Bioinformatics

CS300

Chap 2

Computational Manipulation of DNA

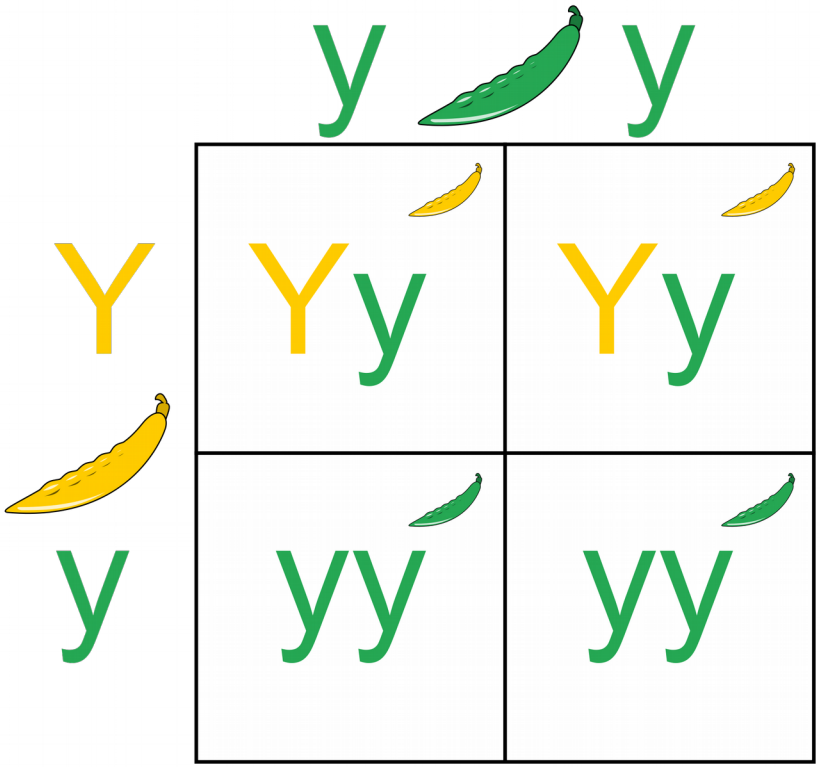
Fall 2017

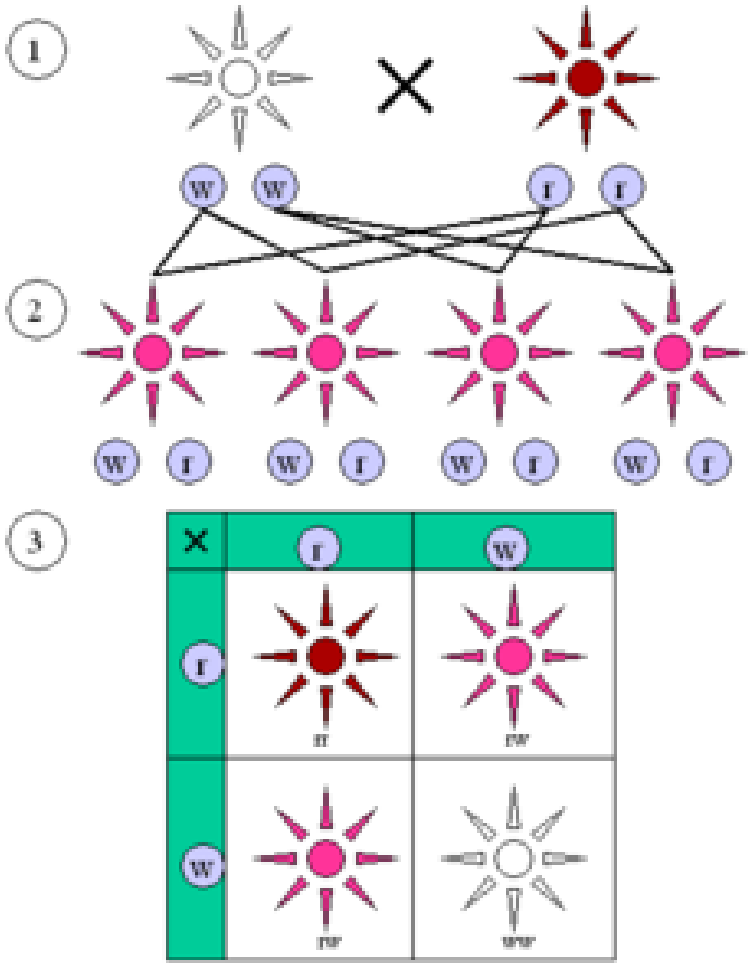
Oliver Bonham-Carter

Consider this...

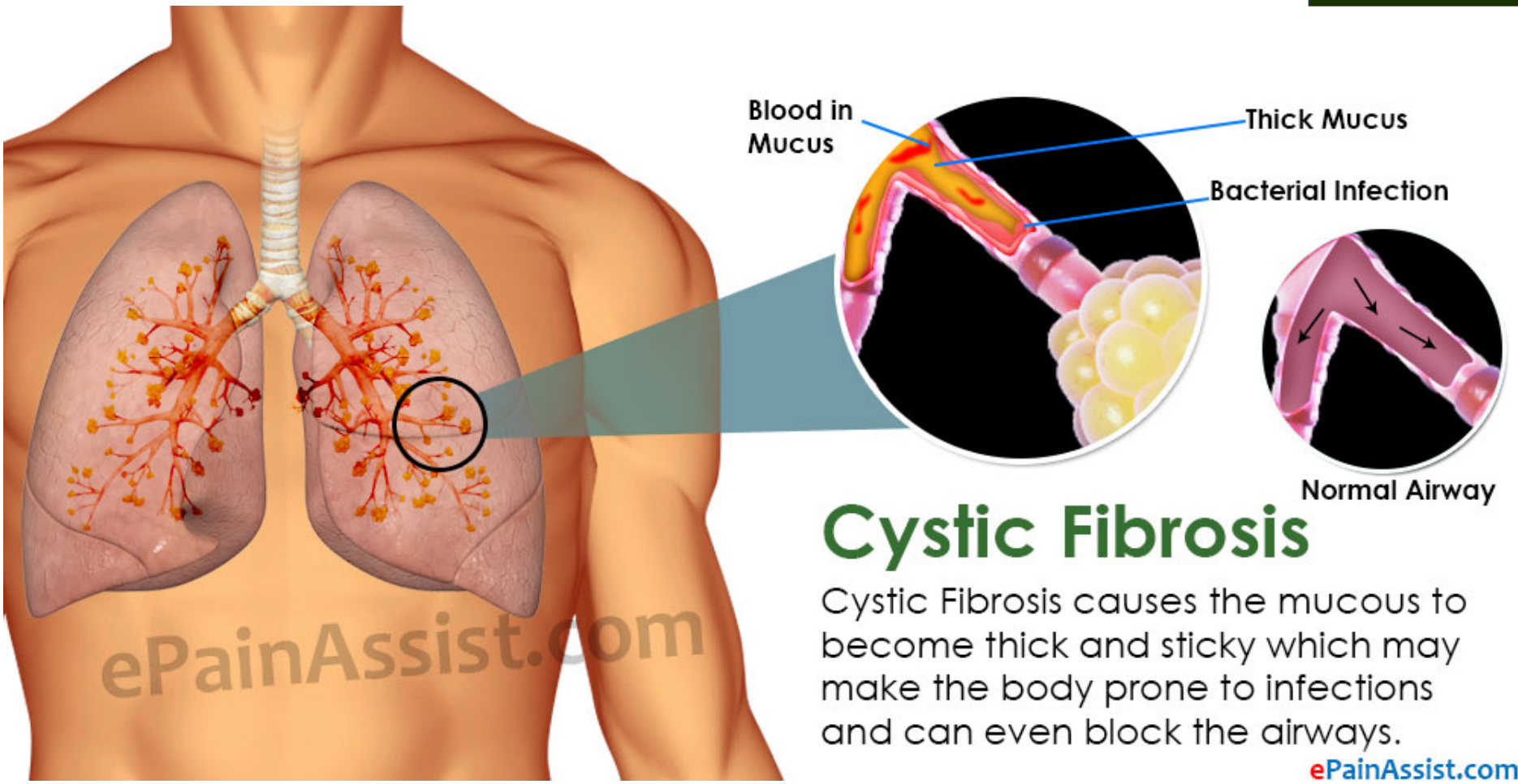
- What is the difference between a gene and an allele?
- Answer in the context of cystic fibrosis and the *CFTR* gene

  Hint: *Think Mendelian Genetics*





Cystic Fibrosis



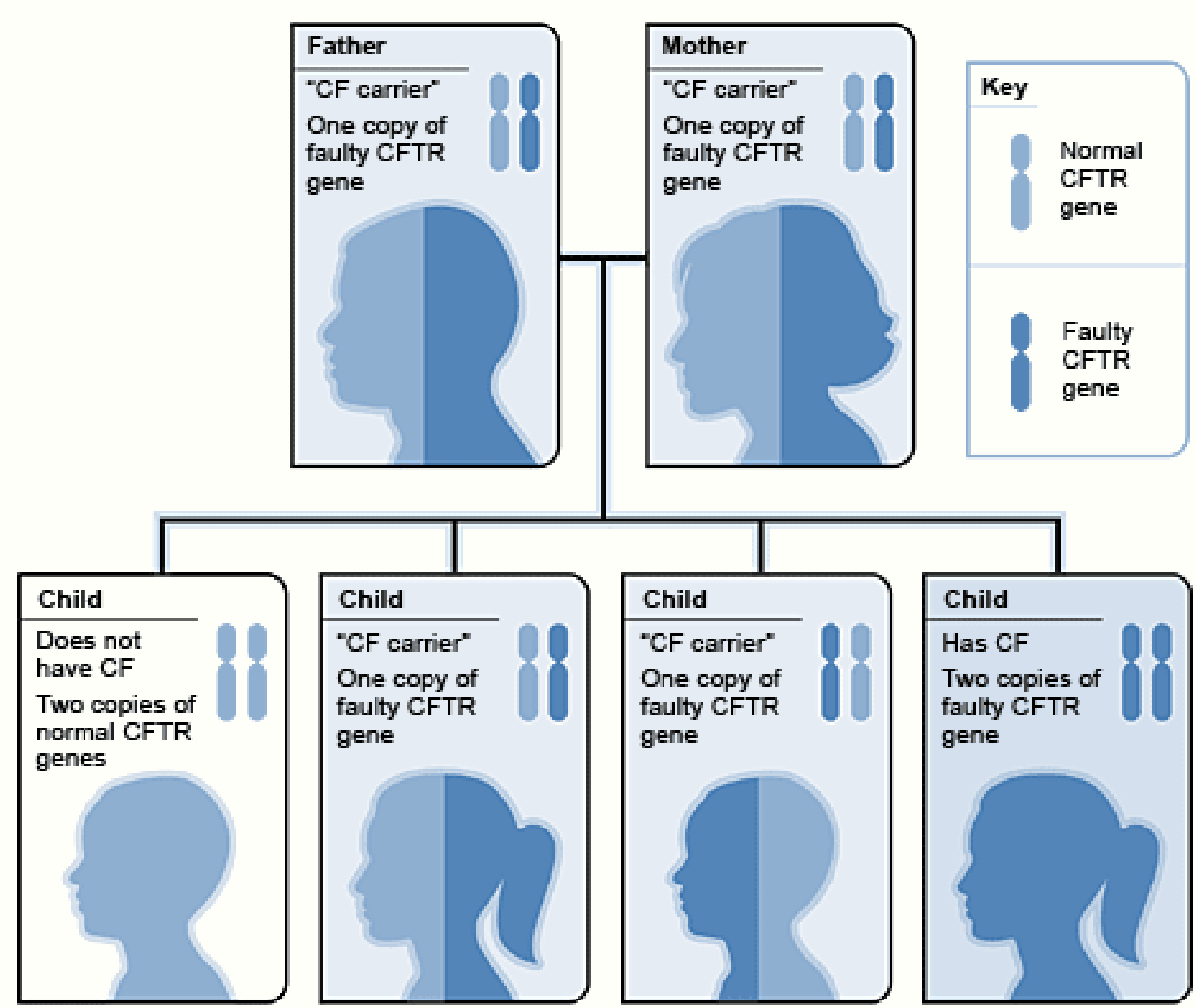
- Inherited medical condition of the secretory glands (producers of mucous and sweat)

Cystic Fibrosis

- Clubbed fingers: occurs in heart and lung diseases that reduce the amount of oxygen in the blood

Cystic Fibrosis

- Autosomal recessive type condition: one faulty gene is inherited from both parents (together) in order for the offspring to get this condition
- Mendelian Genetic
- Impossible to know that someone is sure to get a condition.

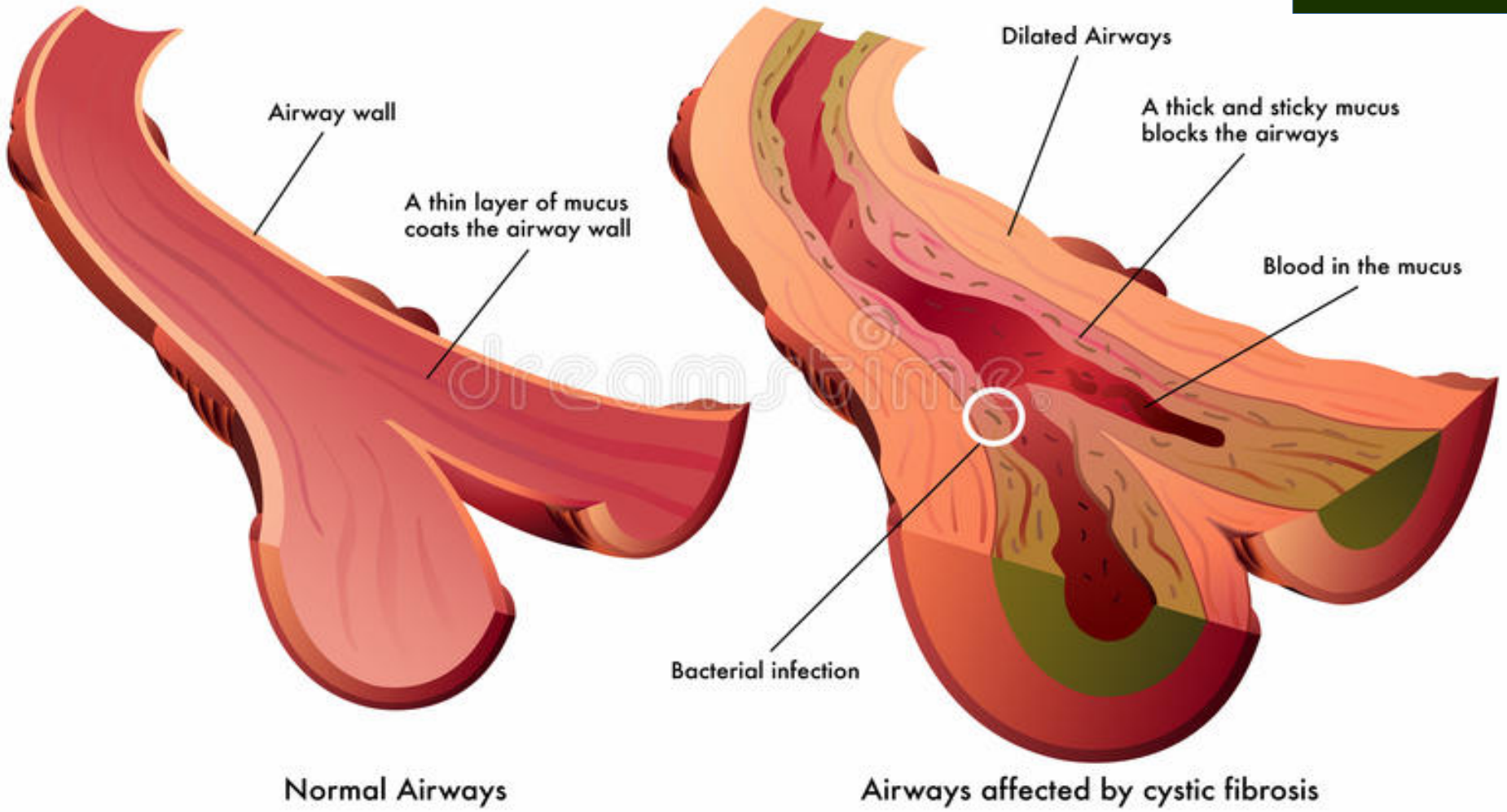


The Cystic Fibrosis Gene

- Cystic Fibrosis Transmembrane conductance: **CFTR**
- Gene product is a bad regulator which fails to move water after displacing chloride ions in epithelial (thin tissue) cells
- Water follows chloride ions by osmosis.

- **What if water regulation were not possible in the cells and organs?**

Cystic Fibrosis



- Restricted flow in airways from mucous build-ups.
- Suffocation

A Build-Up of Anything is Bad

- What if the the garbage collection crews in Paris went on strike (as they did in 2016)?

The Cystic Fibrosis Gene

- Cystic Fibrosis Transmembrane conductance: **CFTR**
- Gene product is a bad regulator which fails to move water after displacing chloride ions in epithelial (thin tissue) cells
- Water follows chloride ions by osmosis.
- https://www.youtube.com/watch?v=EuLVCYrurok

- **What if water regulation were not possible in the cells and organs?**

Three Bad Proteins From the Four

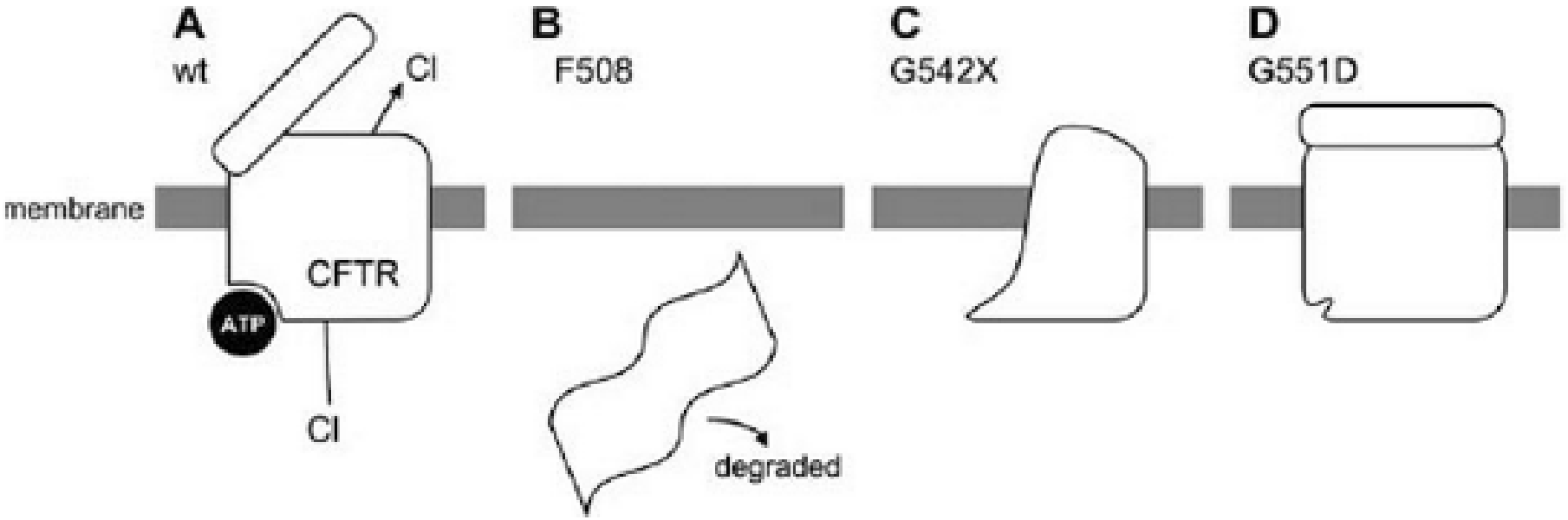
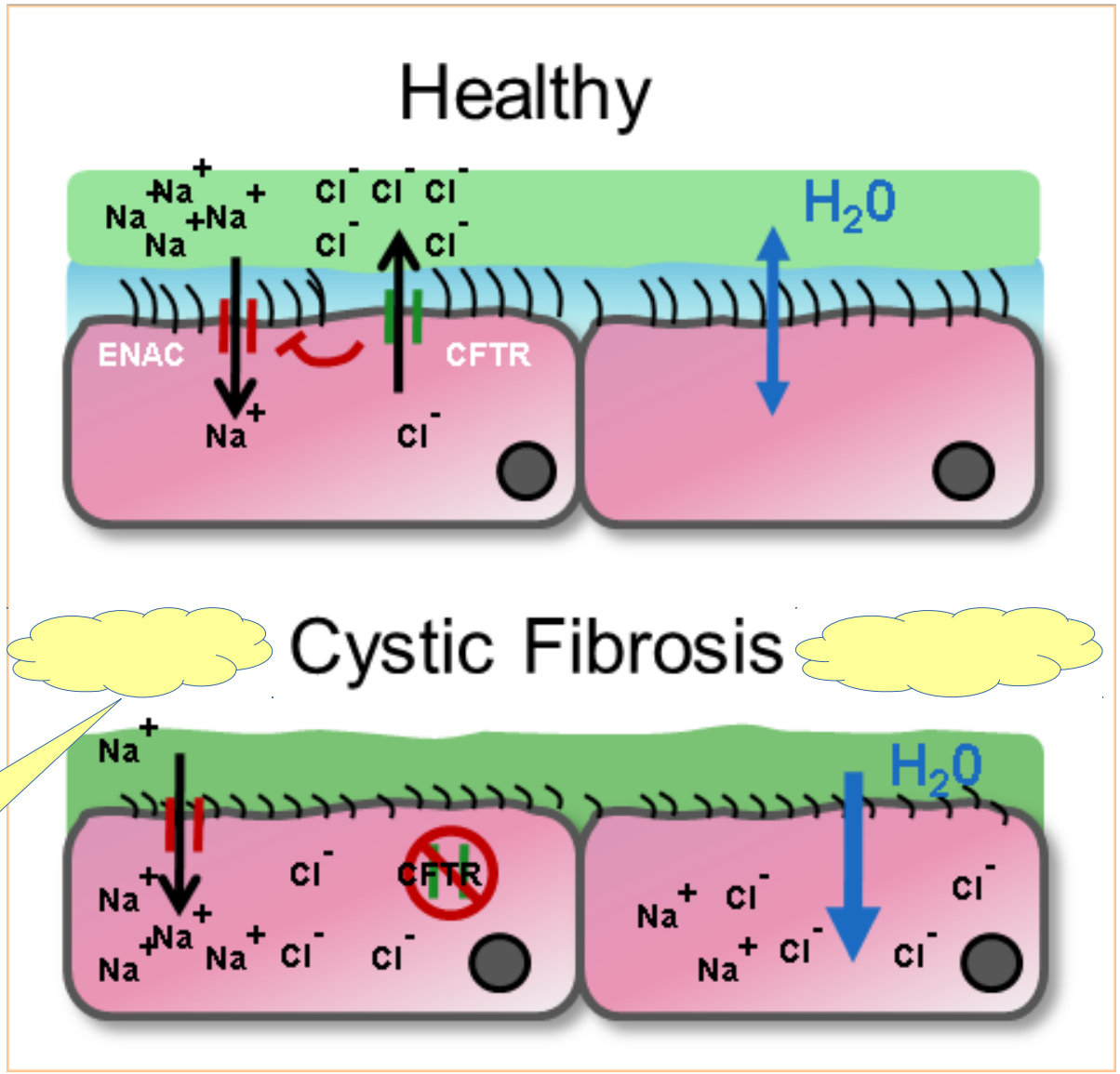


Figure 2.2 The wild-type allele (A) of the CFTR gene produces a chloride transport protein localized in the membrane; three different common CF alleles illustrated here result in variant proteins that are folded incorrectly (ΔF508; B), truncated (G542X; C), or unable to transport chloride (G551D; D).

The Cystic Fibrosis Gene

- Gene codes for four different proteins: only one working type to move chloride ions and enable water displacement.



Open Reading Frames: Explaining Disorders?

- Pam Can See The Man and Dog
- Frame shift by one letter!
- ~~P~~ amC anS eeT heM ana ndD ~~og~~
- Frame shift by two letters!
- ~~Pa~~ mCa nSe eTh eMa nan dDo ~~g~~
- Frame shift by three letters!
- ~~Pam~~ Can See The Man and Dog

Notice how the code changes depending on where you start reading?

Open Reading Frames

Note: RF means *reading frame, where you start reading the words.*

Original: **CAATGGCGAATCGACGTGTATAAA**

RF1 - 5’ - CAA TGG CGA ATC GAC GTG TAT AAA – 3’

RF2 - 5’ - C AAT GGC GAA TCG ACG TGT ATA AA – 3’

RF 3 - 5’ - CA **ATG** GCG AAT CGA CGT GTA **TAA** A – 3’

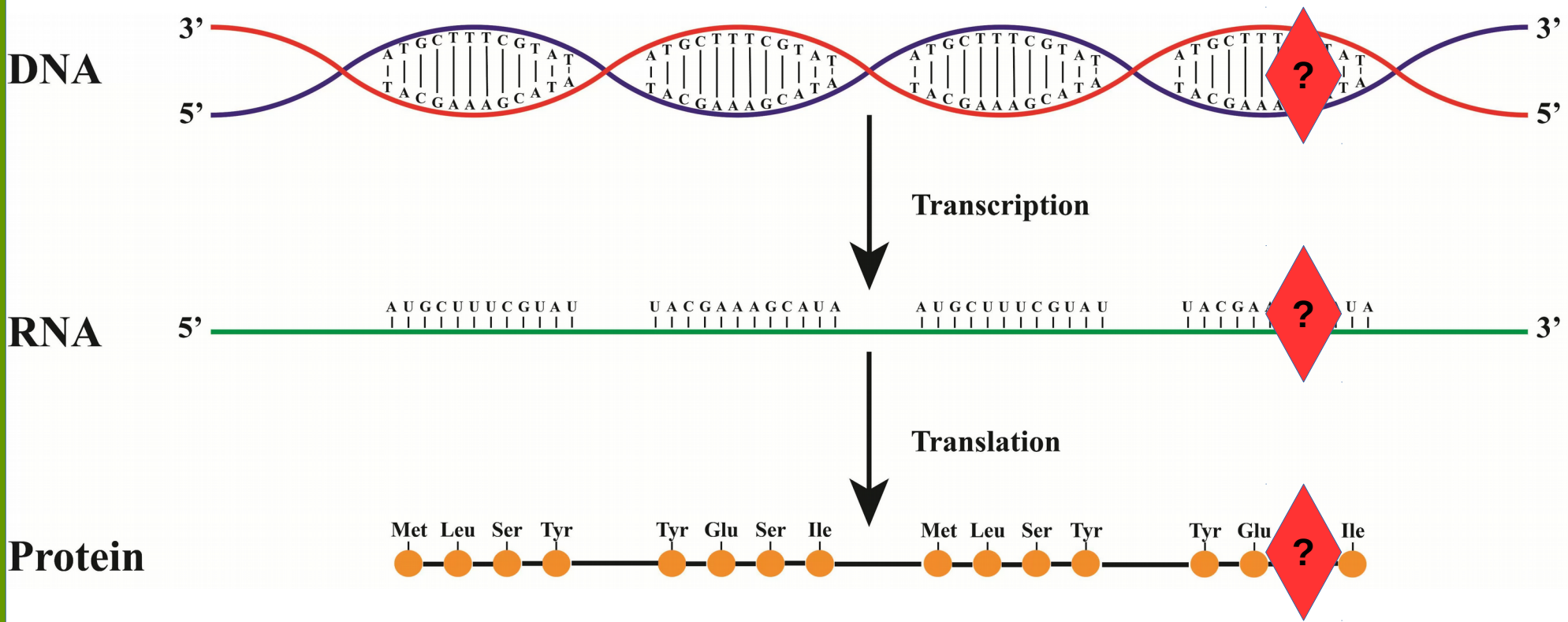
3’ - CAA TGG CGA ATC GAC GTG TAT AAA - 5’ – RF 4

3’ - C AAT GGC GAA TCG ACG TGT ATA AA - 5’ – RF 5

3’ - CA ATG GCG **AAT** CGA CGT **GTA** TAA A - 5’ – RF 6

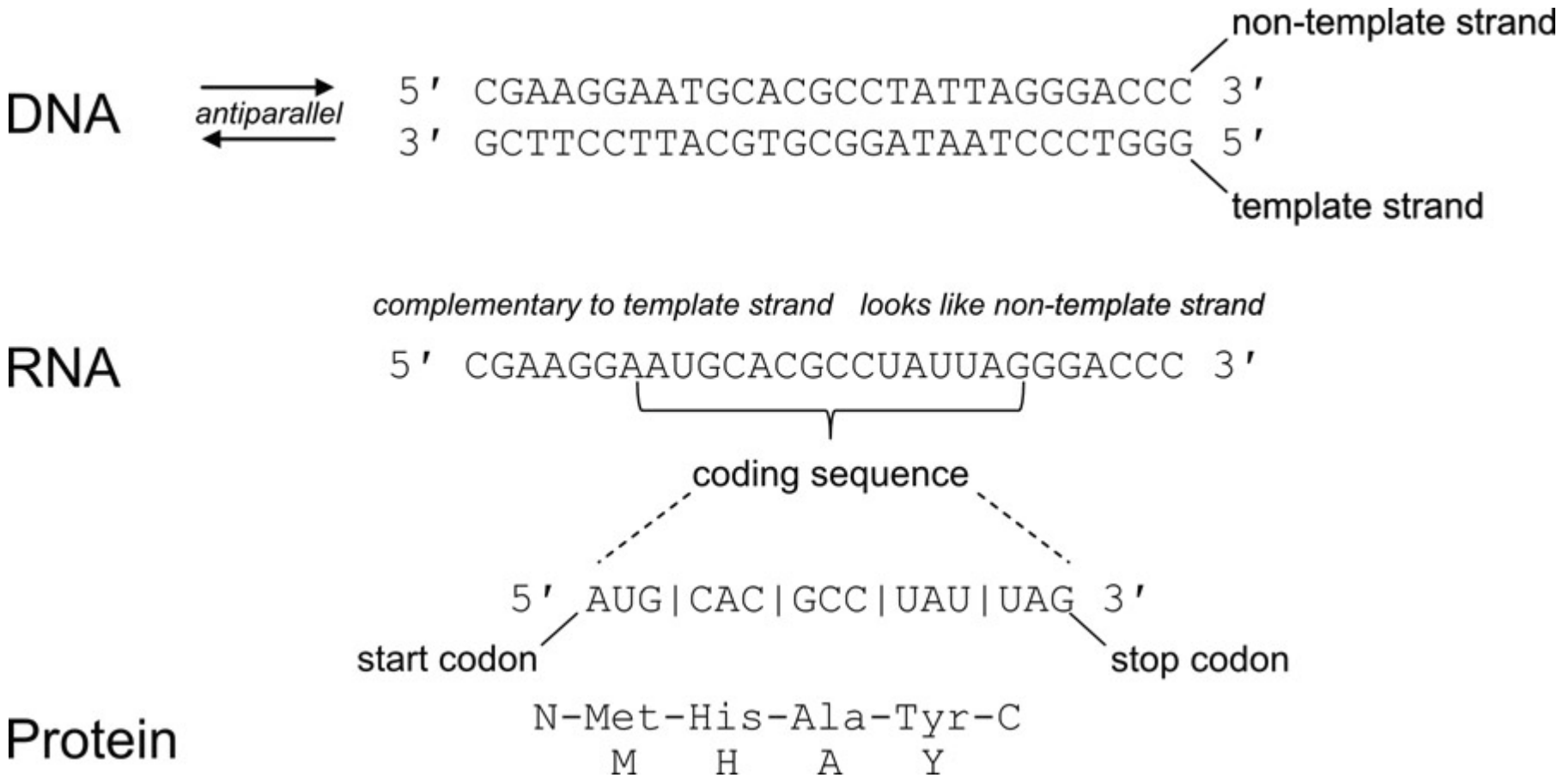
Sequence is Carrier?

- How do we determine if a sequence carries the CF allele?
- Get DNA sample
- Translate DNA to protein: Compare this seq to seq of a “working protein”
- Is difference found between both proteins?



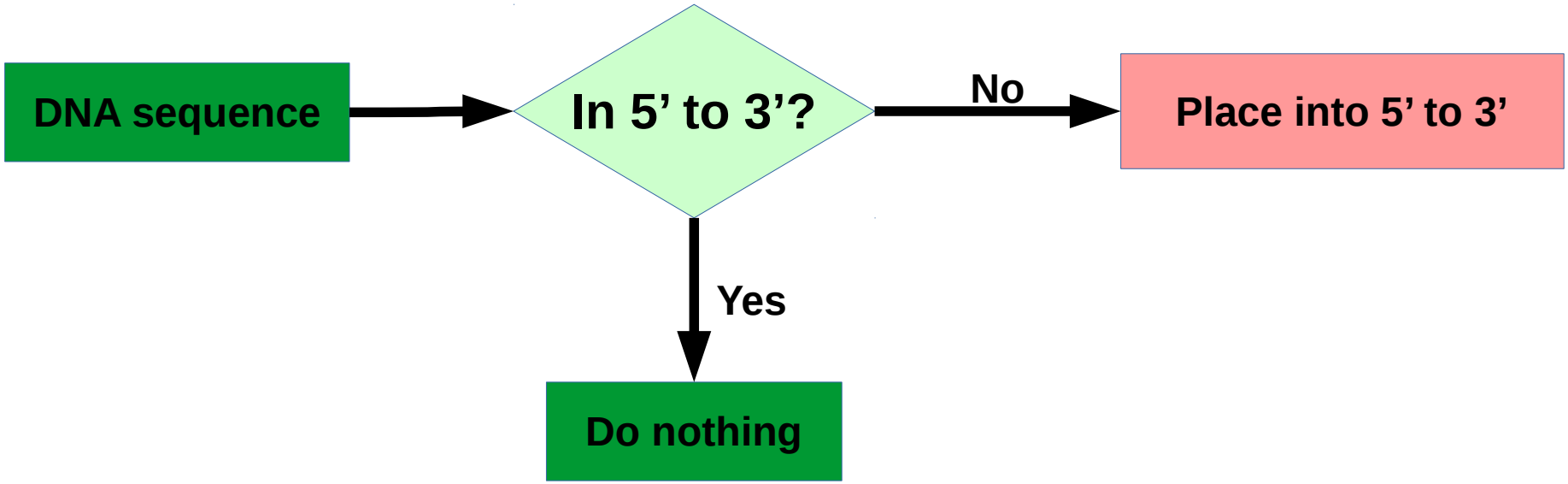
Analyze the Protein

- Translating DNA to find defects



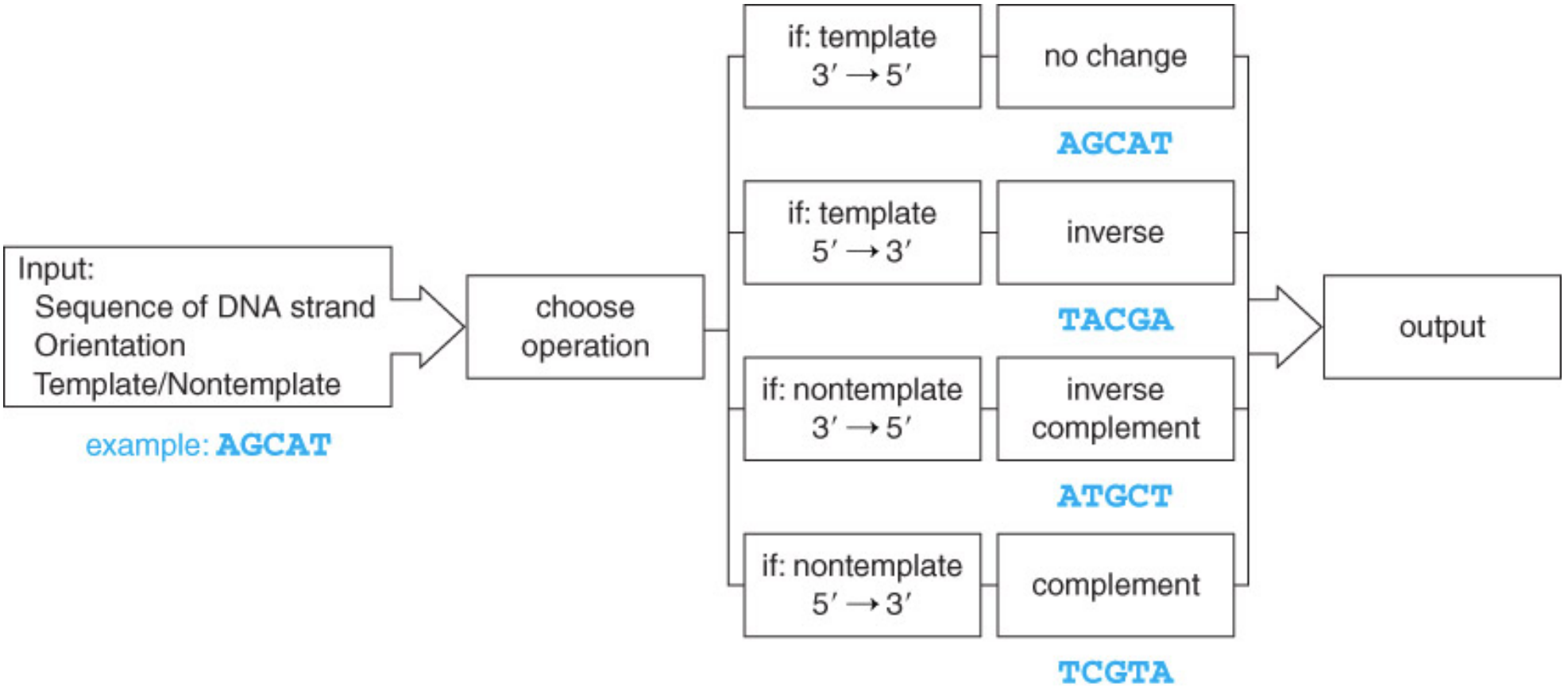
The Unnamed Sequence

- Unlabeled strands of DNA are assumed to be in the 5’ to 3’, (left to right) direction.
- A new sequence is given to us for analysis.
- What are the steps to place this sequence into a format for use with bioinformatics tools?



DNA Manipulation Algorithm

- A series of steps when handling DNA



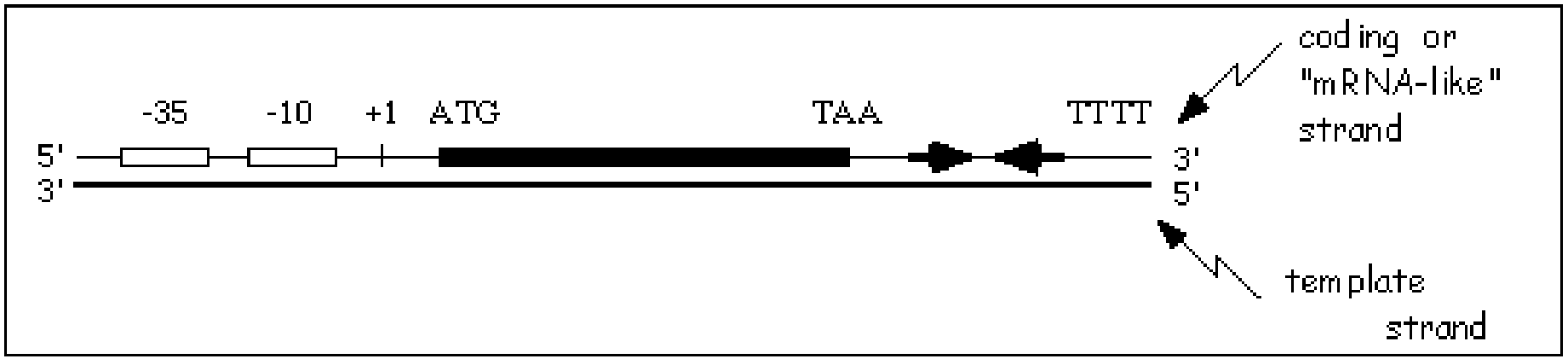
Output DNA in 3' to 5'

The Algorithm in Words

- Input a DNA sequence, including whether or it template or non-template strand and orientation
- Choose the appropriate operation:
  - If it is the template strand and oriented 3’ -> 5’, simply output the same sequence
  - If it is the template strand and oriented 5’ -> 3’, **inverse** the sequence (traverse the string from right to left and add each character to output string)
  - If it is the non-template strand and oriented 3’ -> 5’, generate the **inverse complement** sequence ((i.) traverse the string from right to left and (ii) for each character add the complement to the output string)
  - If it is the non-template strand and oriented 5’ -> 3’, generate the **complement** ((i.) traverse the string from left to right and (ii) for each character add the complement to the output string)
- Output the completed sequence, including 5’ and 3’ end labels

Template vs nonTemplate

- Input:
  - DNA sequence – AGCAT
  - Strand – template (used to make mRNA) or non-template (the compliment of this strand that looks like mRNA)
  - Orientation – 3’ -> 5’ or 5’ -> 3’
- Output:
  - Template strand in 3’ -> 5’ orientation ready for transcription



Codon Table to Translate the Protein Product

- DNA triplets read in groups of three called codons and represent an amino acid

Standard genetic code

1st base	2nd base								3rd base
	T		C		A		G		
T	TTT	(Phe/F) Phenylalanine	TCT	(Ser/S) Serine	TAT	(Tyr/Y) Tyrosine	TGT	(Cys/C) Cysteine	T
	TTC		TCC		TAC		TGC		C
	TTA	(Leu/L) Leucine	TCA		TAA[B]	Stop (*Ochre*)	TGA[B]	Stop (*Opal*)	A
	TTG		TCG		TAG[B]	Stop (*Amber*)	TGG	(Trp/W) Tryptophan	G
C	CTT		CCT	(Pro/P) Proline	CAT	(His/H) Histidine	CGT	(Arg/R) Arginine	T
	CTC		CCC		CAC		CGC		C
	CTA		CCA		CAA	(Gln/Q) Glutamine	CGA		A
	CTG		CCG		CAG		CGG		G
A	ATT	(Ile/I) Isoleucine	ACT	(Thr/T) Threonine	AAT	(Asn/N) Asparagine	AGT	(Ser/S) Serine	T
	ATC		ACC		AAC		AGC		C
	ATA		ACA		AAA	(Lys/K) Lysine	AGA	(Arg/R) Arginine	A
	ATG[A]	(Met/M) Methionine	ACG		AAG		AGG		G
G	GTT	(Val/V) Valine	GCT	(Ala/A) Alanine	GAT	(Asp/D) Aspartic acid	GGT	(Gly/G) Glycine	T
	GTC		GCC		GAC		GGC		C
	GTA		GCA		GAA	(Glu/E) Glutamic acid	GGA		A
	GTG		GCG		GAG		GGG		G

Python Programming

ALLEGHENY COLLEGE

- Biopython
- Translation functions
  - DNA → RNA
  - RNA → DNA
  - RNA → Protein
- Gives a protein sequence to compare to the wild type protein sequence

Follow along in class and save your notes in a text file!!

python