

Bioinformatics

CS300

Crash course:

Mutations

Fall 2019

Oliver BONHAM-CARTER



What is Mutation?

- A natural process that changes the DNA sequence
- A common process
 - during replication of the human genome a “typo” occurs every 100,000 or so nucleotides
 - that’s about 120,000 typos each time one of our cells divides
 - most are repaired





What is Mutation?

- Most mutations are neutral – no consequence
- Some mutations are beneficial – provides advantage in particular environment
- Some mutations are harmful





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COLLEGE

Chocolate Chip Cookies

Ingredients

2 $\frac{1}{4}$ cups all purpose flour
1 teaspoon baking soda
1 teaspoon salt
1 cup (2 sticks) butter, softened
 $\frac{3}{4}$ cup granulated sugar
 $\frac{3}{4}$ cup packed brown sugar
1 teaspoon vanilla extract
2 large eggs
2 cups chocolate chips

PREHEAT over to 375°F

COMBINE flour, baking soda, and salt in a small bowl. Beat butter, sugars, and vanilla extract in a larger mixer bowl until creamy. Add eggs, one at a time, beating well after each addition. Gradually beat in flower mixture. Stir in chocolate chips. Drop by rounded tablespoons onto ungreased baking sheets.

BAKE for 9 to 11 minutes or until golden brown. Cool on baking sheet for 2 minutes; remove to wire rack to cool completely



Wildtype recipe



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Mutation present!



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Point Mutation



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Inversion

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2 cups butterscotch chips



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Substitution



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Types of Mutations

- **Point mutation**
 - A mutation that only affects a single nucleotide of nucleic acid.
- **Inversion mutation**
 - A chromosome rearrangement in which a segment of a chromosome is reversed end to end
- **Substitution mutation**
 - An exchange of one base for another. Such a substitution could: change a codon to one that encodes a different amino acid and cause a small change in the protein produced.



Types of Mutations

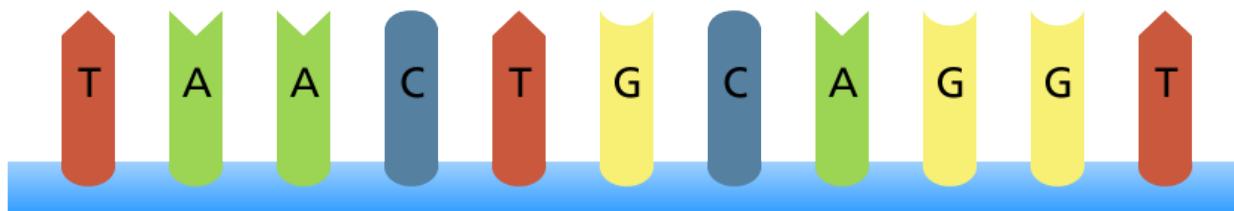
- **Insertions**
 - an addition of one or more nucleotide base pairs into a DNA sequence.
- **Deletions**
 - A mutation (a genetic aberration) in which a part of a chromosome or a sequence of DNA is lost during DNA replication
- **Frameshift mutation**
 - Deletion or an insertion that results in the DNA being read from the wrong starting bases during transcription



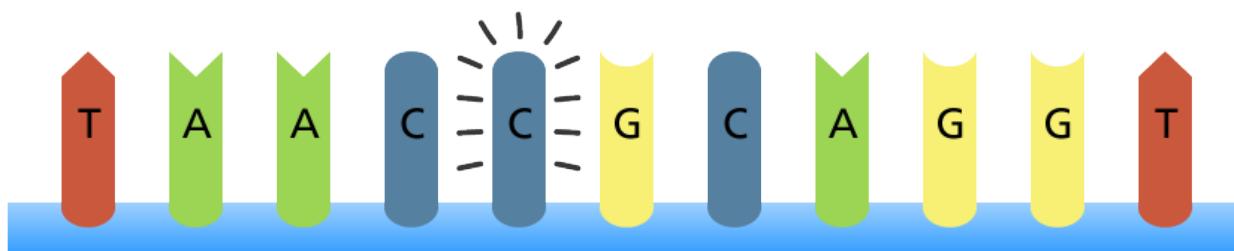
Mutation – Point Mutation

- A point mutation is a mutation that exchanges one base for another

Original sequence



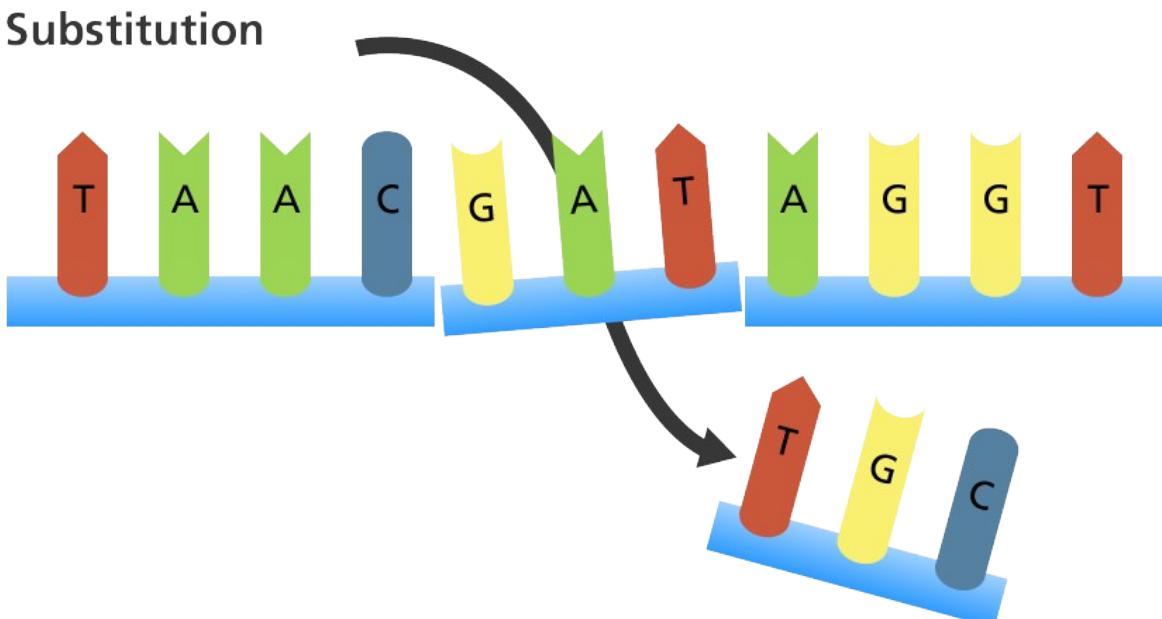
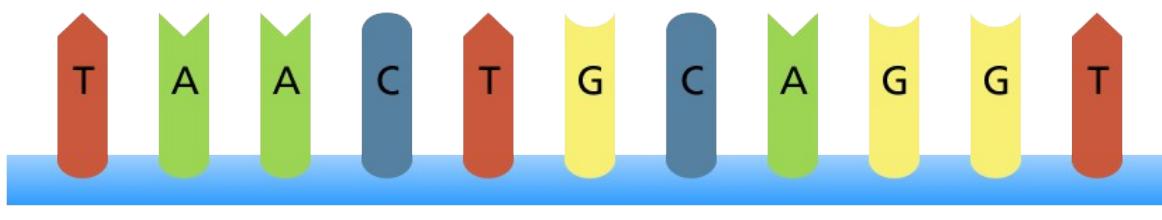
Point mutation





Mutation - Substitution

- A substitution is a mutation where one or more bases in the sequence is replaced by the same number of bases

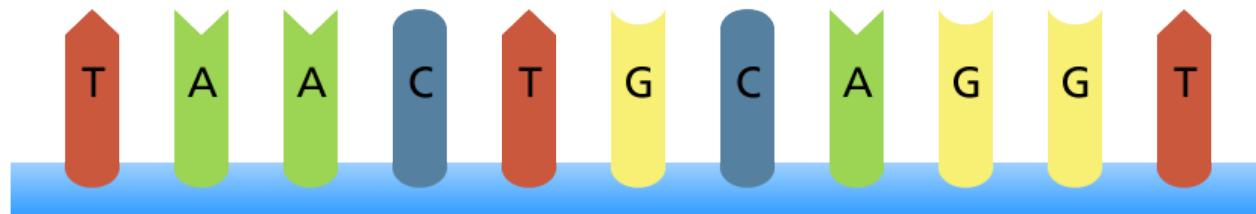




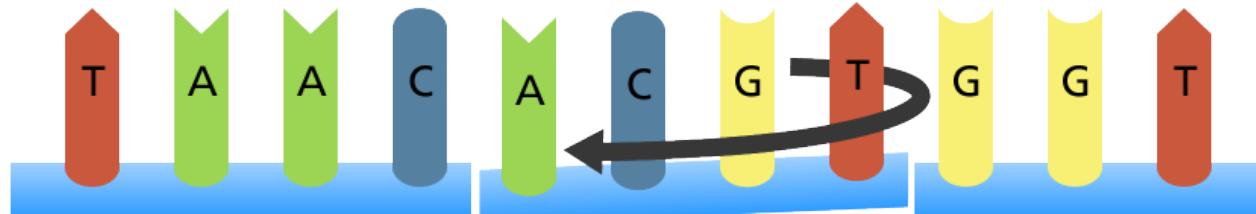
Mutation - Inversion

- An inversion is a mutation where a segment of DNA is reversed

Original sequence



Inversion

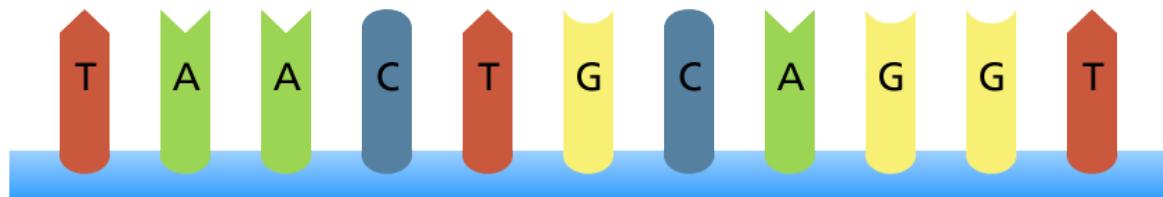




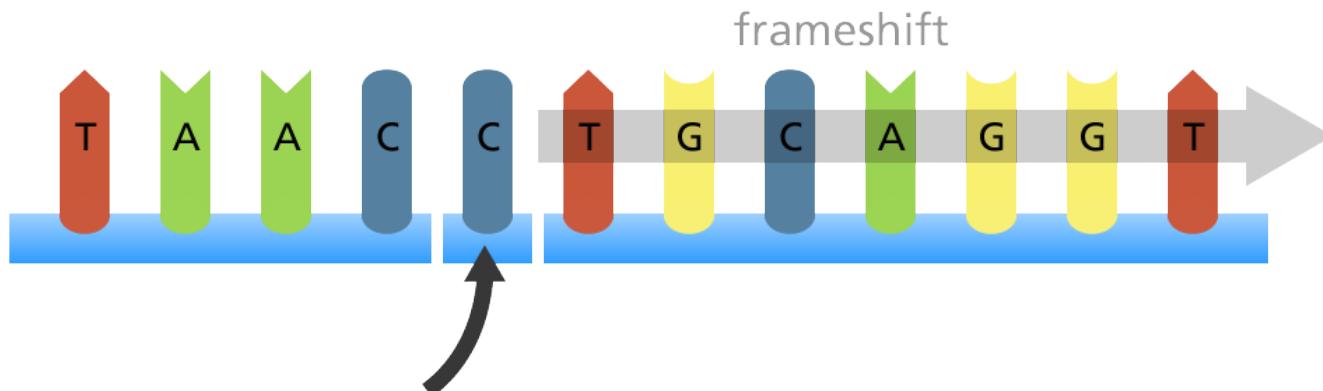
Mutation - Insertion

- An insertion is a mutation in which one or more nucleotides are added into the DNA

Original sequence



Insertion

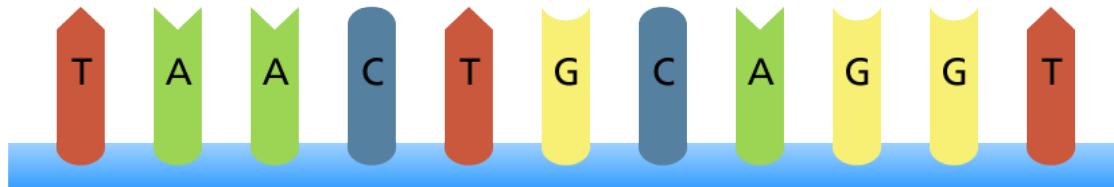




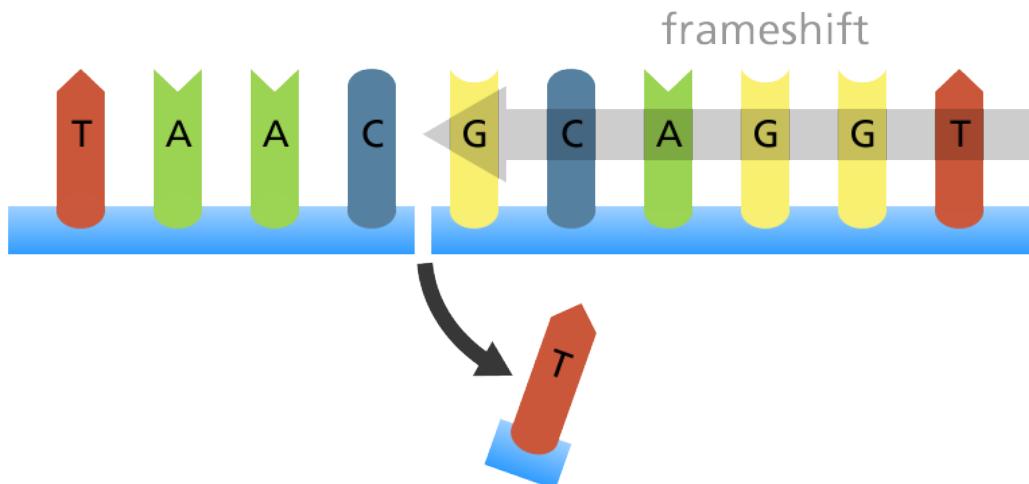
Mutation - Deletion

- A deletion is a mutation in which one or more nucleotides are removed from the DNA sequence

Original sequence



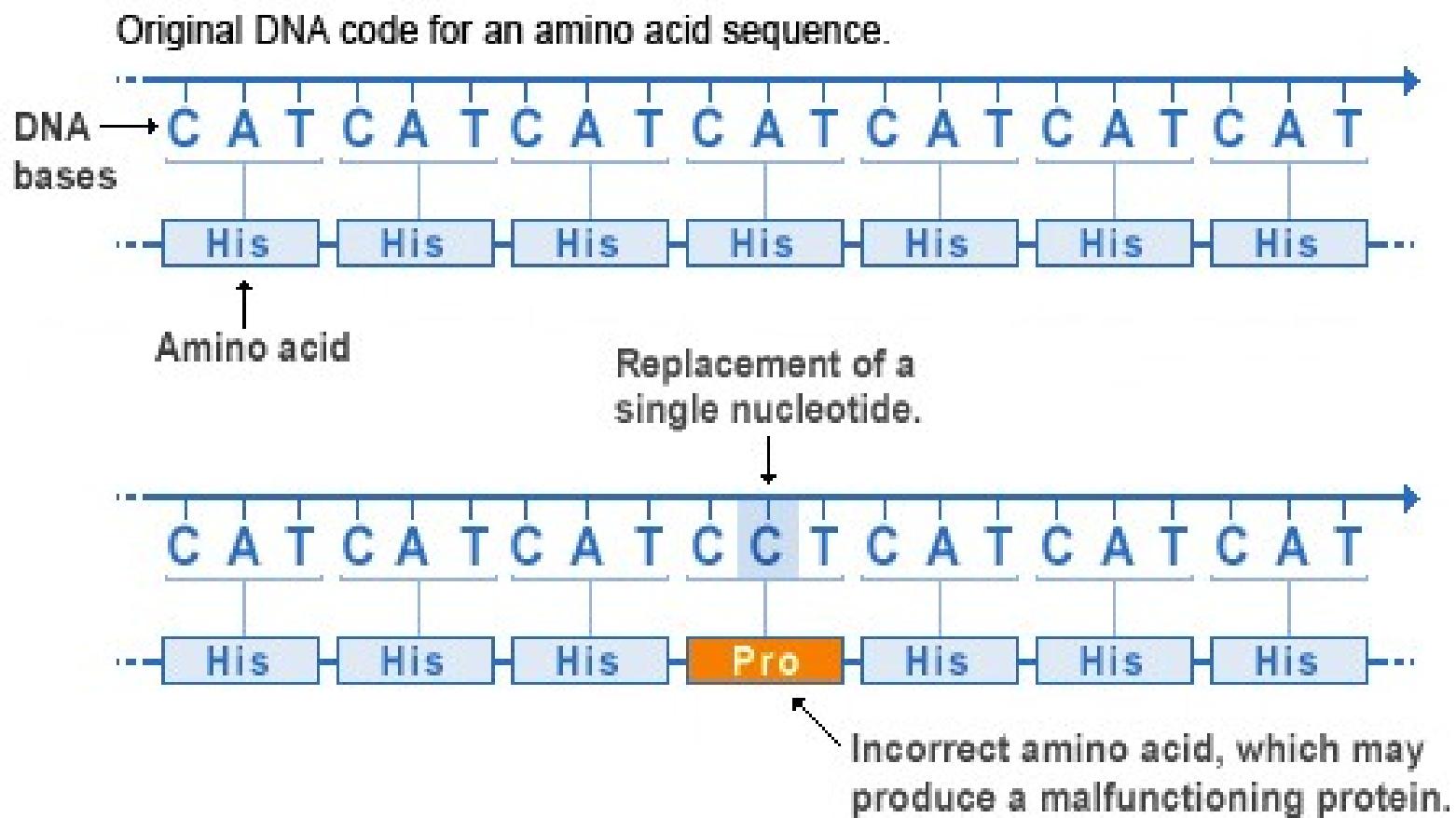
Deletion





Frameshift Mutations

Missense mutation

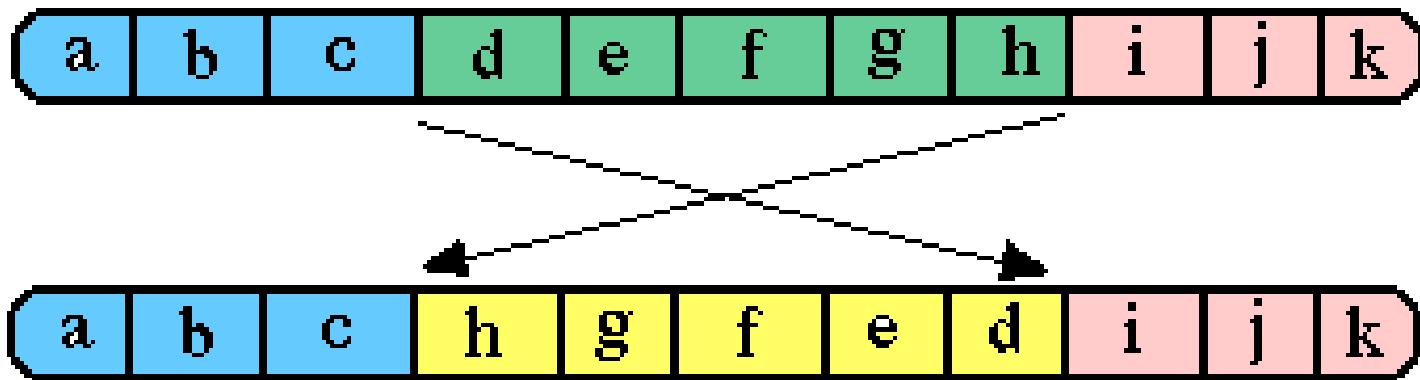


Remember that bases are read in triplets (codons) to make protein.



Where Do Mutations Come From?

- Cell division (meiosis) or can occur if an error is made as DNA copies itself during cell division



- Often no trace of damage to protein as long as gene sequence is not interrupted



Where Do Mutations Come From?

- Mistakes by the DNA polymerase during replication
 - Can be repaired by repair enzymes – not always perfect

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



Where Do Mutations Come From?

- DNA damage and imperfect repair
 - Cell can still divide but DNA sequence has changed



Type of Damage: Double-strand break

Chemical bond between neighboring nucleotides

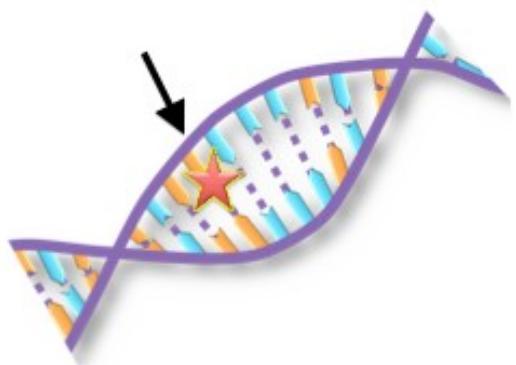
- Common Causes:
- Normal cellular activity
 - Ionizing radiation (including X-rays)
 - Chemotherapeutic drugs
 - DNA repair of other types of damage

- Ultraviolet (UV) light



Where Do Mutations Come From?

- DNA damage and imperfect repair
 - Cell can still divide but DNA sequence has changed



Chemical modification
of a nucleotide

- Reactive oxygen species (ROS)
- Chemotherapeutic drugs
- Other cellular and environmental chemicals
- Normal modifications that regulate what genes are active



Chemical Linkage of
Two Strands

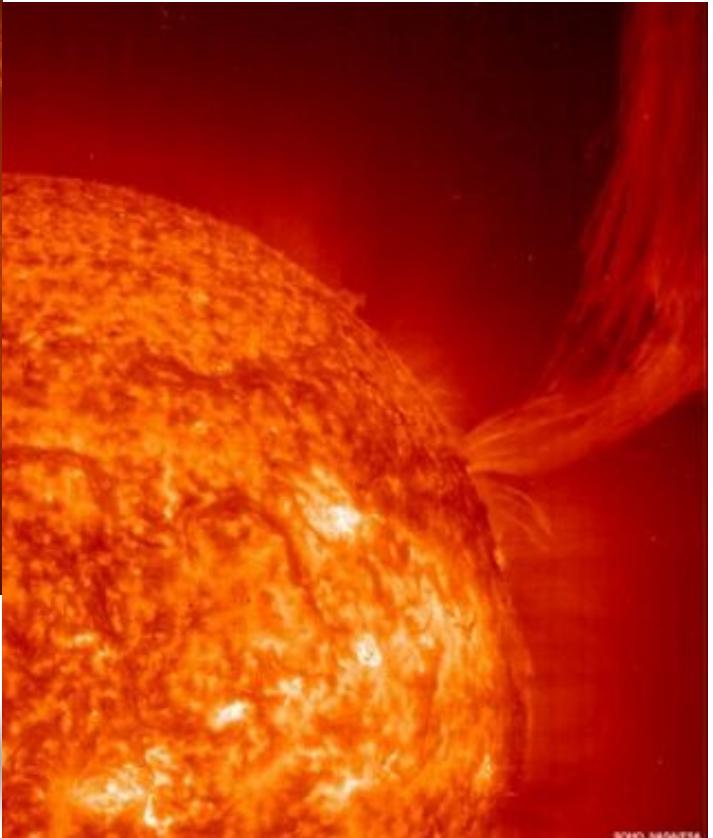
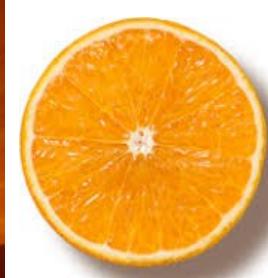
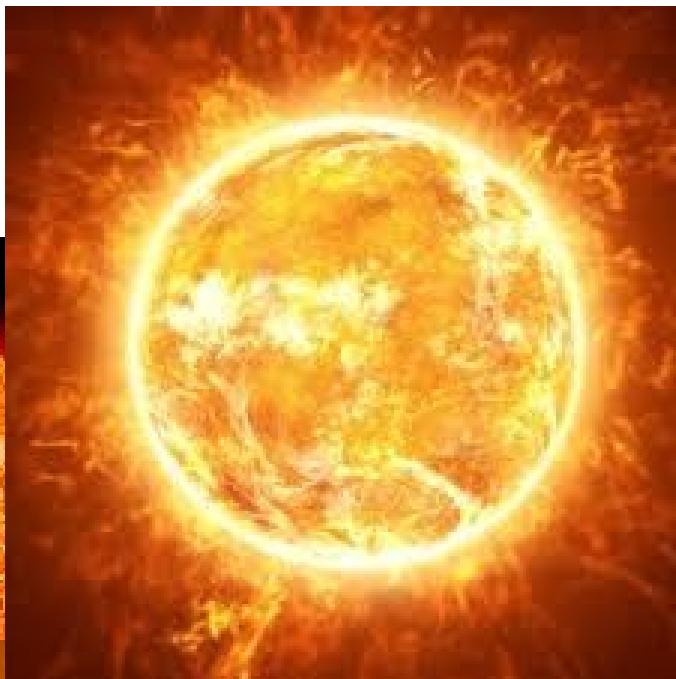
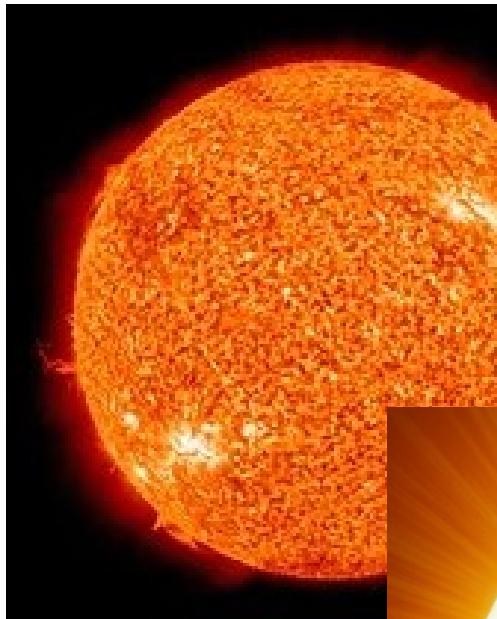
- Reactive oxygen species (ROS)
- Chemotherapeutic drugs
- Other cellular and environmental chemicals



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Where Do Mutations Come From?

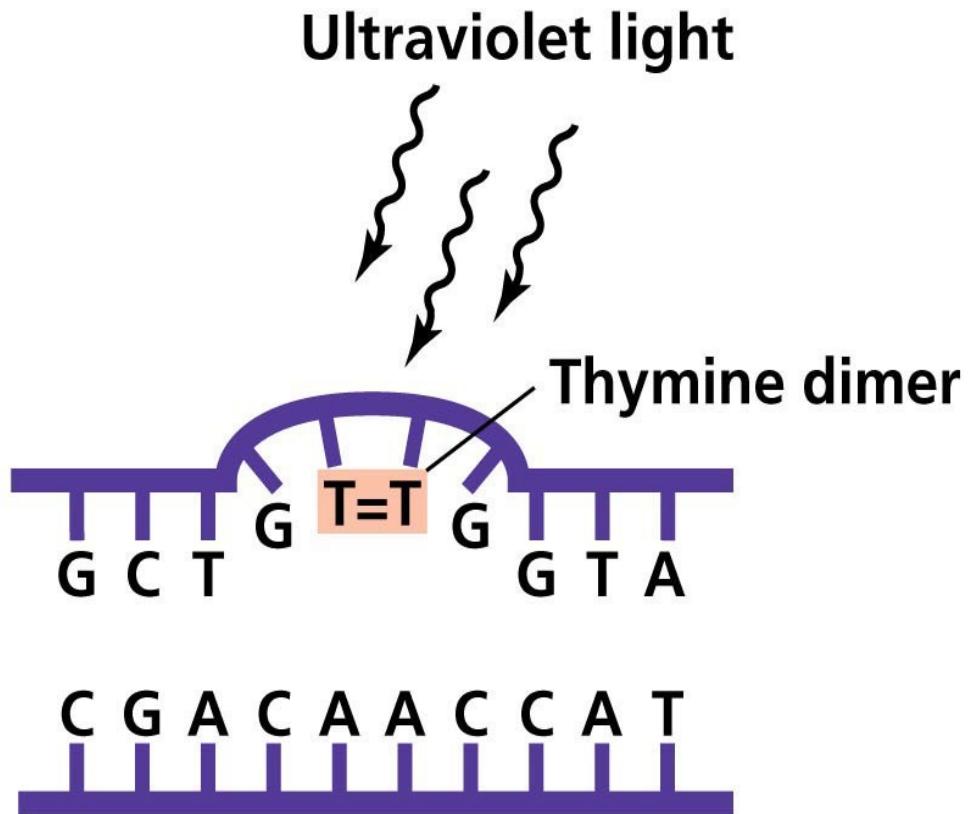
- Environmental factors: ultraviolet radiation from the sun



SOHO/NASA/ESA



Where Do Mutations Come From?



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- UV light causes bond to form between adjacent Ts

If left unrepaired, polymerase “guesses”

- 25% chance per site
- cell can still divide
- hopefully not in a gene

Chance of mistakes during repair process

- polymerase isn't perfect
- cell can still divide
- hopefully not in a gene



Consequences of Mutation?

- Sometimes nothing happens
 - “**Silent mutations**”
 - Mutation does not occur in a gene
 - Humans, just 1.5% of the genome
 - Silent changes
 - occurs in gene, but does not change message
 - genetic code is redundant

TAT

Tyr

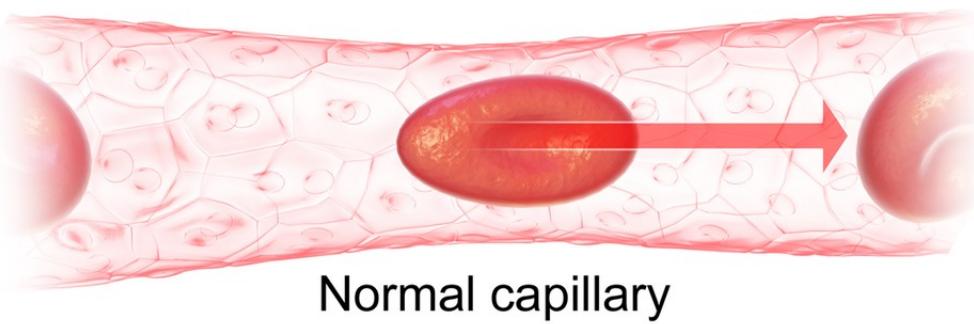
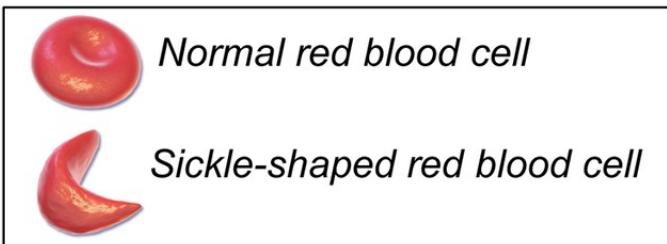
TAC

Tyr

You notice mutations when they interfere with some product production.



Sickle Cell Anemia: A Missense Mutation



- Sickle cells are in the shape of sickles.
- An inherited form of anemia — a condition in which there are not enough healthy red blood cells to carry adequate oxygen throughout your body.
- There's no cure for most people with sickle cell anemia.
- Treatments can relieve pain and help prevent problems associated with the disease.

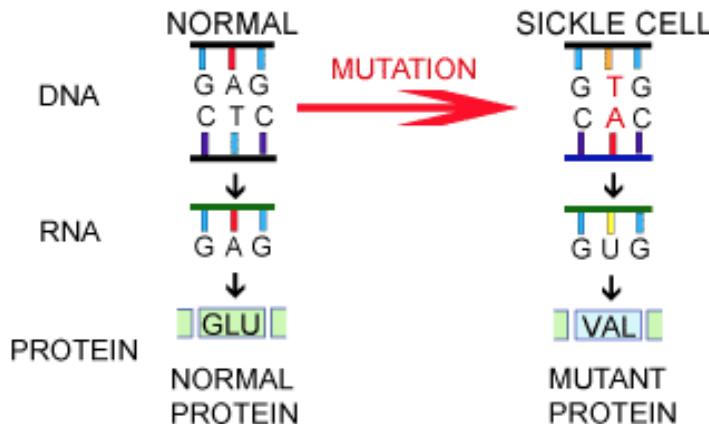
For more information:

<https://www.mayoclinic.org/diseases-conditions/sickle-cell-anemia/symptoms-causes/syc-20355876>

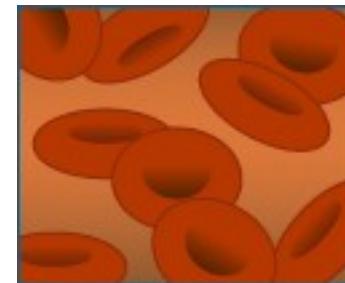


A Mutation Did This?

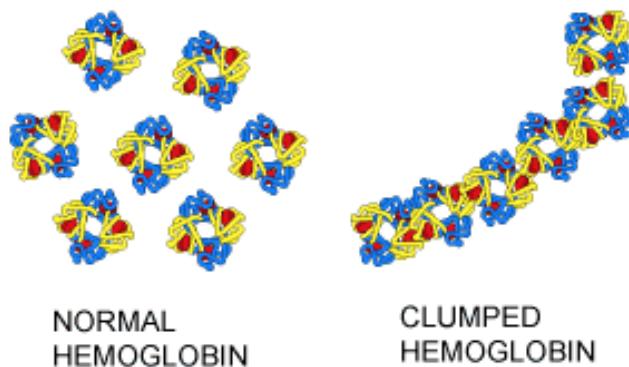
HBB gene - Sickle cell anemia – missense mutation



Normal RBC



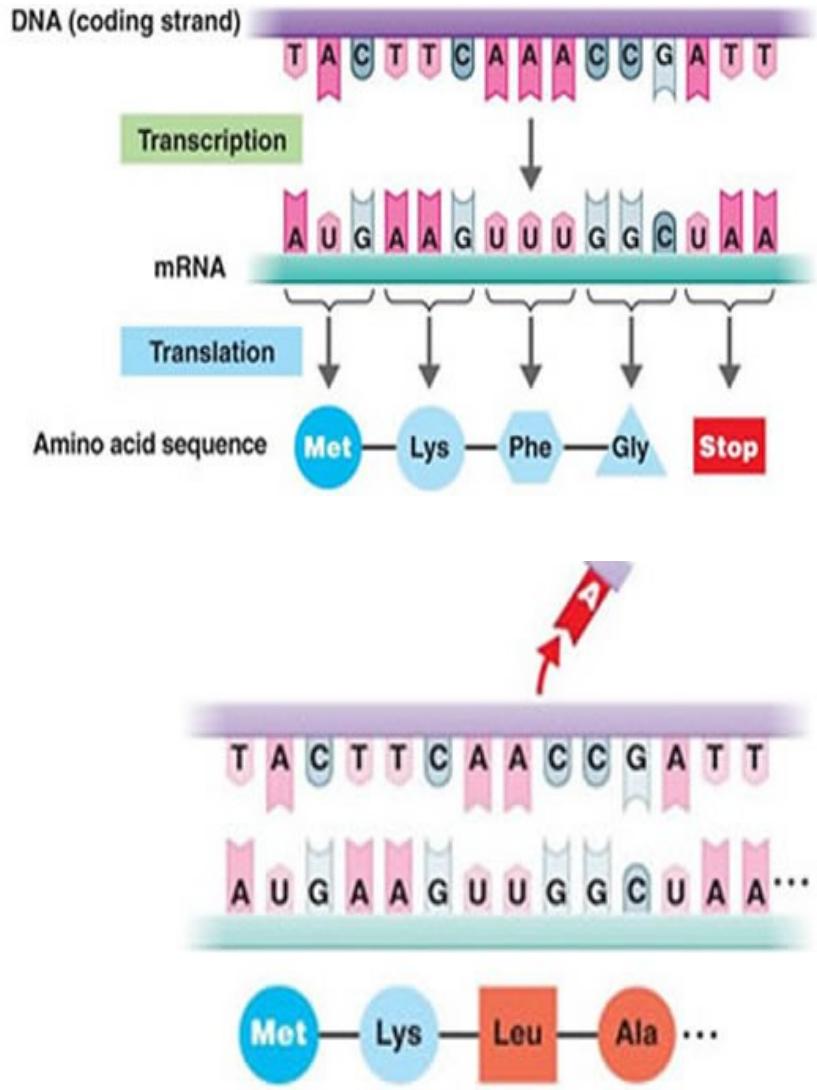
Sickle RBC



- A group of disorders that cause red blood cells to become misshapen and to break down.
- Sickled red blood cells are abnormally shaped and rigid
- Sickle shape can interrupt blood flow



Frame Shift Mutation



- Caused by an Insertion or a Deletion
- Changes codons and corresponding amino acids after mutation site



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Python Programming

- Functions
- Syntax
- General coding

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

