# BC 362: Medical Biochemistry

## CH 4: Protein Structure, Part 2

September 17, 2025

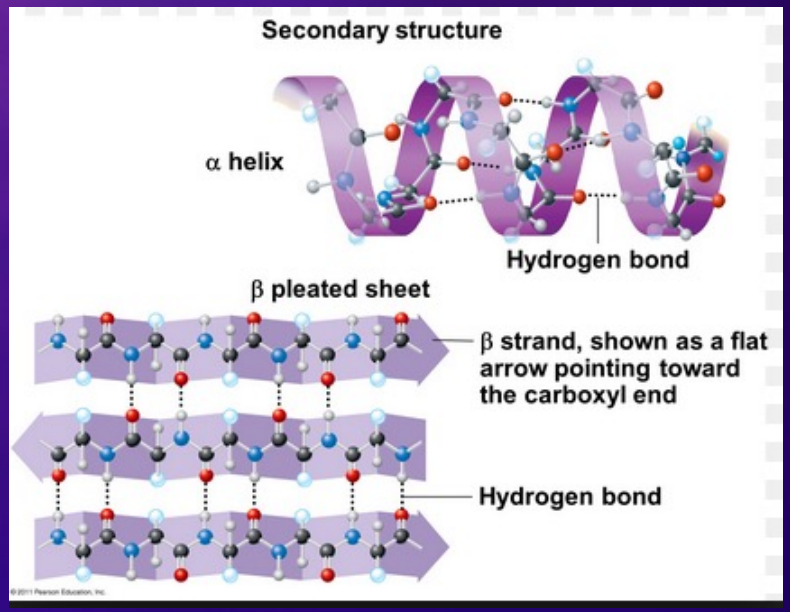
I. Secondary Structure Recap
II. Ramachandran Diagrams
III. Fibrous Proteins
    A. Alpha keratin
    B. Fibroin
    C. Collagen



# Secondary Structure Recap

✦Local spatial arrangement of the peptide chain in a repeated structural motif.

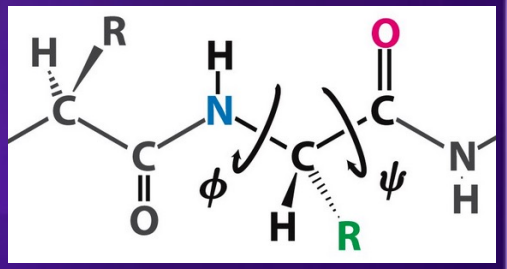
✦Common examples are α–helices and β–sheets.




✦Both are stabilized by H bonds, but beta sheets tend to be more stable because of additional packing interactions between strands and more strands.

Not all amino acid sequences can form these structures (e.g, Pro)!

# Allowed Bond Angles

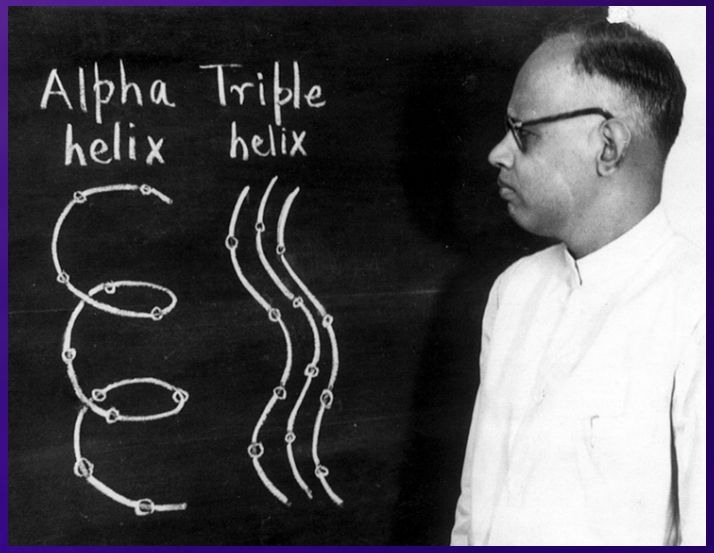



- The work of Pauling, Corey, and Branson suggested that two polypeptide angles have free rotation and thus influence structure.*
  - ✓ $C_\alpha$-N bond angle is phi (φ)
  - ✓ $C_\alpha$-C=O bond angle is psi (ψ)
- The entire path of the peptide backbone is known if all phi and psi angles are specified.
- Some combinations of phi and psi are more likely than others due to steric clash.

*Peptide bond (N—C=O) is planar and doesn't rotate.

# Allowed Bond Angles

- G. N. Ramachandran used peptide models to systematically vary φ and ψ.
- For each conformation, the structure was examined for steric clash between groups.

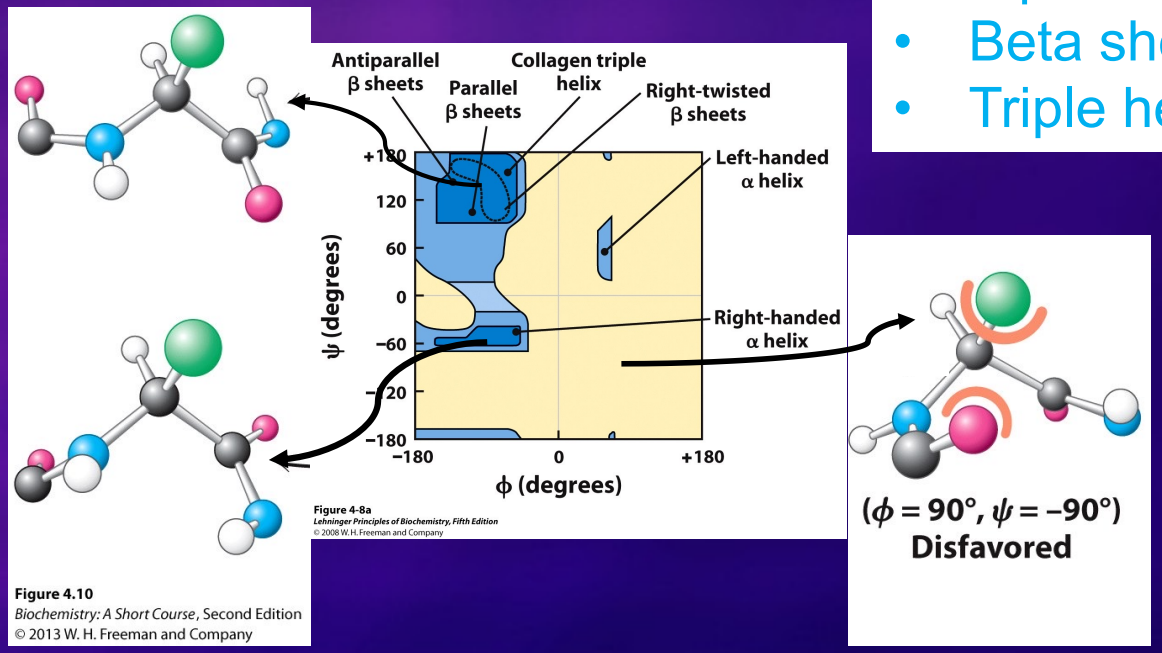



- Combinations of φ and ψ that lead to steric clash are are “disallowed.”
- “Allowed” combinations correspond to defined types of secondary structure.

# Ramachandran Diagram

- The resulting plots are **Ramachandran diagrams.**
- Blue regions are favorable angle combinations.

- Alpha helices
- Beta sheets
- Triple helix

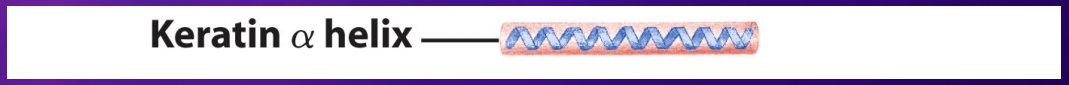


# Fibrous Proteins

- Elongated molecules with a single major type of secondary structure
- Many have *structural* roles (e.g., connective tissue)…mechanically strong yet flexible
- Rich in hydrophobic residues, so generally water insoluble
- Three examples today: keratin, fibroin, collagen

# Fibrous Protein #1: Alpha Keratin

- Alpha keratin is a primary component of epidermal tissues such as hair, wool, skin, horn, and nails.



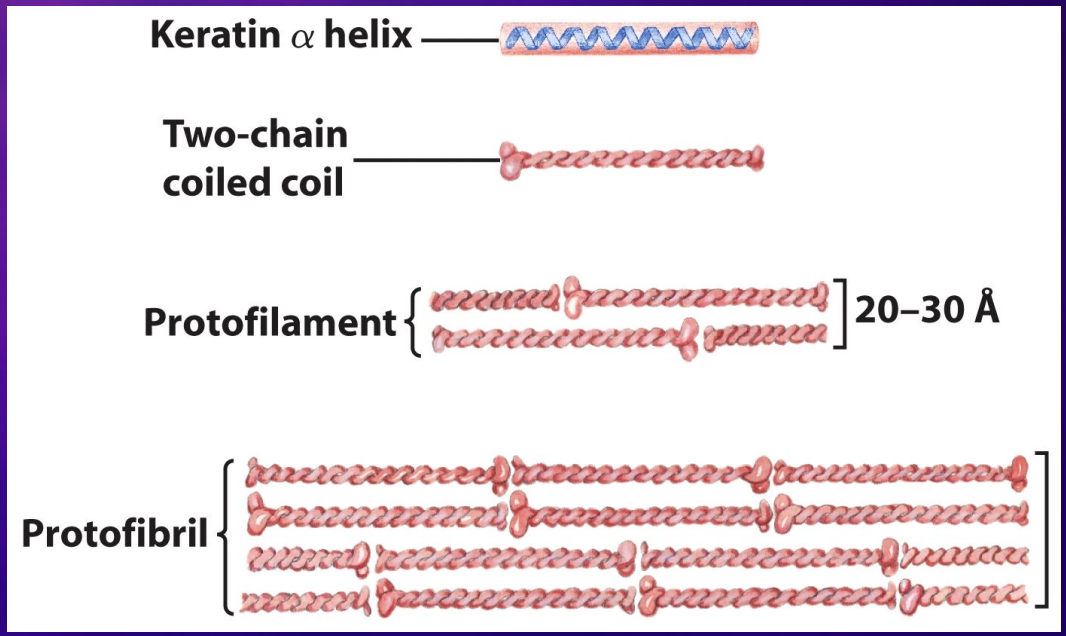

- Fundamental structure is an α–helix.



Fibers retain their shape even under mechanical stress…resist tearing

# Fibrous Protein #1: Alpha Keratin

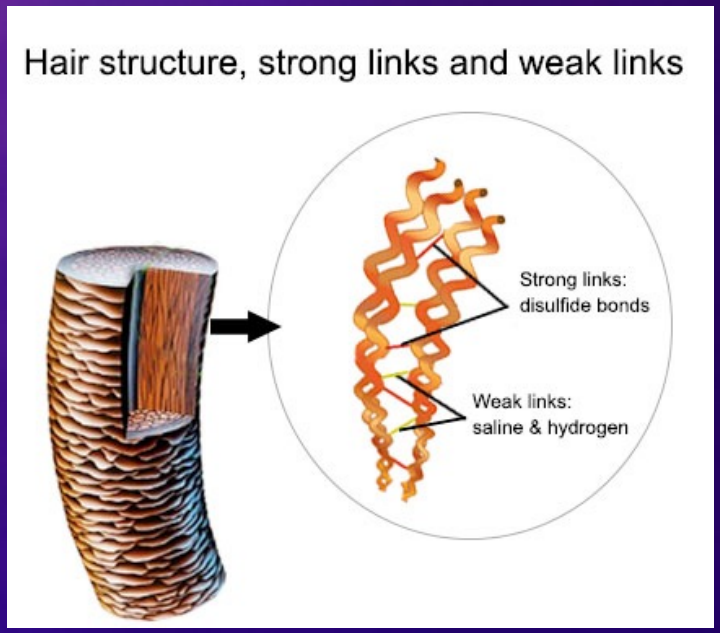
- Alpha keratin is a primary component of epidermal tissues such as hair, wool, skin, horn, and nails.
- Two $\alpha$–helices interact to make a "coiled coil."
- Coiled coils interact to make filaments/fibers.




Like strands of a rope!

# Fibrous Protein #1: Alpha Keratin

- Keratin is a family of proteins (54 keratin genes in humans).

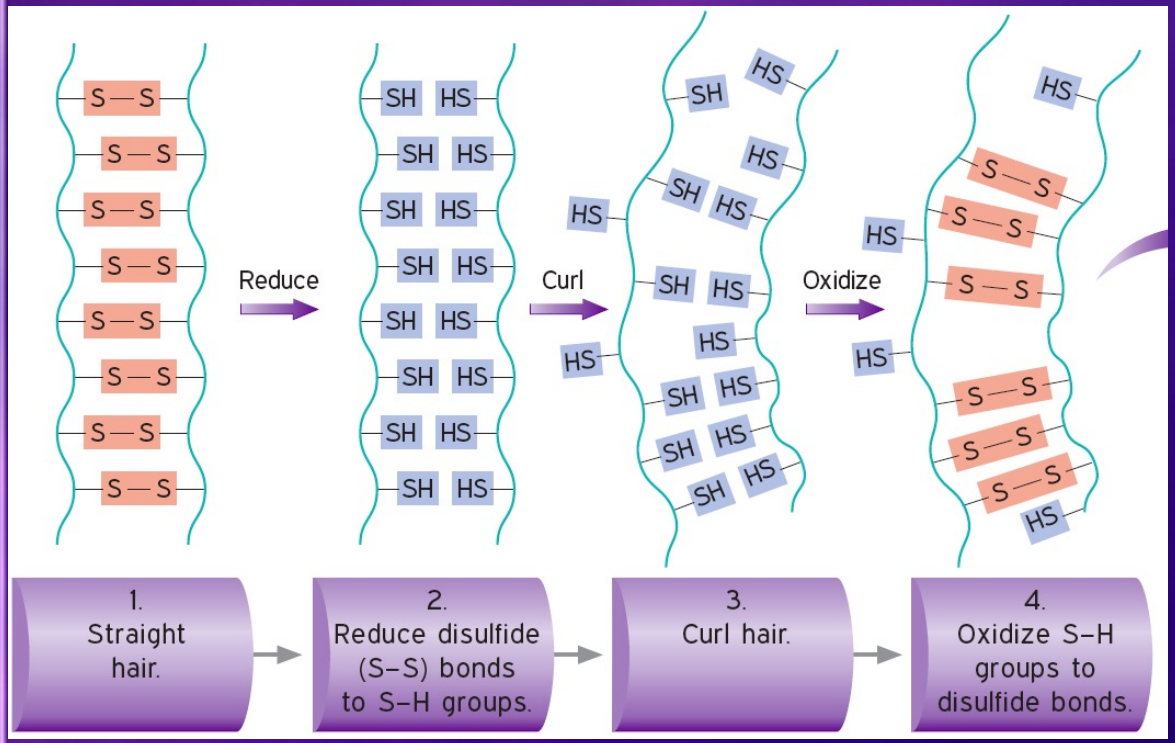



- High cysteine content (7%–20% of the total amino acid residues).

- One of the strongest biological materials, stabilized by intramolecular ($\alpha$–helix) and intermolecular disulfide bonds (between helices).

# Changing hair conformation






- Shown here is curling, as in a "perm."
- Straightening works the same way, except for Step 3!

# In-Class Question

"Hard" alpha-keratins are found in nails and horn, whereas "soft" alpha-keratins are found in skin and hair.

***How might the primary structures differ between these two types of keratins?***

# Fibrous Protein #1: Alpha Keratin

A 55-year-old man asks his PCP about a rough patch of skin on his forehead. He says it feels “like sandpaper” and has been there for months. He works outdoors and rarely uses sunscreen. The doctor takes a look and then explains that this rough patch is due to **hyperkeratosis**, excessive production of keratin in skin cells.

Keratin is an important structural protein in skin cells, but its production is normally regulated.

- How does the patient’s history put him at risk for hyperkeratosis?
- What is the net effect on skin cells and their function?
- Why is it critical to start treatment as soon as possible?

# Fibrous Protein #2: Fibroin

- Fibroin is a primary component of spider webs and insect silk (from silkworms).



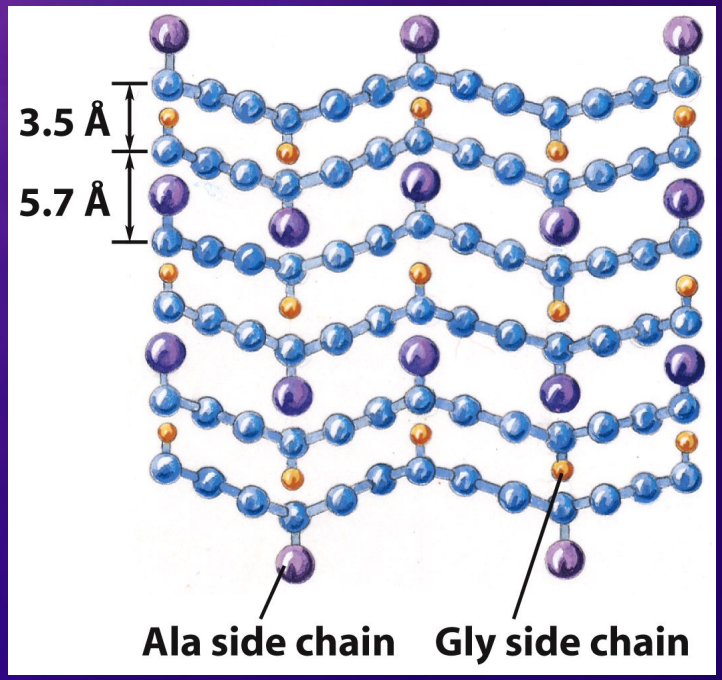


# Fibrous Protein #2: Fibroin



- Fibroin is a primary component of spider webs and insect silk.

- Fundamental structure is an anti-parallel beta sheet.

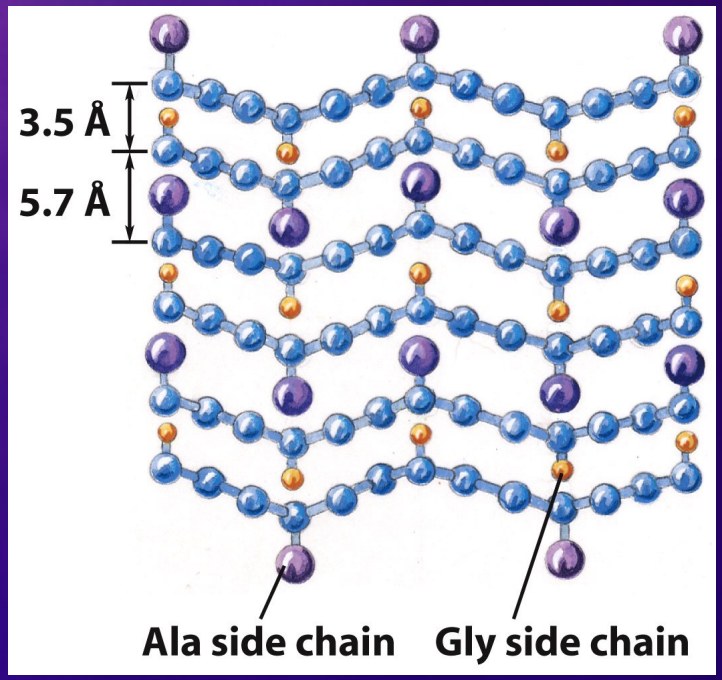



Strong and flexible but not stretchy!

# Fibrous Protein #2: Fibroin

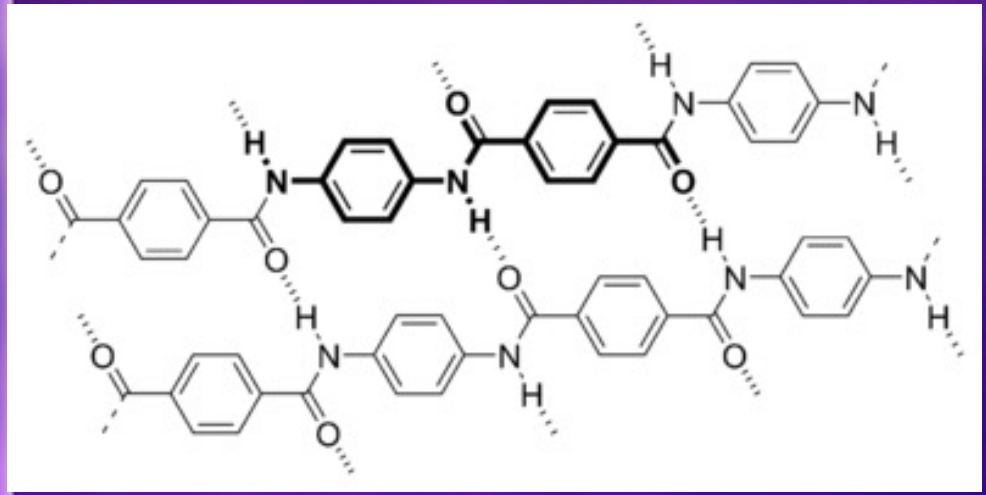
- Fibroin has a repeating motif: –[Gly-Ala-Gly-Ala]$_n$ –

- Close packing of the layers and lots of stabilizing H bonds




- High resistance to breaking under tension (strong) but low density (strength-to-density ratio exceeds that of steel).

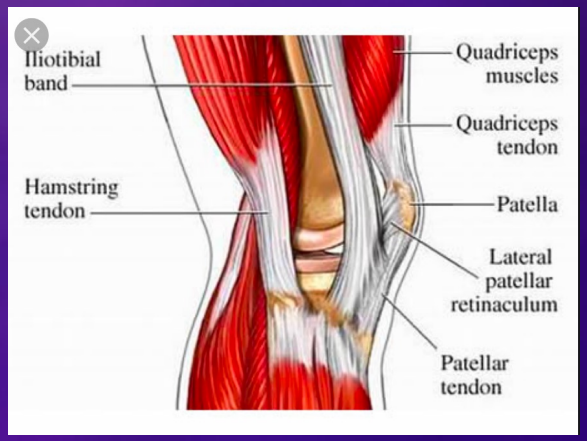
# Imitating Nature: Kevlar



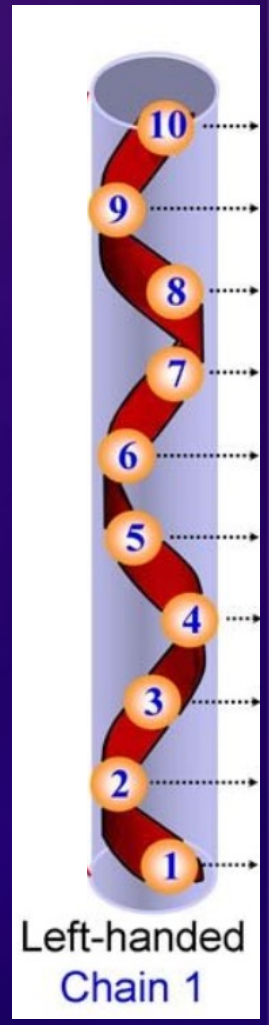


# Fibrous Protein #3: Collagen

- Collagen is a primary component of tendons, ligaments, cartilage, bones, skin, and teeth.

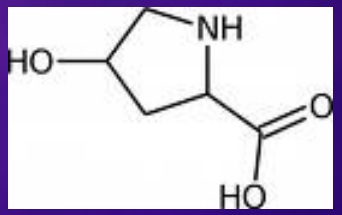



- Fundamental structure is a left-handed helix.

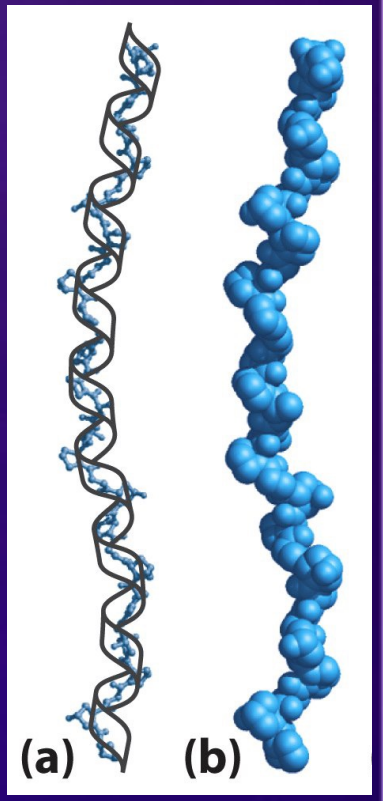


# Fibrous Protein #3: Collagen

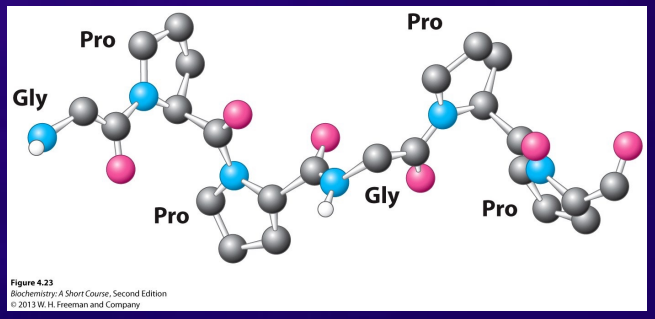
- Collagen is rich in the repeats [Gly-Pro-X] and [Gly-X-Hyp]




Hyp= Hydroxy-Proline

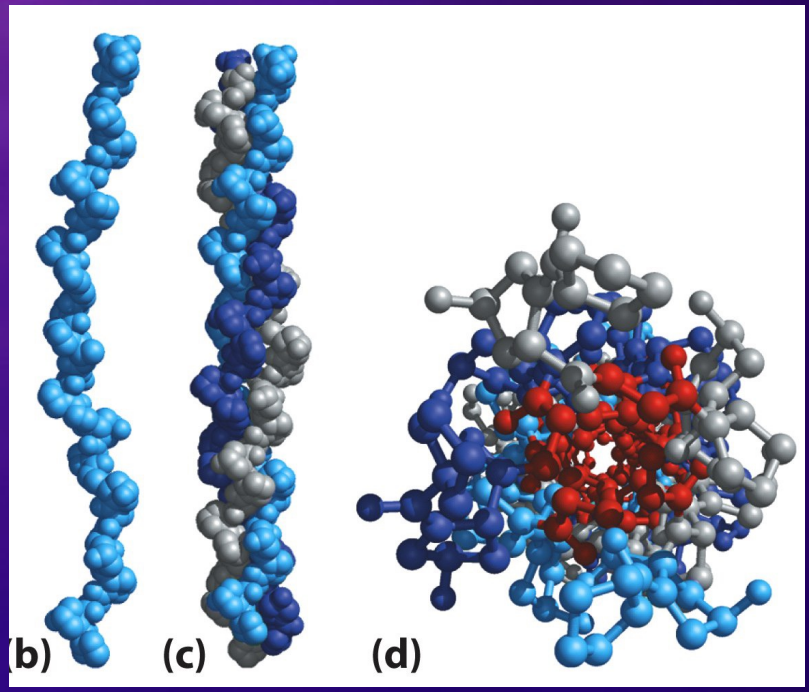



- No stabilizing H-bonds within the helix; Pro leads to an extended chain because of steric repulsion



# Fibrous Protein #3: Collagen

- Three left-handed chains pack closely to form a triple “super” helix
- Gly side chains line the interior.




- Vitamin C is required for hydroxylation of Pro, which enables H-bond interactions between chains.

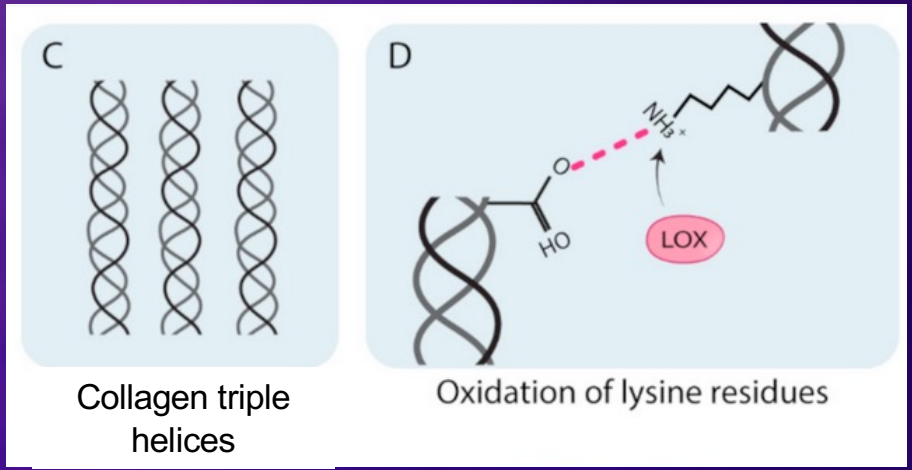
# In-Class Question

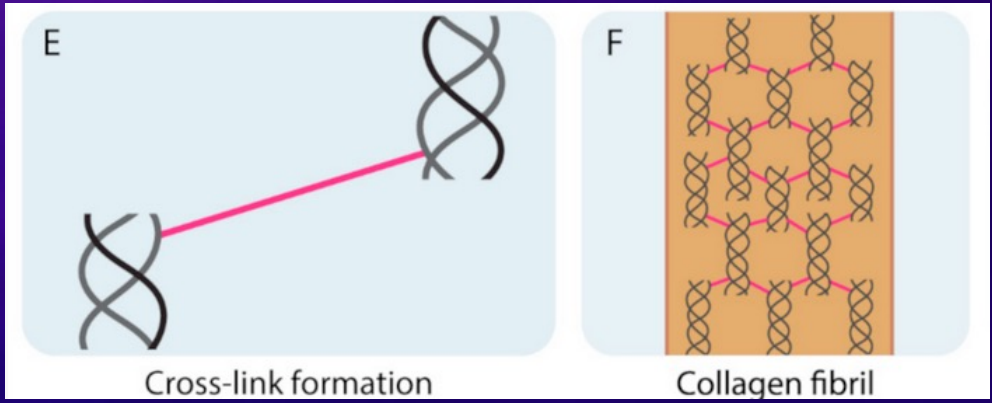
A deficiency of vitamin C leads to “scurvy,” which was historically quite common in sailors without access to fresh fruits and vegetables.

***What might be some signs and symptoms of scurvy? (Think about proteins and tissues affected.)***

# Cross-links

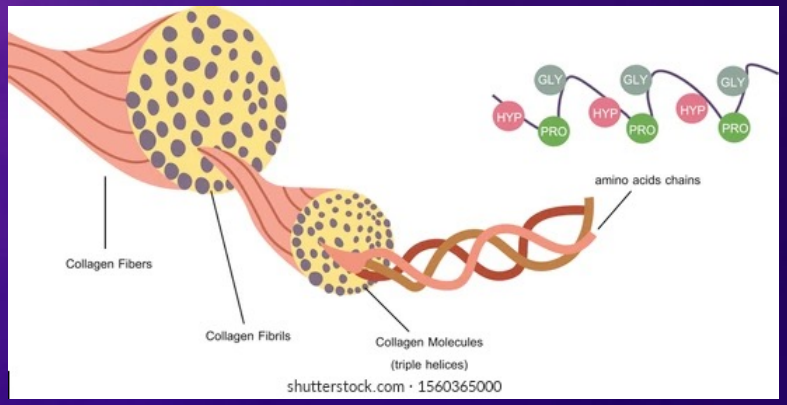
- An enzyme oxidizes some lysine residues
- Covalent cross-links between oxidized lysines stabilize formation of fibers



# Fibrous Protein #3: Collagen

- Collagen is a family of proteins (43 collagen genes in humans).




- Most abundant mammalian protein (25-35% of total body protein).

- Gram-for-gram, stronger than steel. Also has good resilience and can tolerate some stretching.

# Case Study: Collagen Defect

Type 1 collagen, found in skin, tendon, and bone, is assembled from the products of the *COL1A1* and the *COL1A2* genes. A mutation in *COL1A1* that replaces a glycine residue with an arginine in the protein is generally lethal.

***Q1. Why does the collagen structure not tolerate substitution of Arg for Gly?***

***Q2. What might be signs and symptoms of this type of mutation?***

# Case Study: Collagen Defect

## Child Abuse Uncovered in the ER?

Following a routine chest X-ray on an infant with high fever and a cough, Dr. John Carter of County General Hospital finds evidence of rib fractures. He calls Child Protective Services to report a suspected case of abuse and then takes more X-rays to document the case.



# Case Study: Collagen Defect



Osteogenesis imperfecta