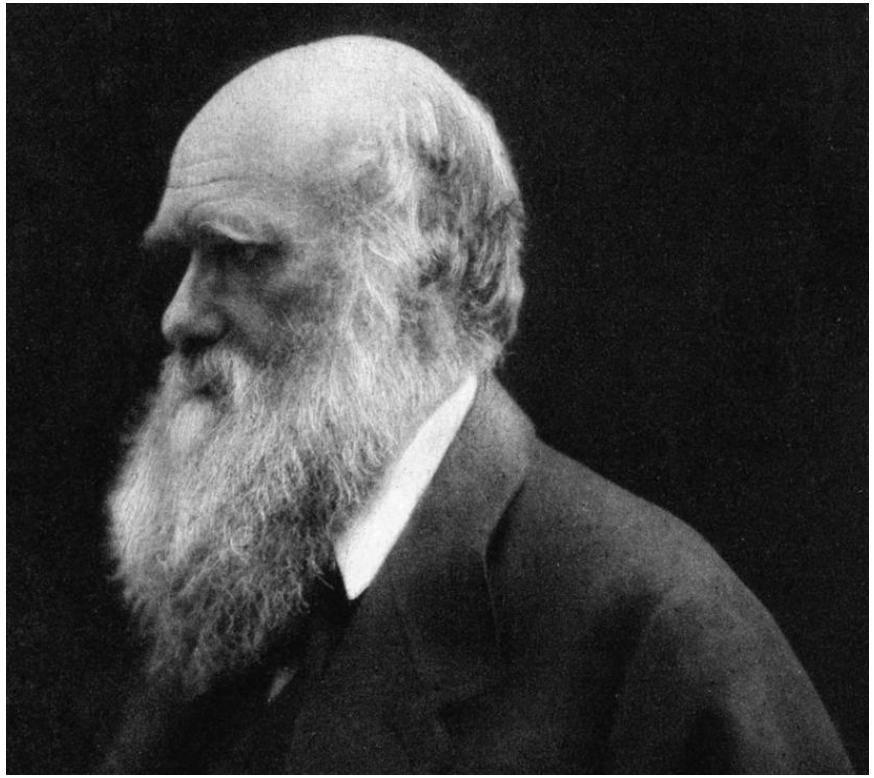
Lecture 1:Syllabus overview and Introduction to Genetics

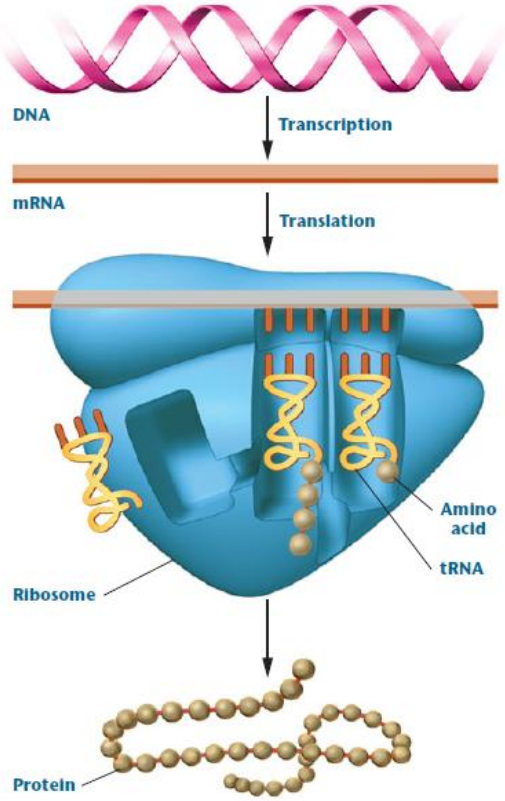
Syllabus overview and advice on success

History of Genetics

Evolutionary Context of Genetics



The Central Dogma



8/25/2025

Image credit: Concepts of Genetics, Klug et al; Wikipedia, https://makeameme.org/meme/good-grades-are-287bqg

Course overview

- Course: BIOL 198 Principles of Genetics MW 9:00-10:15am Hubbell Auditorium
- Professor: Dr. Emery Longan Hutch 216B
- Office hours 12pm-2pm Thursday and Friday
  - End at 1:30 this Thursday
- Email: elongan@ur.rochester.edu
- TAs:
  - Elizabeth Carleton
  - Minnie Sama
  - Sammy Carstens
  - Taylor Speas
  - Mahirah Morshed
  - Lorelei King
  - Elena Barr
  - Gabby Richards
  - Ethan Samora
  - Nicky Faustini
  - Masha Zvereva
  - Kennedy Stark
  - Maia Kurti
  - Ilona Mathis

You are expected to have read and understood the syllabus. Any questions can be directed to me.

4 exams and one writing assignment

Exam 1 = 70 points (5 lectures)
Exam 2 = 115 points (9 lectures)
Exam 3 = 115 points (8 lectures)
Writing assignment (gene therapy) 100 points
Final = 150 points (75 new material, 75 cumulative)

Lots of homework questions, but not graded
Homework questions will be the basis of exams!
If something is in the book but not discussed in class it will not be on the exam
If something is discussed in class that is not in the book, then it is fair game on the exams

Recitation = opportunity to work through material with a TA
Attendance not taken, but almost certainly leaving points on the table of you do not attend!

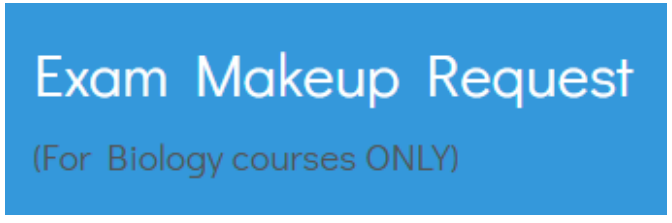
Lecture slides and lecture videos via Panopto will be provided. **This is a guarantee**, not matter if any given recording has technical difficulties. I will post a replacement recording.

For relevant policies on academic honesty, makeup exams, exam regrades, and other aspects of the course, SEE THE SYLLABUS

READ THE SYLLABUS

Missed exams + Exam regrades

- Pass the syllabus quiz to be eligible!!
- Fill out the jotform:
  - https://form.jotform.com/220474760005044
- Send an email addressed to me AND to Lisa Jensen
  - elongan@ur.rochester.edu
  - lbennice@ur.rochester.edu
- Email us as far ahead of time as possible



- If you think a score is incorrect on an exam there is an avenue for regrades
- There will be a window for regrade requests announced after grades are given back for each exam
- Requesting a regrade is done via Gradescope
- Note!!! Submitting a regrade opens you up to losing more points if your appeals are without merit and you are limited to 2 regrade requests per exam
- READ THE POLICY IN THE SYLLABUS
- ***THERE WILL BE ZERO LENIENCY EXTENDED REGARDING THE POLICY IN THE SYLLABUS***

Exams are the bulk of your grade. Plan accordingly!

- Genetics is the foundation of all biology
- The vocabulary and the concepts you learn here will be applicable to most of your other courses
- If I have done my job as a genetics professor, then these terms and concepts should be automatic and retrievable aspects of your working knowledge of biology moving forward
- This is a level of proficiency that I want you to walk away with
- To demonstrate this proficiency, the exams are your opportunity
- Exams are going to be given during the common exam time

Overview of topics in this course

- Exam 1 (Mendelian Genetics):
  - Intro to genetics
  - Mitosis and meiosis
  - Transmission genetics and patterns of heredity
  - DNA structure and replication
- Exam 2 (Central Dogma and how genomes work):
  - Transcription
  - Translation
  - Sex determination and sex chromosomes
  - Chromosomal mutations
  - Recombination and mapping genes in eukaryotes
  - Bacterial genetics and bacterial mapping
  - Genome organization
  - extranuclear inheritance
  - Mutation, transposition, and repair
- Exam 3 (gene regulation + sequencing):
  - Regulation of bacterial gene expression
  - Regulation of eukaryotic gene expression
  - Forward and Reverse Genetics
  - Cancer genetics
  - Recombinant DNA technology
  - Genomics and sequencing
  - Developmental genetics
  - Quantitative genetics
- Final exam (Other aspects of genetics):
  - Population genetics
  - Genetics of adaptation
  - Human evolutionary genetics
  - Forensic genetics
  - Behavior genetics
  - Conservation genetics
  - Cumulative section from each prior unit

Image credit: Wikipedia

Writing assignment (Due December 5th)

- We will be discussing gene therapy
  - Gene therapy = medical technology that makes use of the principles of genetics
  - You will write a short paper in which you apply your knowledge and devise an original gene therapy approach for a genetic disease
  - You will submit : A single draft (3 pages)
  - You will need:
    - To read primary publications about your chosen disease (5 options)
    - Explain the genetics of the disease
    - Explain current gene therapy approaches
    - Devise and explain an alternative strategy given what you have learned in class
    - Properly cite your sources

- Details and instructions are on blackboard

How to succeed in this course

- There is a lot of material, cramming will absolutely not work
- Plan ahead and block off time, spend time with the material every day, at least every other day
- The homework questions are your friend!
  - I recommend starting a text file with each question, and systematically answering them to best of your ability using your notes, the slides, and collaborating with classmates
  - Develop your own model answers
  - I then recommend that you use a notebook or tablet and PHYSICALLY practice answering the questions with no assistance
  - Answering questions accurately with no assistance is what is going to be asked of you on exams
  - Employing this strategy is analogous to the principle of specificity in physical training
  - If I want to be the best figure skater I can be, the bulk of my training time need to be spent practicing figure skating, not running or lifting weights
  - The same principle applies to success in this class
- I am here to help!
- Your TAs are here to help!
- Come to class!
  - I like to be interactive and answer questions in real time, engaging with the material in person will increase your attention and retention

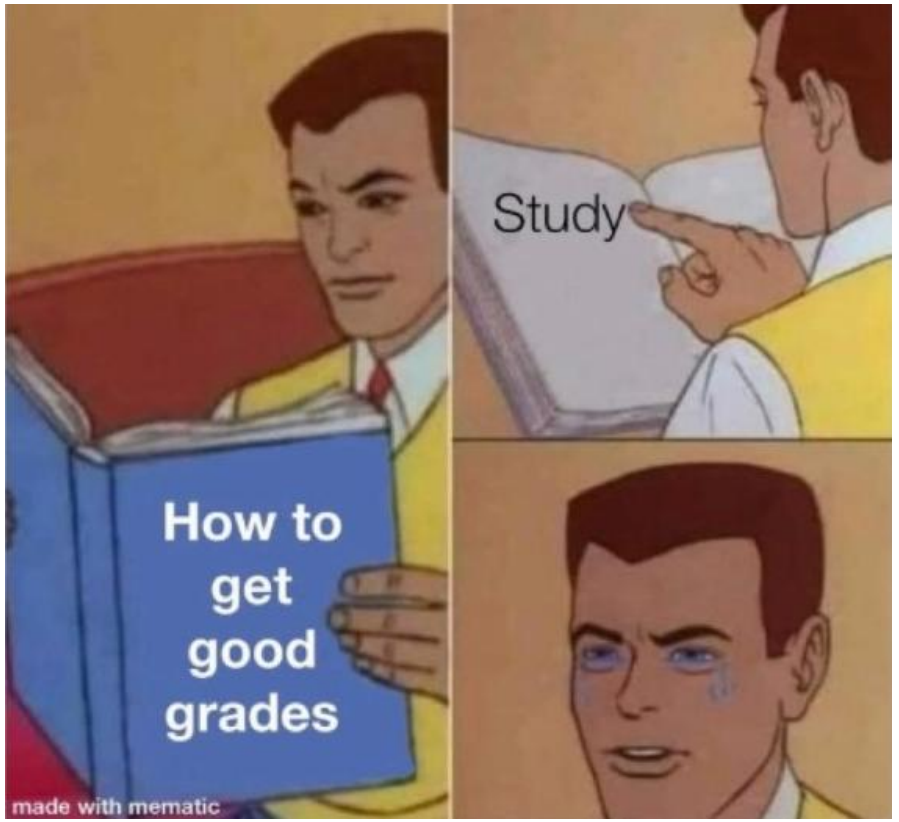


Image credit https://makeameme.org/meme/good-grades-are-287bqg Image credithttps://medium.com/@sarah_r/how-to-get-bad-grades-in-college-436d78d50c92

How to do poorly in this course in 4 easy steps

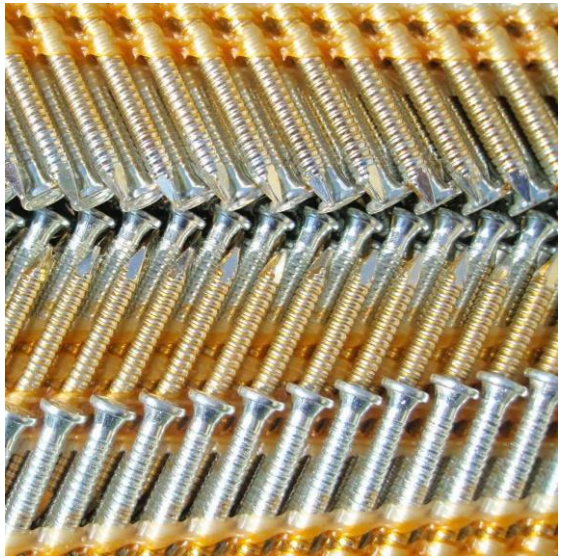
- 1. Cram for exams
- 2. Read the homework questions and only answer them in your head without practicing writing out answers
- 3. Don’t come to class
- 4. Don’t come to office hours

- Obviously, don't do these things!
- All of you can succeed! and I want all of you to succeed!

Image creditthttps://medium.com/@sarah_r/how-to-get-bad-grades-in-college-436d78d50c92

My job and your job

- My job is to give you all of the materials and tools you need to succeed



- Your job is to take those materials and tools and make use of them

Image credit: Wikipedia, https://www.istockphoto.com/illustrations/cartoon-of-house-under-construction

Exam 1 in 2024…and some words of advice

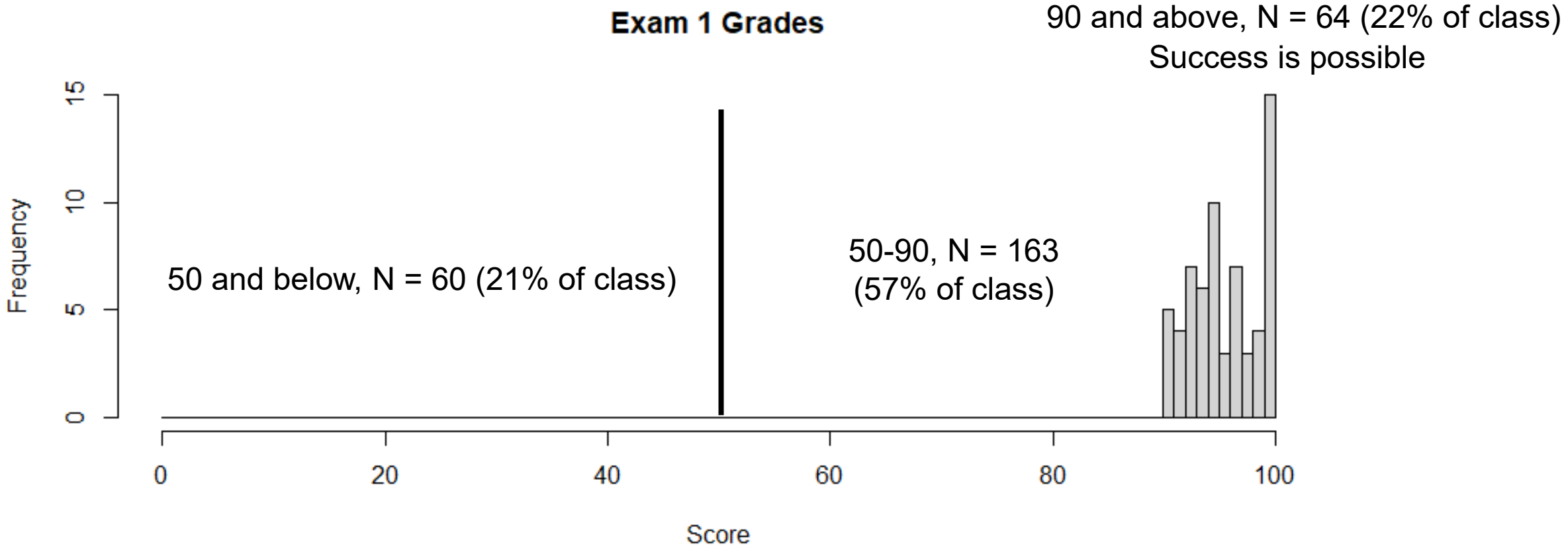
Spend time with the material

Spend time practicing homework questions

Practice being precise with your wording

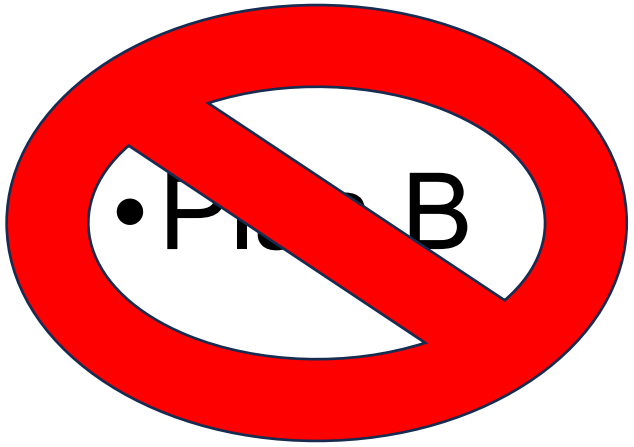
Mode = 100

90 and above, N = 64 (22% of class)
Success is possible



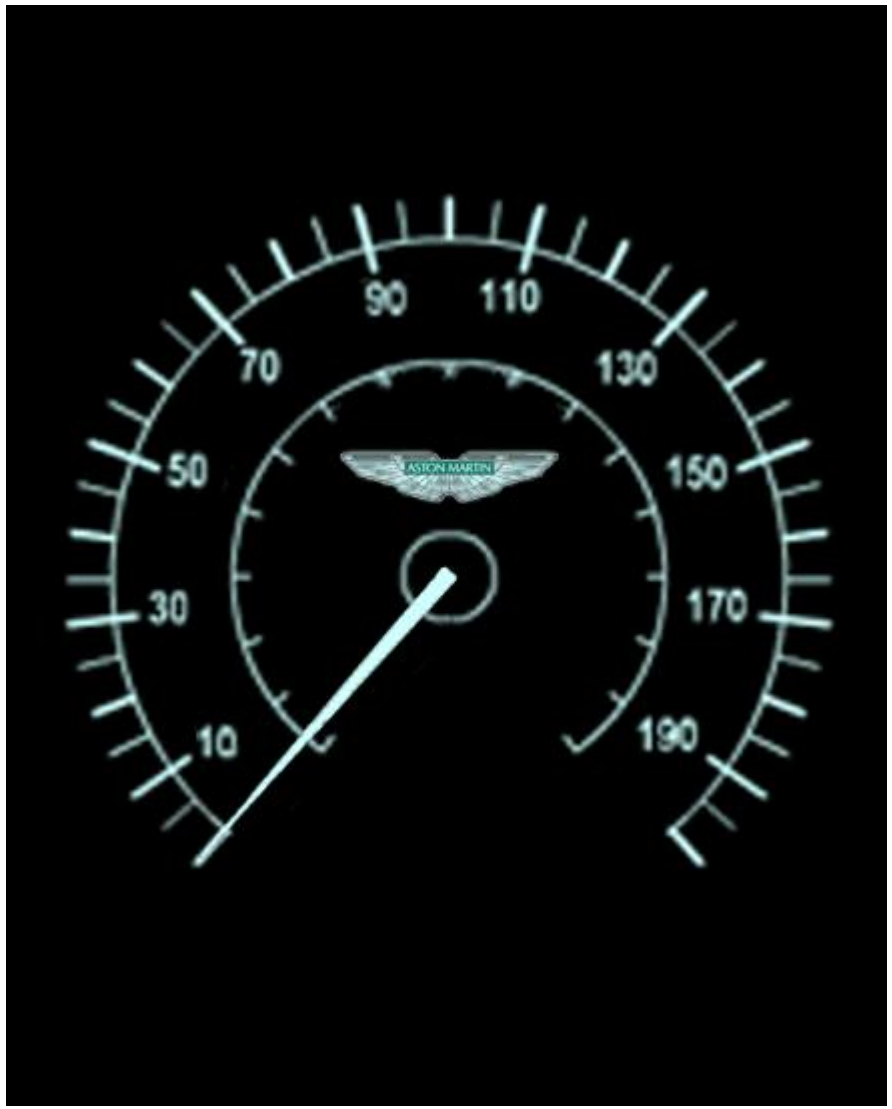
Plan A and Plan B for success

- Plan A
  - Work Hard
    - Spend time with the slides
    - Do the homework questions

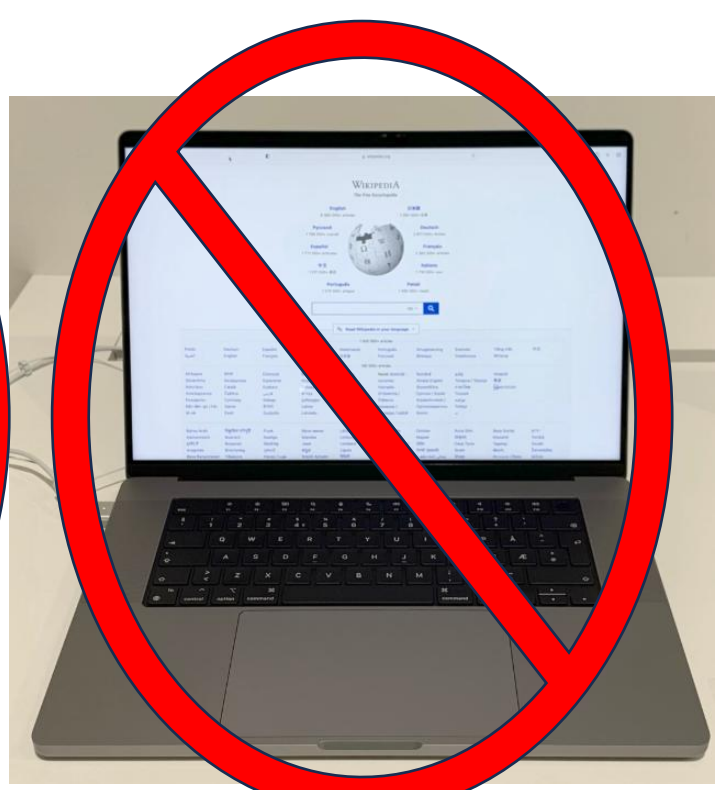


A quick word about pacing…

- This course covers a lot of material
- We will be moving at a pace that is noticeably faster than an intro level class
- This is a variable that cannot and will not be changed
- In order to cover everything we need to, we must move briskly through the material
- Fair warning…The pace will be fast. Plan accordingly!



Phones, laptops, tablets, and notes are not allowed to be out and accessible during exams



Plan accordingly

General slide structure (some exceptions throughout)

- **Terms you should know -** Definition
- **People whose contributions you should be able to identify (usually matching or multiple choice)**
- **Concepts you should be able to apply and explain**
- **Slides are text heavy intentionally!**
  - **The slides should serve as your primary resource for answering the homework questions as you practice**

Images to illustrate the ideas

Graphs or graphics you should be able to understand and in some cases explain/interpret

Learning objectives

- 1. Learn an overview of the history of genetics – including the contributions of the key scientists
- 2. Understand the theory of natural selection and it’s relationship to genetics
- 3. Define key terms that will be used throughout the semester and understand the general concept behind the central dogma
- 4. Refresh your memory on some intro topics

What is genetics?

- **Genetics** is the study of heredity and hereditary material
- Humans have implicitly understood genetics for ~10,000 years
  - (domestication and selective breeding)
- The mechanistic understanding is far younger.
  - Modern genetics began in 1866 when **Gregor Mendel** first published his results on heredity in pea plants
  - (Much more on this to come)

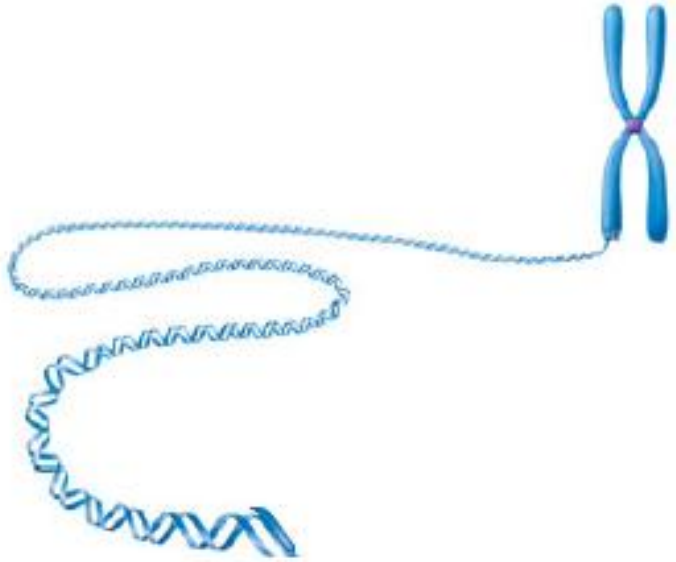
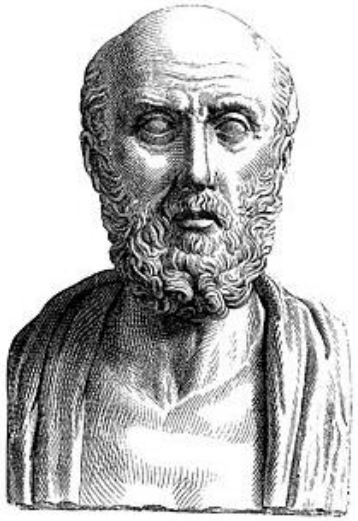


Image credit: Concepts of Genetics, Klug et al; Wikipedia

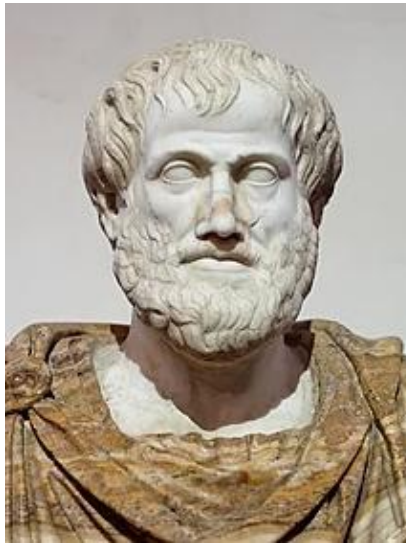
How did people used to think heredity worked?

- In ancient Greece there were two primary ideas about heredity:
  - 1. **Hippocratic school of medicine**: "Humors" derived from different parts of the male body serve as the bearers of hereditary traits and are drawn from various parts of the body to the semen. Humors can either be healthy or diseased and they can change throughout life
  - 2. **Aristotle**: The semen contains a "vital heat" that "cooks and shapes" the menstrual blood into an embryo. Structures formed de novo! (**epigenesis**)
- In the centuries leading to Mendel there were several other ideas about heredity:
  - 1. **Homunculus theory**: The sperm contains a perfectly formed miniature human, whose growth is initiated upon implantation into the uterus
  - 2. **Ovist Theory**: The egg cell contains a perfectly formed miniature human, whose growth is stimulated by the semen
- Critically, these theories lack the concept of **epigenesis** = substances within the embryo *differentiate* into body tissues, rather than body tissues being preformed. **William Harvey** is credited with the first modern explanation of this idea

Hippocrates



Aristotle



Homunculus

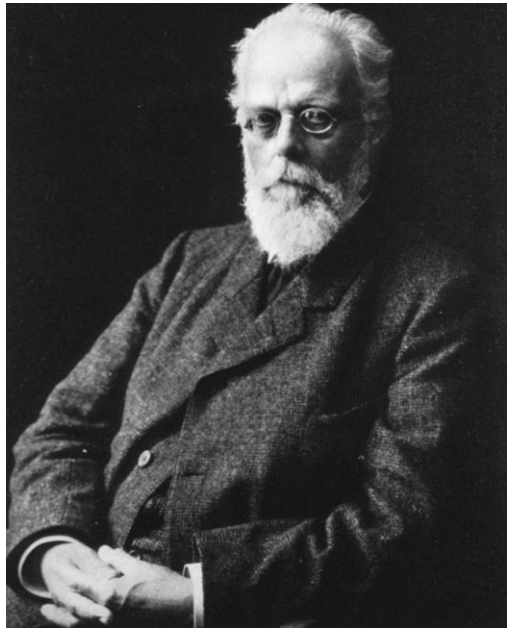
William Harvey

Image credit: Concepts of Genetics, Klug et al; Wikipedia

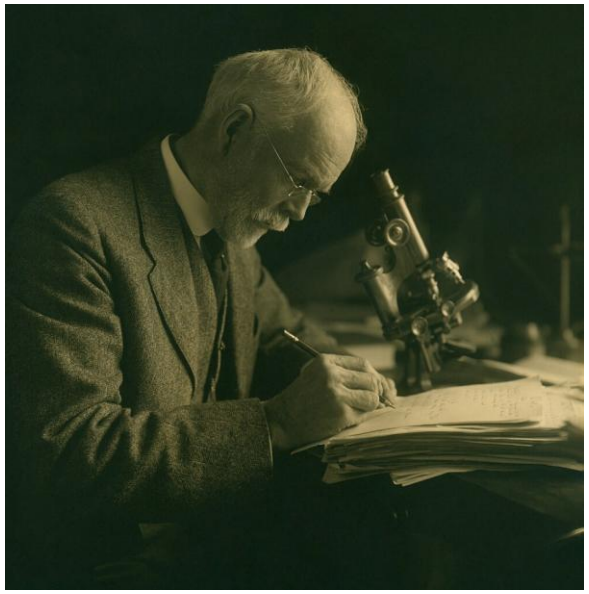
Germ plasm theory, hereditary material, and inherited diseases

- In 1889 **August Weissman** proposed that ovaries and testes each contain full sets of genetic information and that sperm and egg cells carry the information brought together in fertilization
  - This is the germ plasm theory
- 1895 **Edmund Beecher Wilson** proposes that "nuclein" is the hereditary material, and that:
  - "*inheritance may, perhaps, be effected by the physical transmission of a particular chemical compound from parent to offspring*".
- The first characterization of a genetic disorder occurred shortly after by **Archibald Garrod**
  - Alkaptonuria = "Black urine disease" (autosomal recessive)
  - Defect in the breakdown of HGA

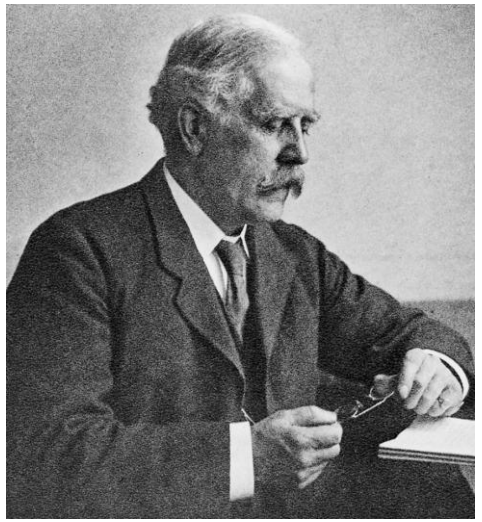
Weissman

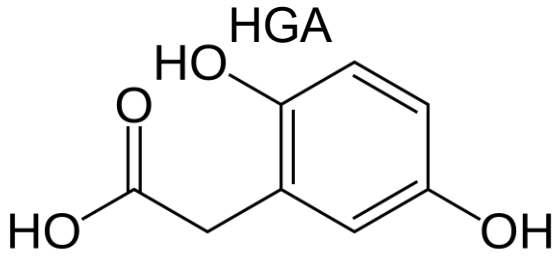


Wilson



Garrod





Fresh sample After left standing

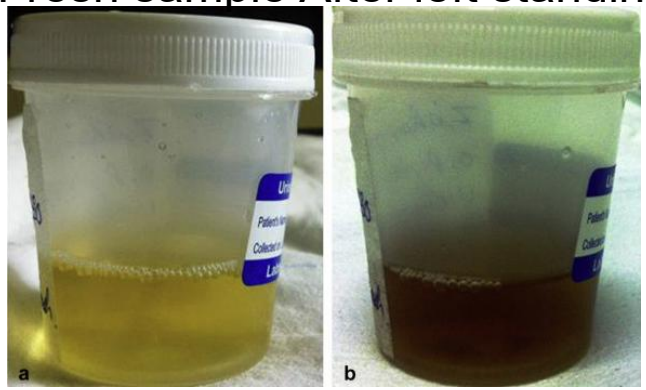


Image credit: Some Info from Moore 1987, Wikipedia, Sharma et al. 2015

What advances potentiated a better understanding?

- **Cell Theory:**
  - 1. All life is made of cells (**Schleiden and Schwann**)
  - 2. All cells come from other cells (**Rudolph Virchow**)
- Refutation of the idea of **spontaneous generation** by **Pasteur**
  - States that life will arise *de novo* from non-living substances
- Widespread rejection of the idea of **fixity of species**
  - Mainly aligning with the idea of special creation, the idea is that all species have not changed since they were formed
- Which leads us into **Darwin** and Natural Selection!

Schleiden

Schwaan

Virchow

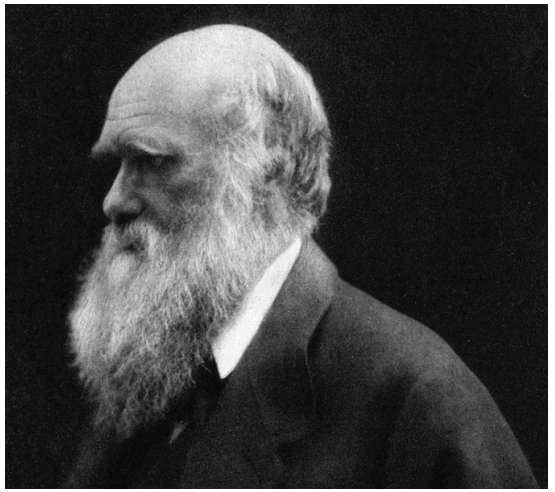
Pasteur

Image credit: Wikipedia

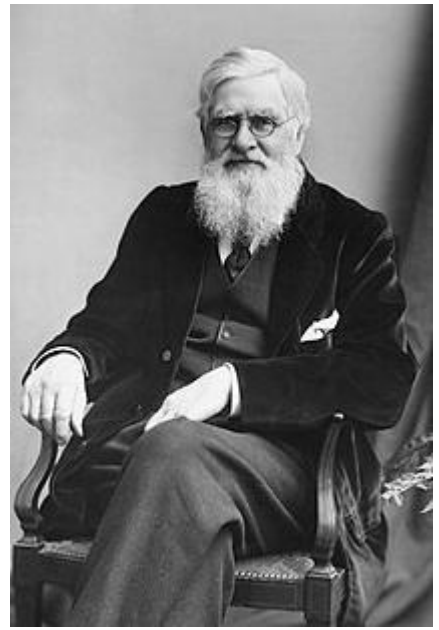
The argument for natural selection (Darwin and Wallace)

- Premise 1: Species are variable and some of this variation is **heritable** (Can be passed from parent to offspring)
- Premise 2: Some of this heritable variation is *meaningful* in terms of survival and reproduction
- Premise 3: Species tend to "over-reproduce", or produce more offspring than the environment can support
- Conclusion 1: There will be a "struggle for existence" among offspring
- Conclusion 2: Those individuals with variations that are most suited to the environment will enjoy higher reproductive success than those individuals with less favorable variations
- Conclusion 3: The population will change through time as adaptive traits accumulate
  - Corollary: If populations of the same species are separated in different environments they may diverge and give rise to distinct species

Darwin



Wallace



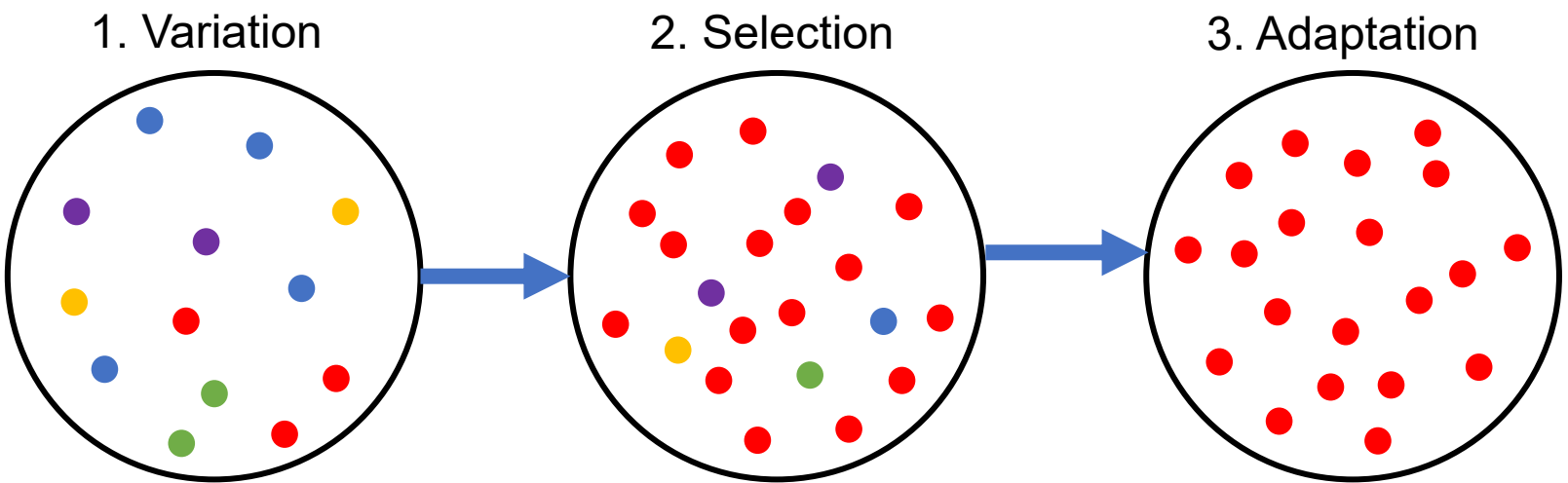
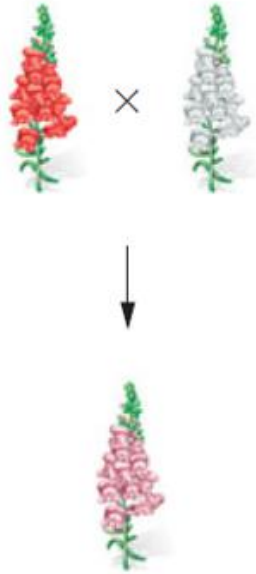


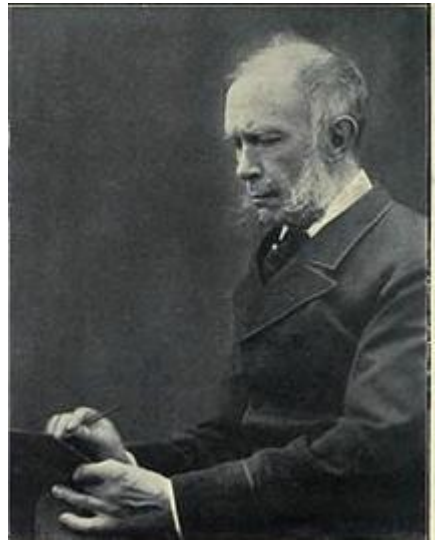
Image credit: Wikipedia

Great! But where do variations come from? How are they inherited?

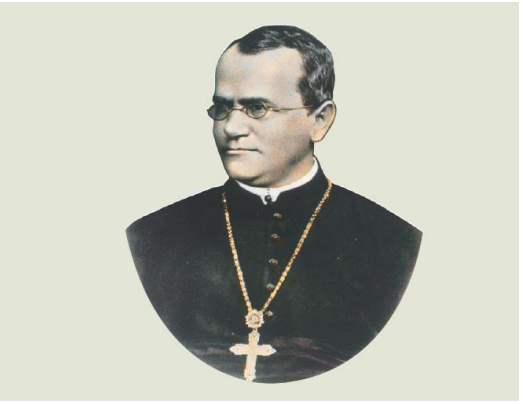
- Darwin believed in **blending inheritance**, the offspring will tend to have trait values near the average of the parents
- **Fleeming Jenkin** -1867 in writing a review of on the origin of species stated that adaptive evolution is not compatible with blending inheritance because it does not matter how advantageous a new variant is, it will tend to be diluted out each generation!
- A contemporary of Darwin, **Gregor Mendel** experimentally demonstrated that inheritance was “particulate” not blending (more on him later)
  - Modern genetics began with Mendel
  - But he published in an obscure journal
  - Darwin never read his work
  - Was not rediscovered until 1900 after his death



Jenkin



Mendel



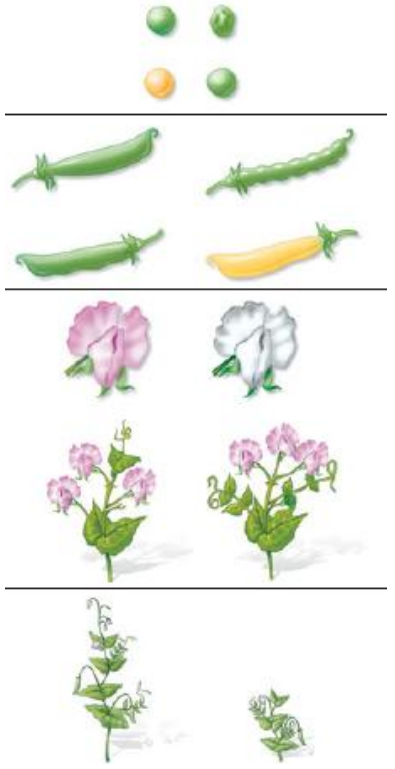


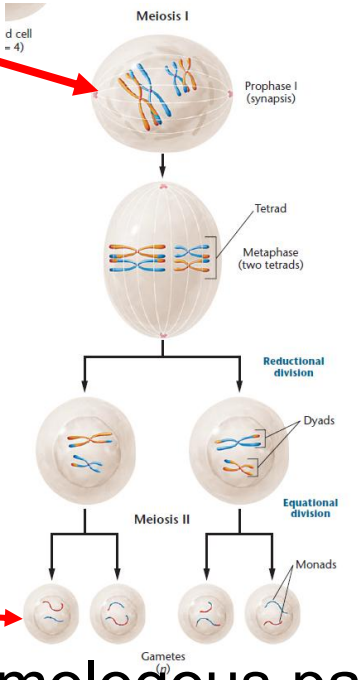
Image credit: Concepts of Genetics, Klug et al; Wikipedia

Discovering Chromosomes

- ~20 years after Mendel, Scientists began observing chromosomes under a microscope (Very large linear DNA molecules)
- Each species has a characteristic **diploid** number
- Human diploid number = 46, 23 **homologous pairs** (maternal and paternal copies of a chromosome)
- Homologous pairs are the same length and contain the same **genes**, though they may carry different **alleles**!
- **Genes** = The functional unit of heredity
- **Allele** = Alternative forms of a gene
- Late in the 19th century, researchers observed two types of cell division:
  - **Mitosis** = Replication and equal division of chromosomes into two daughter cells (Both 2N)
  - **Meiosis** = Two rounds of division yielding 4 **haploid** **gametes**
  - **Haploid** = Having only one copy of each gene in the genome
  - **Gametes** = reproductive cells (eggs and sperm)
- **Sutton** and **Boveri** noted that the behavior of chromosomes was exactly analogous to how **Mendel** described the behavior of genes during gamete formation. This led them to hypothesize that the genetic information is encoded on chromosomes, **the chromosomal theory of inheritance**
- **Walter Fleming** made similar observations

Diploid = 4

Meiosis



Haploid = 2

Homologous pair

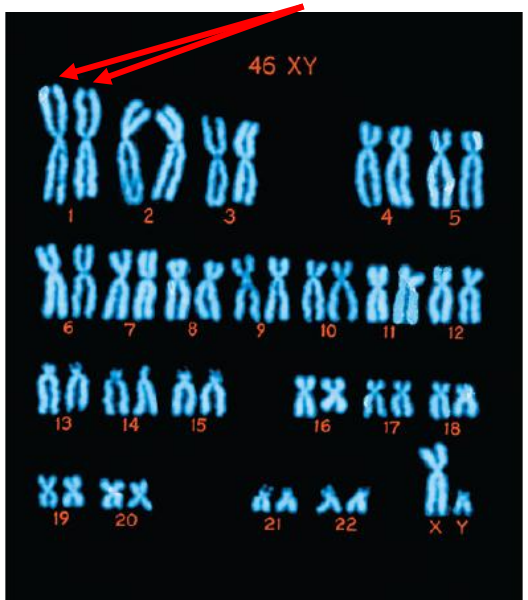
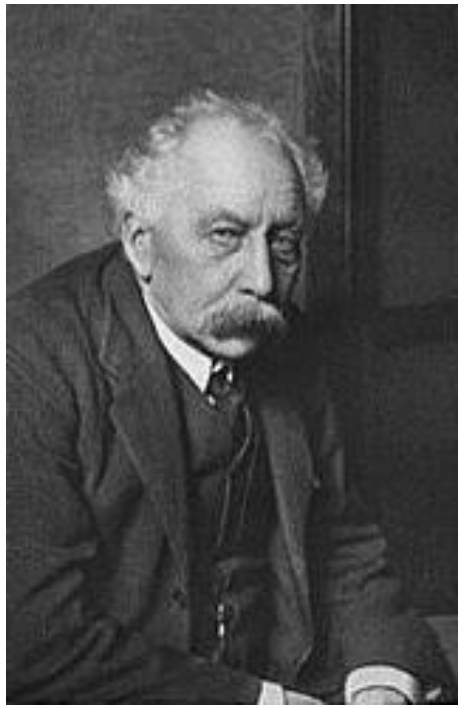


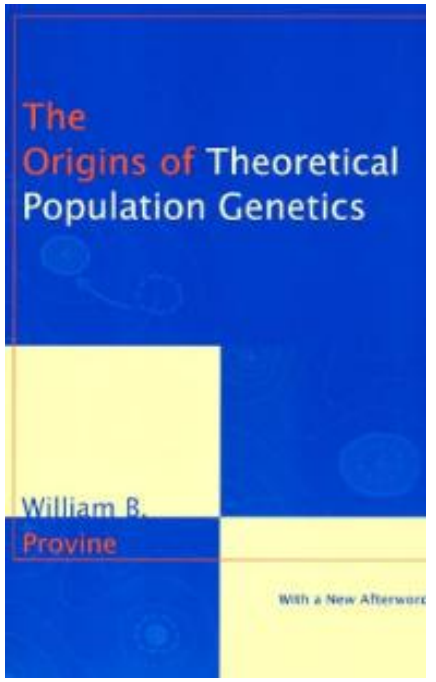
Image credit: Wikipedia, Concepts of Genetics, Klug et al

Rediscovering Mendel

- Several scientists rediscovered Mendel's postulates and his work in 1900
- **William Bateson** was a staunch supporter of the universality of Mendelian inheritance
  - That all traits are fundamentally inherited according to the rules of Mendelian inheritance
  - Bateson was convinced of this on a 1901 train ride as he read a paper by **Garrod** describing alkaptonuria and how it appeared to be inherited as a recessive trait
- There was FIERCE debate about this in the early 20th century (**Biometricians** believed that **continuous characters** could not be explained by Mendelian inheritance)
- The work of **Herman Nilsson-Ehle** and **Edward East** showed that Mendelian inheritance can actually explain inheritance of continuous characters if traits are governed by multiple Mendelian factors

Bateson





THE

AMERICAN NATURALIST

VOL. XLIV *February, 1910* No. 518

A MENDELIAN INTERPRETATION OF VARIATION THAT IS APPARENTLY CONTINUOUS[1]

PROFESSOR EDWARD M. EAST

HARVARD UNIVERSITY

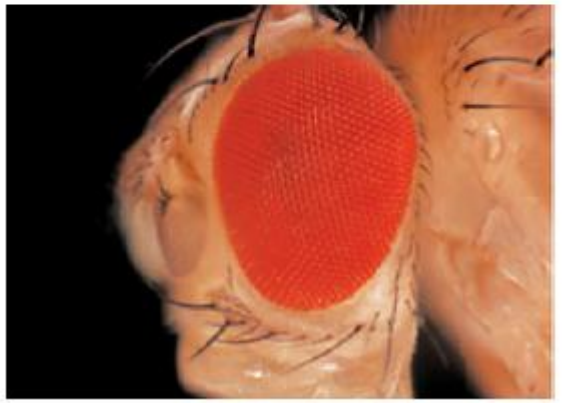
Nilsson-Ehle

Image credit: East 1910, Wikipedia

Heritable changes and terminology: Example

- Shortly after chromosomes were discovered, work on the "white eyes" **mutation** confirmed the chromosomal theory of inheritance (**Thomas Hunt Morgan**)
- **Mutation** = Any heritable change. These are the source of ALL genetic variation
- This mutation causes mutant flies to have white eyes as opposed to the "**wild type**" (typical **phenotype**) of red eyes
- This **gene** for eye color was mapped to the X chromosome and there are 2 **alleles**, the white and red alleles.
- **Alleles** = alternative forms of a gene that differ in DNA sequence, and thus encode slightly different products
- **Genotype** = The genetic makeup of an organism, often referring to the alleles they harbor for one particular gene
- **Phenotype** = the physical manifestation of genotype (appearance or metabolic capability etc.)

Morgan



D. melanogaster X chromosome

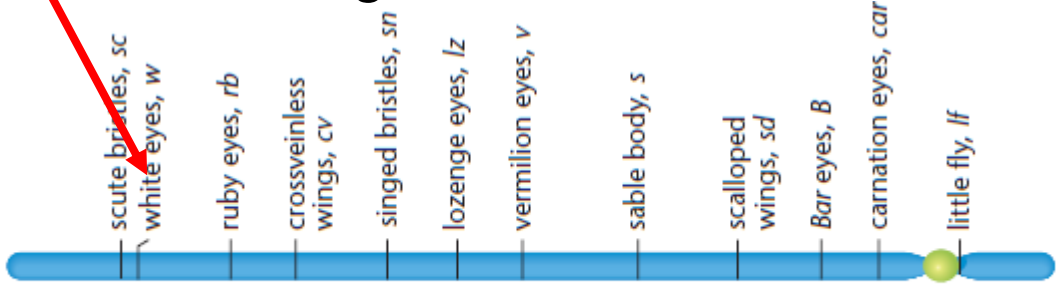
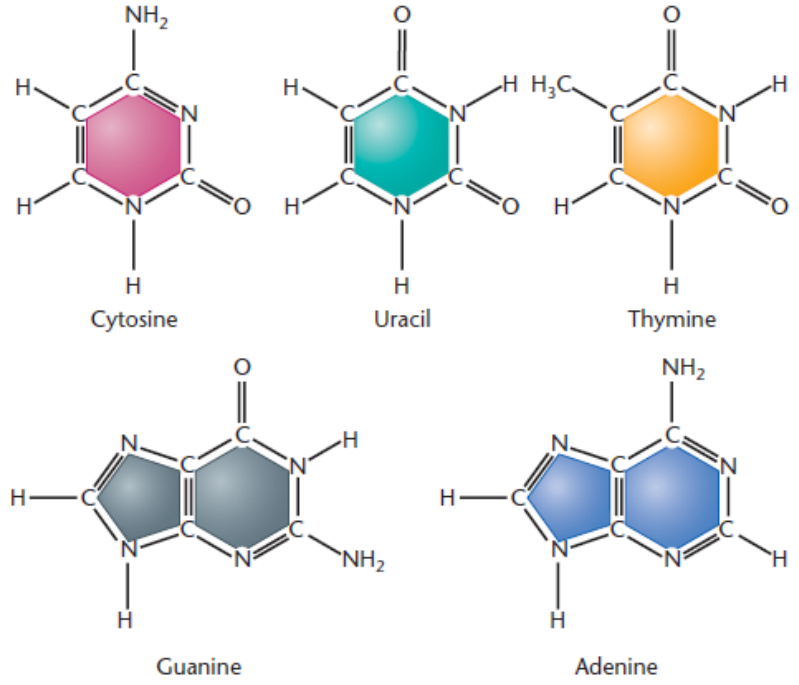


Image credit: Concepts of Genetics, Klug et al; Wikipedia

What is the hereditary material in Chromosomes?

- Chromosomes are ~50% DNA, ~50% proteins
- 4 different monomers in DNA (Nucleotides)
  - (uracil only in RNA)
- 20 different monomers in proteins (amino acids)
- A lot of people thought proteins were the hereditary material due to greater sequence complexity
- Experiments by **Avery**, **McCarty**, and **MaCleod** in bacteria, along with the **Hershey-Chase** experiment demonstrated that the hereditary material was DNA. (More on these later)



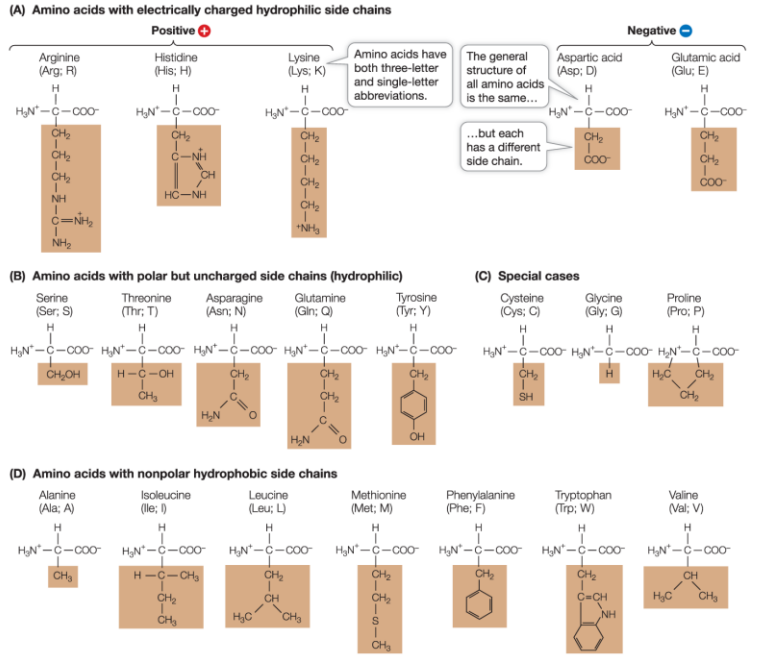
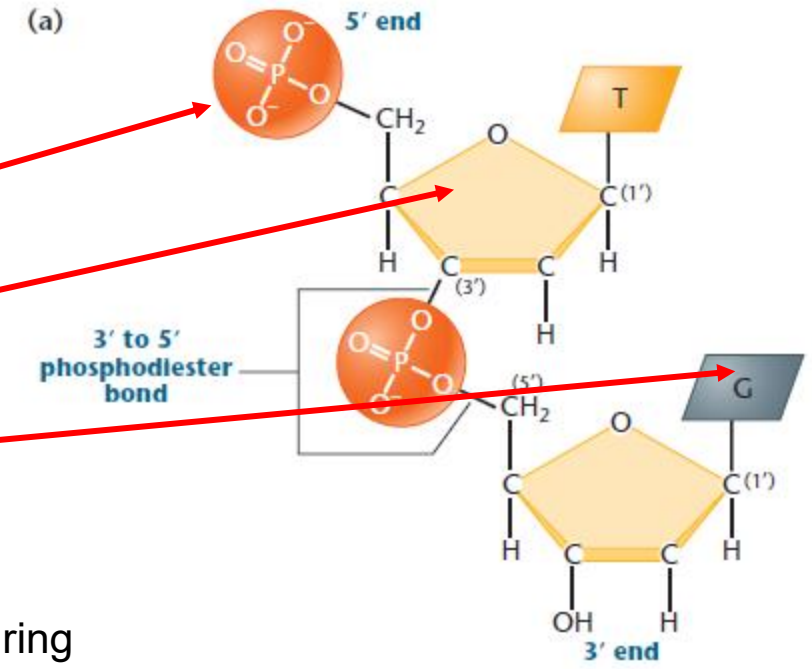


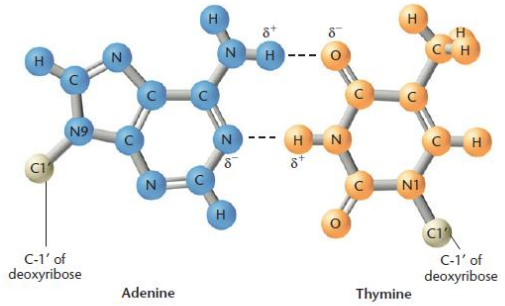
Image credit: Concepts of Genetics, Klug et al. Principles of Life Hillis et al.

What is the structure of DNA?

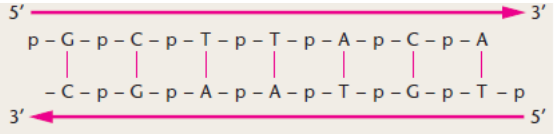
- The basic unit of DNA and RNA is a **nucleotide**
- Nucleotides have 3 components
  - A phosphate
  - A ribose/deoxyribose sugar
  - A nitrogenous base
- Nucleotides are joined into polymers via covalent **phosphodiester bonds**
  - 3' Carbon – P – 5' carbon of another nucleotide
- DNA exists as a **complementary**, **antiparallel**, **duplex** that is held together via hydrogen bonds
  - A always pairs with T (2 H bonds)
  - C always pairs with G (3 H bonds)
  - DNA strands have 5' to 3' polarity and strands in a duplex have opposite polarity



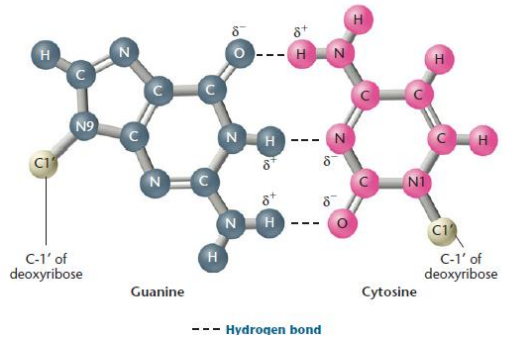
Base pairing



Anti-parallel duplex



Guanine-cytosine base pair



Base pairing + anti-parallel duplex

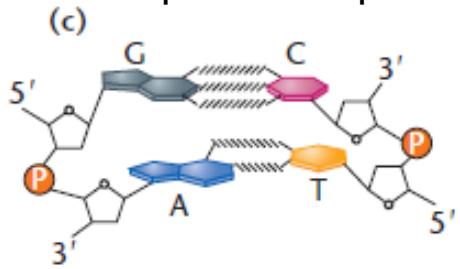
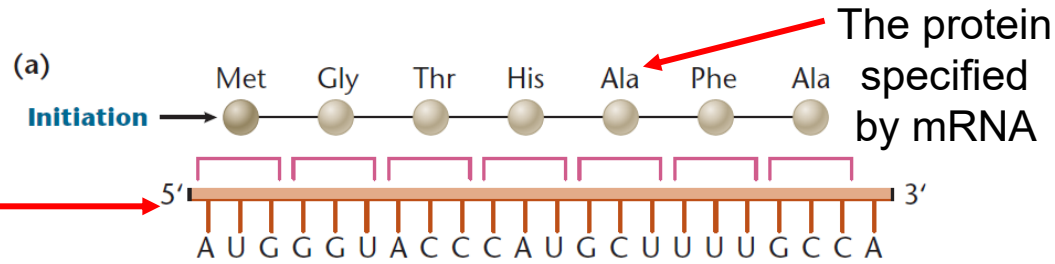
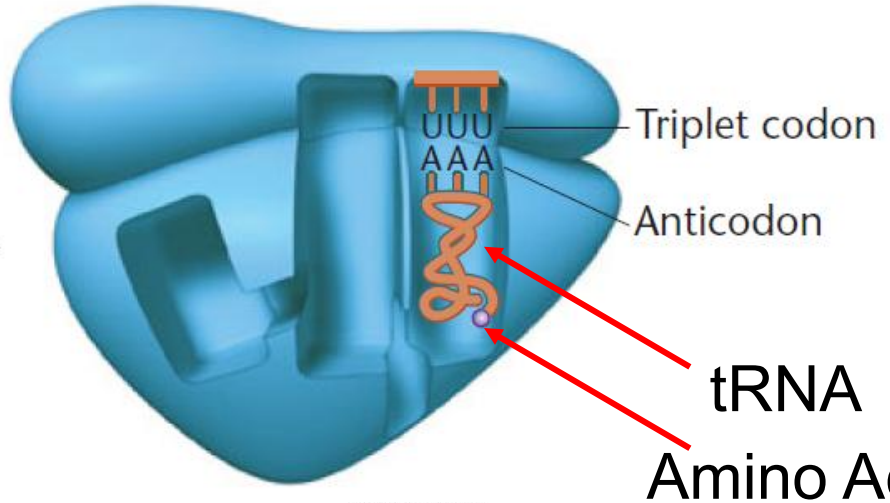


Image credit: Concepts of Genetics, Klug et al; Wikipedia

RNA structure and function

- RNA:
  - Has ribose instead of deoxyribose
  - Has uracil instead of thymine
  - Is typically single stranded
  - Can form complementary structures with DNA
- DNA contains the hereditary information.
- RNA carries this information to the ribosome
- DNA is **transcribed** into RNA
- RNA is **translated** into proteins
- tRNA is the molecule that "translates" the "language" of DNA/RNA into the protein "language"
  - To do this, cells use the genetic code





Second letter

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

Image credit: Wikipedia, Concepts Genetics Klug et al

The central dogma of molecular biology

DNA

transcription

RNA

translation

Protein

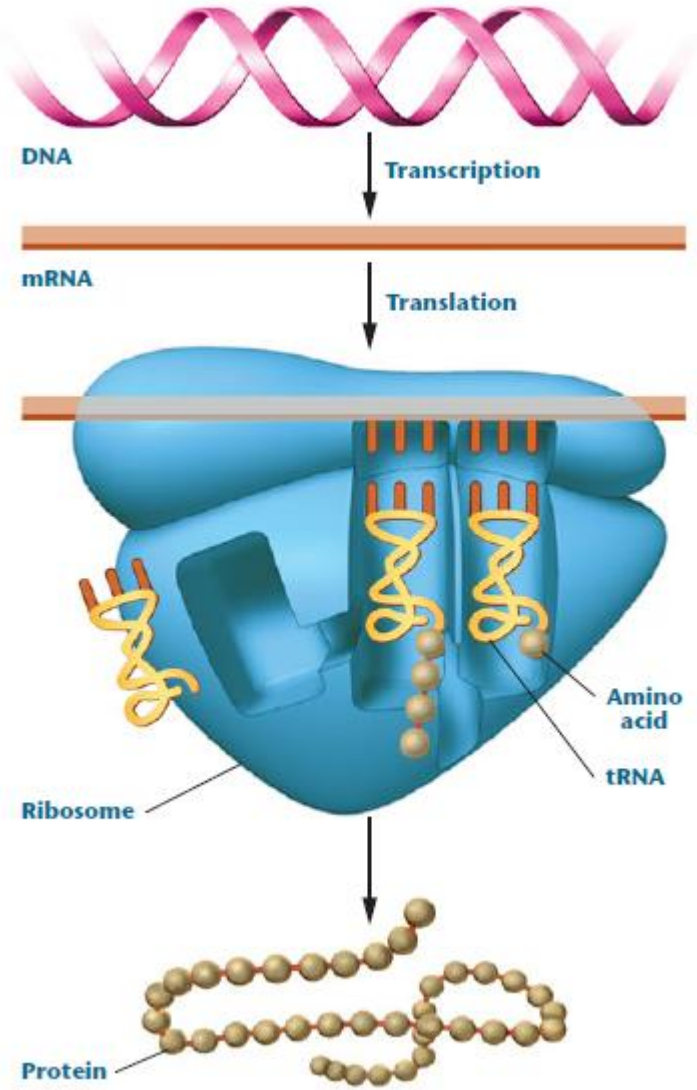


Image credit: Concepts of Genetics, Klug et al

The central dogma of molecular biology is complex!

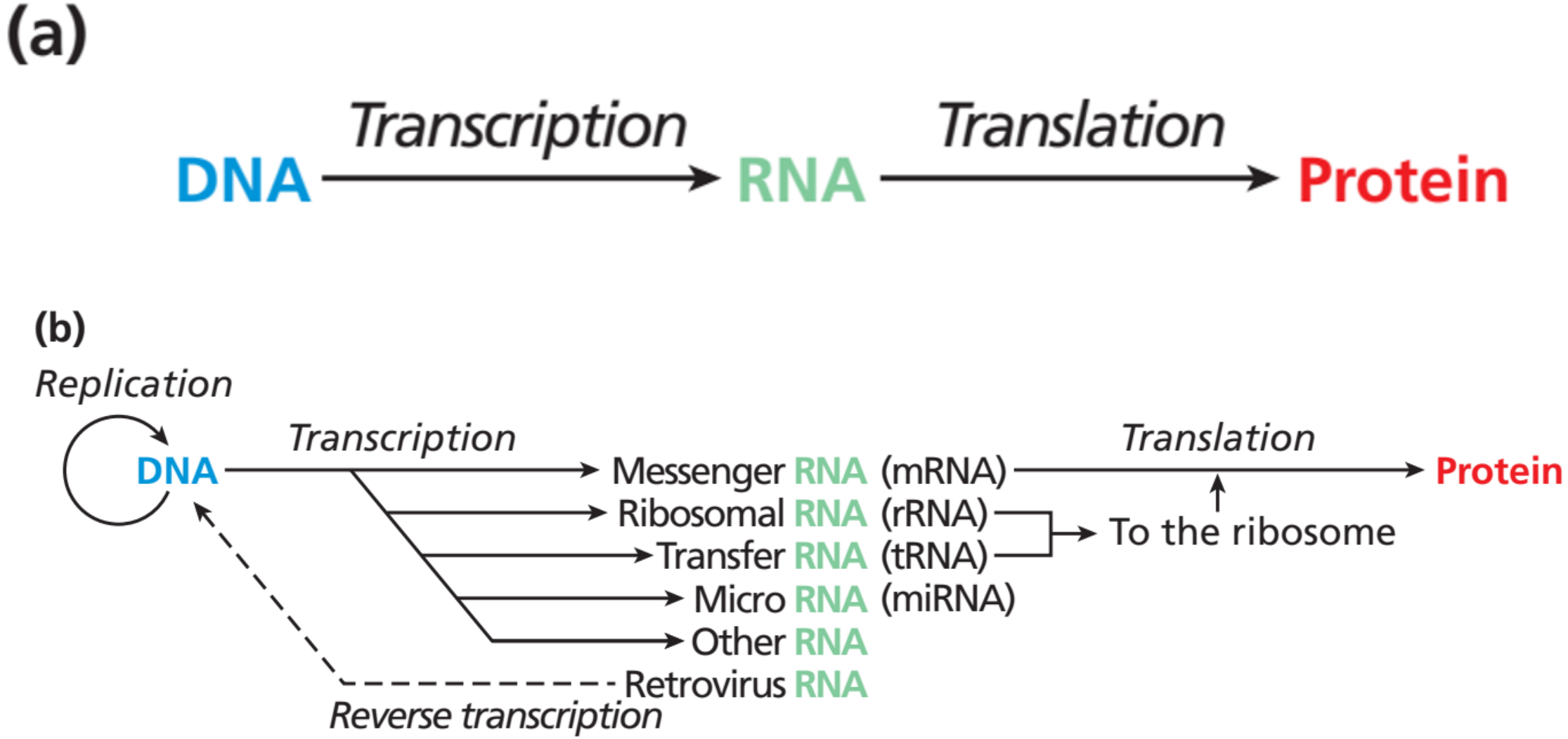
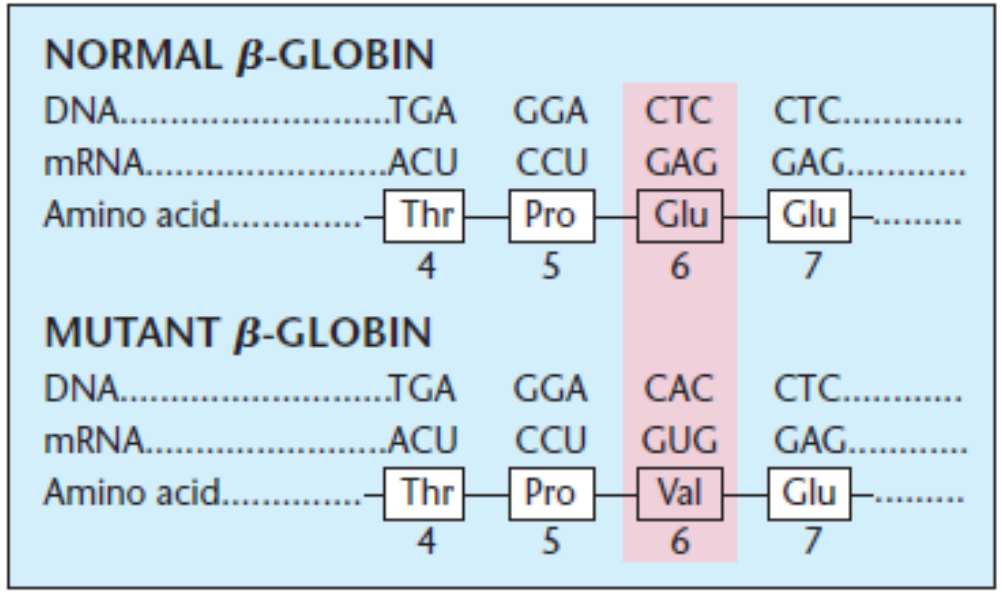


Image credit: Genetic Analysis an Integrated approach Sanders and Bowman

Proteins perform cellular functions and are coded for by DNA

- Example: Hemoglobin
  - Made of alpha and beta globin
  - Carries oxygen from lungs to tissues
- In people that have **sickle cell disease**, a single nucleotide change in beta globin gene alters the amino acid sequence of hemoglobin
- This causes hemoglobin molecules to polymerize which results in fragile sickle shaped red blood cells
- These cells easily break (anemia) and can get stuck in capillaries, causing pain and damage to body tissues.



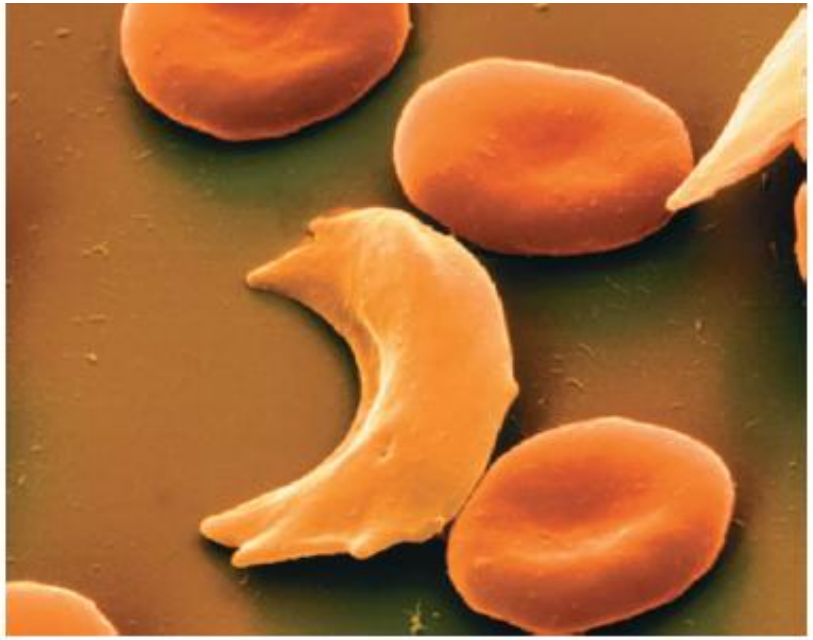


Image credit: Concepts of Genetics, Klug et al

Differences in DNA can be assayed in the lab

- **Gel electrophoresis** is a fundamental technique used in genetics research whereby DNA fragments of different sizes can be differentiated based on their migration pattern through an agarose gel
- This technique can also be applied to proteins
- Larger molecules migrate more slowly than smaller ones

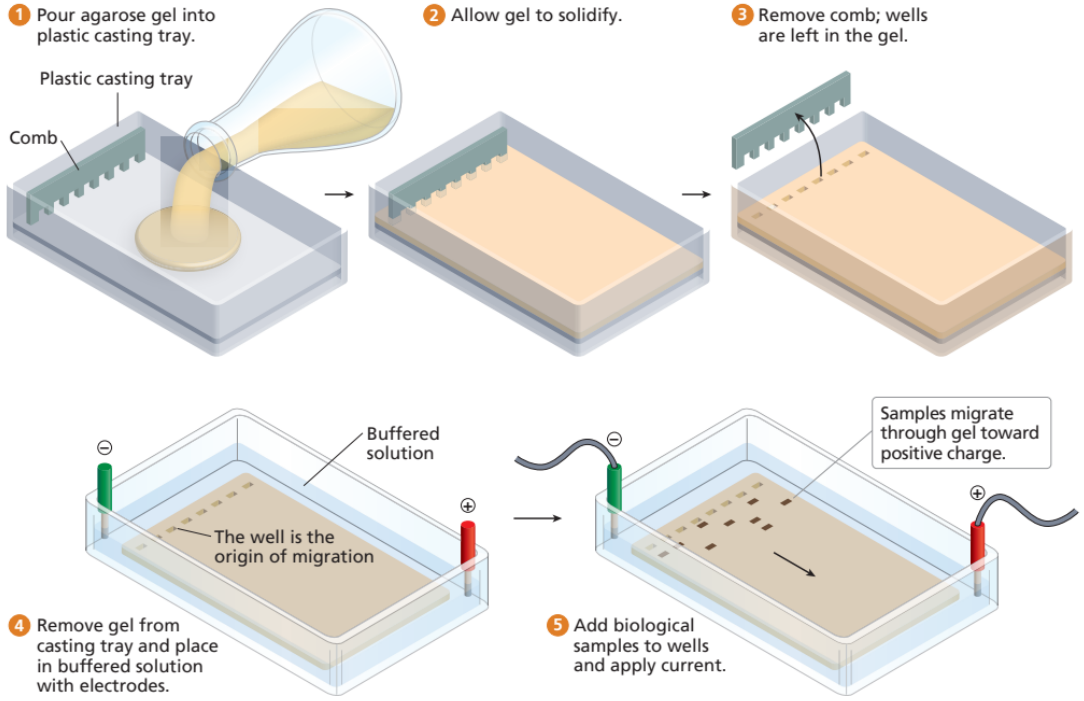


Figure 1.12 Gel electrophoresis, an essential laboratory technique in biological science research.

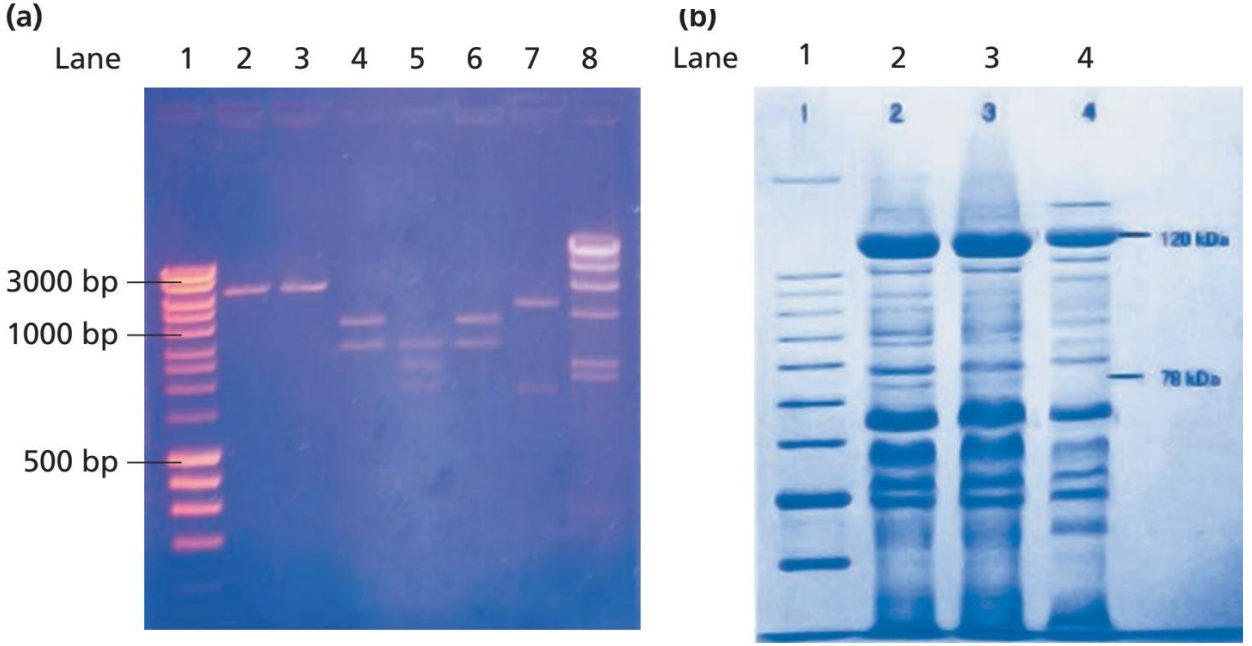
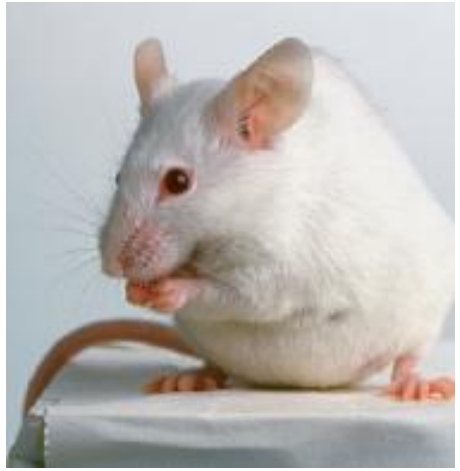
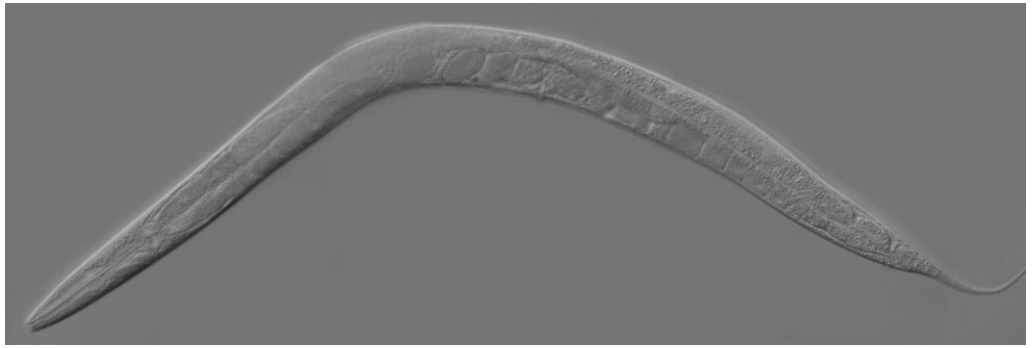


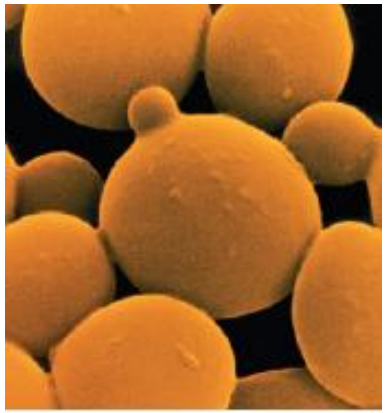
Image credit: Genetic Analysis an Integrated approach Sanders and Bowman

Modern genetic research makes use of full genomes and model organisms

- All life shares a common ancestor (LUCA = Last Universal Common Ancestor)
- The universality of the central dogma and the genetic code evidence this
- Because all life shares a common ancestor, learning about a gene in one organism is usually transferable to humans
- The most commonly used genetic model organisms are bacteria, yeasts, fruit flies, mice, and nematodes.
- Used in research because they have fast generation times and are easy to genetically manipulate in the lab.
- Each of these organisms was sequenced alongside the human genome during the Human Genome Project







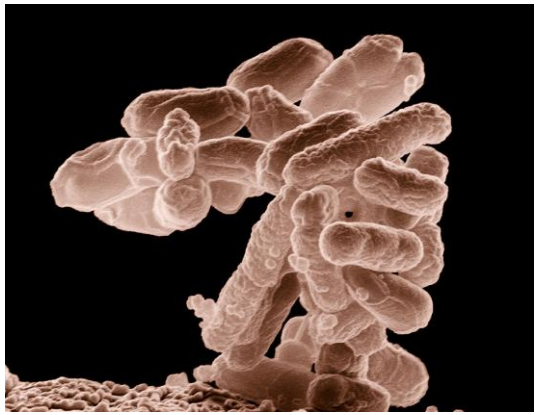
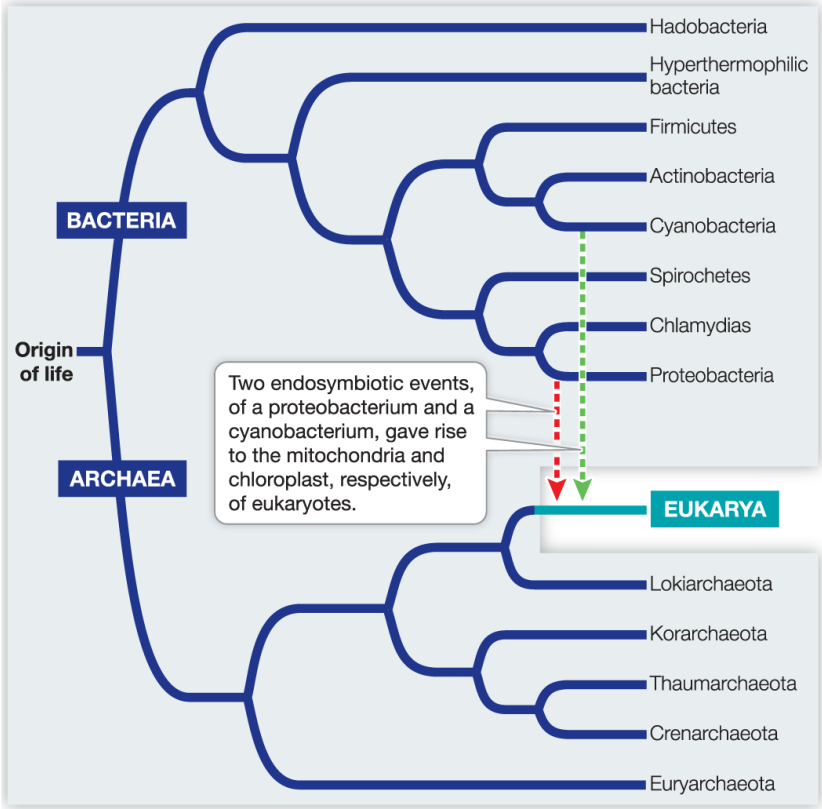


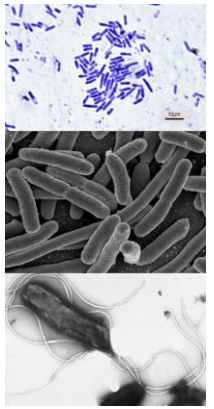
Image credit: Wikipedia

Evidence for LUCA and the three domain model

- Evidence for all life having a universal common ancestor includes that all living organisms:
  - 1. Are composed of a common set of chemical parts (DNA, RNA, amino acids) and structures (membrane bound cells)
  - 2. Contain genetic information that uses a nearly universal genetic code to specify how proteins are assembled
  - 3. Extract energy from their environment
  - 4. Replicate their genetic information in the same manner
  - 5. Share structural similarities among a fundamental set of genes
  - 6. Evolve through gradual changes in their genetic information
- How can we construct the tree of life?
  - DNA sequences diverge over time, such that organisms that are more closely related share more similar sequences
  - **Carl Woese** and colleges examined rDNA genes, common to all forms of life, and based on similarity devised the three domain model of life on Earth



Bacteria



Eukaryotes

Archaeans

Woese

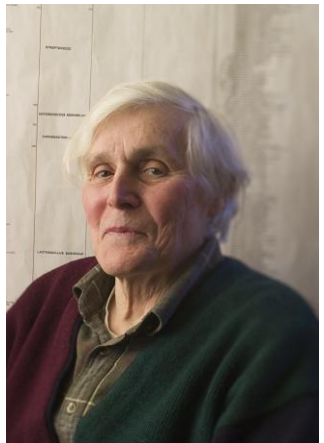


Image credit: Principles of Life Hillis et al. , Wikipedia