Bioinformatics

Announcements

- Homework 8 has been released and will be due **Wed 8/9 11:59pm**
  - There are **two** components --> surveys and written response
  - The surveys are NOT eligible for any extensions
  - The written response is eligible for extensions as usual

- All students who receive full credit on this homework are eligible to receive **1 additional extra credit point** if at least 80% of the course gets full credit on this homework (submits all surveys and completes the written response)

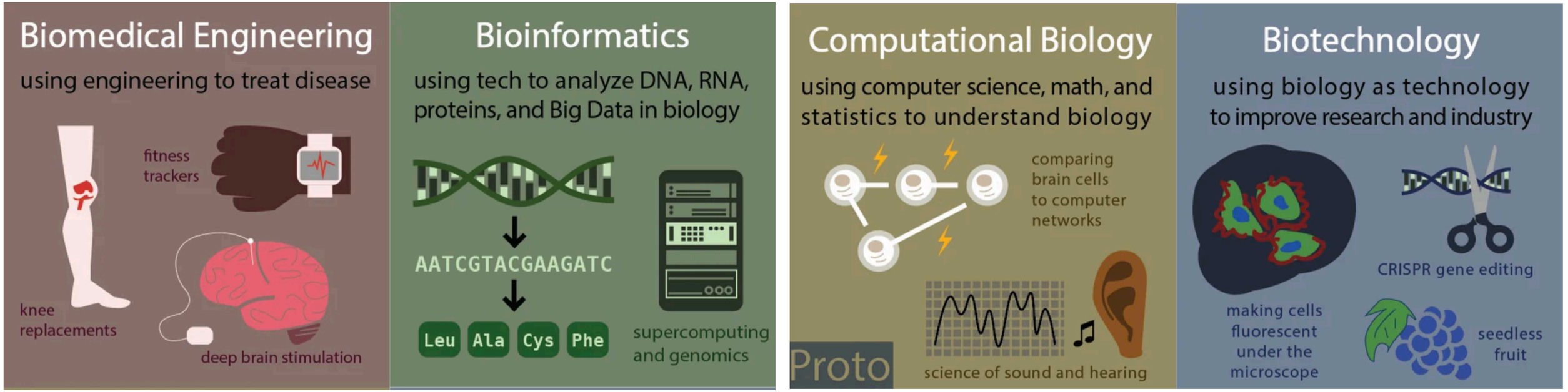
- Exam alterations form priority deadline was yesterday
  - If you need an exam alteration please request ASAP

- HW Recovery 1-4 has been processed
  - No HW Recovery for HW 7 & 8

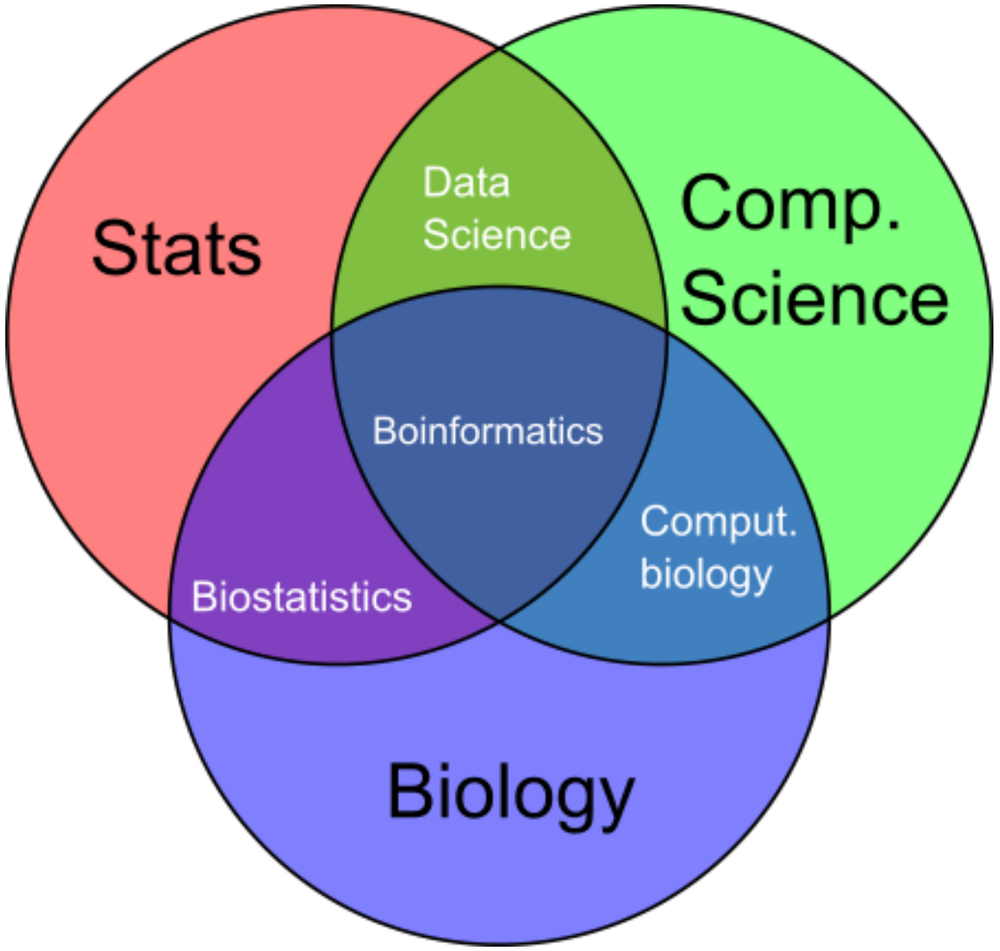
- Lab 13 is optional

- Topical Review Sessions today

Biomedical Engineering vs. Bioinformatics vs. Computational Biology vs. Biotechnology



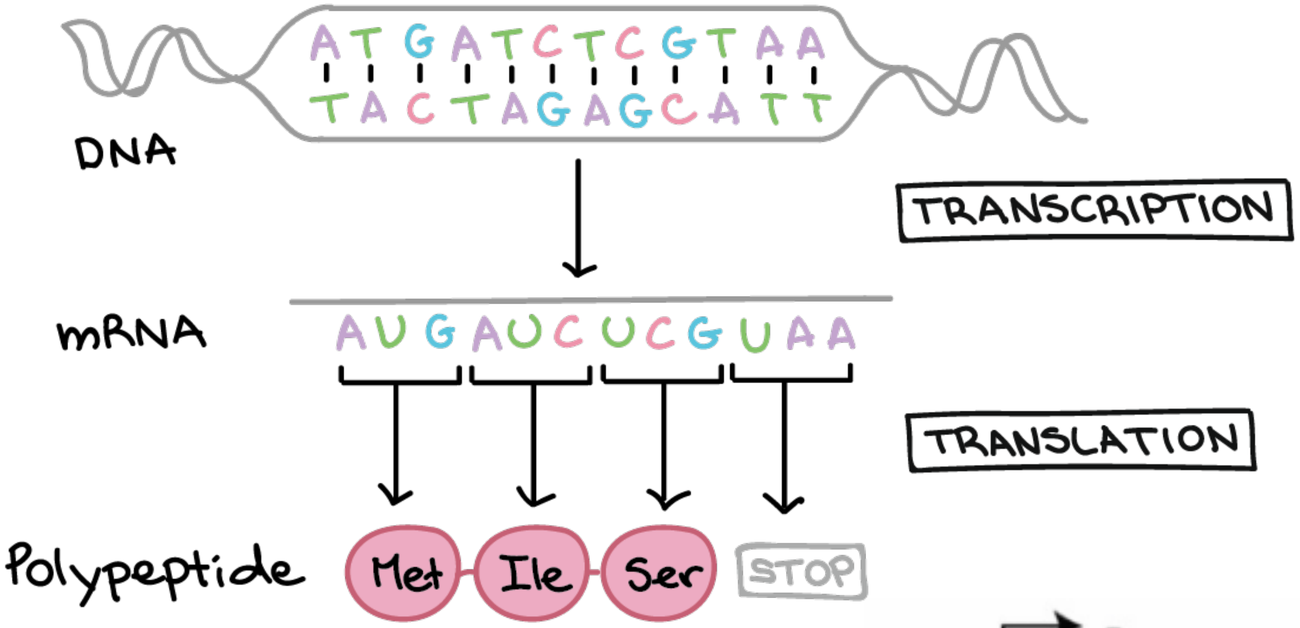
Focus for Today: Bioinformatics

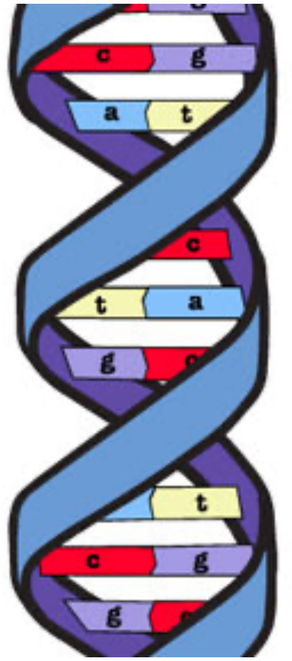


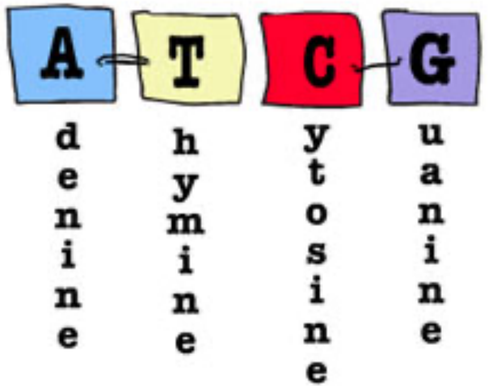
Fields in Bioinformatics

- ***Translational Bioinformatics***– Development of techniques for transforming voluminous biomedical (especially genomic) data to support proactive, predictive, preventive, and participatory health
- ***Clinical Research Informatics***– Development of approaches for enabling the discovery, management, and evaluation of new health knowledge
- ***Clinical Informatics***– Development and application of techniques to improve health care delivery services; clinical informatics is a subspecialty of the American Board of Medical Specialties
- ***Consumer Health Informatics***– Development of information structures and approaches for supporting patient-centric health care needs
- ***Public Health Informatics***– Development of methodologies for supporting public health needs, including surveillance, prevention, preparedness, and health promotion

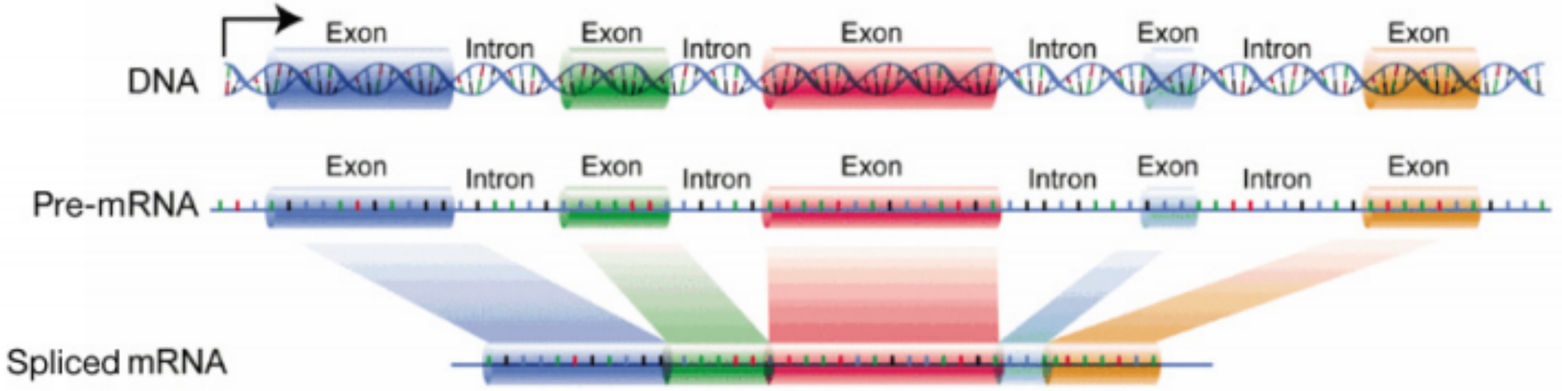
Central Dogma of Biology







REGENERATION Center of Thailand



Genome

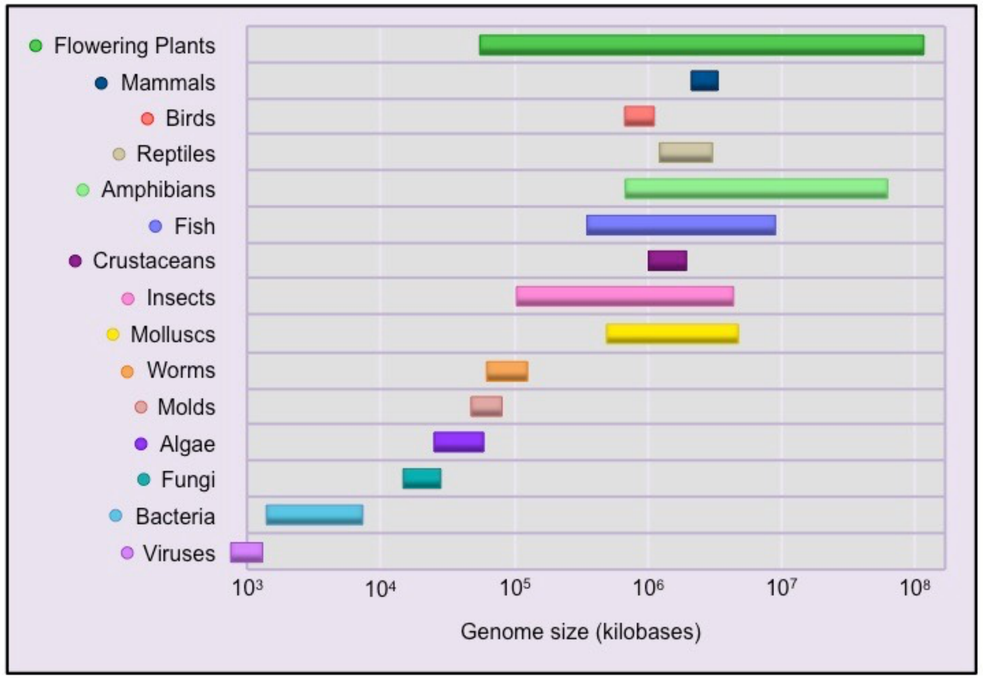
- **DNA:** string of complex molecules called nucleotides. It contains the genetic information and acts as a set of instructions for how to build and maintain you
- **Genome:** complete set of DNA
- **Gene:** DNA is organized into little chunks of information that each carry a specific set of instructions for how to make a certain aspect of you

Genome

- The complexity of an organism increases from the lower single-celled organisms to higher multicellular organisms

- Would an onion or human have a larger genome size?
  - C-Value Paradox: genome size fails to correlate well with apparent complexity
  - Onion: 16 billion bases, Human: 3.2 billion bases

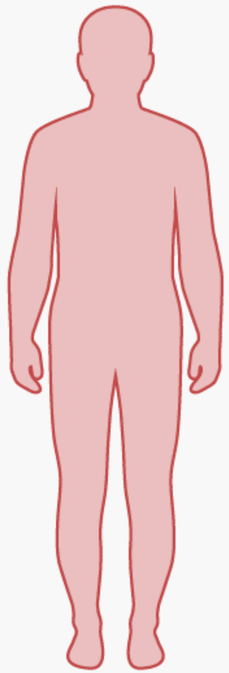
- Size of the genome varies across different groups of organisms



Fun Fact!

The genetic similarity between a **human** and a **mouse** is:

85%



Source: National Human Genome Research Institute

BUSINESS INSIDER

Human Genome Project

- An international scientific research project with the goal of determining the base pairs that make up human DNA
- Launched in October 1990 and completed in April 2003
- Tells us a lot about our genes and how they are organized!

Bioinformatics: Genomic Analysis

How does bioinformatics allow us to understand the similarity in genes?

Algorithms will scan past both ends of the matching sequence

Mouse

. . . A T G C G T A G C C A T A T C C G A A T C G A . . .

Similarities in sequences: Analyze those genes and see how they translate into similar traits

Differences in sequences: Analyze those genes and see how they translate into different traits

Human

. . . A T G C G T A G C C A T A T C C G A A C T T T . . .

Bioinformatics: Genomic Analysis

Cinderella

. . . A T G C G T A G C C A C A T C C G A A T C G A . . .

Is this base difference C/T
significant for disease?

Belle

. . . A T G C G T A G C C A T A T C C G A A T C G A . . .

Conduct a Study

Is this base difference significant for disease?

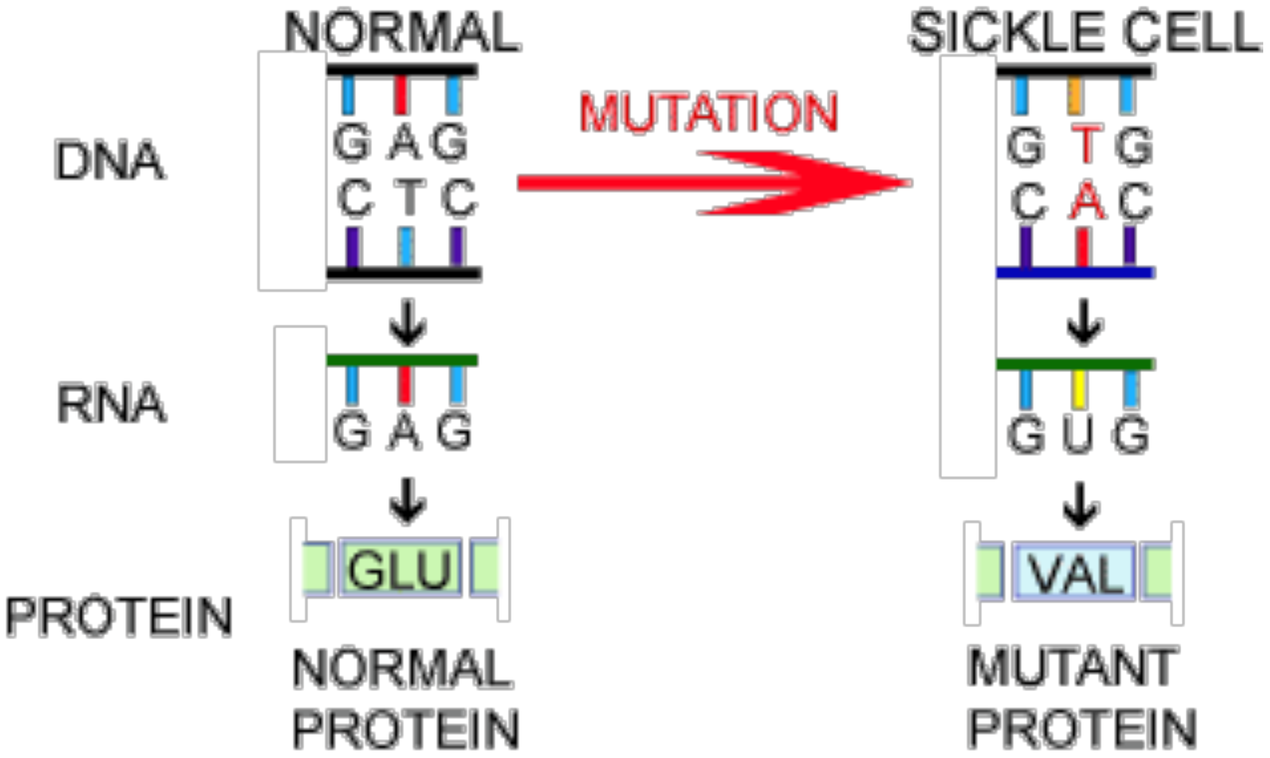
Group A: 100 Healthy Subjects

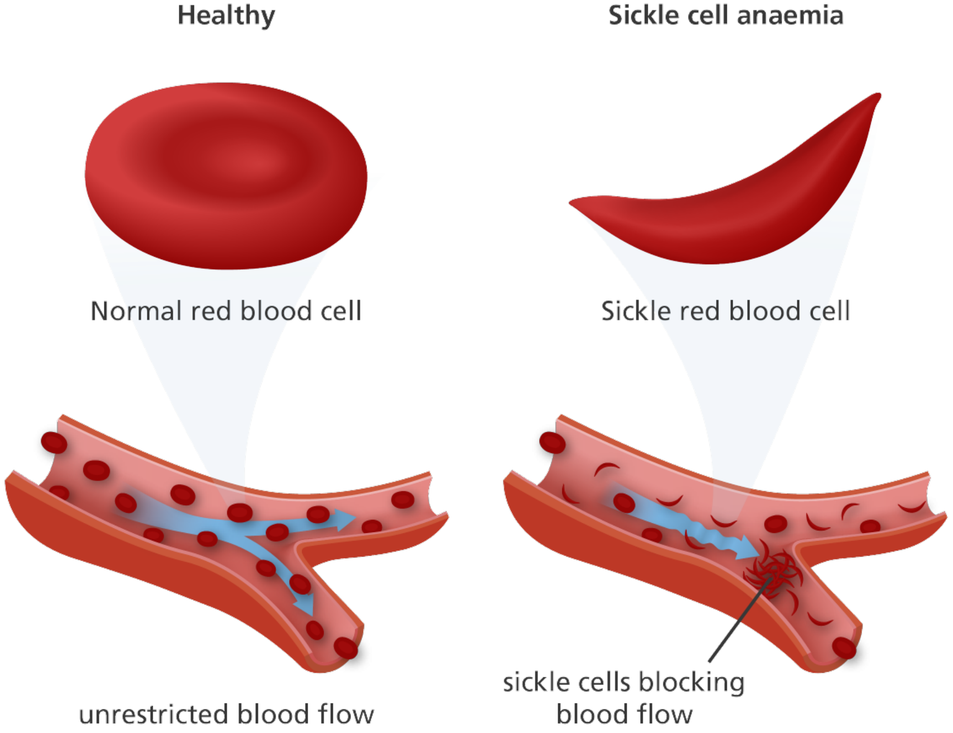
Group B: 100 Diabetic Subjects

Hypothetical Results: **4/100** of group A have a T and **98/100** of group B have T

Base Substitution Sickle Cell Disease

- Sickle cell disease is an inherited disease in which red blood cells contort into a sickle shape and die early, leaving a shortage of healthy red blood cells
- Discovered through genomic analysis, the genetic basis of sickle cell disease is an **A–to–T transversion** in the sixth codon of the HBB gene



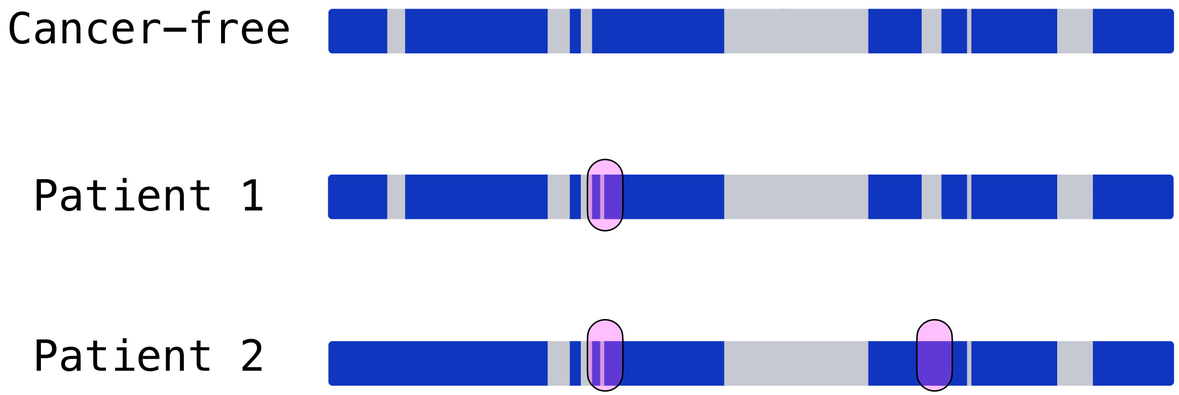


Applications in Neuroscience

- Stroke is a leading cause of death in the US and 87% of strokes are ischemic strokes which cause a lot of irreversible damage
- Ischemic stroke: blood supply to part of the brain is interrupted/reduced
- Arctic ground squirrels: their brain is incredibly resilient!
- **Provides us clues for stroke treatment**

Genomic Analysis for Cancer Treatment and Diagnosis

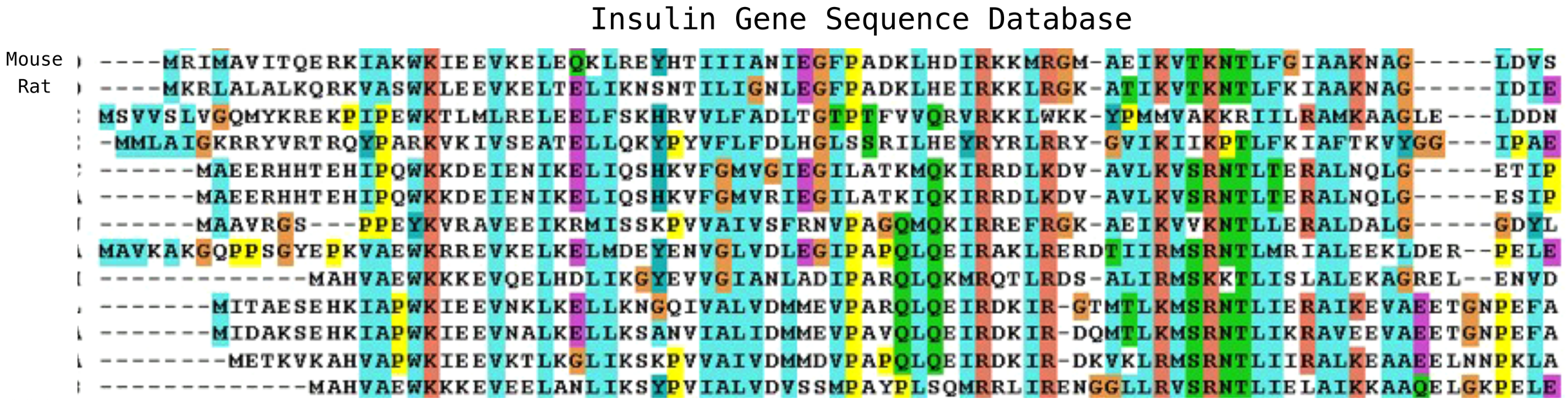
- Clinician’s can order genome sequencing of their patients
- The patient’s cancer cells are compared with the normal genome and genome of many other patients with cancer
  - Pinpoint mutations that are allowing the cancer cells to grow uncontrollably
  - Choose the best treatment



Sequence Alignment

- **Sequence alignment** is a way of arranging the DNA sequences to identify regions of similarity that may be a consequence of functional, structural, or evolutionary relationships between the sequences

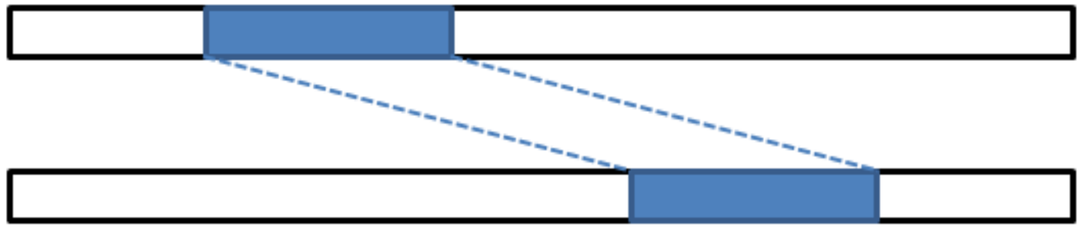
- Aligned sequences are typically represented as rows within a matrix
- Two alignment types are used: **global and local**



Global & Local Alignment

- The global approach compares one whole sequence with other entire sequences
- The output of a global alignment is a one-to-comparison of two sequences
  - Used when comparing two genes of similar function
- The local method uses a subset of a sequence and attempts to align it to subset of other sequences
- Local regions are aligned with the **highest level of similarity**
- Looking for conserved patterns in DNA

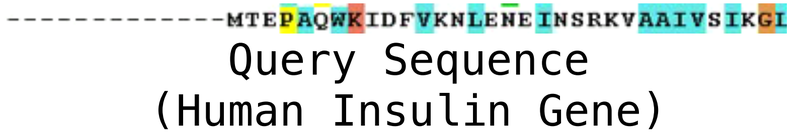
Global Alignment



Local Alignment

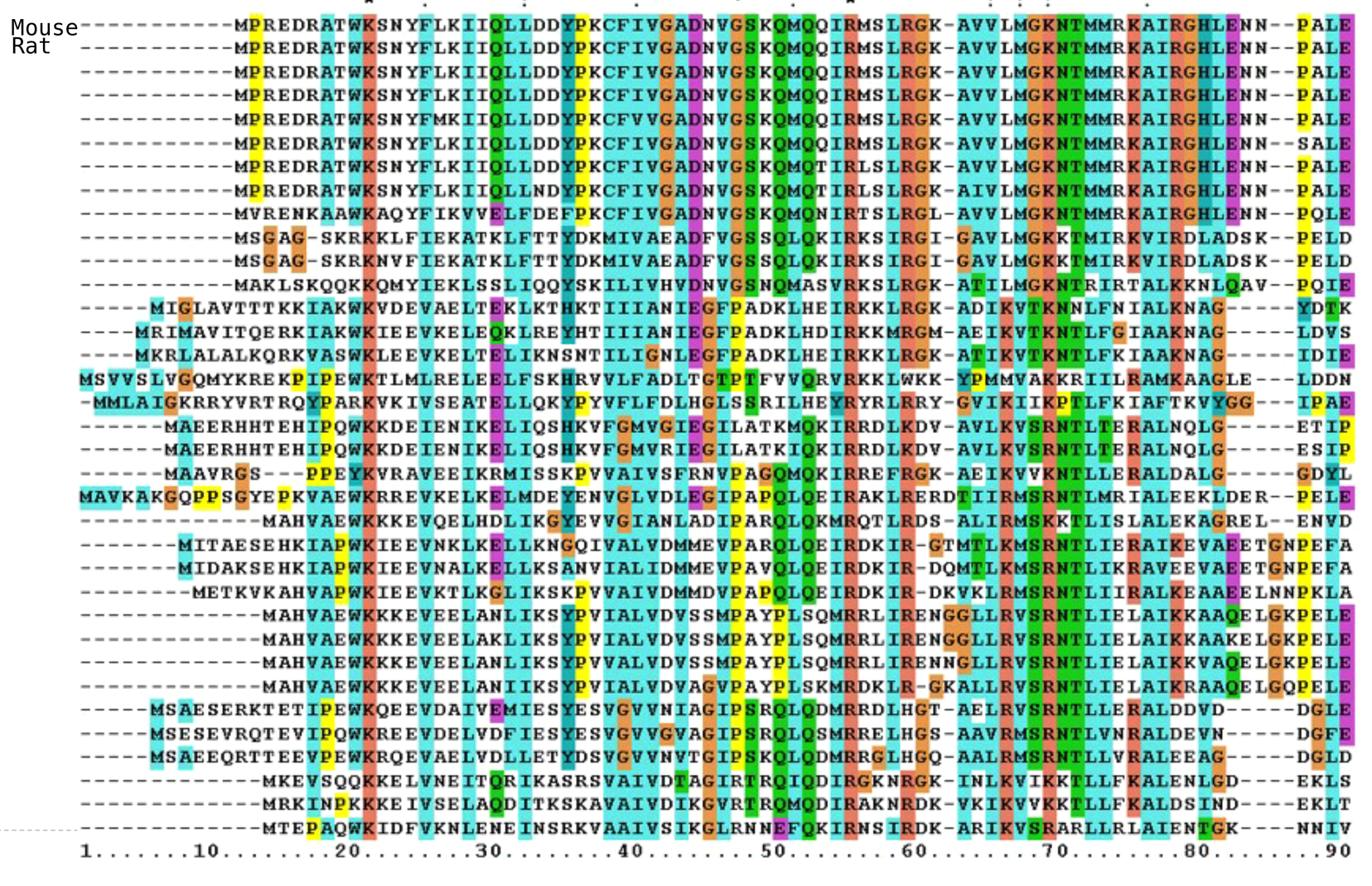
BLAST: Basic Local Alignment Search Tool

- Identifies similarities between sequences by comparing it with database of sequences



Query Sequence
(Human Insulin Gene)

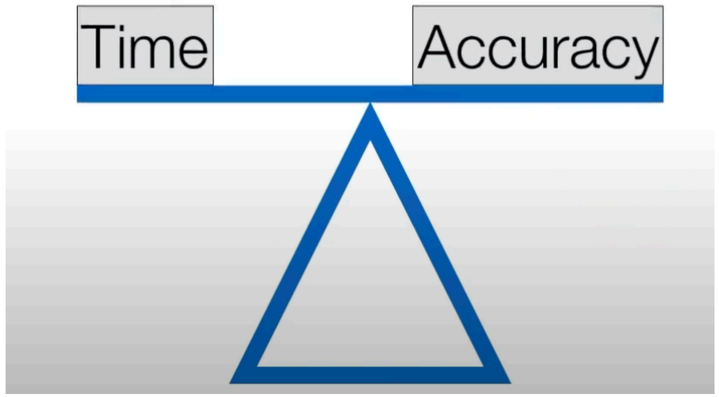
Insulin Gene Sequence Database

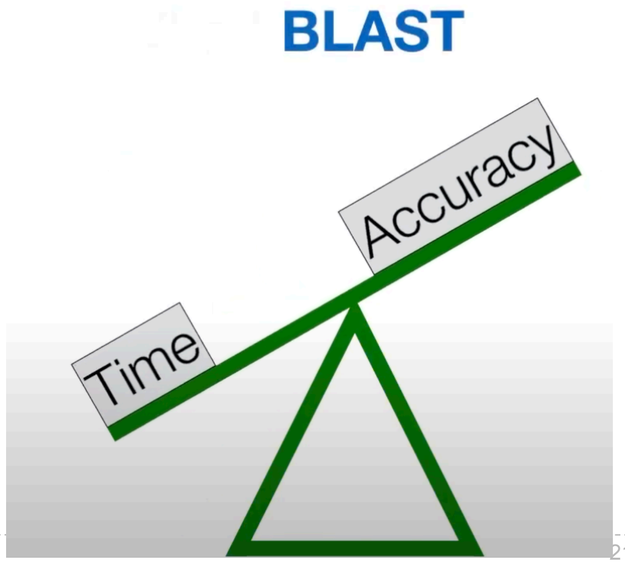


Break

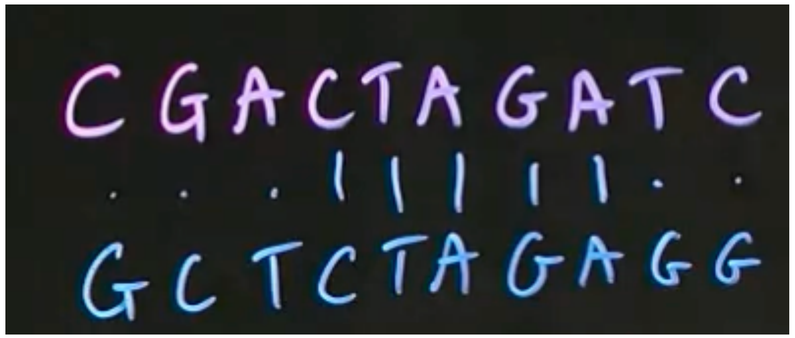
BLAST Algorithm

- BLAST uses a **seed and extend** algorithm
  - Scales with your query sequence and the size of the search database
  - https://www.youtube.com/watch?v=jzSIC2UzxZ4
- It is **heuristic,** based on trial and error and the process of elimination **NOT** precise mathematical formulations
  - BLAST does not look for exact matches because that would be computationally expensive
- Ctrl-F as a Tool for Scanning – is “BLAST” in “Composing Programs”
- BLAST – is something ~60-80% similar to “BLAST” in “Composing Programs”

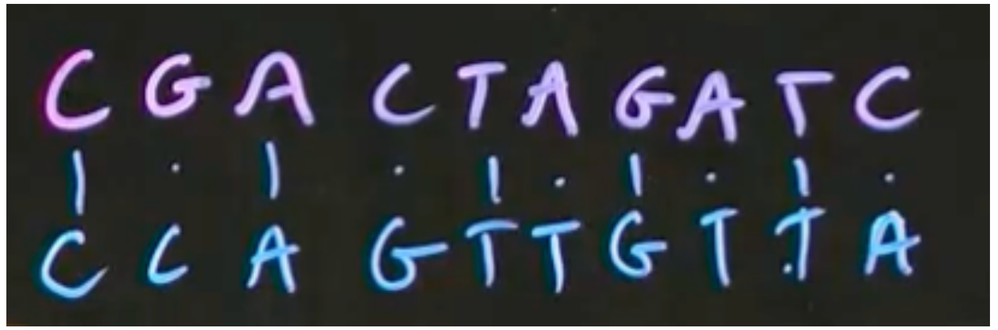




Glance of the BLAST Algorithm



Query Sequence



Target Sequence in the Database

Query Sequence

GACAGC

Database Sequence

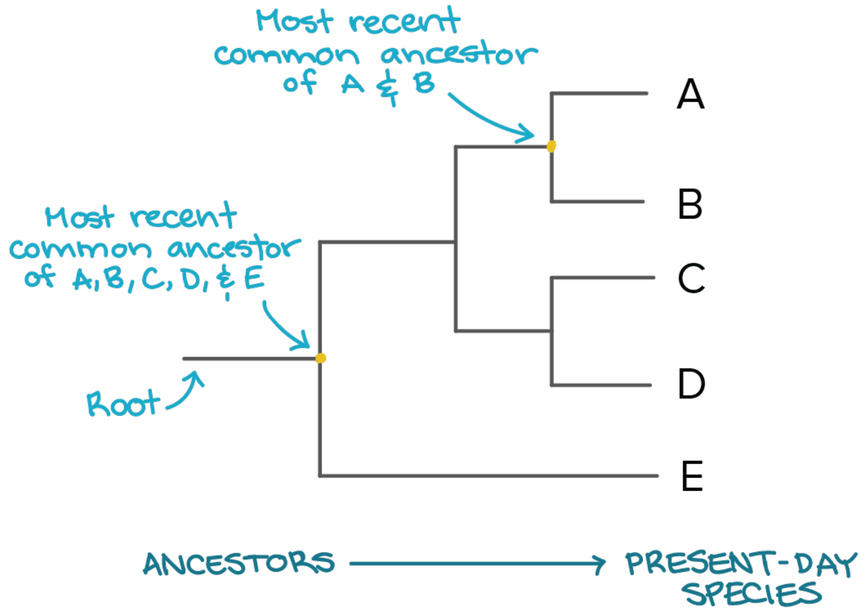
ACGGATTCCATAT

Scoring Scheme	
Match	1
Mismatch	-1
Gap Insertion	-1

		A	C	G	G	A	T	T	C	C	A	T	A	T
	0	0	0	0	0	0	0	0	0	0	0	0	0	0
G	0	0	0	1	1	0	0	0	0	0	0	0	0	0
A	0	1	0	0	0	2	1	0	0	0	1	0	1	0
C	0	0	2	1	0	1	1	0	1	1	0	0	0	0
A	0	1	1	1	0	1	0	0	0	0	2	1	1	0
G	0	0	0	2	2	1	0	0	0	0	1	1	0	0
C	0	0	1	1	1	1	0	0	1	1	0	0	0	0

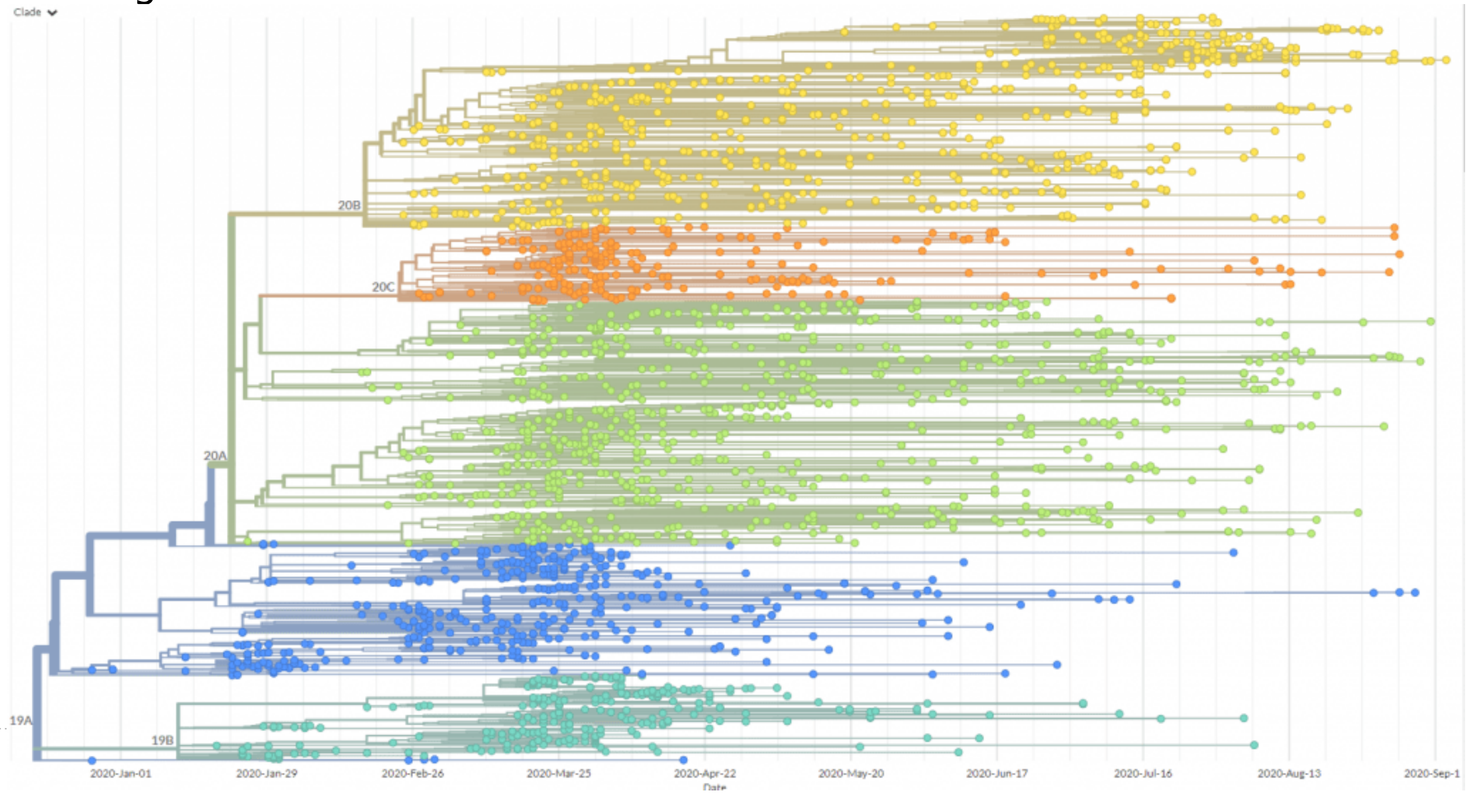
Understanding Evolution: Phylogeny

- How do we track the evolution of a virus? COVID-19 variants, for instance??
- Virus have a VERY HIGH rate of mutation
  - RNA viruses have high mutation rates—up to a **million times higher** than their hosts
- Through genomic analysis of virus samples, we can understand how the sequence of it changes over time
  - Phylogenetic trees allow us to visualize evolution



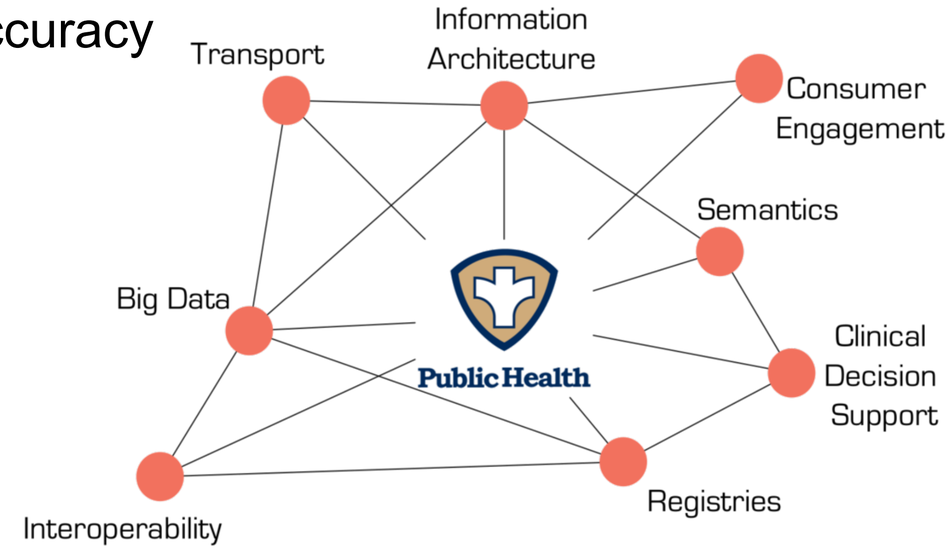
Phylogenetic Trees

- A branching diagram or tree showing the evolutionary relationship among various biological species
- Similarities and differences are based upon physical and genetic characteristics
- Two specifies are more related if they have a more recent common ancestor
- The root is the initial Wuhan SARS-CoV-2 genome



Public Health Informatics

- Capturing, managing and analyzing information to improve population-level health outcomes
- Transmit data to public health officials so they can better monitor and prevent disease
- Providers are already using AI algorithms to gain “unprecedented insights into diagnostics, care processes, treatment variability and patient outcomes”
  - 1 in 18 patients getting the wrong diagnosis in the ER department
  - According to the Society for the Improvement of Diagnosis in Medicine (SIDM) between 40,000 and 80,000 individuals die each year due to misdiagnoses
  - “Differential Diagnosis Tool” that had up to 96% diagnostic accuracy

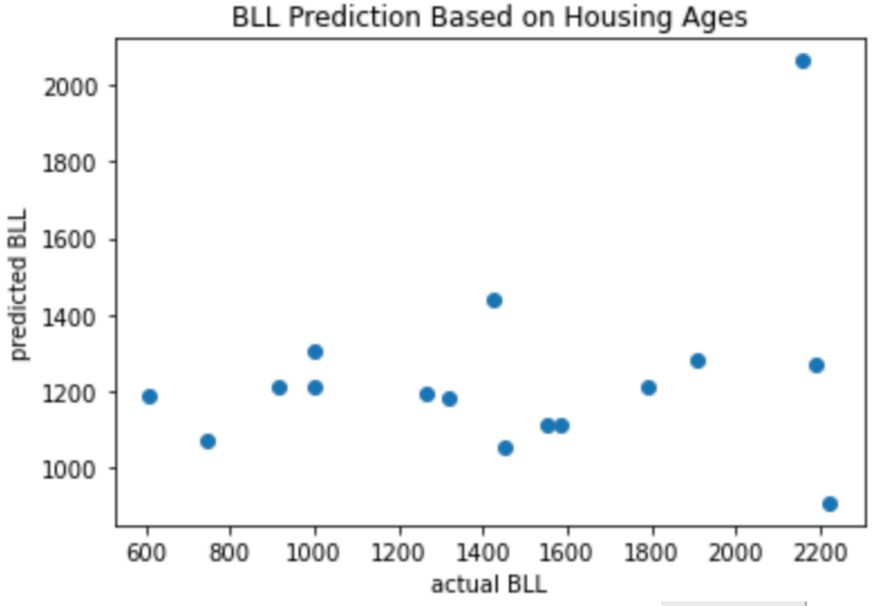


Lead Poisoning Research Project

- There is huge effort for prevention!
- Publicly available data on blood lead levels (BLL) from the Childhood Lead Poisoning Prevention Program (CLPPP)
- Why do some areas have more cases of lead pointing than others?
  - Geographic, demographic, and socioeconomic factors!
  - For instance, I hypothesized there is a positive correlation between the number of severe cases (BLL > 4.5µg/dL) and house age due to likely use of lead paints

Modeling & Testing Hypothesis

- Geographic, demographic, and socioeconomic factors of a zip code can serve as reasonable features for a multiple regression model to predict number of cases in the future



ZIP Code	Postal District Name	Number of BLLs > 4.5…	% of BLLs > 4.5 (0-6)	Total number of BLLs …
95821	Sacramento	118	13.00%	908
95608	Carmichael	56	9.24%	606
94538	Fremont	39	4.76%	819
94087	Sunnyvale	22	4.53%	486
95051	Santa Clara	30	4.26%	705
94109	San Francisco	12	3.82%	314
94536	Fremont	29	3.61%	804
95670	Rancho Cordova	20	3.53%	566
90037	Los Angeles	47	3.24%	1450

Conclusion

- Bioinformatics is a fast-growing area with lots of exciting opportunities!

- **BIO ENG 145** Introduction to Machine Learning for Computational Biology
  - Using machine learning methods for genome-scale experimental data

- **BIO ENG 134** Genetic Design Automation
  - Use of software (lots of OOP) to design and manage genetics experiments

- **BIO ENG C131** Introduction to Computational Molecular and Cell Biology
  - Bioinformatics and Computational biology, with an emphasis on alignment, phylogeny, and ontologies

- Data Science Discovery Program for exposure working on these projects