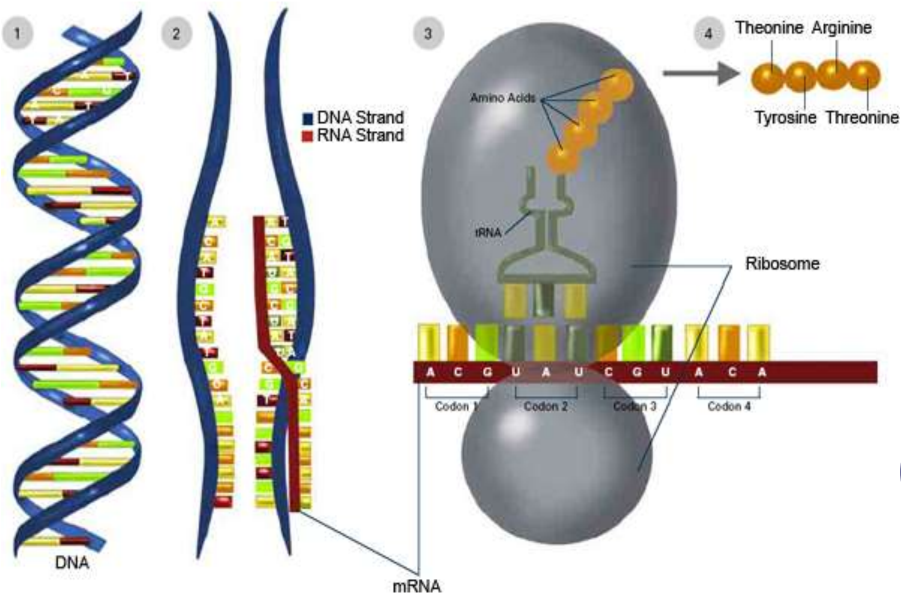
Proteins

By C. Kohn, Waterford, WI

Review – Central Dogma of Molecular Biology

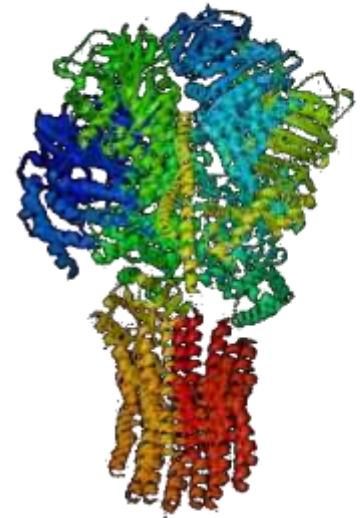
- **DNA is copied by mRNA in a 5 → 3 direction**
- **mRNA is read in groups of three (codons) by a ribosome**
- **Each codon codes for a specific amino acid**
- **That particular amino acid is delivered by tRNA**
- **A string of amino acids creates a polypeptide, and polypeptides join to form a protein.**

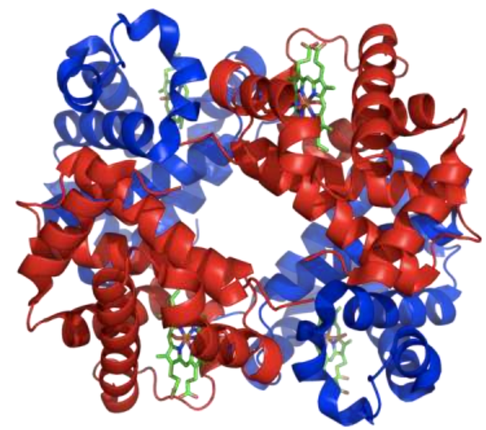


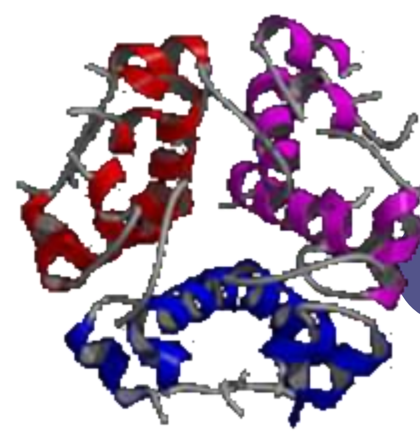
Shape of Proteins

- **Shown here are three examples of proteins.**
  - At the top is ATP Synthase.
  - In the middle is hemoglobin.
  - At the bottom is insulin.
  - Each has a unique shape.

- **We learned earlier that the shape of a protein determines its function.**
  - So how does a protein get its shape?
  - How does it know what shape to take and what to do?
  - What "shapes" a protein?







Shape Determines Function

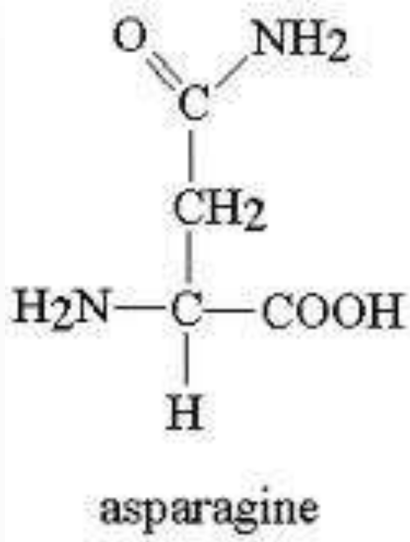
- **The shape of a protein comes from its amino acids, and this shape determines its function.**
  - The amino acids that are used depends directly on the codons in mRNA copied from DNA.

- **Proteins are made from 20-22 amino acids.**
  - Each species may use a different number of amino acids.
  - Humans use 20. Cattle and dogs use 22.

- **Each amino acid has a specific set of properties that help create the shape of the protein**
  - For example, some amino acids are negative charged; some are positively charged. Some are neutral
  - Some like water; some hate it
  - Some really like other amino acids that are the similar. Some are repelled by similar amino acids.

Amino Acid Terminology

- **Amino acids are molecules that either occur naturally or are produced by an organism's cells.**
  - Amino acids our bodies can produce are nonessential amino acids.
  - Amino acids we must consume from other sources are essential amino acids.

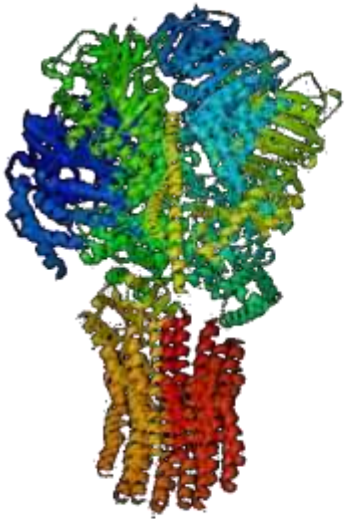


- **Different kinds of amino acids can be written in a number of ways.**
  - 1. You can write the full name of the amino acids.
    - E.g. The first amino acid discovered was *asparagine*
  - 2. You can just write the abbreviation (such as 'asp' for asparagine).
  - 3. You could write the assigned one letter code.
      - E.g Asparagine can be written as just the letter 'N'
      - *Why N? Because we already used A for Alanine*
    - Each amino acid has its own one-letter code *(just like each atomic element has a one- or two letter code; e.g. Oxygen is O, Carbon is C, Gold is Au)*

Image Source: groups.molbiosci.northwestern.edu

Amino Acids → Polypeptides → Proteins

- **Proteins are typically composed of multiple amino acid chains.**
  - Just like a machine usually consists of multiple parts, a protein consists of multiple chains of amino acids.
- **Each chain of amino acids will form a <u>polypeptide</u>.**
  - Multiple polypeptides together will form a protein.
- **In a few cases, the entire protein may be only one polypeptide.**
  - However, most proteins are made of multiple polypeptides.
  - For example, in the ATP Synthase shown here, each color is a different polypeptide.



Rules of Protein Folding

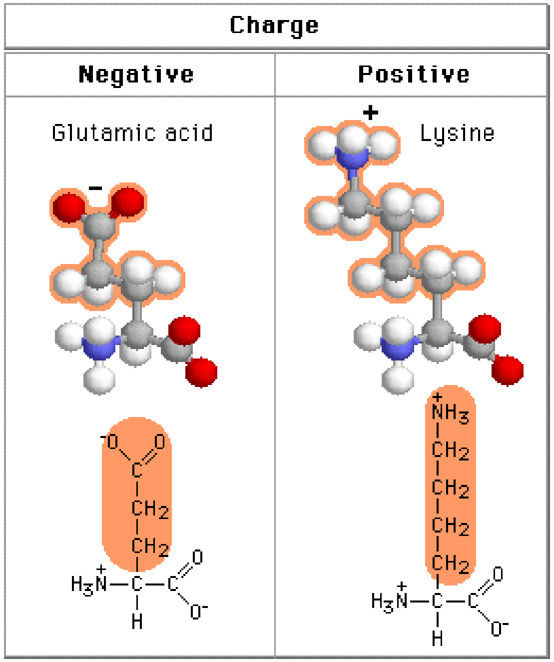
- **When amino acids are assembled in a line to make a protein, they do not stay in an even, straight line.**
  - Different properties of different amino acids result in changes to the shape of the chain of amino acids.

- **This is similar to a line at lunch sometimes…**
  - A couple might move closer to each other without leaving the line
  - Two friends fighting might move away from each other
  - That one kid who really likes pizza might move on one side of the line or the other
  - That other kid who ate too much raw cookie dough might move to the side of the line with the trash can
    - Everyone else would probably move to the opposite side!

Amino Acid Charge

- **Three factors affect how amino acids fold into polypeptides and then into proteins.**

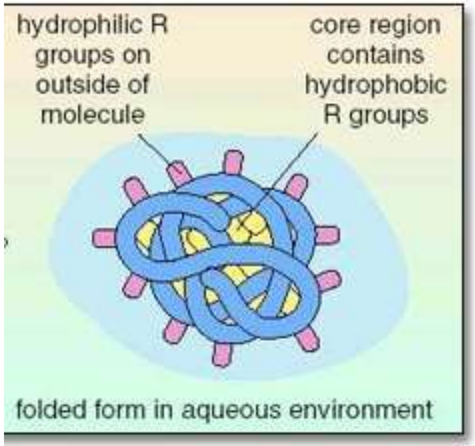
- **The first of these factors is charge. An amino acid can be negatively charged, positively charged, or neutral (no charge).**
  - Opposite charges attract.
    - A negative will move closer to a positive charge and form a bond.
  - Similar charges repel each other; two positive charges will move away from each other.
    - Ditto for two negative charges.



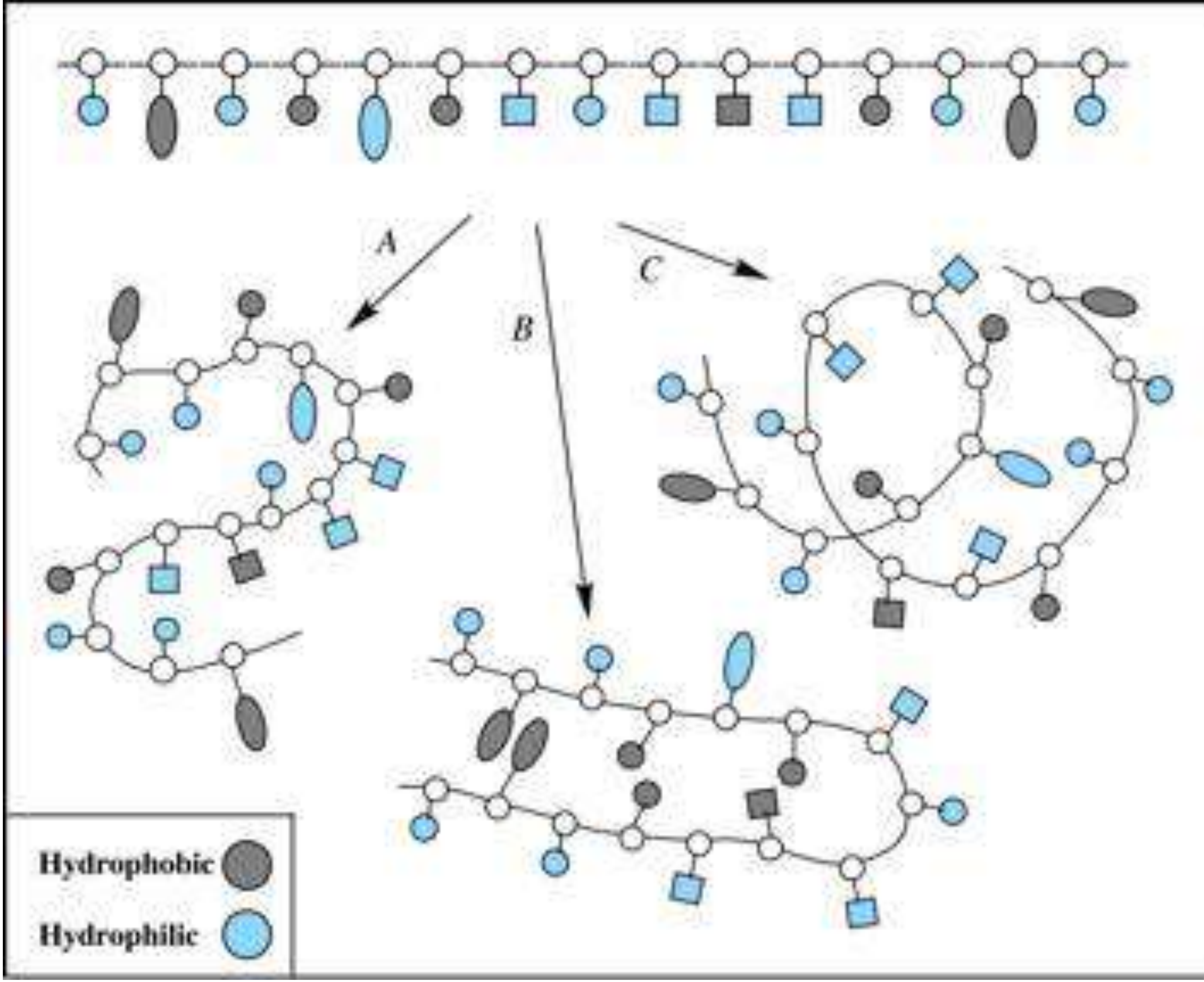
Source: www.phschool.com

Amino Acid Hydrophobicity

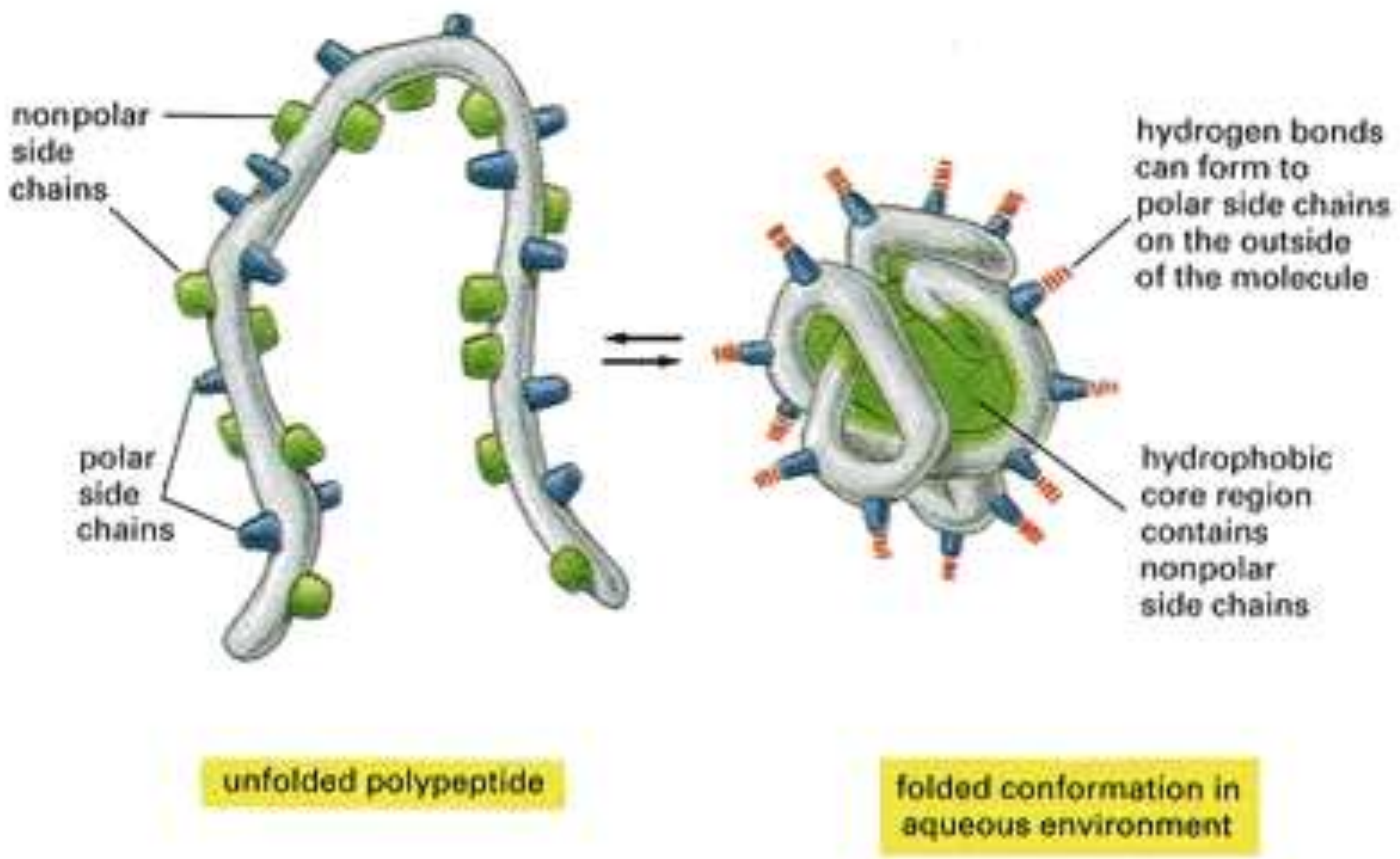
- **The second property is hydrophobicity.**
- **Hydrophobicity simply means whether or not a molecule is attracted to or repelled by water**
  - For example, oil is hydrophobic – it does not mix with water
  - Salt is hydrophilic – it easily dissolves in water
  - Hydrophobic – *water hating* (it has a 'phobia' of water)
  - Hydrophilic – *loves water* (Philadelphia is the city of Brotherly *Love*)
- **Hydrophobic amino acids will move to the inside to get *away* from water**
- **Hydrophilic amino acids will move to the outside to move *towards* water**



Source: labspace.open.ac.uk -



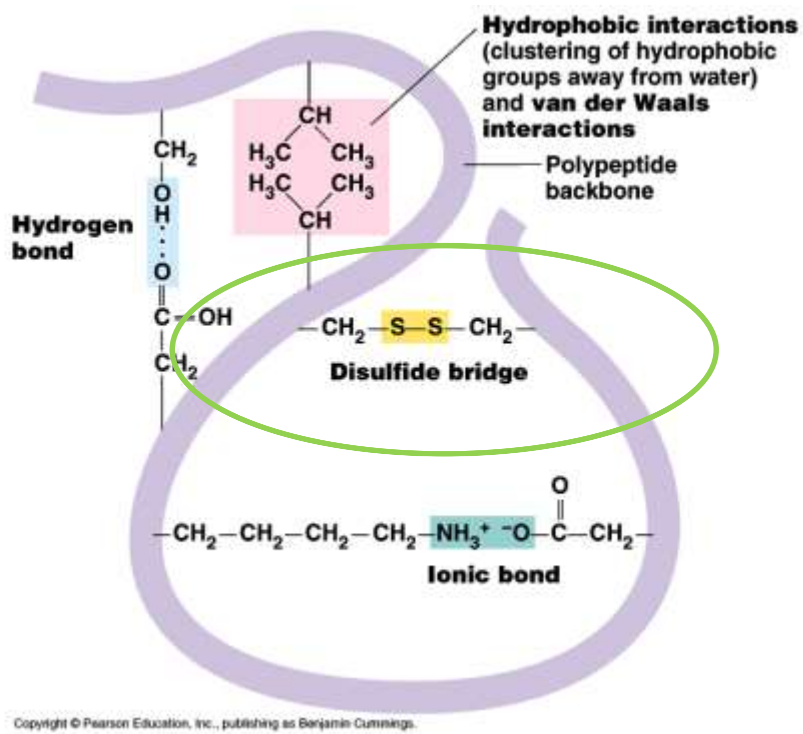
A
B
C
Hydrophobic
Hydrophilic

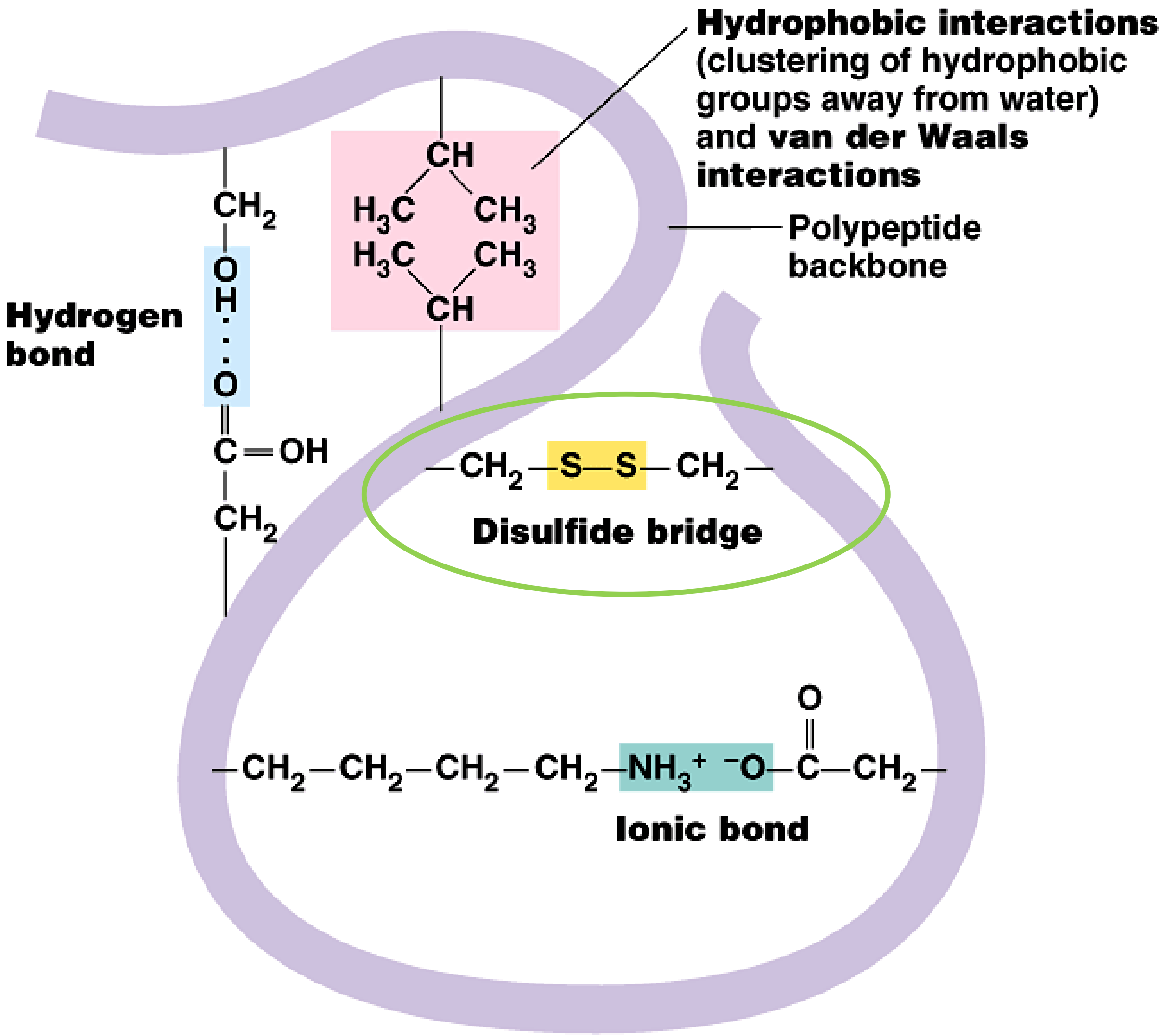

nonpolar
side
chains
polar
side
chains
hydrogen bonds
can form to
polar side chains
on the outside
of the molecule
hydrophobic
core region
contains
nonpolar
side chains
unfolded polypeptide
folded conformation in
aqueous environment

Cysteine Bonds

- **Cysteines are one of the 20 amino acids**
  - Cysteines are like the obnoxious couples that are always together – they can't stand to be apart
  - Two cysteines will always move closer to each other

- **When they move close, they will form what is called a "disulfide bond" or "disulfide bridge".**




Hydrophobic interactions
(clustering of hydrophobic groups away from water) and van der Waals interactions
Polypeptide backbone
Hydrogen bond
Disulfide bridge
Ionic bond

Summary

- **So, three major factors affect how amino acids change from a straight line to a 3D protein**
  - Charge – like charges repel, opposite charges attract
  - Hydrophobicity – some amino acids are attracted to water and move to the outside; others are repelled by water and move to the inside
  - Cysteine bonds – two cysteine amino acids will form a disulfide bond together

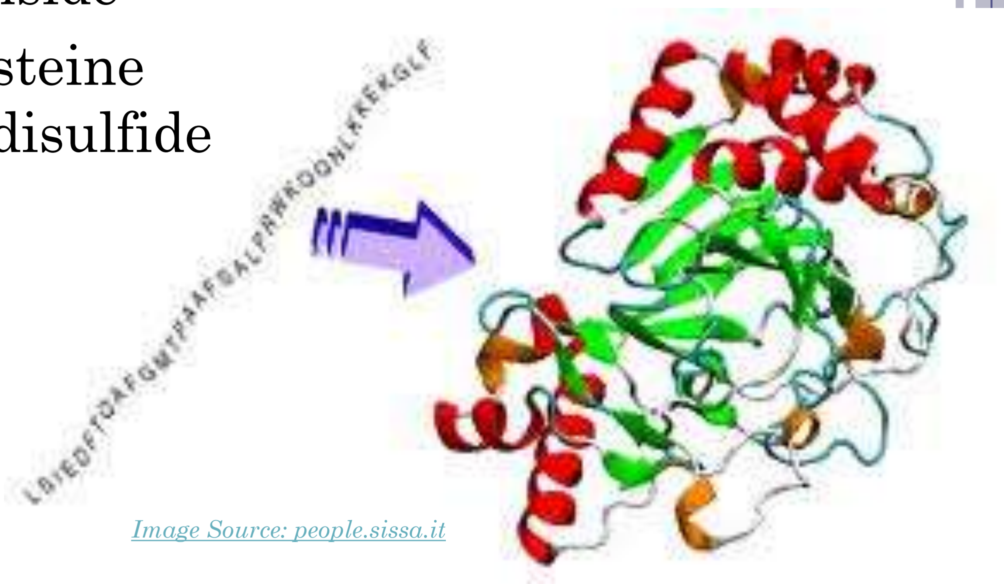
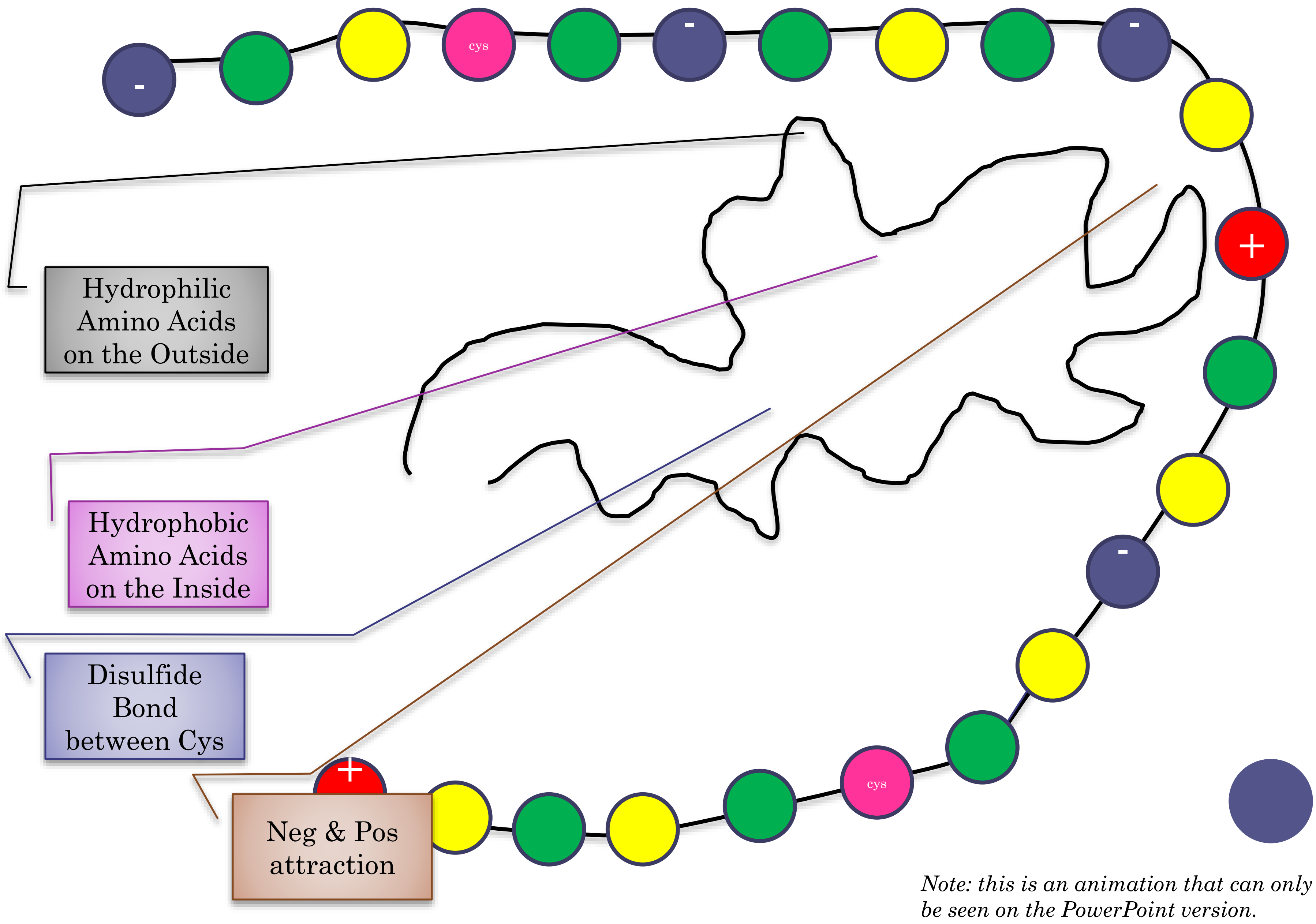
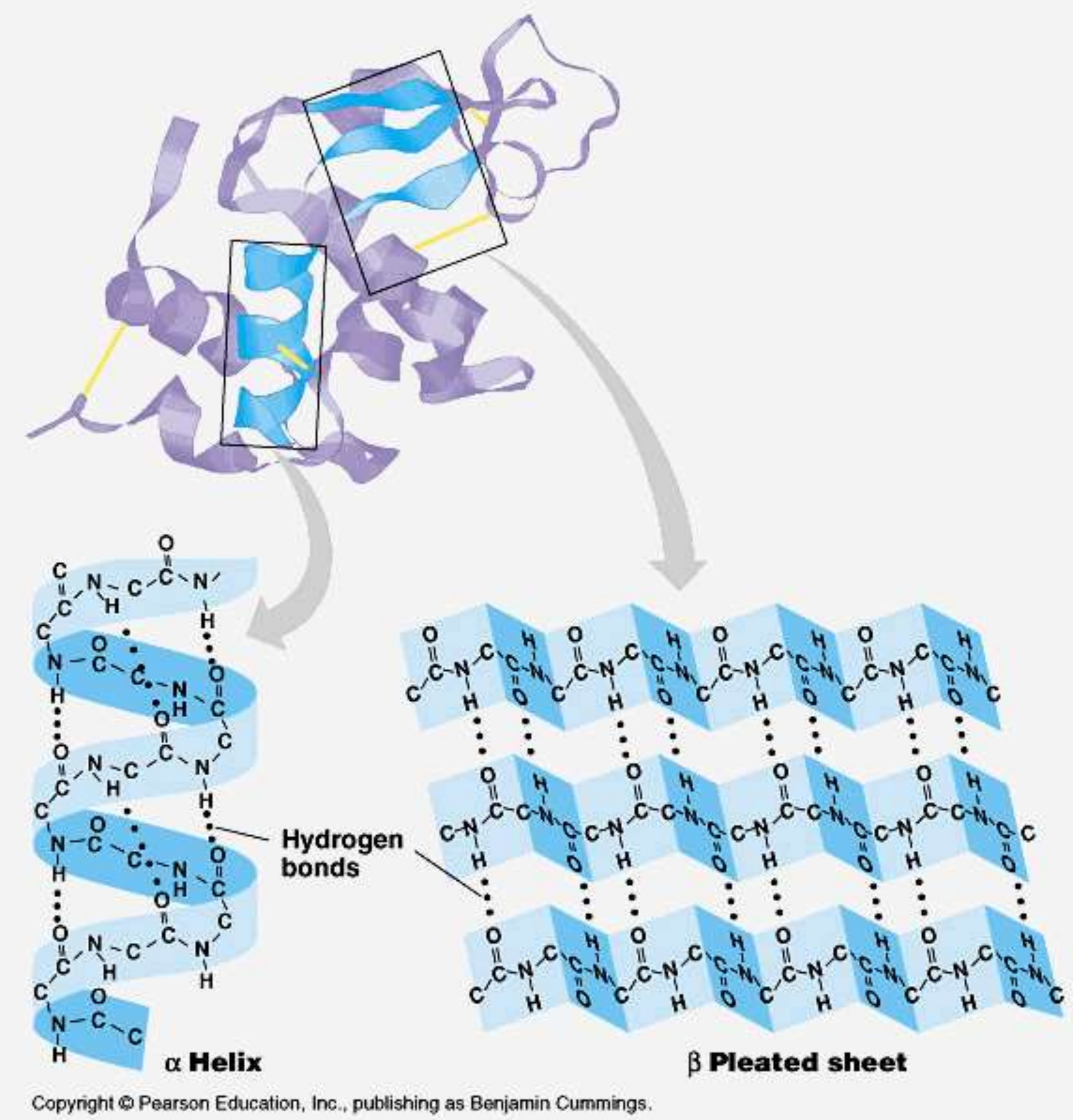


Image Source: people.sissa.it


Hydrophilic Amino Acids on the Outside
Hydrophobic Amino Acids on the Inside
Disulfide Bond between Cys
Neg & Pos attraction
cys
cys
-
-
-
-
+
+
Note: this is an animation that can only be seen on the PowerPoint version.

Shapes of Proteins

- **There are two kinds of shapes that can result because of the factors that affect protein shapes**
  - α helix (pronounced "alpha helix")
  - β sheet (pronounced "beta sheet")



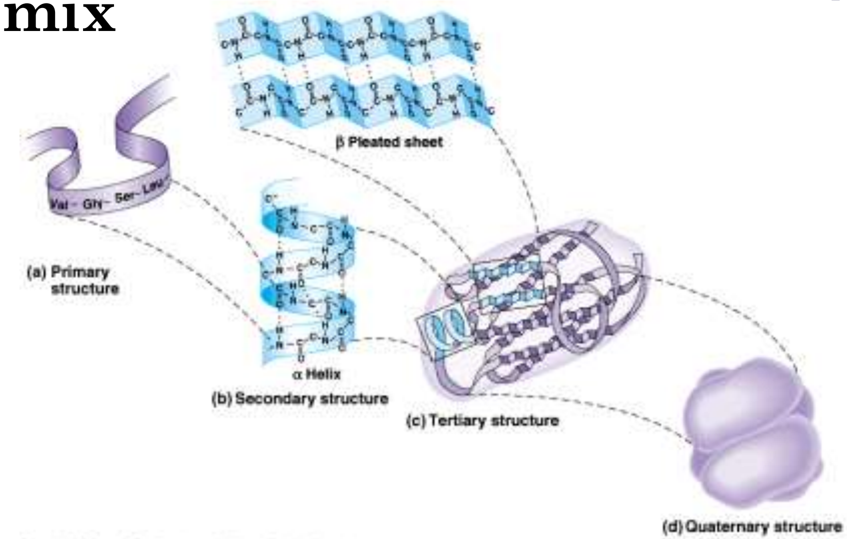
Levels of Protein Organization

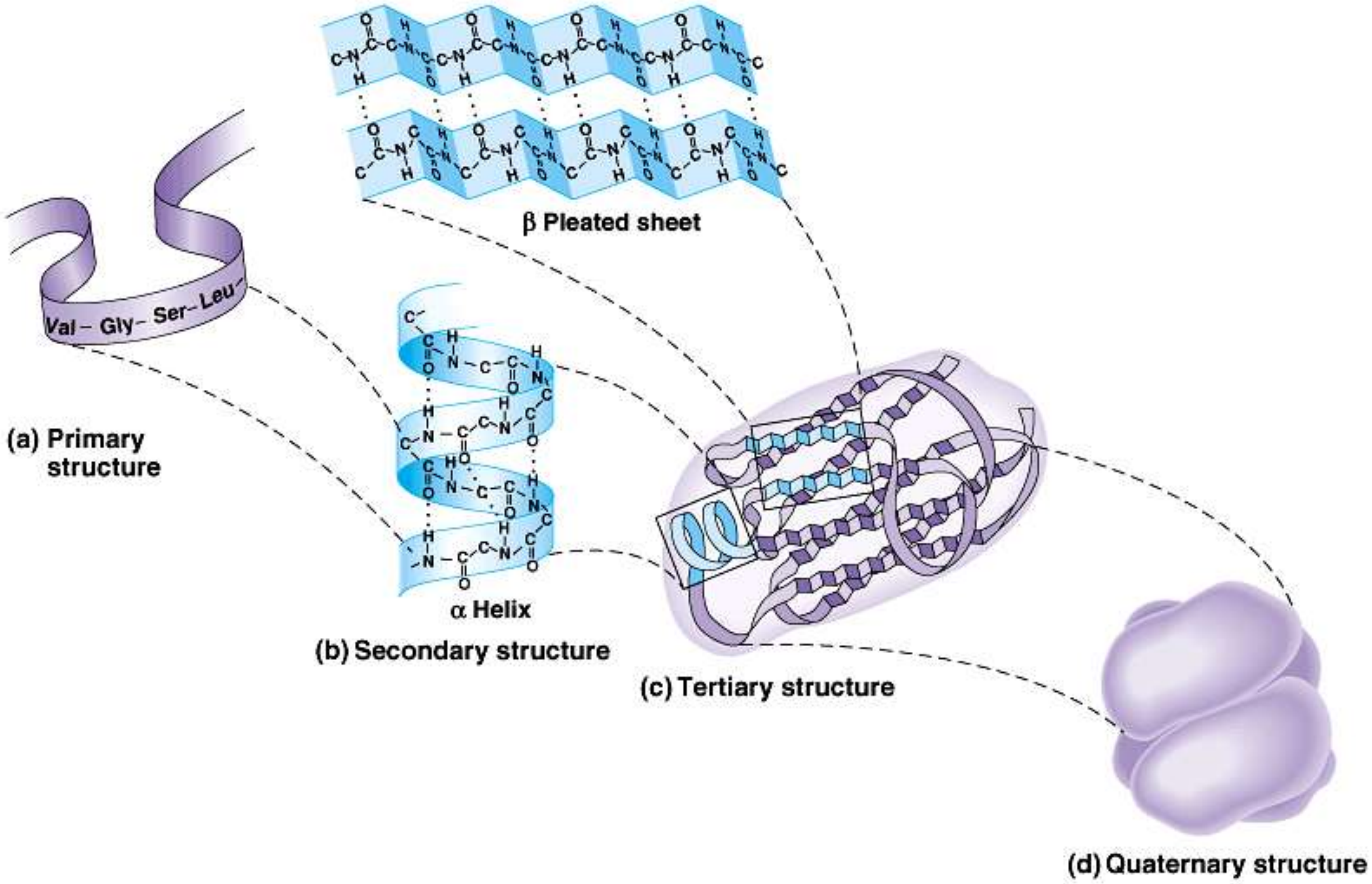
- **The <u>primary</u> level of protein organization is the order of amino acids as determined by mRNA and DNA**

- **The <u>secondary</u> level of protein organization is the shape created by these amino acids.**
  - Only two shapes occur - α helix or ß sheet

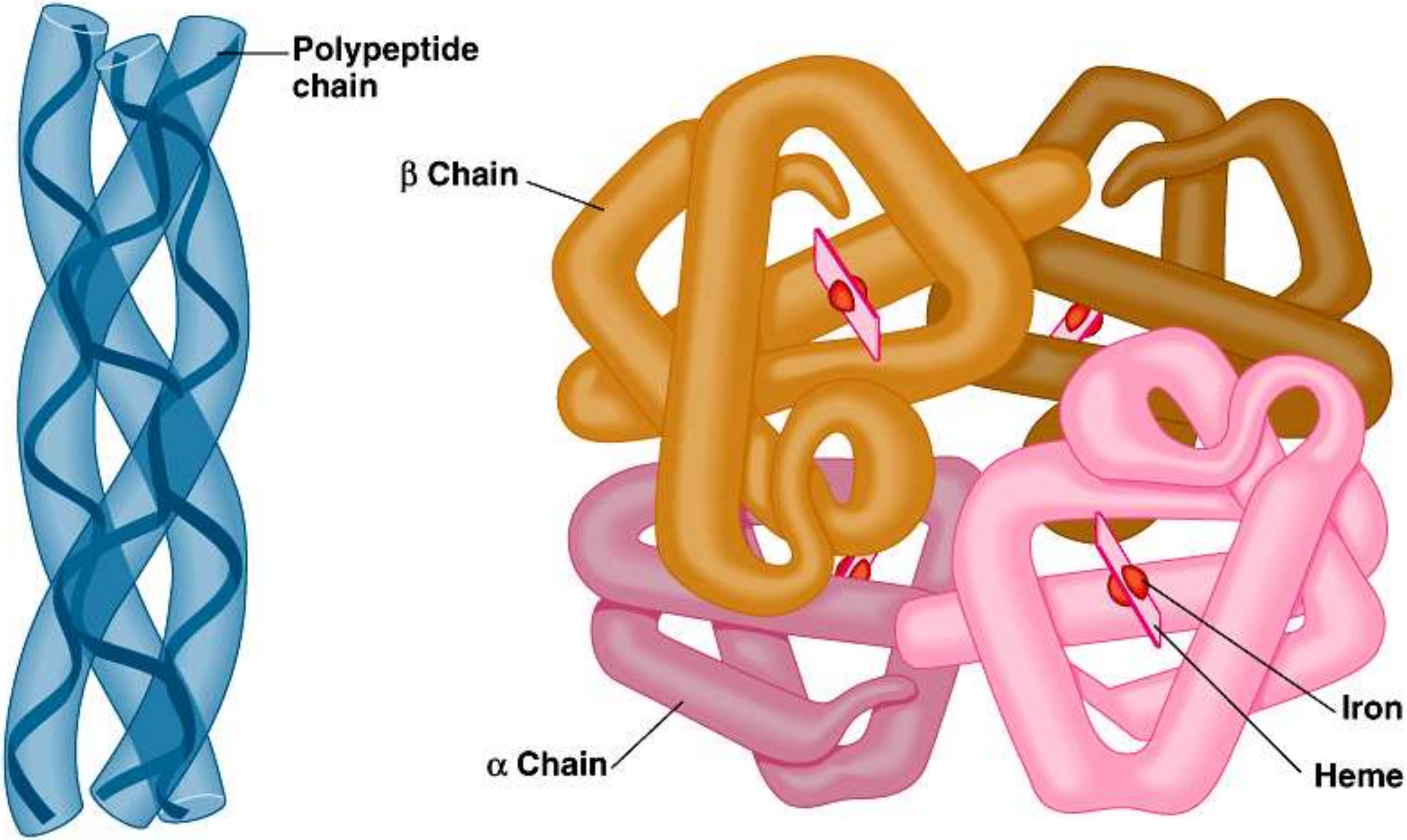
- **The <u>tertiary</u> level is the overall shape of the polypeptide created by the mix of α helixes and β sheets.**

- **The <u>quaternary</u> level, is the mixture of polypeptide subunits to create a functional protein.**



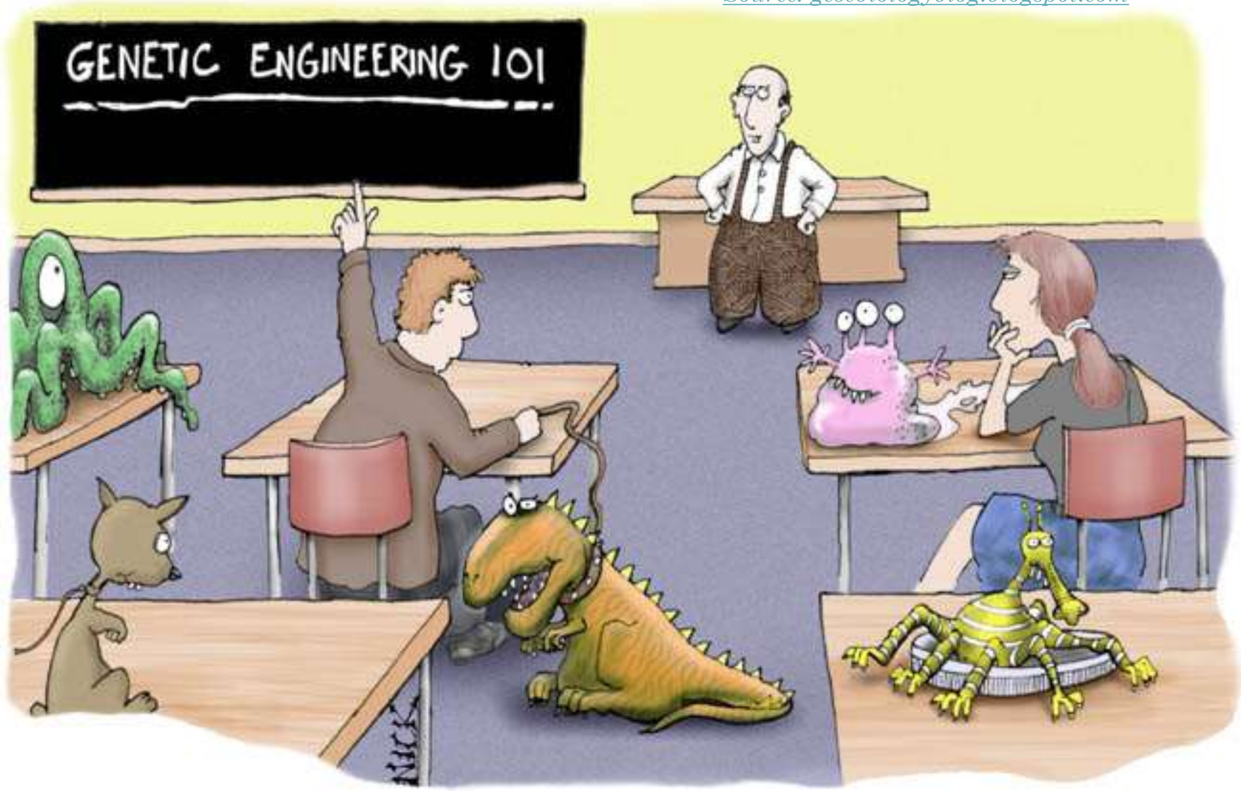


β Pleated sheet
Val – Gly – Ser – Leu –
(a) Primary structure
α Helix
(b) Secondary structure
(c) Tertiary structure
(d) Quaternary structure



(a) Collagen (b) Hemoglobin

Source: gcsebiologyblog.blogspot.com



"Okay—is there anybody ELSE whose homework ate their dog?"

The Impact of Mutations

By C. Kohn, Waterford, WI

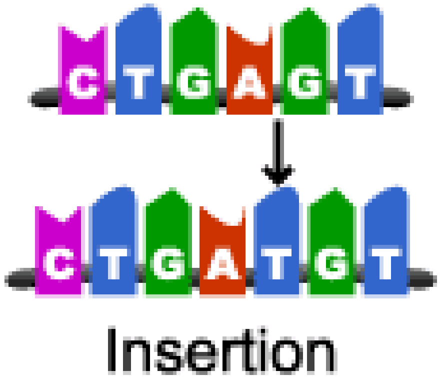
Mutations

- **Any change to the DNA is called a <u>mutation</u>**
  - The effect of a mutation is usually harmful, but it can also be beneficial or even have no impact whatsoever
  - Whether or not a mutation is helpful, harmful, or neither depends on how the protein created from that gene is affected.

- **Mutations are responsible for genetic diseases such as cancer and inheritable disorders.**
  - While genetic mutations can be bad, they can also be good and are responsible for all of the diversity we see in living organisms
  - Mutations drive both evolution by natural selection in nature as well as improvements by artificial selection in agriculture

Types of Mutations

- **Different types of mutations exist**
- **<u>Insertion</u> mutations occur when a base is added**
  - E.g. GATCTA might become GATACTA



- **<u>Deletion</u> mutations occur when a base is completely lost from DNA**
  - E.g. GATCTA might become GATTA

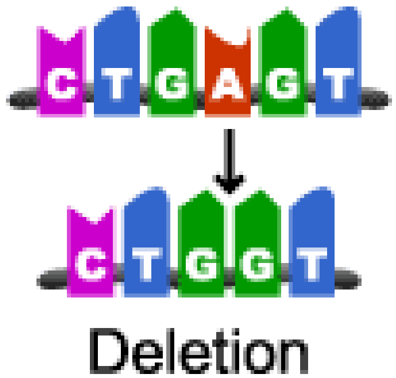
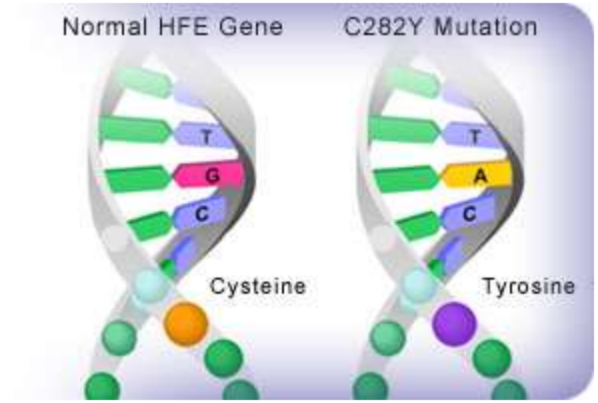


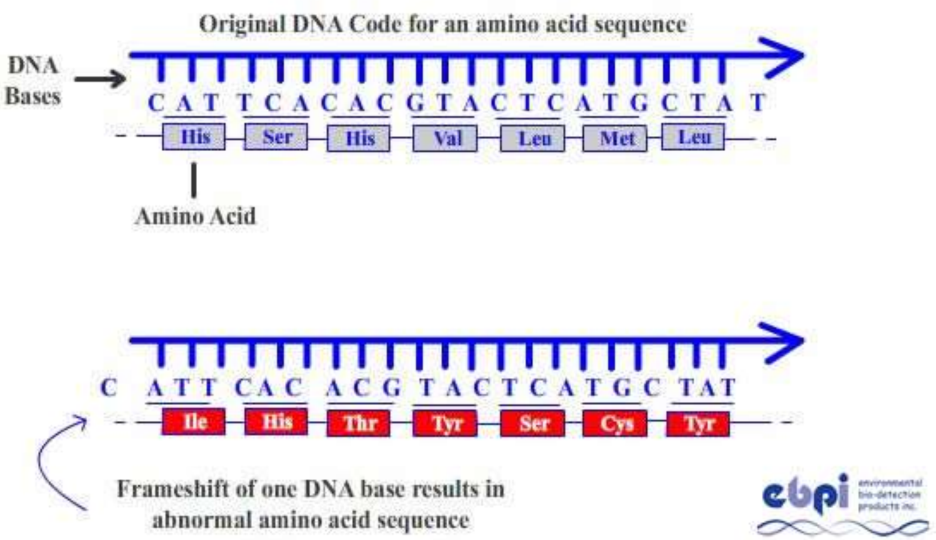
Image Source: learn.genetics.utah.edu



Source: www.cdc.gov

Types of Mutations

- **Substitution mutations occur when one base is switched for another**
  - E.g. GATCTA might become TATCTA
- **If a mutation causes all of the bases downstream to change, it is called a Frameshift Mutation**
  - Deletion and Insertion mutations are frameshift mutations

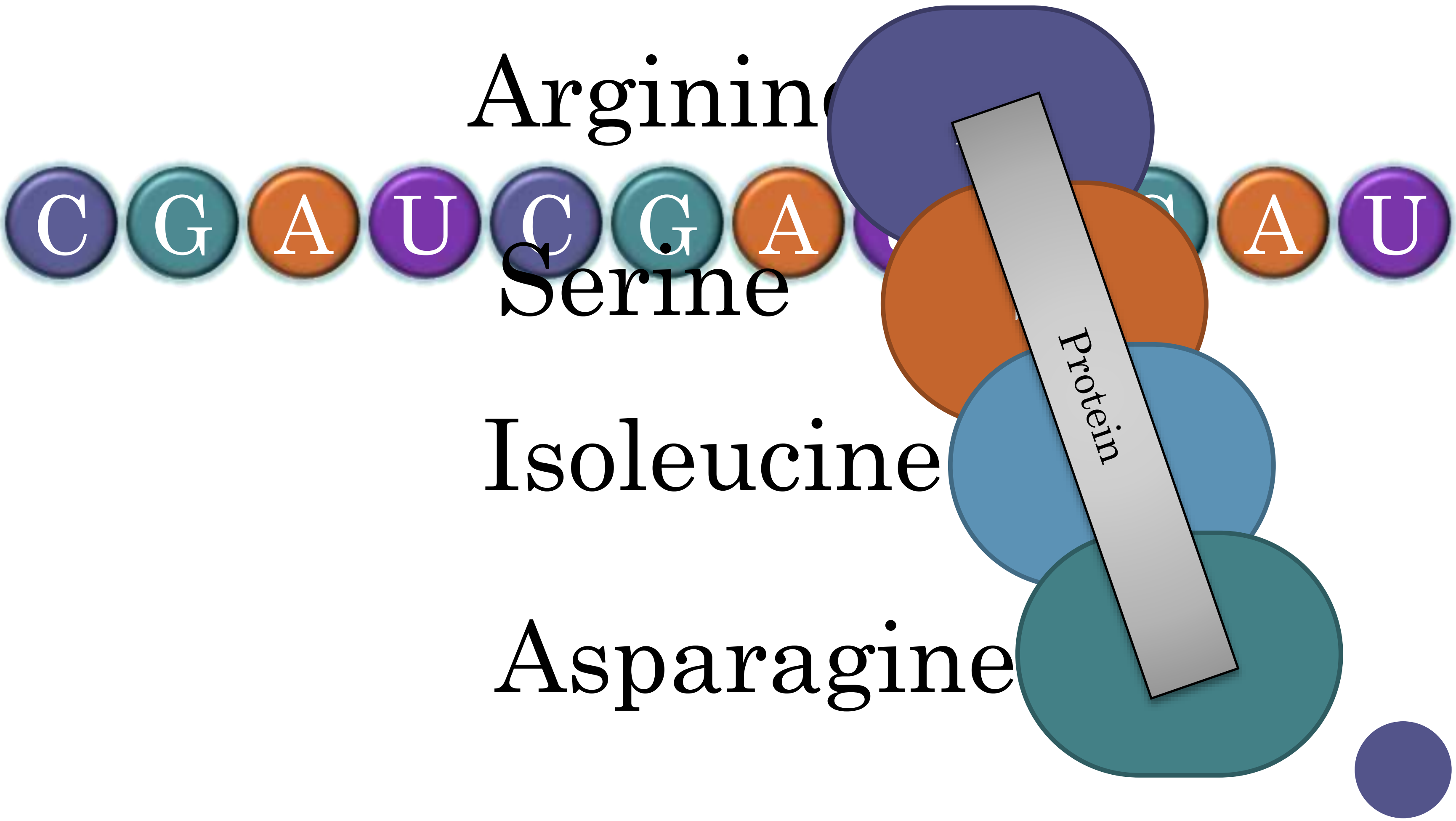


Impact on Proteins

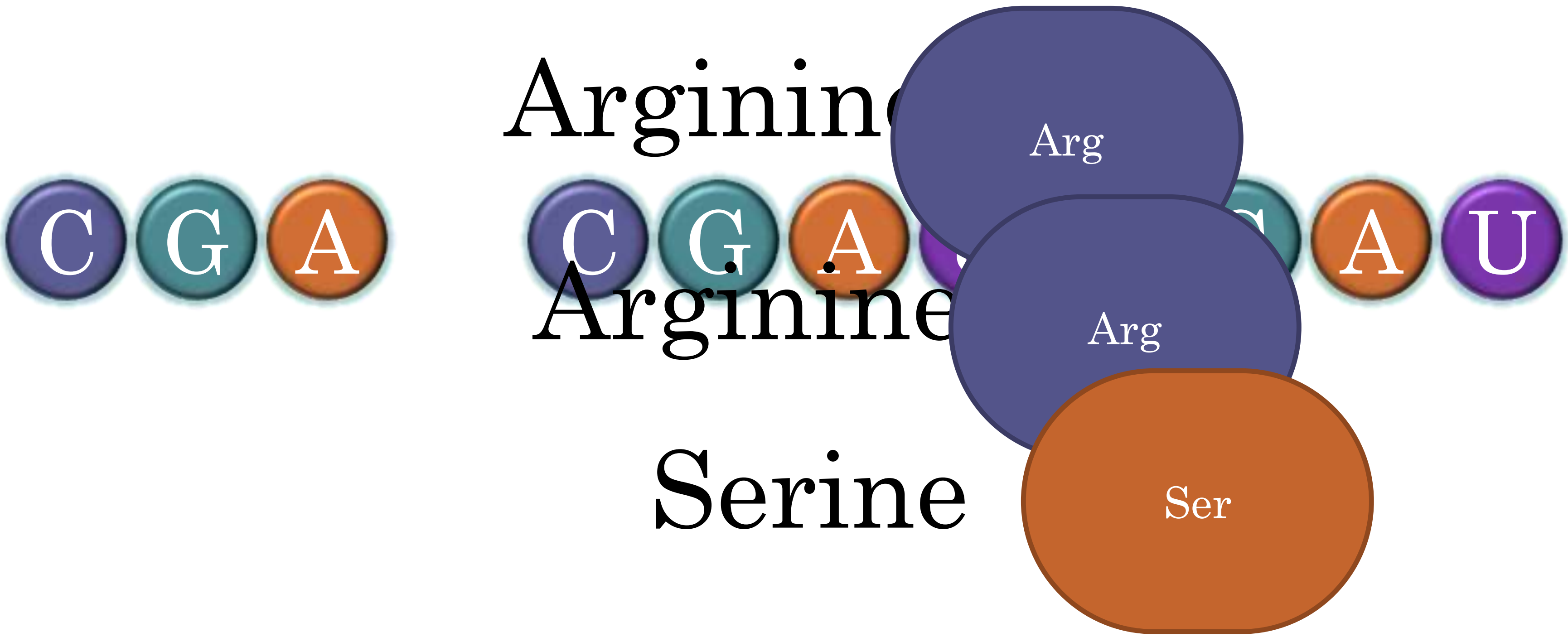
- **So how does a mutation affect a living organism?**
  - First, a mutation may cause a dramatic change to the codons (groups of 3 bases)
  - For example, a deletion mutation in
    5'-GAT-TAC-CTA-TAT-GGA-3'

    would turn it into
    5'-ATT-ACC-TAT-ATG-GA…3'
- **Entirely new amino acids would be added to make a protein because each codon was changed downstream of the mutation**
  - *This again would be a frameshift mutation*

Normal mRNA Strand



Mutated mRNA Strand (Frameshift)



Arginine

Arginine

Serine

Impact of Mutations at Each Level

- **At the <u>primary level</u> of protein organization, the order of amino acids will change, and possibly most or all of the amino acids will be different.**
  - This will cause a major shift in the shape of the protein
- **At the <u>secondary level</u>, the arrangement of α helixes and β sheets will be different.**
- **At the <u>tertiary level</u>, the final look of the polypeptide subunit will be completely different.**
- **At the <u>quaternary level</u>, the protein will have a completely different shape and will not be able to perform its original function.**
  - This can all happen because of one change in one base!

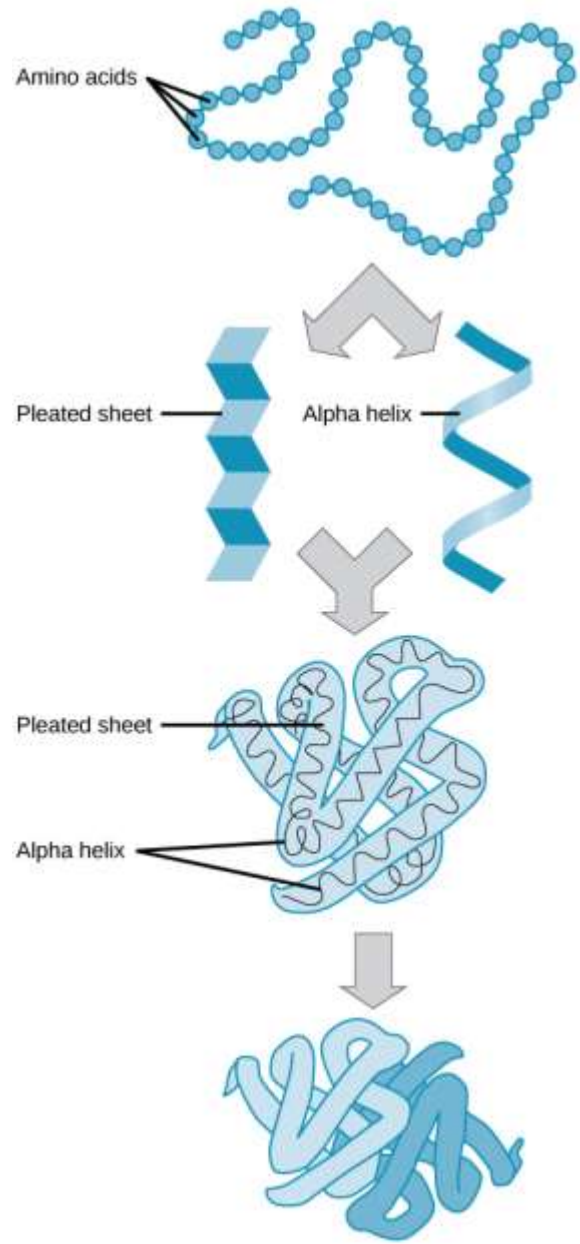


Image Source: cnx.org

Frameshift Mutations

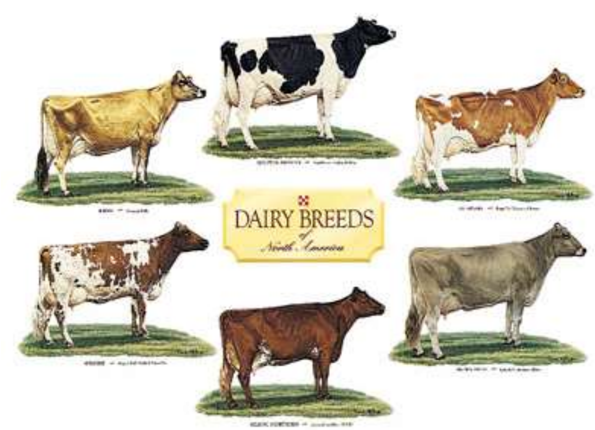
- **Frameshift mutations (insertion or deletion mutations) are especially harmful because they cause every codon to change after the mutation.**
  - This means that almost every amino acid will be different, causing the polypeptide and protein to have an entirely new shape and function.
  - Oftentimes, a codon will change from an amino acid to a TERM command, cutting the amino acid chain short.

- **The result of a frameshift mutation can be devastating to an organism.**
  - For example, the herbicide Agent Orange caused numerous birth defects due to the frameshift mutations it caused in the baby's DNA as it developed.

Mutations Aren't *Always* Bad!

- **Most of the time, mutations will cause the entire protein to be misshaped and malfunction (if the protein is even able to be created).**
  - A mutation that harms an organism is known as a <u>deleterious mutation</u>.
  - A mutation can also have no impact on an organism whatsoever. These are <u>neutral</u> mutations.

- **Very rarely a mutation will be <u>beneficial (or advantageous)</u> and lead to a positive new trait for that organism.**
  - The differences between breeds of livestock and in strains of crops resulted from random mutations that were beneficial.
  - When these productive mutations occur, farmers and geneticists will work to ensure that these traits are selected for when breeding.
    - This ensure that the productive trait becomes more common and widespread.



Norman Borlaug

- **Norman Borlaug was an agricultural researcher who developed strains of wheat that were more productive, more disease-resistant, and more tolerant to temperature extremes.**
  - He did this by selecting for randomly-occurring traits that were the result of mutations in the wheat crop.
  - This selection for beneficial mutations increased wheat yields in his strains by 150%!

- **For his work, Borlaug became known as the "Father of the Green Revolution" and saved countless lives by developing crops that could feed more people.**
  - Because he helped so many people, Borlaug was awarded the Nobel Peace Prize in 1970.

Source: www.nytimes.com