



B1.2 Proteins

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Learning Outcomes

1SL Generalized Structure Of An Amino Acid

Students should be able to recognize and interpret the generalized structure of an amino acid, including the alpha carbon atom with an amine group, a carboxyl group, an R-group and a hydrogen atom. The general structure of an amino acid is provided in the data booklet.

2SL Condensation Reactions Forming Dipeptides And Longer Chains Of Amino Acids

Write the word equation for this reaction and draw a generalized dipeptide after modeling the reaction with molecular models.

3SL Dietary Requirements For Amino Acids

Essential amino acids cannot be synthesized and must be obtained from food. Non-essential amino acids can be made from other amino acids. Students are not required to give examples of essential and non-essential amino acids. Vegan diets require attention to ensure essential amino acids are consumed.

4SL Infinite Variety Of Possible Peptide Chains

Include the ideas that 20 amino acids are coded for in the genetic code, that peptide chains can have any number of amino acids, from a few to thousands, and that amino acids can be in any order. Be familiar with examples of polypeptides.

5SL Effect Of pH And Temperature On Protein Structure

Include the term denaturation.

6HL Chemical Diversity In R-Groups Of Amino Acids For Immense Diversity In Protein Form And Function

It is not required to give specific examples of R-groups. R-groups determine the properties of assembled polypeptides. R-groups are hydrophobic or hydrophilic and hydrophilic R-groups are polar or charged, acidic or basic.

7HL Impact Of Primary Structure On The Conformation Of Proteins

The sequence of amino acids and the precise position of each amino acid within a structure determines the three-dimensional shape of proteins. Proteins therefore have precise, predictable and repeatable structures, despite their complexity.

8HL Pleating And Coiling Of Secondary Structure Of Proteins

Include hydrogen bonding in regular positions to stabilize alpha helices and beta-pleated sheets.

9HL Tertiary Structure Hydrogen, Ionic, And Disulfide Covalent Bonds And Hydrophobic Interactions

It is not required to name examples of amino acids that participate in these types of bonding, apart from pairs of cysteines forming disulfide bonds. Amine and carboxyl groups in R-groups can become positively or negatively charged by binding or dissociation of hydrogen ions and that they can then participate in ionic bonding.

10HL Effect Of Polar And Non-Polar Amino Acids On Tertiary Structure Of Proteins

In proteins that are soluble in water, hydrophobic amino acids are clustered in the core of globular proteins. Integral proteins have regions with hydrophobic amino acids, helping them to embed in membranes.

11HL Quaternary Structure Of Non-Conjugated And Conjugated Proteins

Include insulin and collagen as examples of non-conjugated proteins and hemoglobin as an example of a conjugated protein. **NOS** Technology allows imaging of structures that would be impossible to observe with the unaided senses. For example, cryogenic electron microscopy has allowed imaging of single-protein molecules and their interactions with other molecules.

12HL Relationship Of Form And Function In Globular And Fibrous Proteins

There is a difference in shape between globular and fibrous proteins and their shapes make them suitable for specific functions. Use insulin and collagen to exemplify how form and function are related.

Guiding Questions

What is the relationship between amino acid sequence and diversity in form and function of proteins?

How are protein molecules affected by their chemical and physical environments?

Linking Questions

How do abiotic factors influence the form of molecules?

What is the relationship between the genome and the proteome of an organism?

1 Generalized Structure Of An Amino Acid

Amino acids are monomers of proteins.

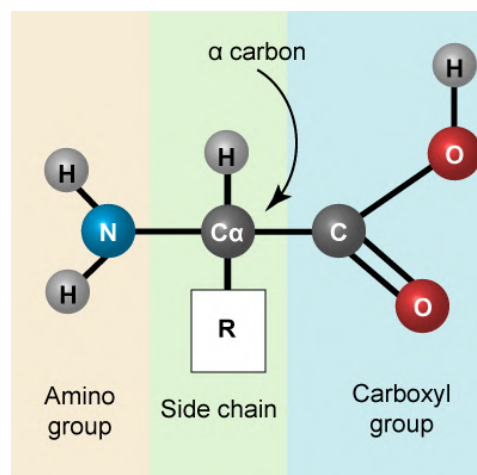
There are 20 amino acids each with a unique R group.

The carboxyl group is acidic as it can donate a proton.

The amine group is basic as it can accept a proton.

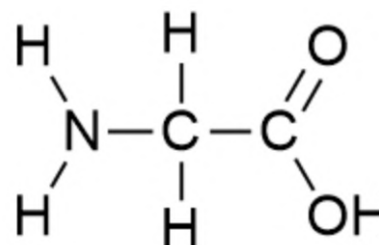
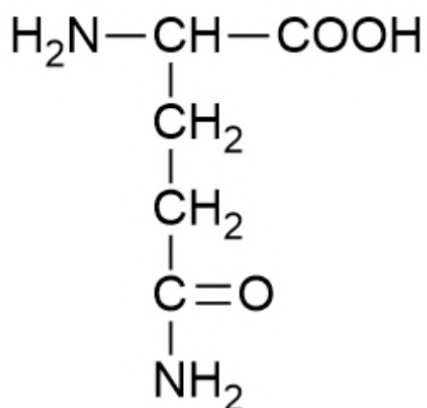
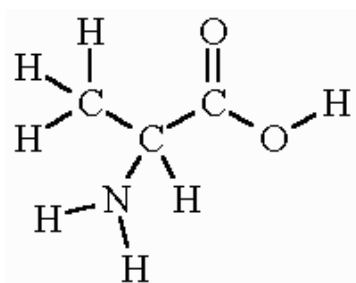
Amphiprotic molecules can act as an acid or a base.

The carbon atoms form strong covalent bonds.



[Libre Texts](#)

Circle and label the parts of each amino acid below:

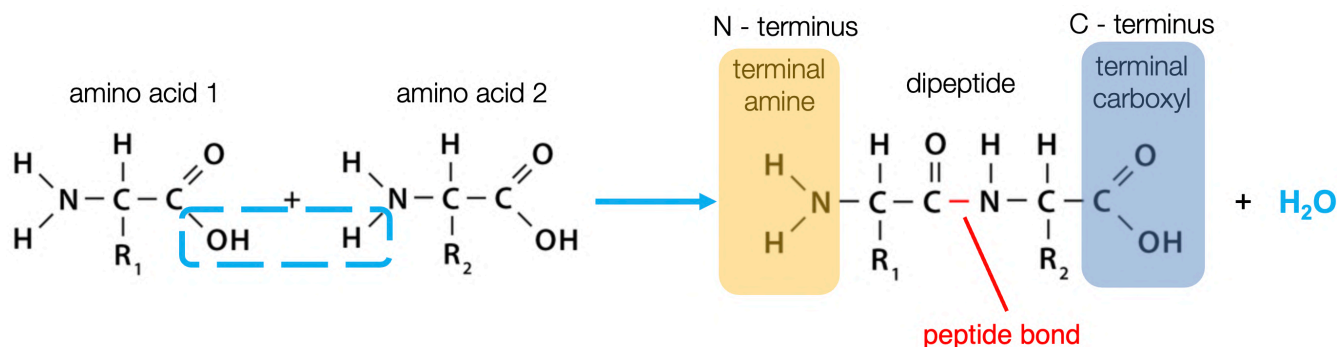


*"It is one of the more striking generalizations of biochemistry ...
that the twenty amino acids and the four bases, are, with minor reservations,
the same throughout Nature."*

Francis Crick

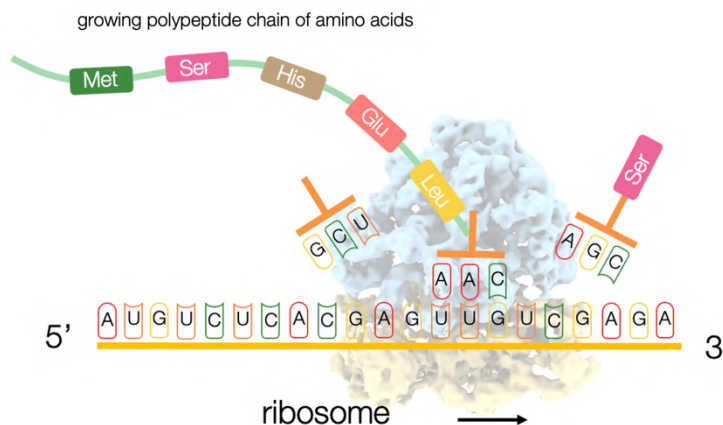
2SL Condensation Reactions Forming Dipeptides And Longer Chains Of Amino Acids

Amino acids are linked by peptide bonds (C-N) to form a dipeptide by a condensation reaction.



Many amino acids are linked to form a long chain called a polypeptide. An oligopeptide is a short chain of polypeptides 3-20 amino acids in length. Ribosomes catalyze the formation of peptide bonds. Proteins are made of one or more polypeptides. The sequence of amino acids determines the three-dimensional shape and function of the polypeptide.

New amino acids are added to the carboxyl end of a growing polypeptide chain.



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Draw a dipeptide below.

Circle the N-terminus and C-terminus – amino acids are always added to the C- terminus.

3SL Dietary Requirements For Amino Acids

Plants can make all 20 amino acids.

Animals obtain their amino acids from plants or other animals.

Humans can synthesize 11 different amino acids but 9 have to come from our diet:

essential amino acids – cannot be synthesized in sufficient quantities so must be obtained in the diet

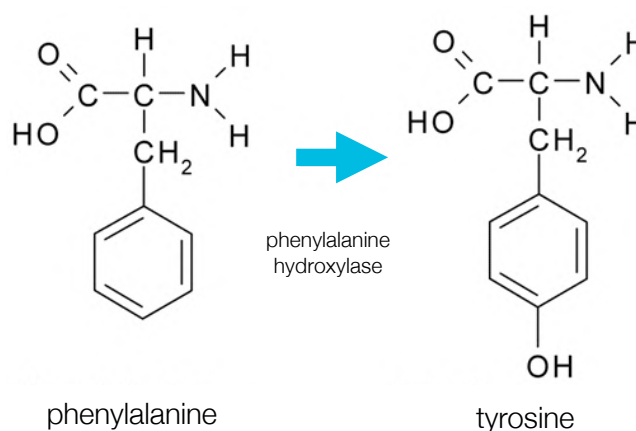
non-essential amino acids – can be synthesized from other amino acids

conditionally essential amino acids – essential in diet due to an illness, mutation or premature birth

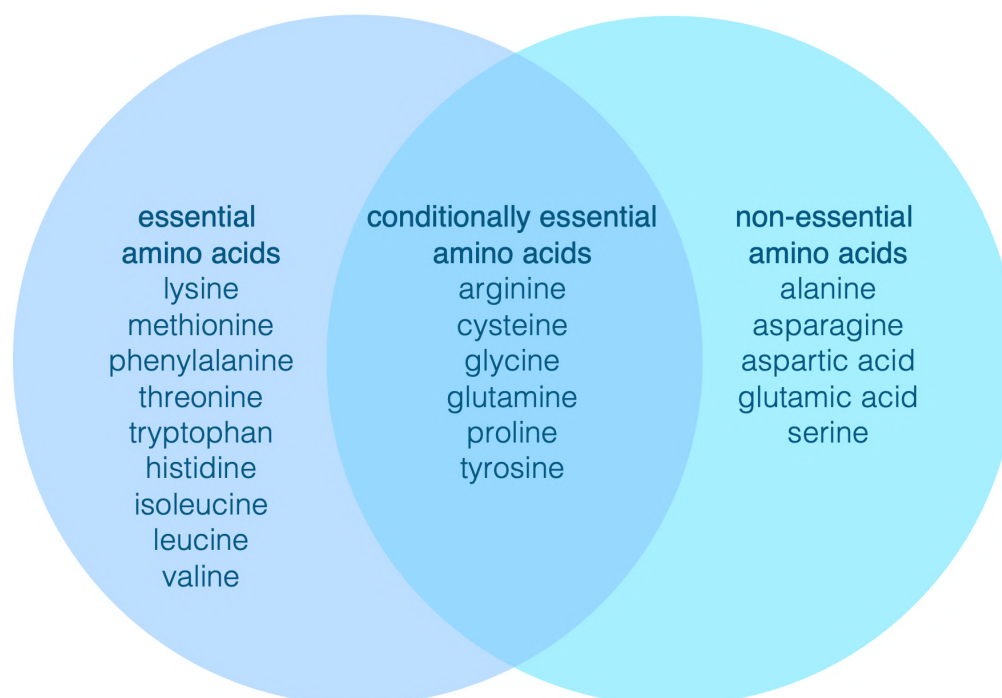
Phenylalanine is essential in the diet. Tyrosine can be made from phenylalanine so it is not essential.

However, if there was a mutation in phenylalanine hydroxylase enzyme then tyrosine would need to come from the diet.

A build-up of phenylalanine in body tissues due to this mutation is called phenylketonuria (PKU) and leads to brain damage without a modified diet.



Nine amino acids are essential in humans – (no need to memorise them all)

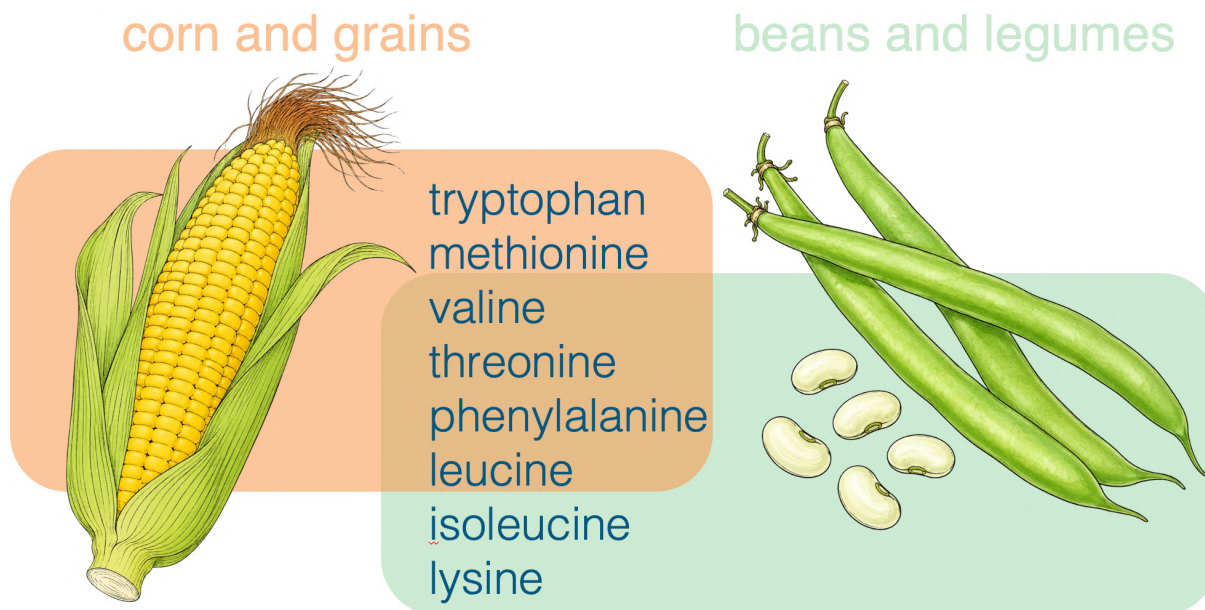


Conditionally essential amino acids only become essential during rapid growth/repair, pregnancy or illness. During these times our bodies may not produce enough.

Amino acids cannot be stored in the body for long.
They are constantly broken down in the liver by deamination.

Meat contains the right balance of amino acids.
It has a high bioavailability of amino acids and other nutrients including iron, zinc, Vit B₁₂, and Vit D.

A vegan diet does not include meat, eggs or dairy foods.
Plants may be low (deficient) in some amino acids.
A variety of plant foods are required in the diet each day to ensure intake of all essential amino acids.



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Corn and grains are low in isoleucine and lysine, while beans and legumes are low in tryptophan and methionine; a varied diet can provide all essential amino acids over the day.

A vegan diet can also be supported with supplements and foods fortified with essential nutrients.

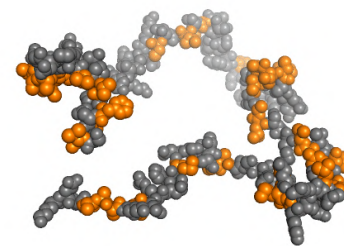
4SL Infinite Variety Of Possible Peptide Chains

DNA specifies 20 amino acids using codons.
Polypeptide chains may contain few to tens of thousands of amino acids.

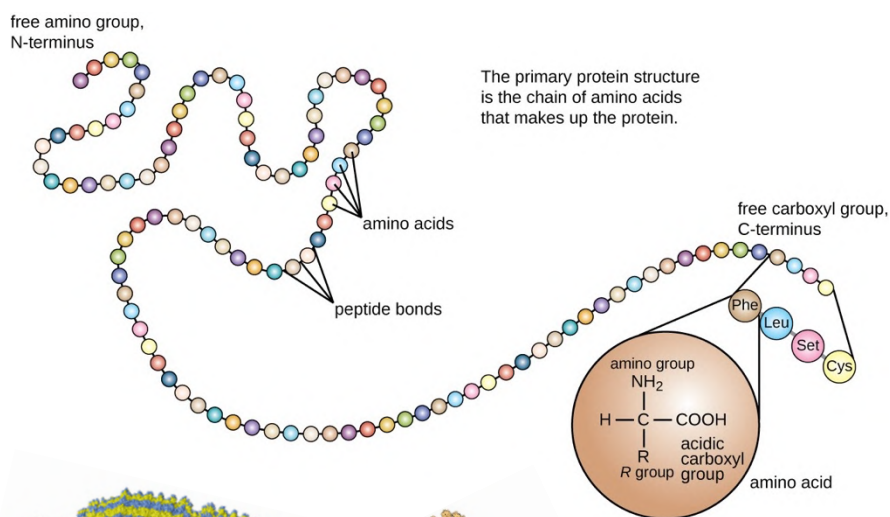
A dipeptide has 20×20 (20^2) possible arrangements.
A tripeptide has $20 \times 20 \times 20$ (20^3) possible unique sequences.
There are (20^n) possible sequences for a polypeptide with n amino acids.

A polypeptide chain of 400 amino acids has 20^{400} possible sequences.
There may be 10^{80} atoms in the universe.
A near infinite array of unique polypeptides can thus be formed so that an endless variety of molecular machinery can be produced.

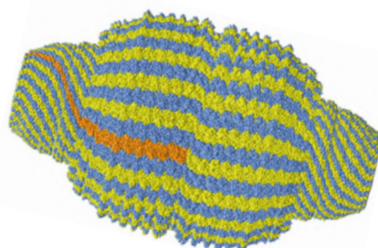
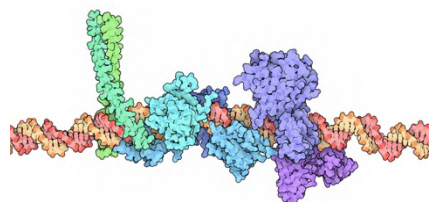
However, most of the random sequences would not be expected to be functional. It would be like reading a book of sentences made up of random letters of the alphabet. Functional proteins require meaningful information to determine a specific sequence of amino acids in the polypeptides.



Protein folding [animation](#) [Jakubowski](#)



[WOU](#)



[PDB](#)

Good introduction to [proteins](#).

protein	function	polypeptides	length of amino acids	description
beta-endorphin	natural pain killer	1	31	secreted by pituitary gland neuropeptide
insulin	hormone	2	21 and 30	signals cells to absorb glucose globular
alpha amylase	enzyme	1	496	contains Cl and Ca atoms globular
titin	elastic protein	1	34 000	in muscle tissue fibrous

5SL Effect Of pH And Temperature On Protein Structure

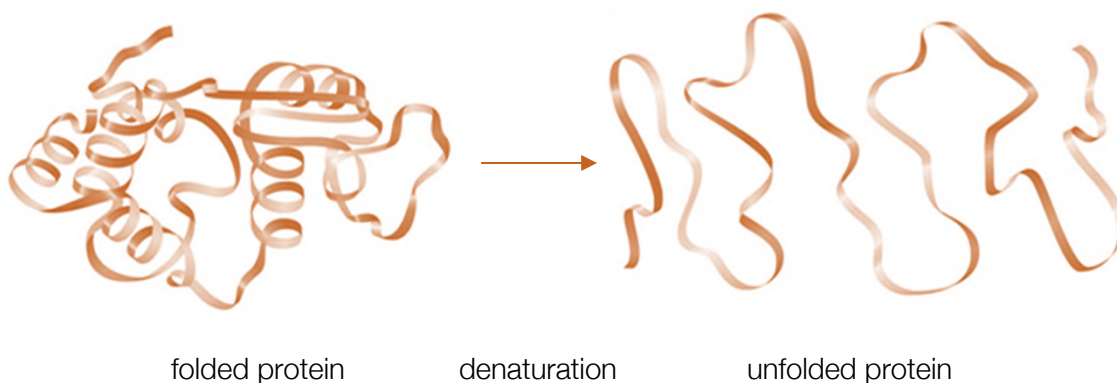
denaturation - a usually permanent change and loss of function in a protein

proteins:

- polypeptide chains fold into a specific 3D shape (conformation) due to amino acid sequence
- bonds between R-groups help determine shape
- breaking of bonds between R groups causes the protein to denature and unfold
- soluble proteins often become insoluble as hydrophobic R-groups become exposed to water

denaturation:

- temperature
 - increased kinetic energy from heat can break bonds by vibration of molecules
 - egg white (albumen) contains albumin protein that turns into an insoluble, opaque, white solid when heated
 - thermophilic bacteria have heat stable enzymes at 80°C or higher
 - Taq DNA polymerase from *Thermus aquaticus* (Taq) bacterium has an optimum of 80°C
- pH
 - extremes of pH break ionic bonds between R-groups that have a + or – charge
 - hydrogen bonds can also break changing the shape of the protein



6HL Variety in R-Groups Enables Immense Diversity In Protein Form And Function

The 20 amino acid R groups allow a great variety of shapes and functions.

Hydrophobic non-polar R groups:

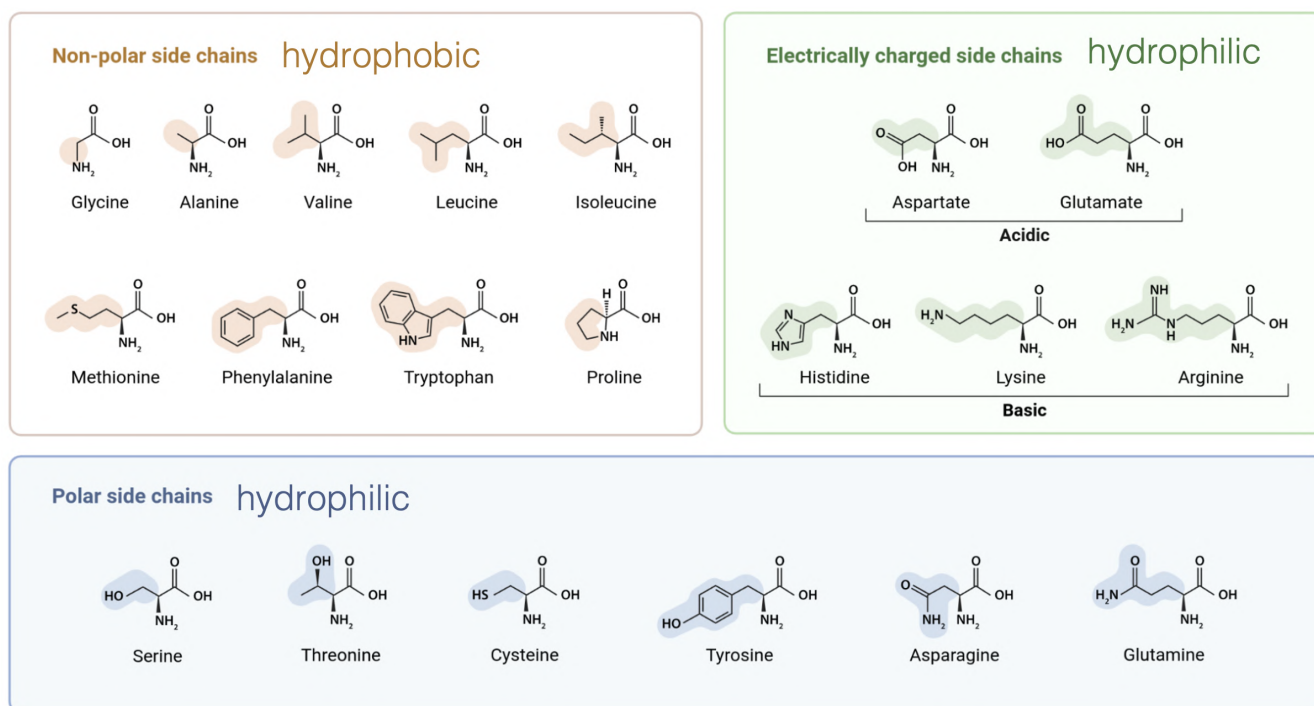
- insoluble in water
- often buried inside water soluble proteins such as enzymes
- are exposed on regions of integral membrane proteins to help lock them into a cell membrane

Hydrophilic polar R groups:

- soluble in water
- carry a partial positive (δ^+) and negative (δ^-) charge allowing hydrogen bonds to form
- face outwards in a water soluble protein

Hydrophilic charged R groups:

- acidic R groups are negatively charged
- basic R groups are positively charged
- can form ionic bonds with other R groups



Sally Kim

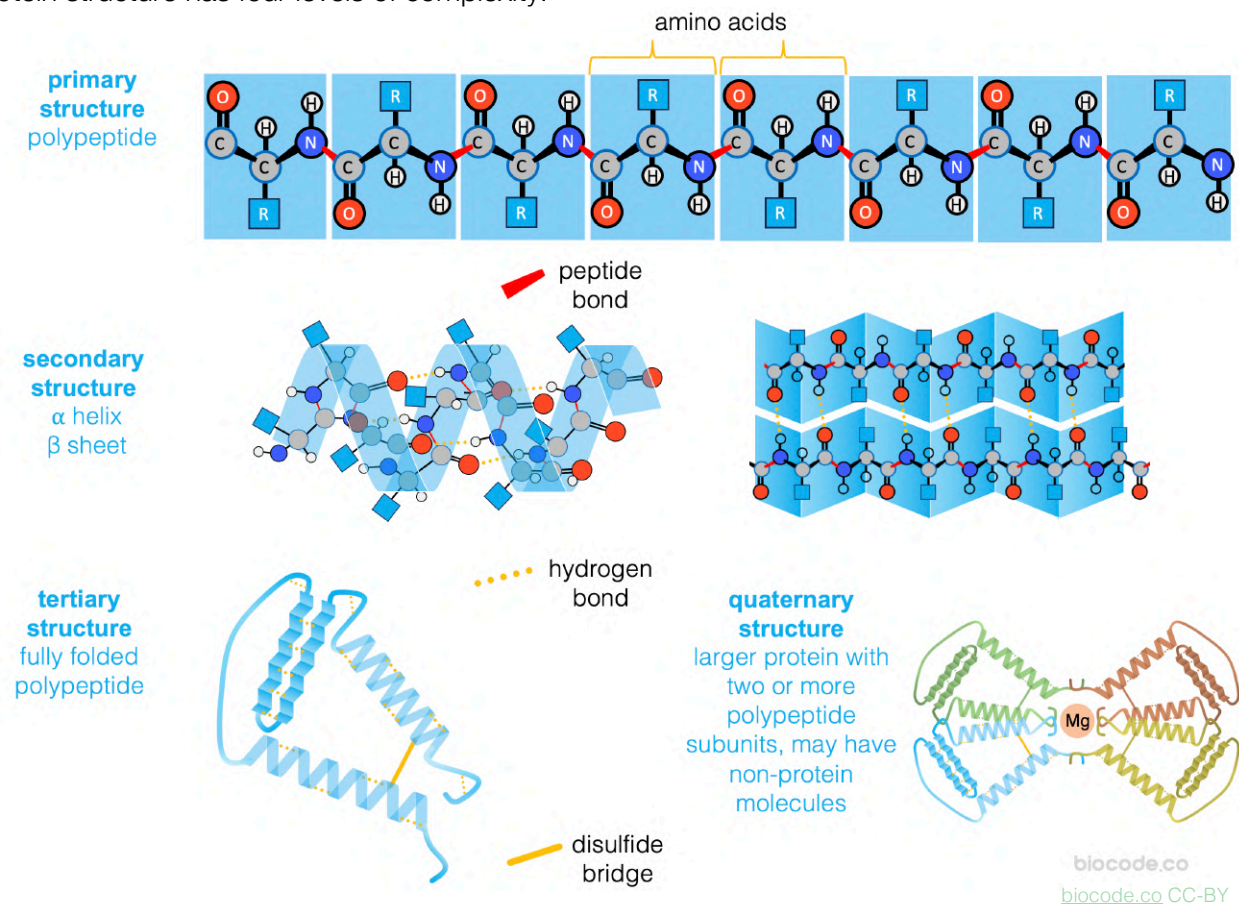
Amino acids can be modified after translation.

Proline is modified by hydroxylase to hydroxyproline in collagen to make it more stable

- vitamin C is needed to make hydroxylase enzyme
- scurvy is caused by reduced hydroxyproline in collagen

7HL Impact Of Primary Structure On The Conformation Of Proteins

Protein structure has four levels of complexity.



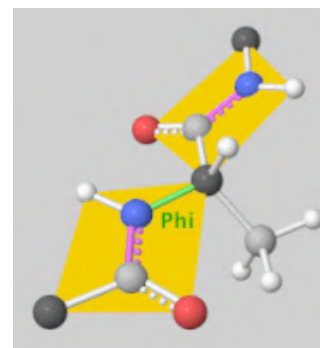
primary structure – determined by the sequence of amino acids in the polypeptide
 - controls all other levels of folding and 3D shape

A particular amino acid sequence is predictable – it will always give the same precise shape and function to a protein no matter how complex the sequence may be. The same complex protein can be made perfectly as many times as needed as long as the correct amino acid sequence is provided.

A polypeptide backbone allows folding into any shape (conformation) by:

- o a repeating sequence of covalent peptide bonds -C- α -N-C- α -N-
- o each with a tetrahedral bond angle
- o rotation of the backbone occurs around each alpha carbon atom

Imagine a very large Lego set but, with only 20 different kinds of pieces and this Lego set must be put together in a long string – this seems too limiting. However, each piece can rotate, is very small, can make side chain connections and non-protein elements can be inserted - now an almost infinite variety of sophisticated and complex engineering solutions can be constructed.



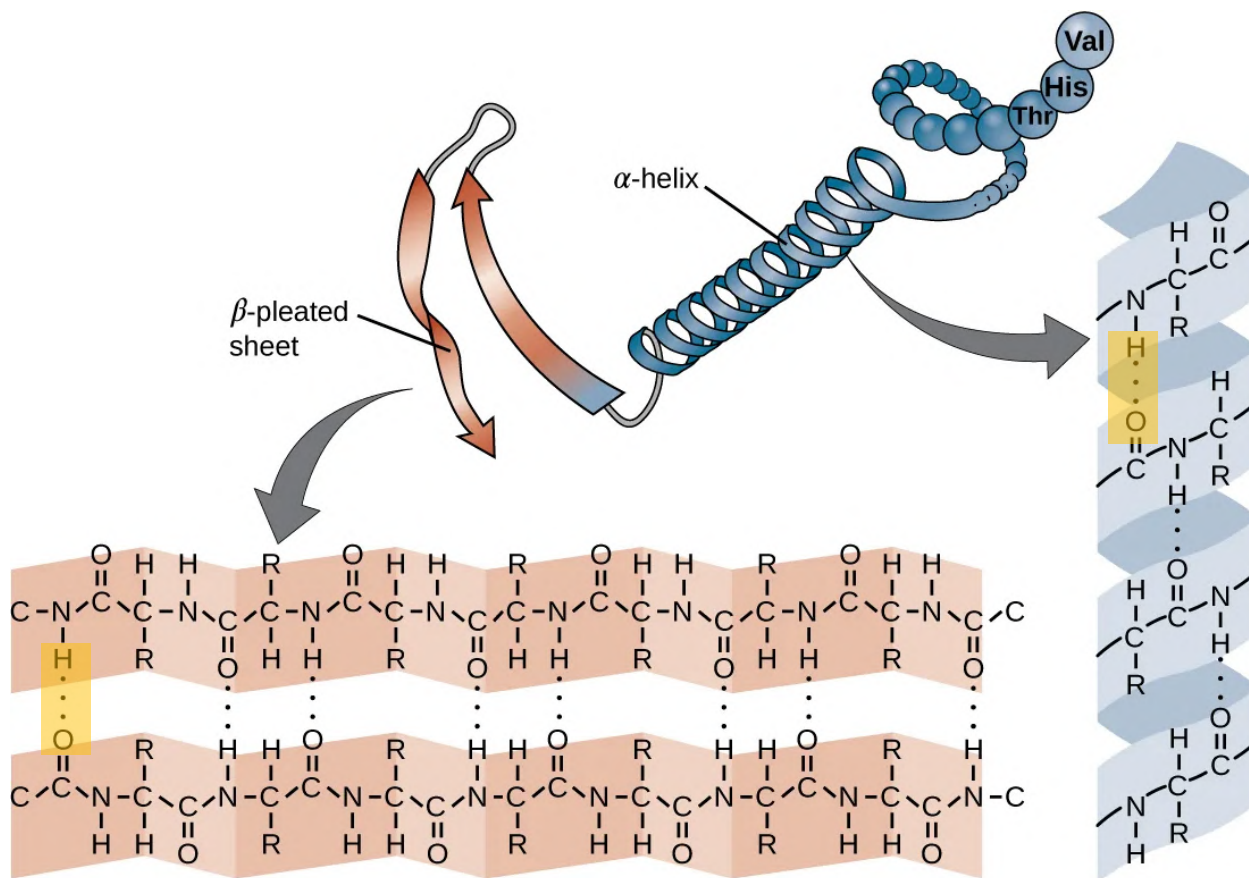
Animation Herraez

Over 180 000 proteins have been filed in the [Protein Data Bank](https://www.rcsb.org/) (PDB) – with more to be discovered.

8HL Pleating And Coiling Of Secondary Structure Of Proteins

secondary structures - formed by **hydrogen bonds** between non-adjacent amino acids

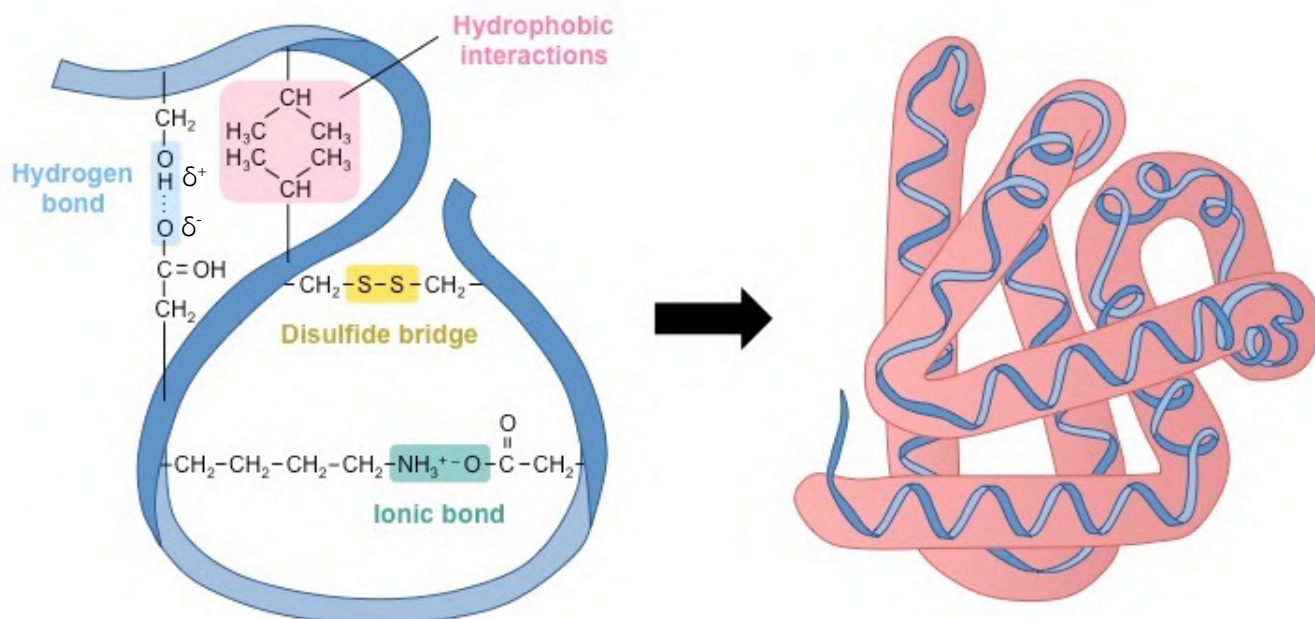
- between C=O and N-H groups along the polypeptide
- H is slightly positive and O is slightly negatively charged
- two common structures are the alpha helix and beta pleated sheet



[Download for free at OpenStax](#)

9HL Tertiary Structure

tertiary structure - three-dimensional shape of a polypeptide determined by R-groups



[bioninja](#)

Includes the following bonds:

ionic bonds

- form between oppositely charged R groups
- acidic R-groups can lose H^+ and become negatively charged, $COOH$ becomes COO^-
- basic R-groups can gain H^+ and become positively charged, NH_2 becomes NH_3^+
- sensitive to pH changes

hydrogen bonds

- weak / common
- between polar R groups
- H has a partial positive charge (δ^+) when covalently bound to an electronegative atom eg N or O
 - allows H to weakly attract a nearby electronegative atom which has a slight negative charge (δ^-)
 - recall that electronegative atoms pull shared electrons strongly toward themselves

disulfide bonds

- between pairs of cysteines
- strong covalent bond

hydrophobic interactions

- between nonpolar R groups
- tend to form in the middle of the protein away from contact with water

Folding occurs as a polypeptide forms during translation from the ribosome. Sometimes chaperone proteins help a polypeptide to fold correctly.

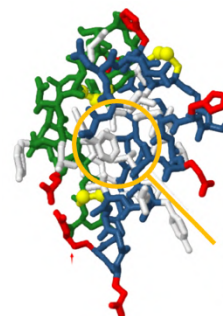
10HL Effect Of Polar And Non-Polar Amino Acids On Tertiary Structure Of Proteins

globular proteins are often:

- water soluble with hydrophilic amino acids on their surface and hydrophobic amino acids are found at their centre
example – insulin

integral membrane proteins

- have hydrophobic amino acids on parts of their surface to embed into the fatty acid tails of the membrane



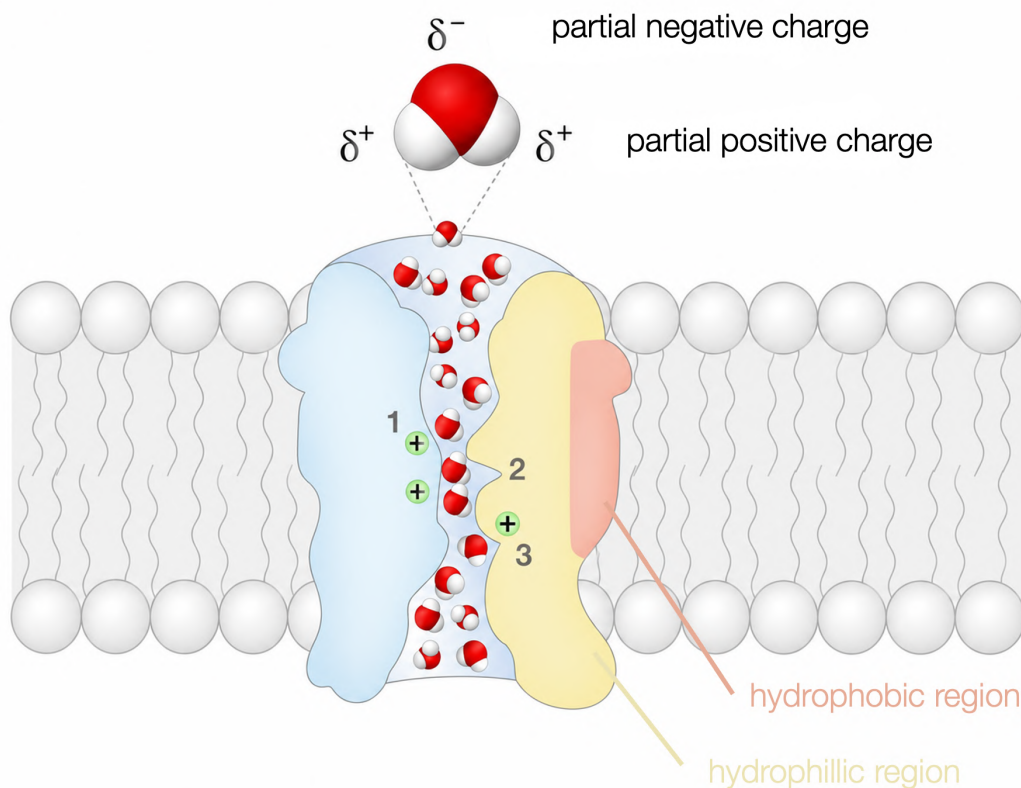
hydrophobic core of insulin

[PDB](#)

channel proteins are transmembrane integral proteins:

- a belt of surface hydrophobic amino acids face the fatty acid tails to embed into the membrane
- have hydrophilic amino acids lining the pore to control width and charge of channel
 - both ends of the protein have hydrophilic amino acids

aquaporin – channel protein that allows only water across a membrane one molecule at a time



[adapted Wolber](#)

11HL Quaternary Structure Of Non-Conjugated And Conjugated Proteins

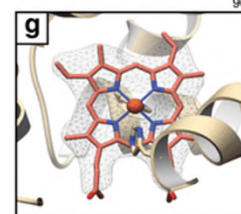
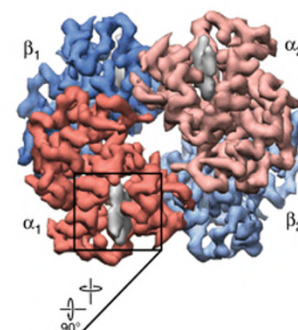
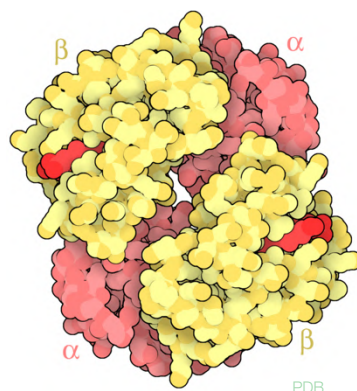
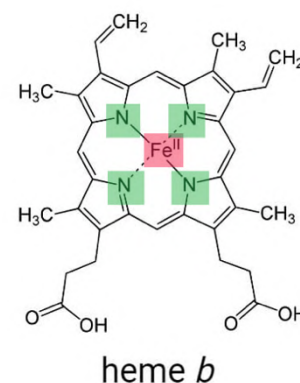
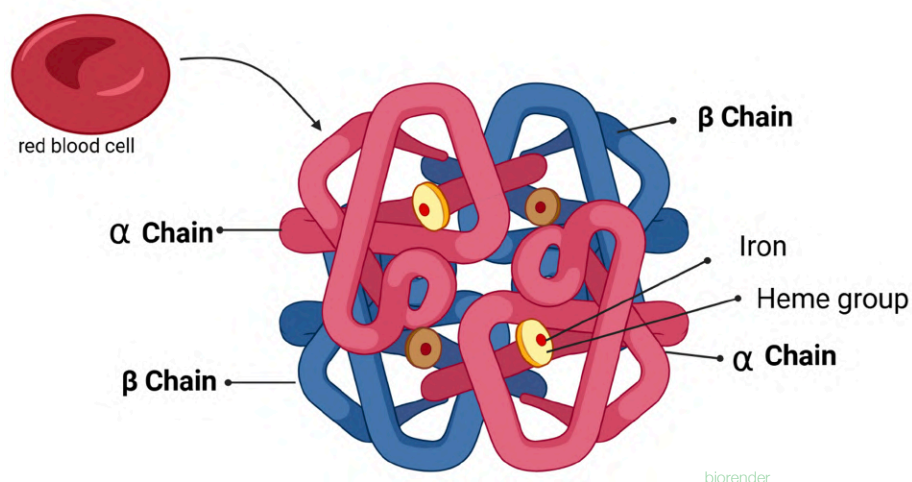
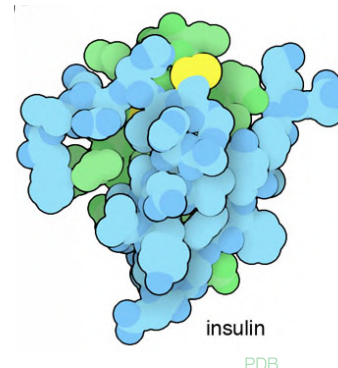
quaternary structure – 3D shape determined by two or more polypeptides

non-conjugated protein:

- have one or more polypeptides and no prosthetic group
- insulin has two polypeptides linked by 3 disulfide bonds
- collagen has three polypeptides, insulin has two polypeptide chains

conjugated protein:

- have one or more polypeptides and one or more prosthetic groups
- hemoglobin has four polypeptides and four iron containing heme groups



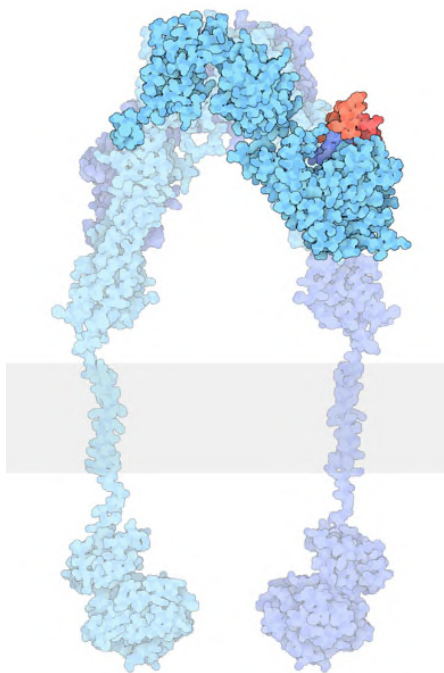
Hemoglobin is 5nm wide.

Cryo-EM is accurate up to about 0.12nm

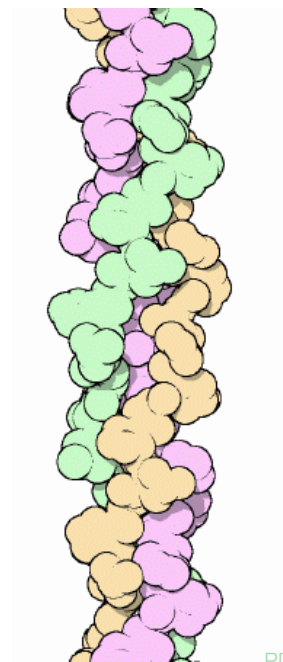
- can determine location of atoms
- reveal conformational changes frozen in place during sample preparation that are usually too rapid to observe
- allows function of a protein to be predicted
- not possible without powerful computer processors and image processing software
- many discoveries can now be made

12HL Relationship Of Form And Function In Globular And Fibrous Proteins

globular proteins	fibrous proteins
specific rounded shape	long polypeptides form fibers or sheets
specific amino acid sequence	repetitive amino acid sequence
often water soluble often hydrophobic R groups in centre	often water insoluble often hydrophobic R groups on surface
enzymes, receptors, transporters, hormones	structural support
sensitive to pH, temperature	less sensitive to pH, temperature
insulin is a hormone, small and water soluble to move through bloodstream, has a specific shape to match an insulin receptor	collagen – has three polypeptides that form a triple helix, each polypeptide has three repeating amino acids, has high tensile strength for connective tissues



insulin (red) insulin receptor (blue) [PDB](#)



[PDB](#)

collagen – a three stranded cord is not easily broken