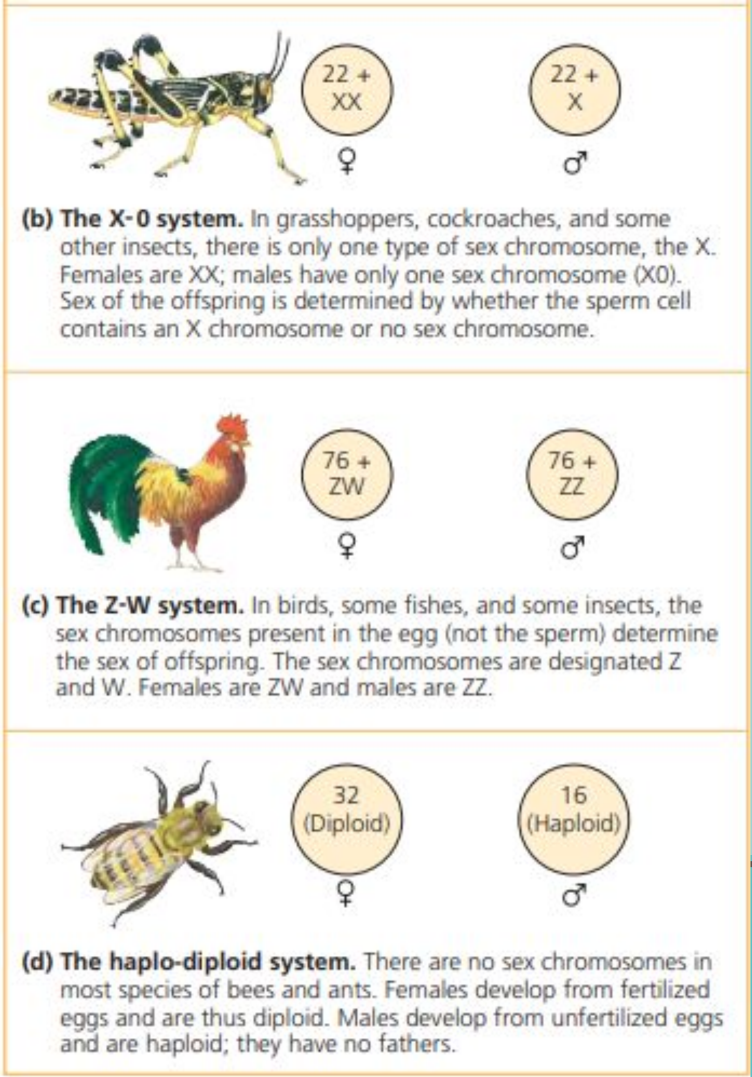
Gene Regulation

- Operons

Eukaryotes

- Control elements
- RNA splicing





Diseases

← And Chromosome stuff

Recessive

- **Tay-Sachs disease**
  - Recessive
  - Enzyme that breaks down lipids in brain does not work properly, leading to destruction of nervous system
  - How we classify a disease really depends on what level we look at it: at organismal level - dominant/recessive; at biochemical level - incomplete; at molecular level - codominant
- **Cystic fibrosis**
  - Recessive
  - Most common lethal genetic disease
    - In Europe, 4% of pop is carrier
  - Produces thicker mucus, often resulting in things like lung infections or problems with digestive system, leading to death.
    - Caused bc intracellular [Cl^-] is greater and cells absorb more water

Recessive

- **Sickle-cell disease**
  - Recessive
  - Results in red-blood cells having sickle shape
    - Not good for flowing through blood vessels, leading to pain and blood clots
    - Also means less oxygen transport
    - **Bilirubin** (yellow) from dead blood cells causes **jaundice**
  - Heterozygous is resistant to malaria *(Plasmodium) (Anopheles)*
  - **Glu** --> **Val** at position 6
- Phenylketonuria (PKU)
  - Recessive disease
  - Babies screened for
  - Can't metabolize phenylalanine, but can be treated with diet

Dominant

- **Huntington's disease**
    - Dominant
    - Symptoms take effect later in life (usually 35-45) giving enough time for people with disease to have children and pass on the alleles
    - Nervous system is destroyed
        - Huntingtin gene has CAG repeat expansion
        - Normally repeats 20 times, but in HD repeats >40 times
- Achondroplasia
    - Dominant
    - Causes dwarfism

X-linked

- **Color blindness**
  - X-linked
  - Red-green color blindness
  - More common in males
- **Duchenne muscular dystrophy**
  - X-linked
  - Muscles gradually weaken
  - Affected individuals rarely live past early 20's
- **Hemophilia**
  - X-linked
  - Some blood clotting proteins are missing, so affected individuals bleed a lot
  - Hemophilia A (Classic) = factor VIII
  - Hemophilia B (Christmas disease) = factor VII

Mitochondrial

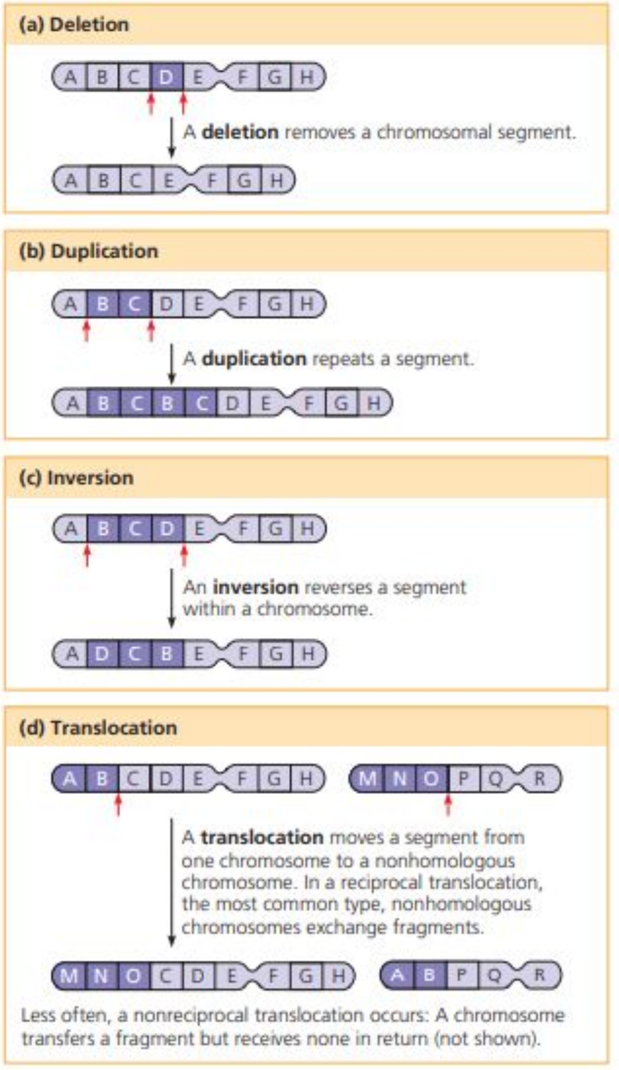
- Mitochondrial myopathy
    - Mitochondrial
    - Makes ppl weak
- Leber's hereditary optic neuropathy
    - Mitochondrial
    - Makes ppl go blind

Chromosome number wrong

- **Down syndrome (Trisomy 21)**
  - Usually not lethal, but learning disorders, sterile, etc.
- **Klinefelter syndrome (XXY)**
  - They're a guy, but they have more feminine features and are sterile
  - May have impaired intelligence
- **XYY (Jacob syndrome)**
  - Mostly normal male, except usually taller
- **Trisomy X (XXX)**
  - Mostly normal female, except usually taller
- **Turner syndrome/ Monosomy X (X0)**
  - Females are mostly normal, but sterile

Chromosome deletion/translation

- **Cri du chat**
  - Caused by deletion in chromosome 5
  - Individuals die in infancy or early childhood
- Chronic myelogenous leukemia
  - **Reciprocal translocation** - tip of chromosome 9 is switched with chromosome 22
  - **Philadelphia chromosome** - name for the shortened chromosome 22
  - Happens during mitosis of white blood cells
  - Leads to cancer
- Translocation down syndrome
  - Robertsonian translocation - an extra chromosome 21 is attached to chromosome 14

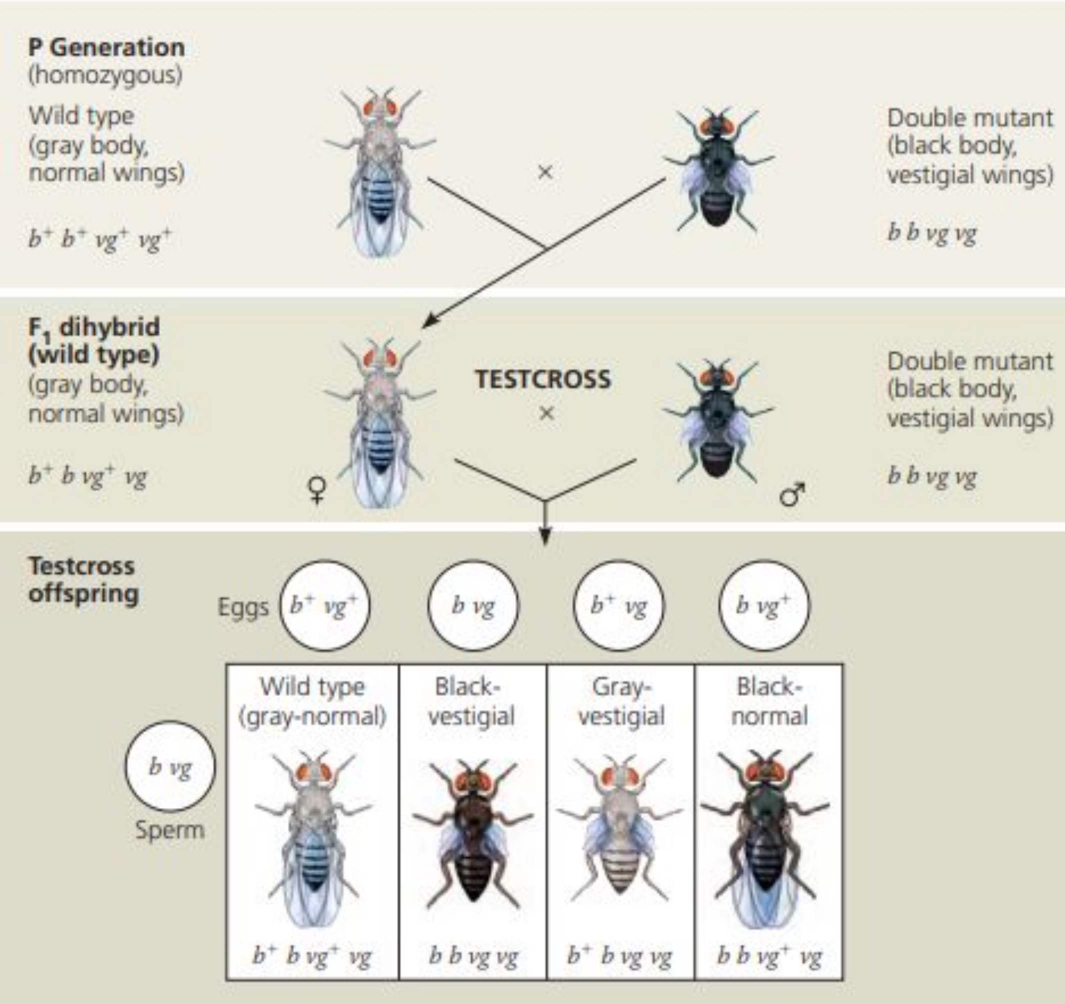


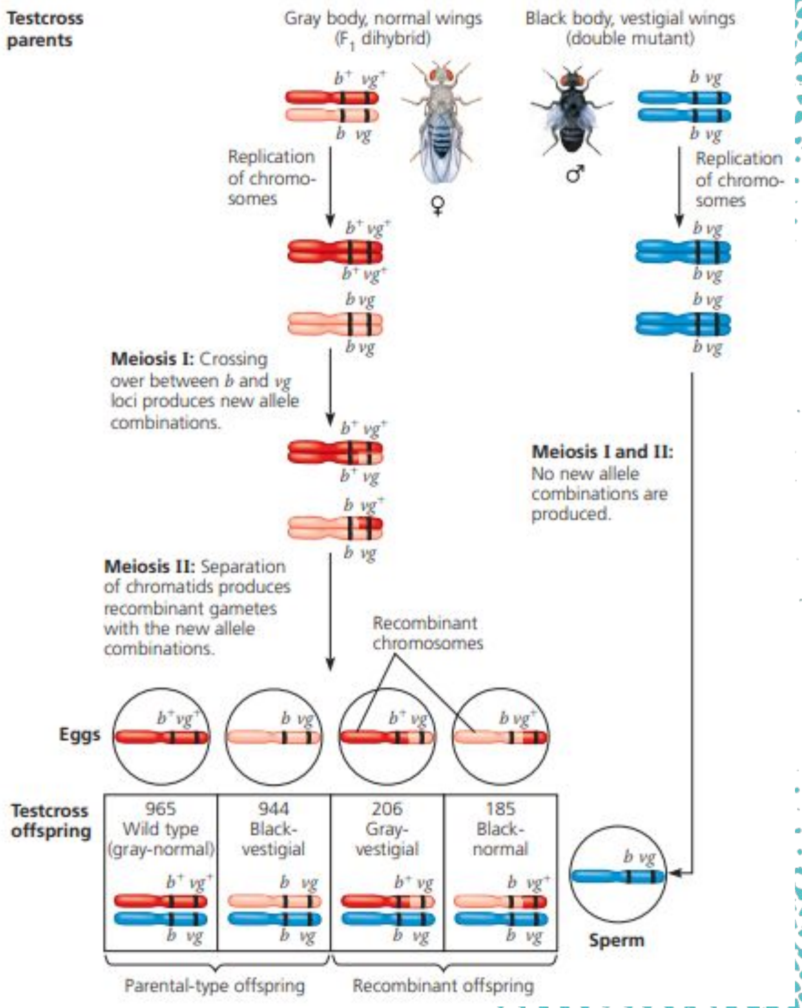
Diseases - Prion

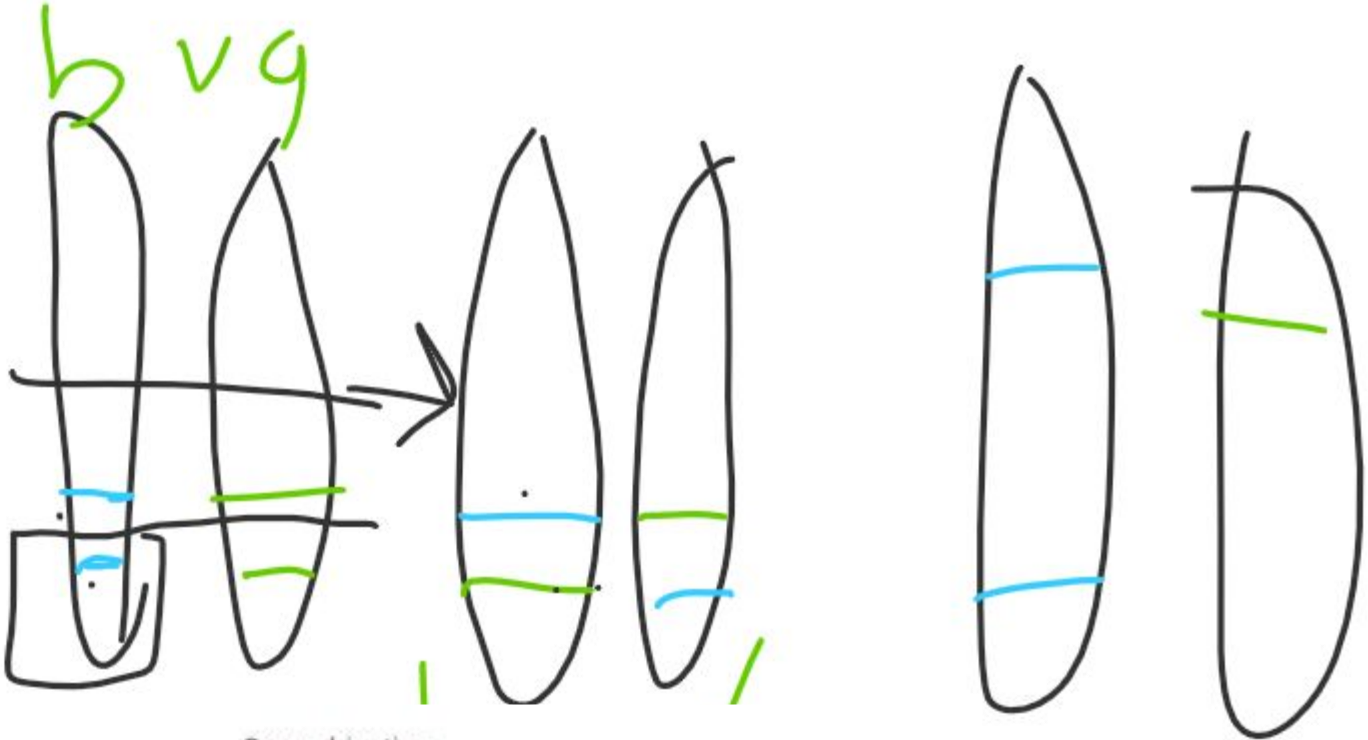
- **Creutzfeldt-Jakob disease**
  - **Prion**
  - Leads to degradation of the brain
- Mad Cow disease
- Kuru (Laughing Sickness)
  - Ritualistic cannibalism

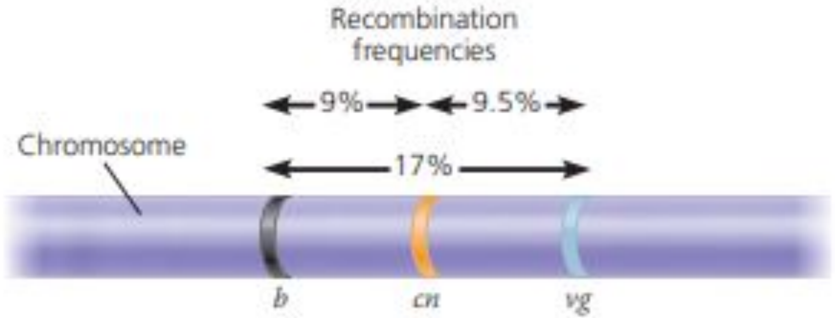
Gene linkage

- Also discovered by Morgan
- Exception to the law of independent assortment
- Alleles that are close together on the same chromosome are paired together more often
    - These genes are known as **linked genes** and do not obey Mendel's traditional laws of inheritance
- **Recombination frequency** - determines how linked they are
    - It can be calculated!
    - Do a **test cross** - homozygous recessive individual is mated with heterozygous individual
    - **Parental types**, and **recombinant types**
    - #recombinant/total = %
- **Linkage map** - map based on recombination frequency
    - 1 map unit = 1%
    - Alfred H Sturtevant - student of Morgan that created genetic maps
    - **cytogenetic map** - mapping chromosome with respect to features like certain stained bands
    - **physical map** - just nucleotide sequence


P Generation
(homozygous)
Wild type
(gray body,
normal wings)
b+ b+ vg+ vg+
×
Double mutant
(black body,
vestigial wings)
b b vg vg
F1 dihybrid
(wild type)
(gray body,
normal wings)
b+ b vg+ vg
TESTCROSS
×
Double mutant
(black body,
vestigial wings)
b b vg vg
Testcross
offspring
Eggs
b+ vg+
b vg
b+ vg
b vg+
b vg
Sperm
Wild type
(gray-normal)
b+ b vg+ vg
Black-
vestigial
b b vg vg
Gray-
vestigial
b+ b vg vg
Black-
normal
b b vg+ vg

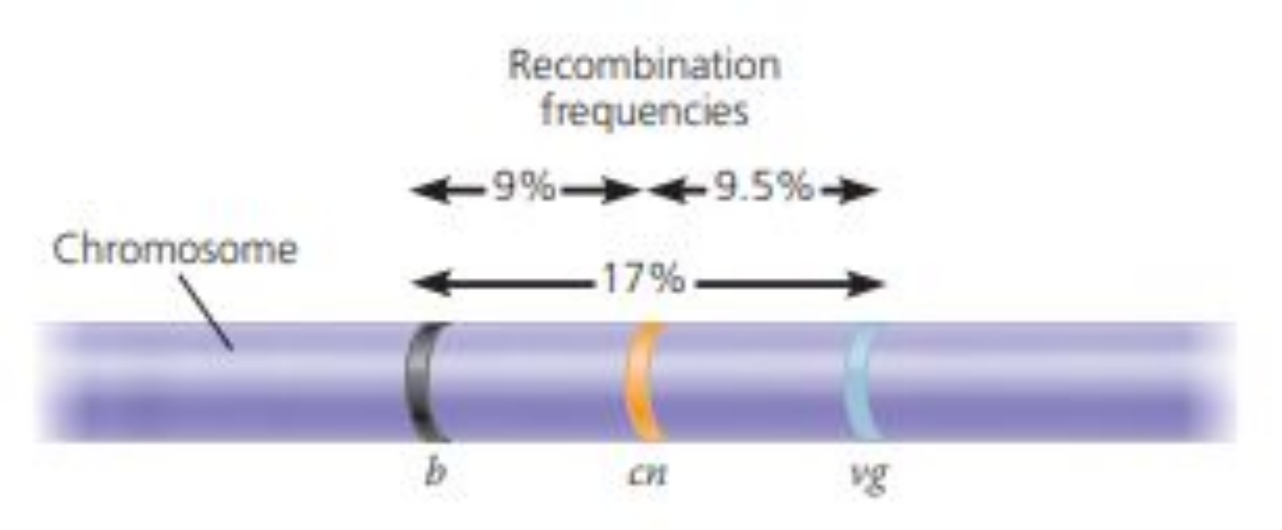

Testcross
parents
Gray body, normal wings
(F1 dihybrid)
Black body, vestigial wings
(double mutant)
b+ vg+
b vg
b vg
b vg
Replication
of chromo-
somes
Replication
of chromo-
somes
Meiosis I: Crossing
over between b and vg
loci produces new allele
combinations.
Meiosis I and II:
No new allele
combinations are
produced.
Meiosis II: Separation
of chromatids produces
recombinant gametes
with the new allele
combinations.
Recombinant
chromosomes
Eggs
b+ vg+
b vg
b+ vg
b vg+
Testcross
offspring
965
Wild type
(gray-normal)
944
Black-
vestigial
206
Gray-
vestigial
185
Black-
normal
b vg
Sperm
Parental-type offspring
Recombinant offspring


b v g


Recombination frequencies
9%
9.5%
17%
Chromosome
b
cn
vg

Linkage - Coincidence

Just do it twice!



Which of the following types of genes violates Mendel’s principle of independent assortment?

W) Linked

X) Codominant

Y) Dominant

Z) Epistatic

What is the correct linkage map for the genes P, Q, R, and S

given the following recombination frequencies between each gene: P-Q, 22%; P-R, 8%;

P-S, 6%; S-Q, 30%; R-Q, 13%; and R-S, 15%?

(3 points) Susan has recently been observing the characteristics of boomtastic bunnies for a school project. In boomtastic bunnies, pink fur is dominant to white fur, small paws are dominant to large paws, and short ears are dominant to long ears. Susan wanted to find the distance between the genes for fur color and ear size, so she conducted a 3 point test cross where she mated a pink, small-pawed, short eared boomtastic bunny with a white, large pawed, long eared boomtastic bunny. She recorded the characteristics of the resulting baby boomtastic bunnies in the following table.

Phenotype	Genotype	Observed
Pink, small pawed, short eared	FfPpEe	26
Pink, small pawed, long eared	FfPpee	16
White, small pawed, short eared	ffPpEe	3
White, small pawed, long eared	ffPpee	115
Pink, large pawed, short eared	FfppEe	115
Pink, large pawed, long eared	Ffppee	3
White, large pawed, short eared	ffppEe	16
White, large pawed, long eared	ffppee	26
	Total	320

What is the distance, in centimorgans, between the fur color and ear size genes?

A. 11.9 cM
B. 18.1 cM
C. 30 cM
D. 15.6 cM
E. 12.8 cM

Linkage Practice

(2 points) Interference (I) occurs when crossing over in one part of a chromosome influences crossing over in other regions of the same chromosome. Calculate the coefficient of coincidence (C) using data from the three-point cross in the previous question.

$$I = 1 - C$$

$$C = \frac{observedDCO}{expectedDCO}$$

A. -8.4%
B. -2.8%
C. 14.3%
D. 15.9%
E. 20.4%