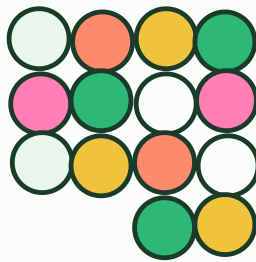


REVISION GUIDE

Twenty amino acids, *endless* shapes

Proteins

Every protein in you is a chain of the same twenty building blocks. The order they are joined in decides the shape the chain folds into, and the shape decides the job. Heat or the wrong pH and the shape, and the job, are gone.



12 chapters

The interactive guide, with every animation:

biologybybradford.com/guides/ib-biology-b1-2-proteins



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06	The R groups decide how a chain behaves HL	17
07	The sequence sets the shape HL	19
08	Coils and pleats held by hydrogen bonds HL	22
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11	More than one chain: quaternary structure HL	28
12	Balls and ropes: globular and fibrous proteins HL	30
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By the end you can

- ☐ Draw a generalised amino acid and name the four groups on its alpha carbon B1.2.1
- ☐ Explain how condensation joins amino acids with peptide bonds, write the word equation and draw a dipeptide B1.2.2
- ☐ Explain why some amino acids must come from food, and what that means for a vegan diet B1.2.3
- ☐ Explain why the number of possible polypeptides is practically endless B1.2.4
- ☐ Explain how heat and pH denature a protein, and why it then stops working B1.2.5
- ☐ Classify R groups and explain how they set the properties of a polypeptide B1.2.6
- ☐ Explain how the sequence of amino acids gives every copy of a protein the same precise shape B1.2.7
- ☐ Describe the alpha helix and beta-pleated sheet and the hydrogen bonds that hold them B1.2.8
- ☐ Name the four kinds of bond that hold a tertiary structure, and say where polar and non-polar R groups end up B1.2.9, B1.2.10
- ☐ Compare insulin, collagen and haemoglobin: chains, conjugated or not, globular or fibrous, and how form suits function B1.2.11, B1.2.12

Tick each one when you can do it without the book.

01

B1.2.1 GENERALISED STRUCTURE OF AN AMINO ACID

Every amino acid is built on the same *core*

A protein is a polymer (B1.1), a long chain of the same kind of unit joined end to end. The units are **amino acids**, and every one of them starts from the same pattern.

At the middle sits one carbon atom, the **alpha carbon**. Carbon always makes four bonds, and here they go to four different things: an **amine group** (-NH_2), a **carboxyl group** (-COOH), a single hydrogen atom and an **R group**. The name says it: "amino" from the amine group, "acid" from the carboxyl group, which can give up a hydrogen ion.

The R group is the only part that varies. The genetic code uses twenty different R groups, so there are twenty amino acids. The smallest R group is a single hydrogen atom, and others are chains or rings, some containing oxygen, nitrogen or sulfur. At standard level you do not need to name any of them.

KEY POINTS

- Draw the alpha carbon in the middle, the amine group on one side and the carboxyl group on the other, hydrogen and R above and below.
- Show every atom and every bond, in the un-ionised form (-NH_2 and -COOH), as the markschemes do.
- Count the bonds: four on carbon, three on nitrogen, two on oxygen, one on hydrogen.

KEY TERMS

amino acids

The monomers of proteins. Each has an amine group, a carboxyl group, a hydrogen atom and an R group on one central carbon.

alpha carbon

The central carbon of an amino acid. It makes four single bonds, to an amine group, a carboxyl group, a hydrogen atom and an R group.

amine group

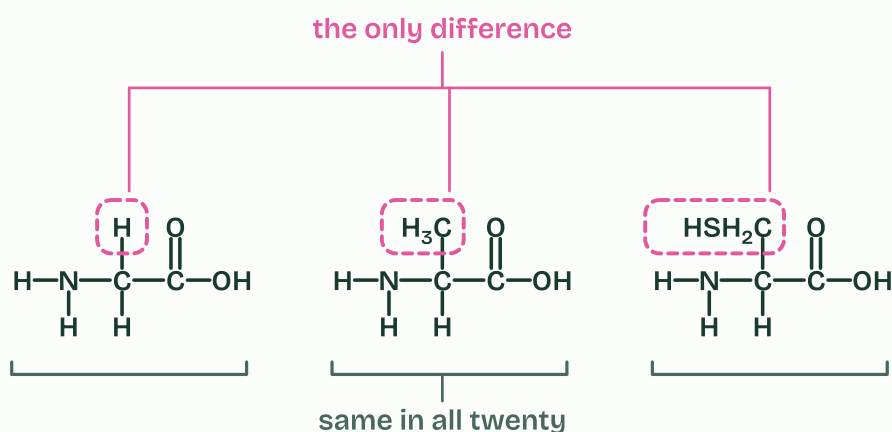
The group -NH_2 : a nitrogen atom bonded to two hydrogens. It is the amino part of the name.

carboxyl group

The group -COOH : a carbon with a double bond to one oxygen and a single bond to an OH. It can give up a hydrogen ion, which is why it is an acid.

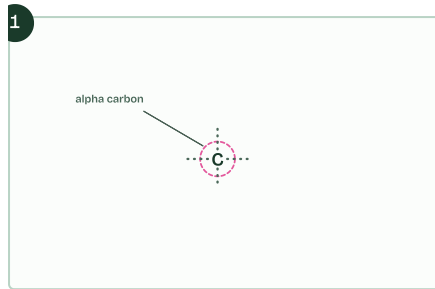
R group

The side chain of an amino acid: the one part that differs between the twenty. R stands for whatever group it is, not for an element.

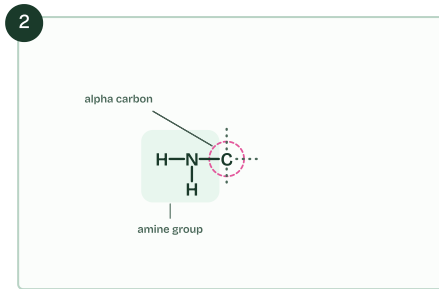


STEP BY STEP

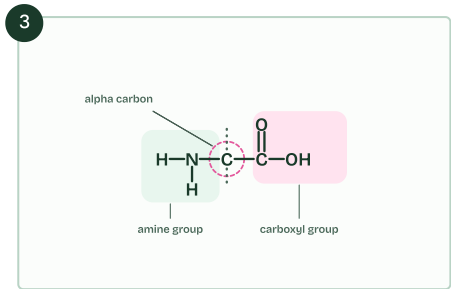
6 STEPS



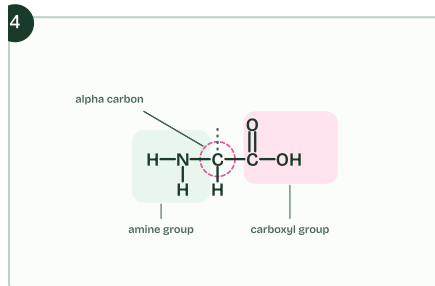
The **alpha carbon** makes four bonds.



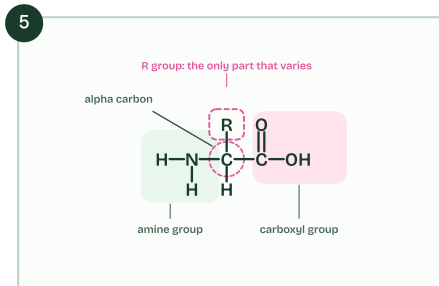
An **amine group** goes on the left bond: a nitrogen with two hydrogens.



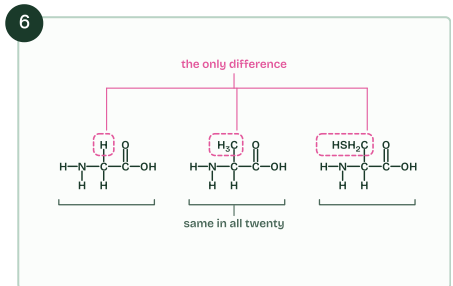
A **carboxyl group** goes on the right bond: a carbon with a double bond to one oxygen and a single bond to an OH.



One **hydrogen** atom goes on the bottom bond.



The last bond carries the **R group**. It stands for whatever side chain this amino acid has.



Three different amino acids: the same core in each, and only the **R group** differs.

REMEMBER IT

The four groups on the alpha carbon

A A Amine group -NH₂, on one side	C Cat Carboxyl group -COOH, on the other side	H Has Hydrogen one H atom	R Rhythm R group the only part that varies
--	---	---	--

WATCH OUT

R is not an element. It stands for the side chain, whatever it is in that amino acid. And check every drawing by counting bonds: four on every carbon, three on nitrogen, two on oxygen, one on hydrogen.

PREDICT

A student draws an alpha carbon bonded to -NH₂, -COOH, R and -OH. What is wrong with the drawing?

- (A) Nothing is wrong: the alpha carbon can carry any four groups, as long as it makes four bonds
- (B) The fourth group should be a single hydrogen atom, not -OH
- (C) The R group is in the wrong place: it should be bonded to the nitrogen of the amine group

Decide before you look. Answer on page 34.

B1.2.2 CONDENSATION REACTIONS FORMING DIPEPTIDES AND LONGER CHAINS

02 Peptide bonds join amino acids, and *water* leaves

Amino acids join by the same move as every other monomer in B1.1, a condensation reaction. The OH from the carboxyl group of one amino acid and an H from the amine group of the next leave together as a molecule of water. The carbon of the carboxyl group is then left bonded to the nitrogen of the amine group, and that C-N bond is a **peptide bond**, a strong covalent bond. Two amino acids make a **dipeptide**.

The word equation is **amino acid + amino acid → dipeptide + water**.

The dipeptide still has a free amine group at one end and a free carboxyl group at the other, so more amino acids can join on in the same way. A long chain is a **polypeptide** (a short chain of a few amino acids is sometimes called an oligopeptide). A chain of n amino acids has $n - 1$ peptide bonds, and $n - 1$ molecules of water were released making it. Hydrolysis, adding water back, reverses it, which is what digestion does to the proteins in food. In cells, ribosomes make the peptide bonds, in the order a gene sets (D1.2).

A protein is one or more polypeptides folded into a working shape. Model this reaction with a kit first (see Teach), then try the bond builder below and draw a dipeptide.

KEY TERMS

peptide bond

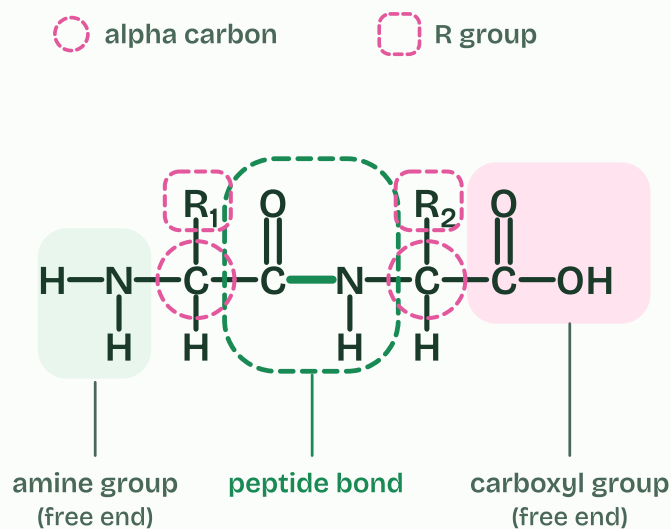
The covalent bond between the carbon of one amino acid's carboxyl group and the nitrogen of the next amino acid's amine group. It forms in a condensation reaction.

dipeptide

Two amino acids joined by one peptide bond.

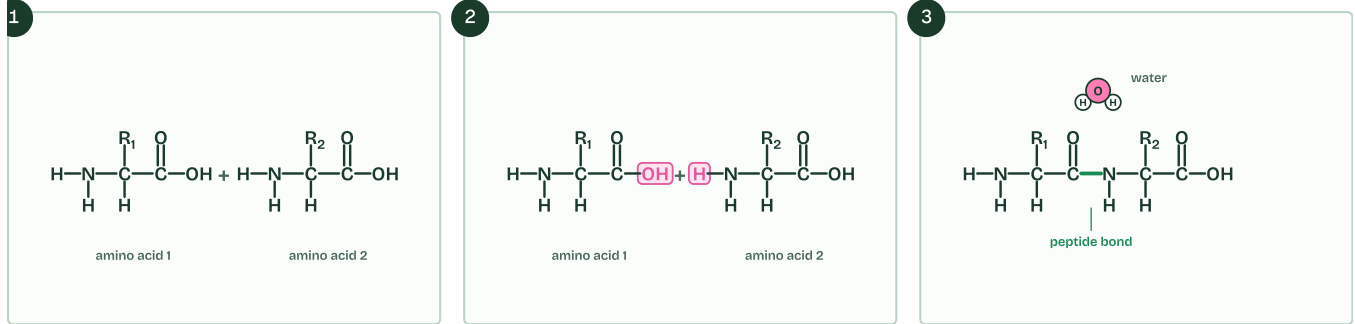
polypeptide

A chain of many amino acids joined by peptide bonds.



STEP BY STEP

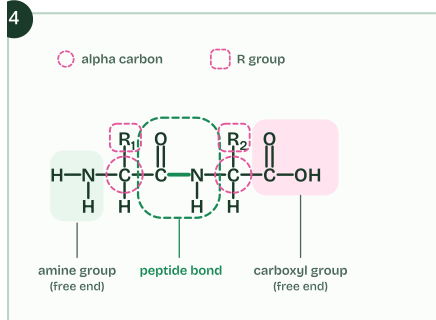
4 STEPS



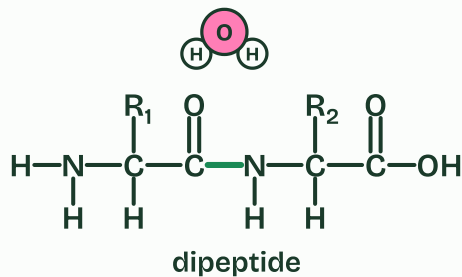
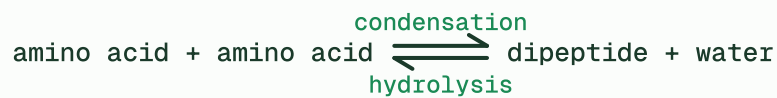
Two amino acids, **R₁** and **R₂**, with the carboxyl group of the first facing the amine group of the second.

The **OH** from the carboxyl group and one **H** from the amine group are lit: they will leave as **water**.

The carbon bonds to the nitrogen and the water drifts away. The new C-N bond is a **peptide bond**.



A **dipeptide**, drawn as an examiner wants it. It still has an amine group at one end and a carboxyl group at the other.

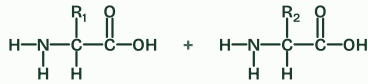


Join the amino acids, both ways round, then add water to split them again. Count the peptide bonds and the water released.

STEP BY STEP

4 STEPS

1

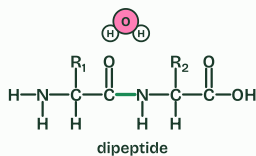


Two amino acids.

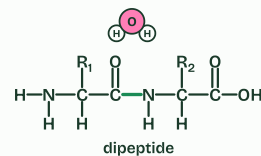
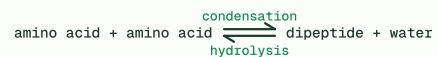
2

The OH of one's **carboxyl group** and an H of the other's **amine group** face each other.

3

They leave as **water**, and a **peptide bond** joins the carbon to the nitrogen: **condensation**, making a **dipeptide**.

4

Add water and the peptide bond splits again, the OH back to the carbon and the H to the nitrogen: **hydrolysis**.

WATCH OUT

The peptide bond is not between the two alpha carbons, not through an oxygen (C-O-N), and never involves an R group. And the water takes its OH from one amino acid and its H from the other, not both from the same one.

EXAMPLE

Insulin has two polypeptides. The shorter has 21 amino acids and so 20 peptide bonds, and the longer has 30 and so 29. (Insulin itself comes back at higher level.)

PREDICT

Two different amino acids, A and B, are joined by one peptide bond. How many different dipeptides could they make?

- (A) One: A joined to B is the same molecule as B joined to A, because the same two amino acids are used
- (B) Four: any group on one amino acid can join any group on the other, so there are four ways to do it
- (C) Two: A's carboxyl to B's amine, or B's carboxyl to A's amine, and these are different molecules

Decide before you look. Answer on page 34.

03

B1.2.3 DIETARY REQUIREMENTS FOR AMINO ACIDS

Some amino acids you must *eat*

Your cells need all twenty amino acids to build their proteins. They can make some of them from other amino acids: these are **non-essential amino acids**. They cannot make the rest, which must come from food: **essential amino acids**. For an adult, nine of the twenty are essential. You do not need to name any of them.

“Essential” is about the diet, not importance: a protein needs every amino acid in its sequence, so the non-essential ones matter just as much. You just do not need to eat them.

The body keeps no store of spare amino acids, as it does for glycogen and fat, so essential ones are needed regularly. Food protein is digested (hydrolysed) to amino acids, which are absorbed and built into your own proteins. If one essential amino acid runs short, every protein that needs it cannot be finished: the gene sets the sequence, and no other amino acid can stand in.

Plants and animals differ here. A plant makes all twenty amino acids itself, from sugars and nitrate taken up from the soil, so it needs no amino acids from food. An animal cannot make all of them and must eat the essential ones. Some amino acids are conditional: the body can make them, but not fast enough at certain times such as infancy, pregnancy or illness. Vegan diets take all their protein from plants. Most plant foods contain every essential amino acid, but some have little of one: cereals are low in one, and beans and lentils in a different one. A variety over the day, such as rice with lentils or hummus with bread, supplies them all, and soya and quinoa have all of them in good amounts. A vegan diet needs attention, not luck. Meat, eggs and dairy carry all of them in proportions close to what we need.

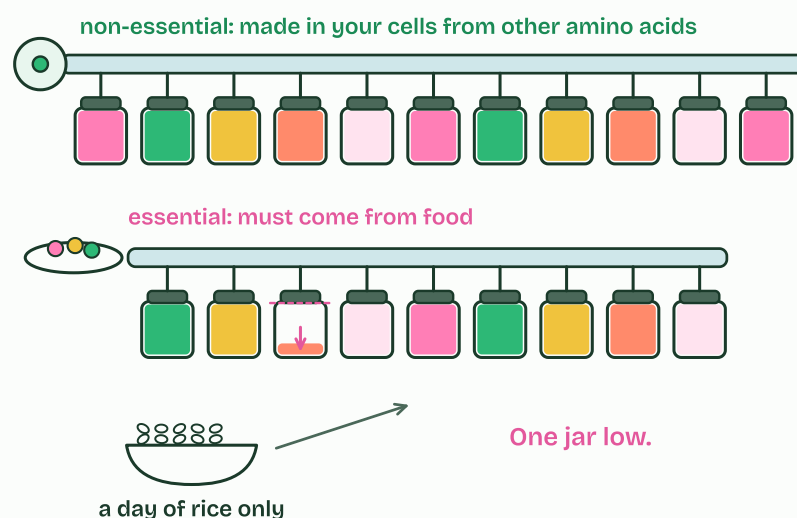
KEY TERMS

non-essential amino acids

Amino acids that the body can make from other amino acids, so they do not have to come from food.

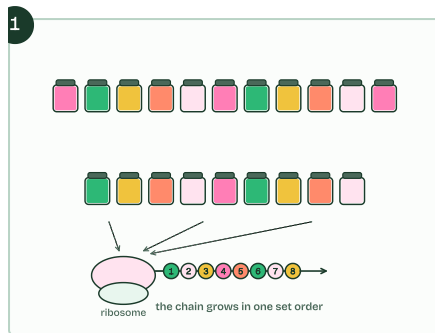
essential amino acids

Amino acids that the body cannot make, so they must be obtained from food.

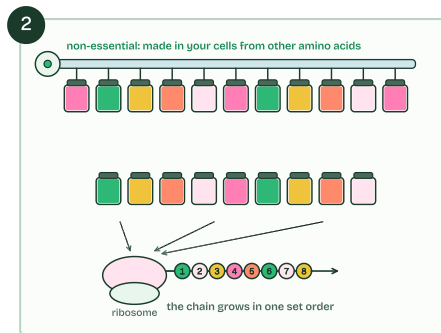


STEP BY STEP

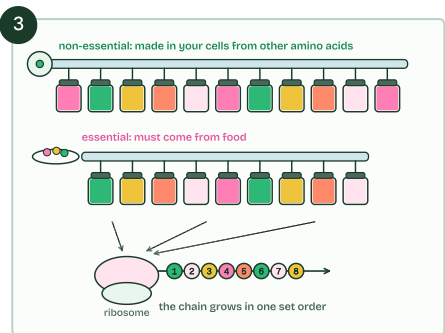
5 STEPS



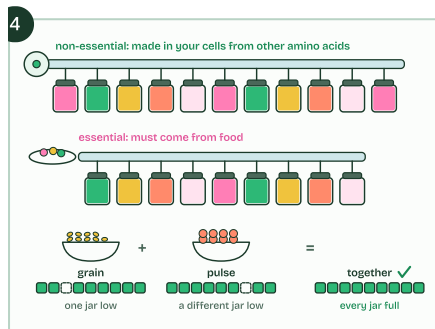
Twenty jars feed the line, and the chain grows in **one order**, set by the gene.



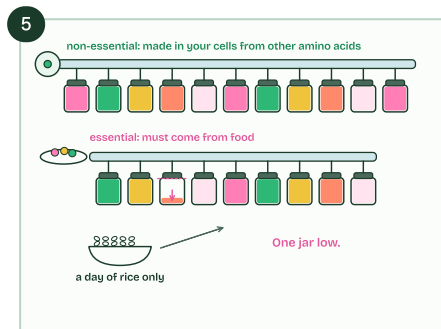
Eleven jars are filled by a pipe from the cells: **non-essential** amino acids, which your cells can make from other amino acids.



Nine jars are filled only from the plate: **essential** amino acids, which must come from food.



A varied plant plate: grain runs a little low in one jar and pulses in a different one, and together they fill every jar. A **vegan** diet covers all nine with **variety**.



A day of rice only: one jar runs low.

WATCH OUT

Non-essential amino acids are not unimportant: they are in your proteins too, you just do not need them in food. And “vegans cannot get essential amino acids” is false: they need a variety of plant proteins.

PREDICT

You eat plenty of protein, but it lacks one essential amino acid. What happens to the proteins that need it?

- (A) They cannot be completed, because no other amino acid can take its place in the sequence
- (B) Your cells make the missing amino acid from other amino acids that are in plentiful supply
- (C) Nothing changes, as long as the total amount of protein eaten is high enough
- (D) A different amino acid is put in its place, so the proteins are still finished, if slightly altered

Decide before you look. Answer on page 34.

B1.2.4 INFINITE VARIETY OF POSSIBLE PEPTIDE CHAINS

04 Twenty amino acids, *endless* chains

The **genetic code** (A1.2) codes for twenty amino acids. A polypeptide can have any number of them, from a few to thousands, in any order, and the same amino acid can appear again and again.

That makes the number of possible chains enormous. There are $20 \times 20 = 400$ different dipeptides, $20 \times 20 \times 20 = 8,000$ tripeptides, and 20^n chains of length n . Past about 62 amino acids there are more possible sequences than there are atoms in the observable universe, and real proteins are much longer than that.

Living things use only a tiny fraction of the possible sequences. Most protein-coding genes code for one polypeptide, and all the proteins an organism makes are its **proteome**. You should know some examples of polypeptides:

KEY POINTS

- **Glucagon**, a hormone, has 29 amino acids.
- **Insulin**, a hormone, has 51 in two chains of 21 and 30.
- **Lysozyme**, an enzyme in egg white and tears, has 129.
- Each **haemoglobin** chain has 141 or 146.
- A **collagen** chain has about 1,000.
- **Titin**, a springy protein inside muscle, has about 34,000, the largest known in humans.

KEY TERMS

genetic code

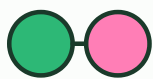
The rules a cell uses to turn the sequence of bases in a gene into the sequence of amino acids in a polypeptide. It codes for twenty amino acids.

proteome

All the proteins that an organism, or a cell, makes.

choices at each position

20 20



2 amino acids

SWITCH IT

6 SETTINGS

1

choices at each position

20 20 20 20 20 20 20 20 20 20 20 20 ...



150 amino acids (12 drawn)

2

choices at each position

20 20 20 20 20 20 20 20 20 20 20 20 ...



150 amino acids (12 drawn)

10

3

choices at each position

20 20 20 20 20 20 20 20 20 20 20 20 ...



150 amino acids (12 drawn)

51

4

choices at each position

20 20 20 20 20 20 20 20 20 20 20 20 ...

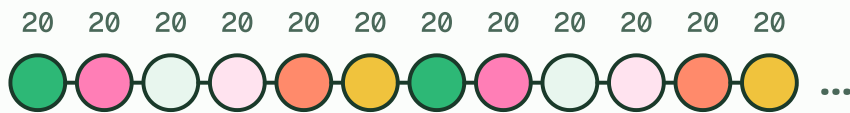


150 amino acids (12 drawn)

62

5

choices at each position

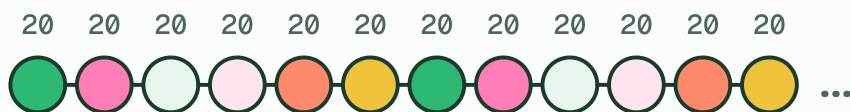


150 amino acids (12 drawn)

100

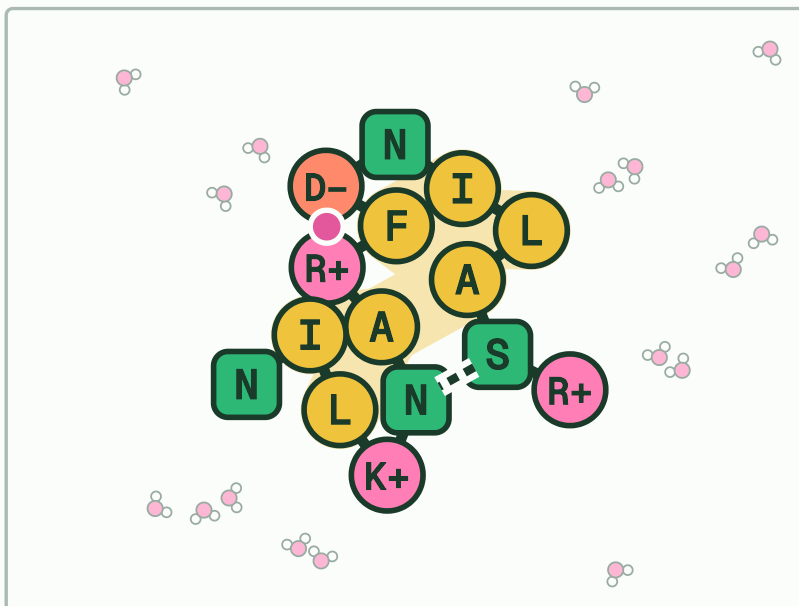
6

choices at each position



150 amino acids (12 drawn)

146



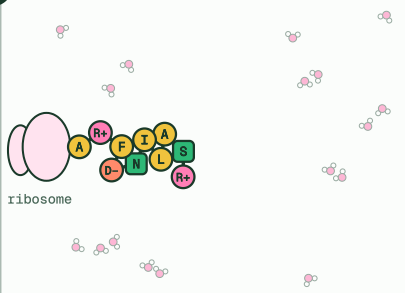
- non-polar
- polar
- polar, with a charge
- cysteine (C)
- 8 weak bonds hold its shape
- S-S 0 strong bonds between two cysteines

Type your name: it is a polypeptide.

STEP BY STEP

2 STEPS

1



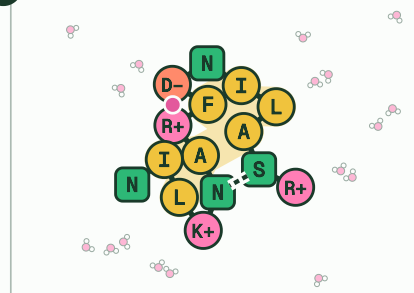
Each letter is an amino acid

15 amino acids leave the ribosome one at a time

ribosome

Type **ROSALIND FRANKLIN**: each letter is the code for one amino acid (the O is skipped: no amino acid has that letter). Its 15 amino acids are joined by 14 peptide bonds: one of 20^{15} (about 3×10^{19}) possible chains this long. A ribosome makes the chain one amino acid at a time, and it starts to fold as it comes out.

2



● non-polar
■ polar
● polar, with a charge
○ cysteine (C)

8 weak bonds hold its shape

0 strong bonds between two cysteines

It folds into a shape of its own, held by **weak bonds** between its side chains.

WATCH OUT

Twenty amino acids do not mean twenty proteins. And a protein's identity is its order: the same amino acids in a different order make a different polypeptide.

LINKING QUESTION

What is the relationship between the genome and the proteome? The genome is all of an organism's genes, and most of them code for a polypeptide, so the genome sets which proteins the organism can make, its proteome. Different cells use different parts of it, so a liver cell's proteins differ from a muscle cell's (D1.2, and D2.2 at higher level).

PREDICT

How many different dipeptides can be made from the 20 amino acids?

- (A) 20, because there are only twenty amino acids to choose from
- (B) 40, because each of the twenty amino acids can sit first or second
- (C) 190, because a pair in either order counts once and a repeated amino acid is not allowed
- (D) 400, because there are twenty choices at each of the two positions

Decide before you look. Answer on page 34.

05

B1.2.5 EFFECT OF PH AND TEMPERATURE ON PROTEIN STRUCTURE

Heat and pH *unfold* a protein

A protein works because of its precise three-dimensional shape: a pocket that fits one molecule, a surface that binds one partner. That shape is held in place by many weak bonds between parts of the folded chain, hydrogen bonds (met in A1.1) and attractions between charged groups.

At higher level you will meet the four kinds of bond in chapter 9.

Heat. The atoms vibrate more and more, and past a point the weak bonds break. The chain unfolds, its shape is lost and it can no longer do its job: it is **denatured**. The peptide bonds are covalent and much stronger, so the sequence of amino acids is unchanged.

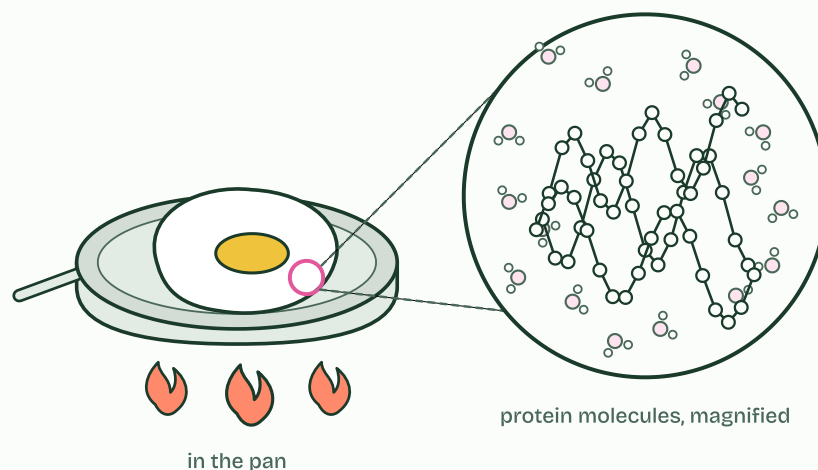
pH. Hydrogen ions attach to groups in the R groups, or leave them, and so change their charges. The attractions between oppositely charged groups are lost and the shape changes. Each protein keeps its shape over a range of pH, and far outside it the protein denatures.

Denaturation is usually permanent. Heated chains tangle with each other and do not refold when cooled, which is why an egg white stays white and solid. Each protein's limits suit where it works: proteins in the stomach keep their shape at about pH 2, and the proteins of microbes in hot springs stay folded at temperatures that would denature ours. Cooling slows a protein down but does not unfold it.

KEY TERMS

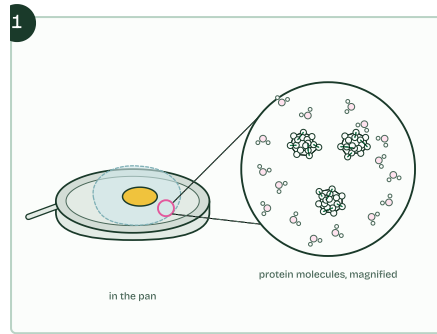
denatured

Having lost its three-dimensional shape because the bonds that hold it have broken, so that the protein can no longer do its job. The amino acid sequence is unchanged.

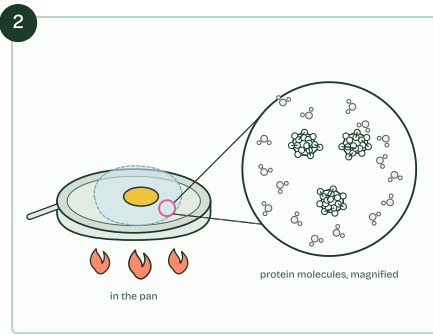


STEP BY STEP

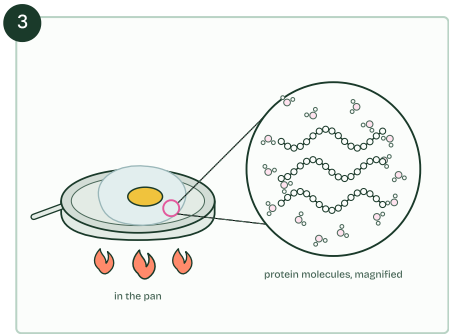
4 STEPS



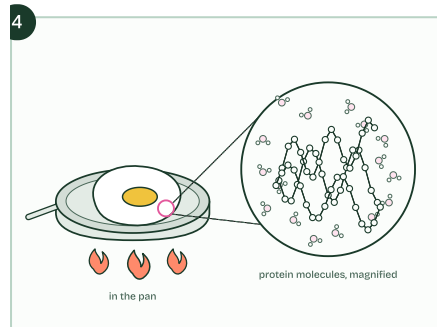
Raw egg white: clear and runny. Magnified, the proteins are **folded**, each on its own among the water molecules.



Heat makes the molecules jiggle harder and breaks the bonds that hold the folds.



The chains **unfold**: with the bonds gone, their shape is gone.



Unfolded chains **tangle** together and the egg white sets, white and solid. The proteins are **denatured**.

ANIMATION · HEAT IT, CHANGE THE PH

3 MOMENTS

1 37 °C, PH 7

37 °C bonds holding the fold: 0 of 8 no shape yet
pH 7 no small molecule yet

2 37 °C, PH 7

37 °C bonds holding the fold: 8 of 8 folded
pH 7 small molecule fits

A new chain of amino acids among water molecules: as yet it has **no shape**.

A small molecule **fits** its pocket: one precise shape, one job.

3 37 °C, PH 7

37 °C bonds holding the fold: 0 of 8 unfolded, tangled
pH 7 small molecule cannot fit

Cooled again, it does not refold: the unfolded chains **tangle** together instead.

Watch it move, and change it as it runs: biologybybradford.com/guides/ib-biology-b1-2-proteins#denaturation

WATCH OUT

Denatured does not mean dead (a protein was never alive), melted or dissolved. Cold does not denature: a protein in the fridge is slow but whole. And cooling a heat-denatured protein does not usually bring its shape back.

TRY IT

The enzyme in your spit, a home lab in C1.1, times salivary amylase breaking down starch at cold, room and warm temperatures. Amylase is a protein, and denaturation is the reason the hottest tube behaves as it does.

LINKING QUESTION

How do abiotic factors influence the form of molecules? Temperature and pH change a protein's shape by breaking the bonds that hold it. The same idea runs through the course: heat breaks hydrogen bonds between water molecules (A1.1), warmth melts fats with more C=C bonds sooner (B1.1), and every enzyme has an optimum (C1.1).

PREDICT

When an egg sets in a hot pan, which bonds break?

- (A) The peptide bonds, so the chains fall apart into separate amino acids as the egg cooks
- (B) Neither: the protein just melts, like fat, and goes solid again as it cools
- (C) The weak bonds that hold the fold, while the peptide bonds stay intact
- (D) Both the weak bonds and the peptide bonds, so everything comes apart

Decide before you look. Answer on page 34.

06

B1.2.6 HL CHEMICAL DIVERSITY IN THE R GROUPS

The R groups decide how a chain *behaves*

R groups differ in size, shape and chemistry, and those differences give a polypeptide its properties: which parts face water, what binds to what, and where the chain carries charge. You do not need to name any R group, but you do need to sort them.

There are two big classes. **Hydrophobic** R groups are non-polar, mostly carbon and hydrogen, and water does not attract them. **Hydrophilic** R groups are attracted to water, and they are either **polar**, with partial charges that let them form hydrogen bonds, or **charged**.

Charged R groups are **acidic** or **basic**. An acidic R group contains a carboxyl group, which loses a hydrogen ion and becomes negative (-COO^-). A basic R group contains an amine group, which gains a hydrogen ion and becomes positive (-NH_3^+). At the pH inside a cell both are charged, and a change in pH changes that (chapters 5 and 9).

KEY TERMS

hydrophobic

Not attracted to water.

Hydrophobic R groups are non-polar, made mostly of carbon and hydrogen.

hydrophilic

Attracted to water. Hydrophilic R groups are either polar or charged.

polar

Having slightly positive and slightly negative regions, as in an O-H or N-H group, so that it can form hydrogen bonds with water.

charged

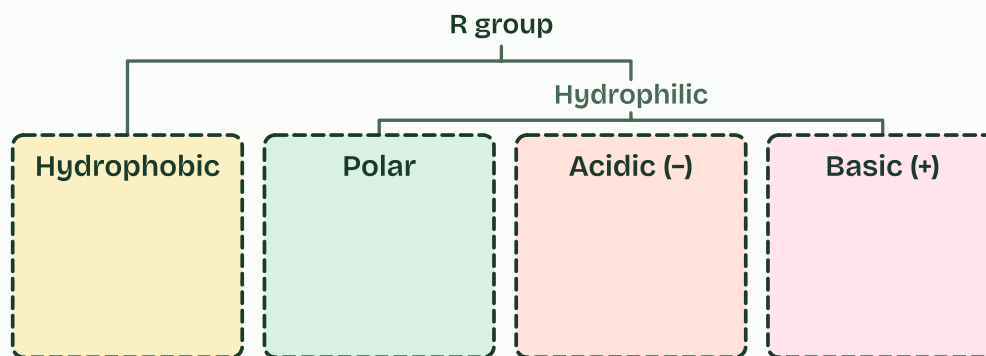
Carrying a whole positive or negative charge, because a group in the R group has gained or lost a hydrogen ion.

acidic

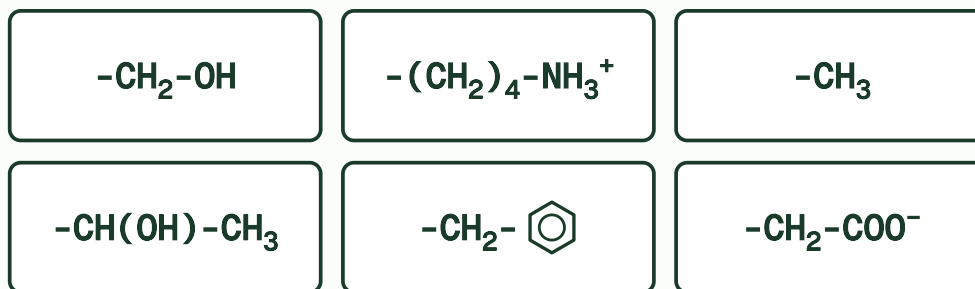
An acidic R group contains a carboxyl group, which loses a hydrogen ion and becomes negatively charged.

basic

A basic R group contains an amine group, which gains a hydrogen ion and becomes positively charged.



Six R groups to sort



Six R groups, drawn as condensed formulas, and four bins. Which bin does each belong in, and what tells you?

REMEMBER IT

The four kinds of R group

H Hungry	P Pandas	A Ate	B Bamboo
Hydrophobic non-polar, hides from water	Polar partial charges, hydrogen bonds	Acidic loses H^+ , negative	Basic gains H^+ , positive

WATCH OUT

Hydrophilic does not mean charged: polar R groups are hydrophilic with no overall charge. Acidic R groups are negative, not positive. And a charge can come and go with pH.

PREDICT

An R group contains a carboxyl group. Inside a cell, at about pH 7, it is:

- (A) Uncharged and hydrophobic, so water does not attract it
- (B) Negatively charged, because it has lost a hydrogen ion
- (C) Positively charged, because it has gained a hydrogen ion

Decide before you look. Answer on page 34.

07

B1.2.7 HL IMPACT OF PRIMARY STRUCTURE ON CONFORMATION

The sequence sets the *shape*

The **primary structure** of a protein is the sequence of amino acids in its polypeptide, and a gene sets it. The sequence, and the exact position of each amino acid in it, decide the three-dimensional shape (its conformation): where the chain coils or pleats (secondary structure, chapter 8), how the whole chain folds (tertiary, chapters 9 and 10) and how chains fit together (quaternary, chapter 11).

So proteins have precise, predictable and repeatable structures, despite their complexity. Every insulin molecule your pancreas makes has the same shape, and fits insulin receptors anywhere in your body. Change one amino acid in a key position and the shape can change: in D1.3 you will meet a single changed amino acid in haemoglobin with large effects.

KEY TERMS

primary structure

The sequence of amino acids in a polypeptide, set by its gene.

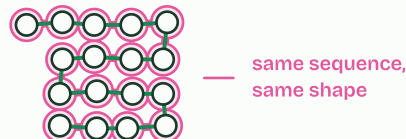
1 primary
the sequence



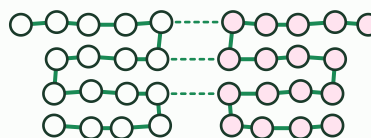
2 secondary
coils and pleats



3 tertiary
the whole chain folded

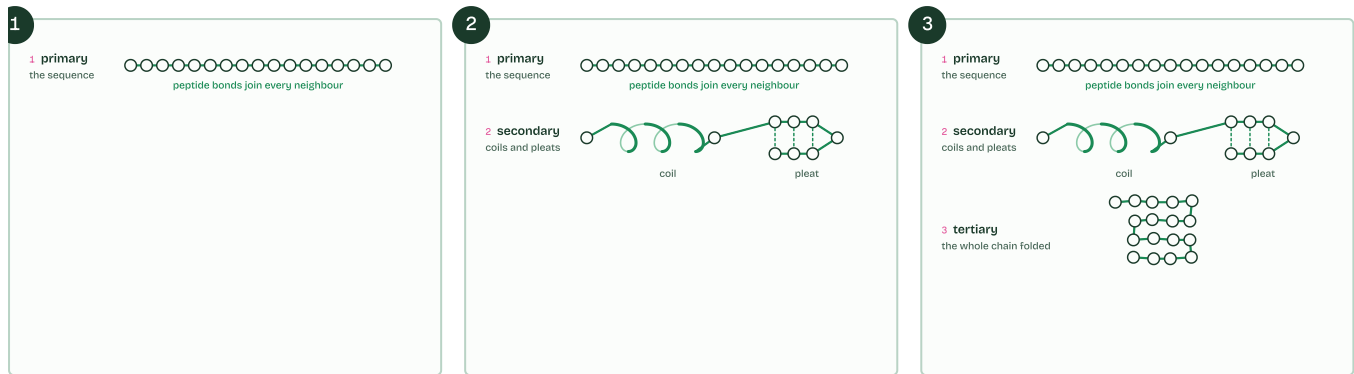


4 quaternary
two or more chains



STEP BY STEP

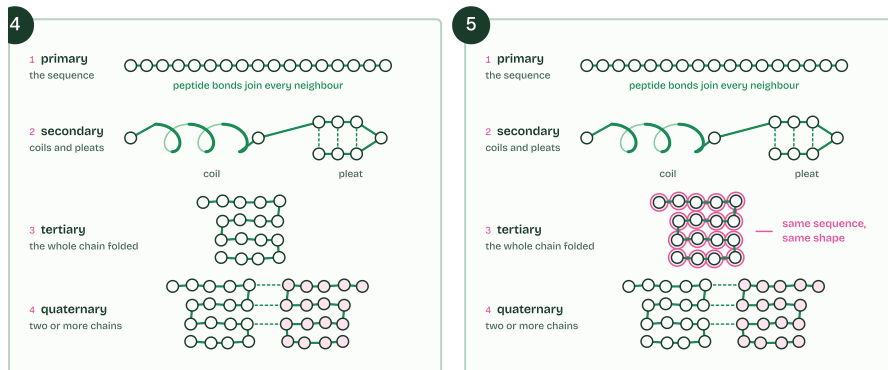
5 STEPS



Primary structure: a sequence of amino acids, each joined to the next by a peptide bond.

Secondary structure: one stretch coils and another pleats beside itself, held by dashed hydrogen bonds.

Tertiary structure: the whole chain folded into a compact shape.



Quaternary structure: two or more folded chains together. Not every protein has one.

A second copy of the same sequence folds into the same shape: same sequence, **same shape**, every time.

WATCH OUT

Primary structure is the sequence, not a shape, but it decides every level after it. Folding is not random.

HOW WE KNOW

Christian Anfinsen unfolded the enzyme ribonuclease with chemicals and then removed them. The chains refolded by themselves into the working shape, so the information for the shape is in the sequence (Nobel Prize in Chemistry, 1972). Since 2020 a computer model trained on known structures, AlphaFold, has predicted the shape of many proteins from their sequence alone, often close to what experiments find, and its database holds predictions for over 200 million proteins. Models earn trust by being tested against evidence.

PREDICT

**Two people make insulin from the same gene sequence.
Do their insulin molecules have the same shape?**

- ☐ A Yes, exactly: the same sequence folds the same way every time
- ☐ B Roughly: folding is random, so every molecule differs a little from the next
- ☐ C Only if the two people are related, because they share the same alleles for it

Decide before you look. Answer on page 34.

08

B1.2.8 HL PLEATING AND COILING OF SECONDARY STRUCTURE

Coils and pleats held by *hydrogen bonds*

The polypeptide backbone is the repeating N-C-C pattern (the amine nitrogen, the alpha carbon, the carboxyl carbon) with the R groups hanging off it. Every peptide bond sits between a C=O group, whose oxygen is slightly negative, and an N-H group, whose hydrogen is slightly positive. These backbone groups are polar (A1.1), so a C=O and an N-H further along the chain can form a hydrogen bond. Where the chain makes these bonds in regular positions, it settles into a regular shape, its **secondary structure**.

In an **alpha helix** the chain coils, and each C=O bonds with the N-H four amino acids further along. The bonds fall in regular positions along the coil, and the R groups point outwards. In a **beta-pleated sheet**, stretches of the chain lie side by side, running the same way or opposite ways, and C=O groups in one stretch bond to N-H groups in the next. The chain zigzags, which makes the pleats, and the R groups point alternately above and below the sheet.

Each bond is weak, but hundreds in regular positions make the structure stable. One protein usually has stretches of both, joined by less regular loops.

KEY TERMS

secondary structure

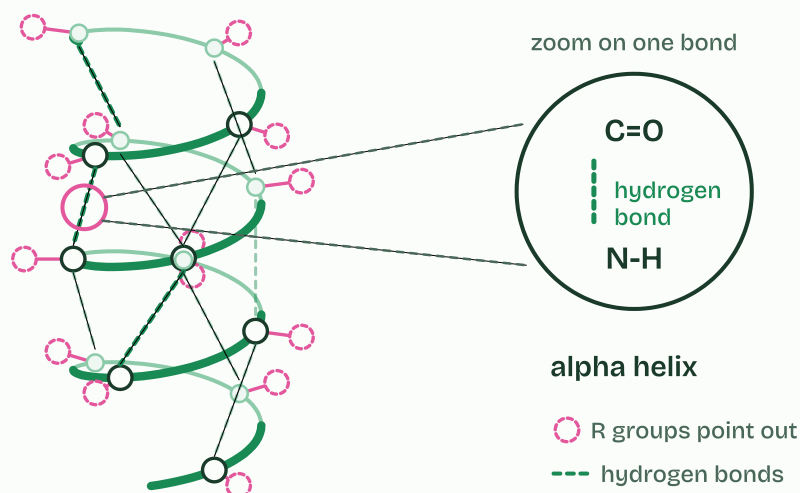
The regular coils and pleats that a polypeptide forms, held by hydrogen bonds between groups in the backbone.

alpha helix

A secondary structure in which the polypeptide is coiled like a spring. Each C=O forms a hydrogen bond with the N-H four amino acids further along.

beta-pleated sheet

A secondary structure in which stretches of the polypeptide lie side by side, held by hydrogen bonds between their backbones. The chain zigzags, so the sheet is pleated.



Hydrogen bond the O of a C=O group in one amino acid and the H of an N-H group four amino acids further along. Both groups are in the backbone.

Hydrogen bond the O of a C=O group in one amino acid and the H of an N-H group four amino acids further along. Both groups are in the backbone.

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Hydrogen bond the O of a C=O group in one amino acid and the H of an N-H group four amino acids further along. Both groups are in the backbone.

Hydrogen bond the O of a C=O group in one amino acid and the H of an N-H group four amino acids further along. Both groups are in the backbone.

Hydrogen bond the O of a C=O group in one strand and the H of an N-H group in the strand beside it. Both groups are in the backbone.

Hydrogen bond the O of a C=O group in one strand and the H of an N-H group in the strand beside it. Both groups are in the backbone.

Hydrogen bond the O of a C=O group in one strand and the H of an N-H group in the strand beside it. Both groups are in the backbone.

Hydrogen bond the O of a C=O group in one strand and the H of an N-H group in the strand beside it. Both groups are in the backbone.

Beta-pleated sheet stretches of the chain side by side, held by hydrogen bonds between backbone groups.

Hydrogen bond the O of a C=O group in one amino acid and the H of an N-H group four amino acids further along. Both groups are in the backbone.

Hydrogen bond the O of a C=O group in one strand and the H of an N-H group in the strand beside it. Both groups are in the backbone.

Hydrogen bond the O of a C=O group in one strand and the H of an N-H group in the strand beside it. Both groups are in the backbone.

Hydrogen bond the O of a C=O group in one strand and the H of an N-H group in the strand beside it. Both groups are in the backbone.

Alpha helix one stretch of the chain coiled, held by hydrogen bonds between backbone groups in regular positions.

Loops the less regular stretches that join the helices and sheets together.

SWITCH IT

3 SETTINGS

1

zoom on one bond

C=O
hydrogen bond
N-H

alpha helix

R groups point out
hydrogen bonds

Helix

2

beta-pleated sheet

three strands side by side, running opposite ways

R groups alternate above and below

Sheet

3

alpha helix

beta-pleated sheet

loops

One chain usually has stretches of both, joined by less regular loops.

In a protein

WATCH OUT

Secondary structure bonds are between backbone groups, not R groups. An alpha helix is one coiled polypeptide, nothing to do with the double helix of DNA. And collagen's helix is not an alpha helix (chapter 11).

PREDICT

Which groups form the hydrogen bonds that hold an alpha helix?

- (A) The R groups of neighbouring amino acids, in regular positions
- (B) Water molecules around the helix, bonded to two parts of the chain
- (C) The amine and carboxyl groups at the two ends of the chain
- (D) The C=O and N-H groups of the peptide bonds in the backbone

Decide before you look. Answer on page 34.

09

B1.2.9 HL DEPENDENCE OF TERTIARY STRUCTURE ON FOUR KINDS OF BOND

Four kinds of bond hold the *fold*

Tertiary structure is the three-dimensional shape of the whole polypeptide. It is held by bonds between R groups, often far apart in the sequence.

KEY POINTS

- **Hydrogen bonds** between polar R groups.
- **Ionic bonds** between a positively charged (basic) and a negatively charged (acidic) R group. The amine and carboxyl groups in R groups become charged by gaining or losing a hydrogen ion, and only then can they form ionic bonds.
- **Disulfide bonds**, covalent bonds between the sulfur atoms of two **cysteines**, the only amino acid you need to name. This is the strongest of the four.
- **Hydrophobic interactions**: non-polar R groups cluster together, away from water.

This links back to chapter 5. Heat breaks hydrogen bonds, ionic bonds and hydrophobic interactions, and a change of pH alters charges and so breaks ionic bonds. The disulfide bonds are covalent, so they survive much more.

KEY TERMS

tertiary structure

The three-dimensional shape of a whole polypeptide, held by bonds between R groups that are often far apart in the sequence.

ionic bonds

The attraction between a positively charged R group and a negatively charged one.

disulfide bonds

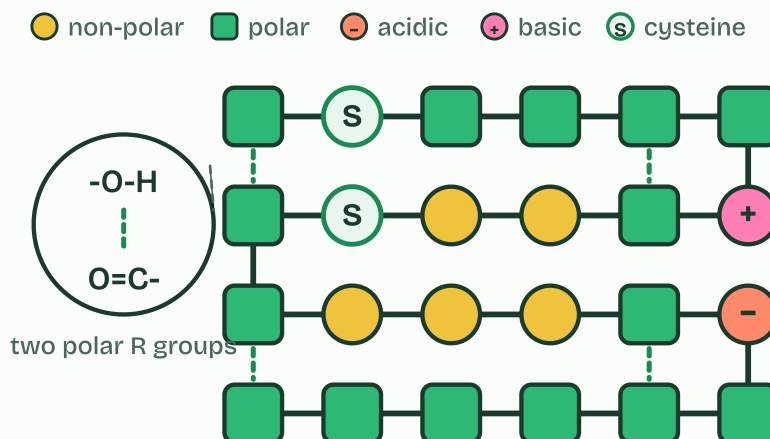
A covalent bond between the sulfur atoms of two cysteines.

cysteines

The amino acid whose R group ends in a sulfur atom, so that two of them can form a disulfide bond. It is the only amino acid you need to name.

hydrophobic interactions

The clustering of non-polar R groups together, away from water, in the middle of a folded protein.



SWITCH IT

6 SETTINGS

1

two polar R groups

Hydrogen

2

acidic meets basic

Ionic

3

two cysteines

Disulfide

4

Hydrophobic

5

All

6

the carboxyl gains H+

Lower the pH

REMEMBER IT

The bonds that hold a tertiary structure

H Happy	H Hippos	I Ignore	D Dentists
Hydrogen bonds between polar R groups	Hydrophobic interactions non-polar R groups huddle away from water	Ionic bonds between + and - R groups	Disulfide bonds two cysteines; the only covalent one

WATCH OUT

A disulfide bond is covalent and forms only between two cysteines: it is not a kind of hydrogen bond. Ionic bonds need charged R groups, not just polar ones. And hydrophobic interactions are not attractions between the R groups and water.

PREDICT

An ionic bond holds two parts of a protein together. The pH falls to 2. Why might the bond break?

- (A) Acid breaks the peptide bonds, so the chain falls apart into amino acids
- (B) The negative carboxyl R group gains a hydrogen ion and loses its charge
- (C) The positive R group loses its charge, so nothing is left to attract the negative one
- (D) Hydrogen ions break the disulfide bonds, which are the weakest of the four

Decide before you look. Answer on page 35.

10

B1.2.10 HL EFFECT OF POLAR AND NON-POLAR AMINO ACIDS ON TERTIARY STRUCTURE

Oily inside, *watery* outside

In proteins that dissolve in water, such as the globular proteins of chapter 12, the hydrophobic R groups cluster in the core, away from the water. The hydrophilic R groups, polar and charged, sit on the surface, where they interact with water. That watery surface is why the protein dissolves.

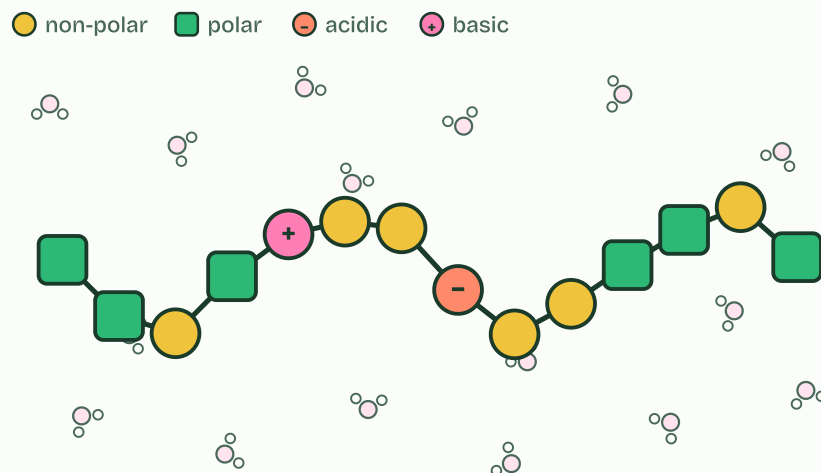
Why? Water molecules form hydrogen bonds with each other and with polar groups, but not with non-polar ones, so the non-polar R groups end up pushed together. This drives much of the folding. Water does not push them away as a magnet would: it simply bonds to itself and to polar groups instead.

Integral proteins work the other way round. They have regions of hydrophobic amino acids where they cross the membrane, lying among the hydrophobic tails of the phospholipids (B1.1), and hydrophilic regions where the protein meets water on each side (B2.1). A stretch of about 20 hydrophobic amino acids, coiled as a helix, is enough to cross the bilayer once. In a channel protein the chain crosses several times, and the hydrophilic amino acids face inwards to line the pore that ions or water pass through, while the hydrophobic ones face the lipids outside.

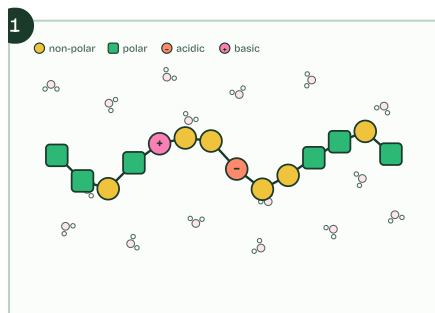
KEY TERMS

integral proteins

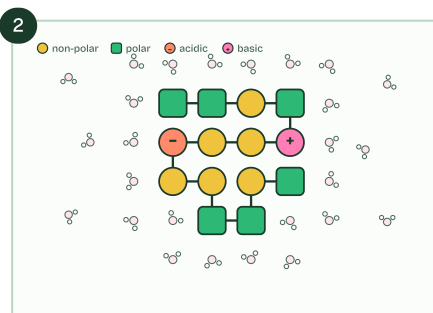
Proteins that are embedded in a cell membrane, with part of the chain lying among the hydrophobic tails of the phospholipids.



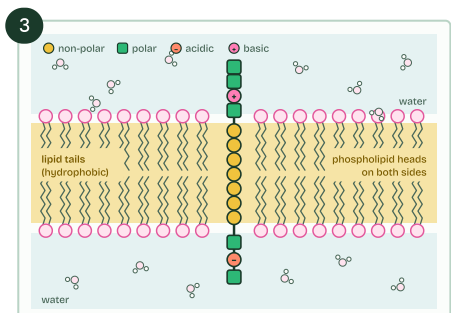
SWITCH IT



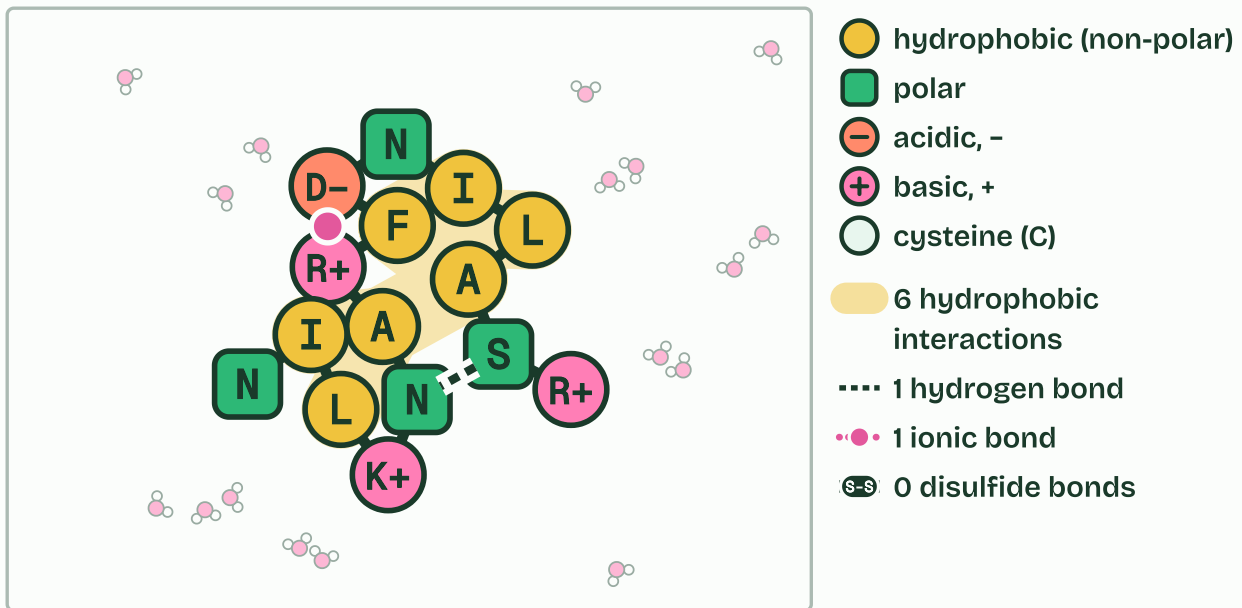
Unfolded



In water



In a membrane



Type your name or pick a gene, press Fold and watch which bonds form and where the non-polar amino acids end up. Fold the made-up membrane protein across a membrane. Then change one base: try the sickle cell change and make a second copy, then a frameshift.

STEP BY STEP

2 STEPS

1

Each letter is an amino acid
 15 amino acids leave the ribosome one at a time

Type **ROSALIND FRANKLIN**: each letter is the code for one amino acid (the O is skipped: no amino acid has that letter). A ribosome makes the chain one amino acid at a time, and it starts to fold as it comes out.

2

● hydrophobic (non-polar)
 ■ polar
 ● acidic, -
 ● basic, +
 ○ cysteine (C)
 6 hydrophobic interactions
 ---- 1 hydrogen bond
 ●● 1 ionic bond
 S-S 0 disulfide bonds

In water it folds: the **non-polar** ones gather inside, away from the water (6 of 7), and the polar ones face outwards. Hydrophobic interactions, hydrogen bonds and ionic bonds hold it.

WATCH OUT

Hydrophobic amino acids are not “bad”: without them there would be no core and no membrane protein. And a chain does not fold because someone puts it there: it folds by itself as it jostles in water.

PREDICT

A protein dissolves in blood plasma. Where are most of its hydrophobic R groups?

- (A) On the surface, where they touch the water and help the protein to dissolve
- (B) At the two ends of the chain, where they are free to move about
- (C) Clustered in the core of the protein, away from the water
- (D) Spread evenly through it, so that no part of the chain is more water-loving

Decide before you look. Answer on page 35.

11

B1.2.11 HL QUATERNARY STRUCTURE OF NON-CONJUGATED AND CONJUGATED PROTEINS

More than one chain: *quaternary* structure

Some proteins are a single polypeptide. Others are two or more polypeptides held together, and their arrangement is the **quaternary structure**, held by the same kinds of bond as the tertiary.

A **non-conjugated protein** is made of polypeptide only. **Insulin** has two polypeptides, of 21 and 30 amino acids, linked by two disulfide bonds, with a third disulfide bond within the shorter chain. **Collagen** has three polypeptides, each about 1,000 amino acids long, wound round each other into a triple helix like a rope. Every third amino acid is the smallest one, which lets the chains pack tightly, and hydrogen bonds between the chains hold the rope together.

A **conjugated protein** includes a part that is not polypeptide, a **prosthetic group**. **Haemoglobin** has four polypeptides, two of one kind and two of another, each holding a haem group with an iron ion at its centre. Each haem binds one oxygen molecule, so one haemoglobin carries up to four.

KEY TERMS

quaternary structure

The arrangement of two or more polypeptides in one protein, held by the same kinds of bond as the tertiary structure.

non-conjugated protein

A protein made of polypeptide only.

conjugated protein

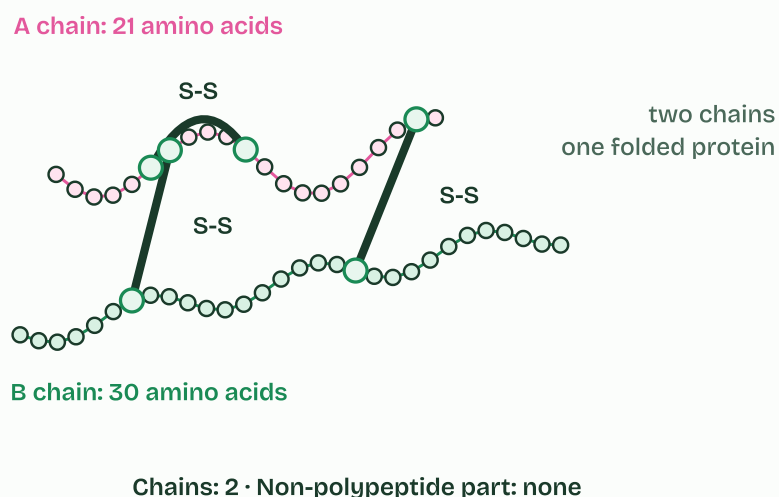
A protein that includes a part that is not polypeptide, called a prosthetic group.

prosthetic group

The non-polypeptide part of a conjugated protein, such as the haem group of haemoglobin.

cryogenic electron microscopy

Cryo-EM: freezing proteins so fast that the water around them turns to glass-like ice, then imaging single molecules with electrons and combining thousands of images into a 3D structure.



SWITCH IT

3 SETTINGS

1

A chain: 21 amino acids
B chain: 30 amino acids
two chains one folded protein
Chains: 2 · Non-polypeptide part: none

Insulin

2

three chains wound into a rope
every third amino acid is the smallest one
dashed: hydrogen bonds between the chains
Chains: 3 · Non-polypeptide part: none

Collagen

3

haem
iron ion
four chains: two of one kind, two of another
Chains: 4 · Non-polypeptide part: haem (one in each chain)

Haemoglobin

REMEMBER IT

The three named proteins, in order of chains

I I	S See	H Him
Insulin 2 chains; globular; non-conjugated	Collagen 3 chains; fibrous; non-conjugated	Haemoglobin 4 chains plus haem; globular; conjugated

WATCH OUT

Quaternary means more than one chain, not four (haemoglobin just happens to have four). Conjugated means joined to a non-protein group, not to another protein. And collagen's triple helix is not three alpha helices: each chain is a narrower helix of its own.

HOW WE KNOW

Technology lets us see what our senses cannot. A haemoglobin molecule is about 5 to 6 nm across, and a light microscope cannot resolve anything smaller than about 200 nm. **Cryogenic electron microscopy** (cryo-EM) freezes proteins so fast that the water around them turns to glass-like ice, not crystals, then images single molecules with electrons. A computer combines thousands of images of molecules lying at different angles into a 3D structure, so it shows single proteins and the molecules they bind without growing crystals, as X-ray crystallography needs (Nobel Prize in Chemistry, 2017).

PREDICT

A haemoglobin molecule is about 5 to 6 nm across.

Could you see one with the best light microscope?

- (A) Yes, at the highest magnification, if the best objective lens and a bright enough light are used
- (B) No: it is far smaller than the smallest thing light can resolve, about 200 nm
- (C) Only if it is stained, because a stain makes any molecule large enough to see

Decide before you look. Answer on page 35.

12

B1.2.12 HL RELATIONSHIP OF FORM AND FUNCTION IN GLOBULAR AND FIBROUS PROTEINS

Balls and ropes: globular and *fibrous* proteins

Globular proteins are folded into compact, rounded shapes. Their hydrophilic surfaces make most of them soluble, and their precise shapes let them bind specific molecules: enzymes, hormones, transport proteins and antibodies.

Insulin shows how form suits function. It is small and compact. It is soluble, so it is carried dissolved in the blood plasma from the pancreas to every tissue. Its precise shape binds the insulin receptor on target cells (liver, muscle and fat cells), and its disulfide bonds keep that shape stable.

Fibrous proteins are long and narrow, often with a repeating sequence, usually insoluble and strong, and have structural jobs. **Collagen** is three chains wound into a rope. The ropes lie side by side, staggered, and are cross-linked into fibrils, which are bundled into fibres. It is insoluble and has great tensile strength, which means it resists pulling. It is in skin, tendons, ligaments, bone, cartilage and blood vessel walls, and it is the most abundant protein in the human body.

The rule of thumb is that globular proteins do something and fibrous ones are something. It has exceptions: actin and tubulin are globular units that link into structural filaments.

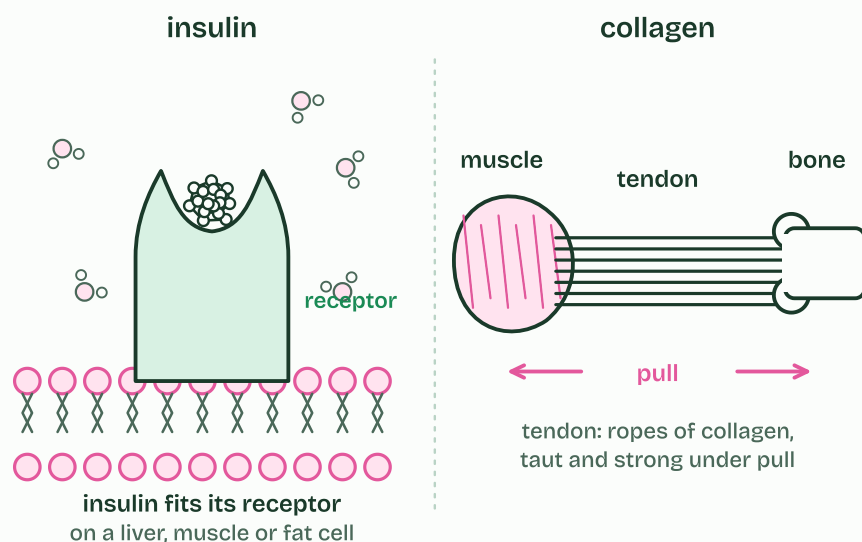
KEY TERMS

globular proteins

Proteins folded into compact, rounded shapes. Most are soluble in water and bind specific molecules: enzymes, hormones, transport proteins and antibodies.

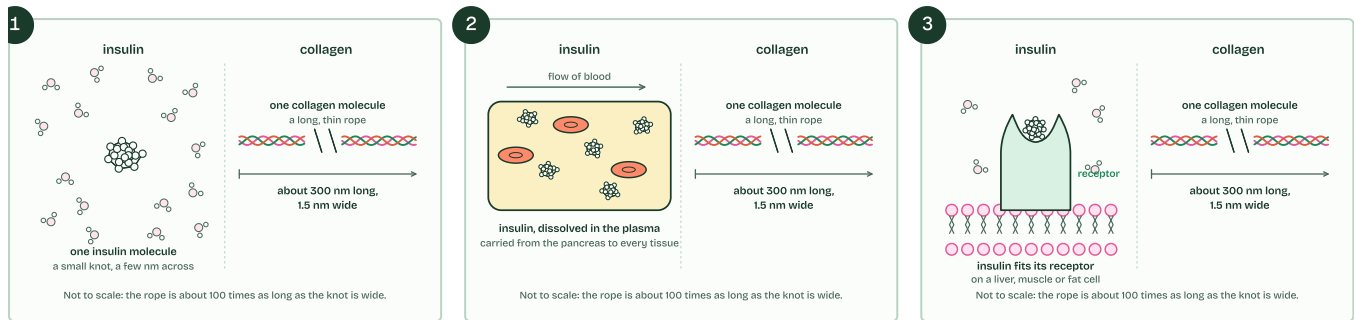
fibrous proteins

Proteins that are long and narrow, often with a repeating sequence. Most are insoluble and strong, and have structural jobs.



STEP BY STEP

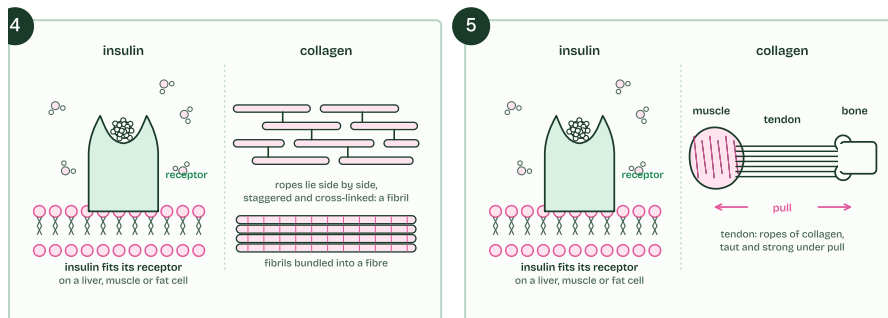
5 STEPS



One **insulin** molecule is a small rounded knot among water molecules. One **collagen** molecule is a long, thin rope, about 100 times longer than the knot is wide.

Insulin is **soluble**: dissolved in the plasma, it is carried round the body in the blood.

Insulin has a **precise shape** that fits the receptor on its target cells, liver, muscle and fat cells, like a key in a lock.



Collagen ropes lie side by side, staggered and **cross-linked**, into fibrils, and fibrils are bundled into fibres.

In a tendon, collagen fibres are **insoluble** and strong: they stay taut when muscle pulls on bone.

WATCH OUT

The functional and structural rule is only a rule of thumb (actin and tubulin). And a fibrous protein is fibrous in shape as a single molecule: it is not "made of fibres".

PREDICT

A protein is long and thin, has a repeating sequence and does not dissolve in water. What is its most likely job?

- (A) A hormone carried in the blood, because it has to dissolve and reach its target
- (B) An enzyme, because enzymes are always long and thin so that they reach their substrate
- (C) An antibody, which has to be long and thin to wrap round the microbes it destroys
- (D) A structural protein, as found in tendons, skin and blood vessel walls

Decide before you look. Answer on page 35.

Key terms

Every term this guide defines, A to Z, with the chapter it is in. Cover the right-hand side and test yourself.

acidic 06

An acidic R group contains a carboxyl group, which loses a hydrogen ion and becomes negatively charged.

alpha carbon 01

The central carbon of an amino acid. It makes four single bonds, to an amine group, a carboxyl group, a hydrogen atom and an R group.

alpha helix 08

A secondary structure in which the polypeptide is coiled like a spring. Each C=O forms a hydrogen bond with the N-H four amino acids further along.

amine group 01

The group -NH₂: a nitrogen atom bonded to two hydrogens. It is the amino part of the name.

amino acids 01

The monomers of proteins. Each has an amine group, a carboxyl group, a hydrogen atom and an R group on one central carbon.

basic 06

A basic R group contains an amine group, which gains a hydrogen ion and becomes positively charged.

beta-pleated sheet 08

A secondary structure in which stretches of the polypeptide lie side by side, held by hydrogen bonds between their backbones. The chain zigzags, so the sheet is pleated.

carboxyl group 01

The group -COOH: a carbon with a double bond to one oxygen and a single bond to an OH. It can give up a hydrogen ion, which is why it is an acid.

charged 06

Carrying a whole positive or negative charge, because a group in the R group has gained or lost a hydrogen ion.

conjugated protein 11

A protein that includes a part that is not polypeptide, called a prosthetic group.

cryogenic electron microscopy 11

Cryo-EM: freezing proteins so fast that the water around them turns to glass-like ice, then imaging single molecules with electrons and combining thousands of images into a 3D structure.

cysteines 09

The amino acid whose R group ends in a sulfur atom, so that two of them can form a disulfide bond. It is the only amino acid you need to name.

denatured 05

Having lost its three-dimensional shape because the bonds that hold it have broken, so that the protein can no longer do its job. The amino acid sequence is unchanged.

dipeptide 02

Two amino acids joined by one peptide bond.

disulfide bonds 09

A covalent bond between the sulfur atoms of two cysteines.

essential amino acids 03

Amino acids that the body cannot make, so they must be obtained from food.

fibrous proteins 12

Proteins that are long and narrow, often with a repeating sequence. Most are insoluble and strong, and have structural jobs.

genetic code 04

The rules a cell uses to turn the sequence of bases in a gene into the sequence of amino acids in a polypeptide. It codes for twenty amino acids.

globular proteins 12

Proteins folded into compact, rounded shapes. Most are soluble in water and bind specific molecules: enzymes, hormones, transport proteins and antibodies.

hydrophilic 06

Attracted to water. Hydrophilic R groups are either polar or charged.

hydrophobic 06

Not attracted to water. Hydrophobic R groups are non-polar, made mostly of carbon and hydrogen.

hydrophobic interactions 09

The clustering of non-polar R groups together, away from water, in the middle of a folded protein.

integral proteins 10

Proteins that are embedded in a cell membrane, with part of the chain lying among the hydrophobic tails of the phospholipids.

ionic bonds 09

The attraction between a positively charged R group and a negatively charged one.

non-conjugated protein 11

A protein made of polypeptide only.

non-essential amino acids 03

Amino acids that the body can make from other amino acids, so they do not have to come from food.

peptide bond 02

The covalent bond between the carbon of one amino acid's carboxyl group and the nitrogen of the next amino acid's amine group. It forms in a condensation reaction.

polar 06

Having slightly positive and slightly negative regions, as in an O-H or N-H group, so that it can form hydrogen bonds with water.

polypeptide 02

A chain of many amino acids joined by peptide bonds.

primary structure 07

The sequence of amino acids in a polypeptide, set by its gene.

prosthetic group 11

The non-polypeptide part of a conjugated protein, such as the haem group of haemoglobin.

proteome 04

All the proteins that an organism, or a cell, makes.

quaternary structure 11

The arrangement of two or more polypeptides in one protein, held by the same kinds of bond as the tertiary structure.

R group 01

The side chain of an amino acid: the one part that differs between the twenty. R stands for whatever group it is, not for an element.

secondary structure 08

The regular coils and pleats that a polypeptide forms, held by hydrogen bonds between groups in the backbone.

tertiary structure 09

The three-dimensional shape of a whole polypeptide, held by bonds between R groups that are often far apart in the sequence.

**Check yourself**

The check for this guide is online: a fresh paper of past-paper style questions from the exam bank on B1.2 each time, marked as you go, and saved to your Exam practice progress when you are signed in. Scan the code, or type the link.

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Answers

PREDICTIONS IN THE CHAPTERS

01 A student draws an alpha carbon bonded to -NH_2 , -COOH , R and -OH . What is wrong with the drawing?

B The fourth group should be a single hydrogen atom, not -OH

The alpha carbon always carries a single hydrogen atom. With -OH in its place the drawing is not an amino acid, and an examiner would not award the mark for the alpha carbon's groups. Check every drawing for the H.

02 Two different amino acids, A and B, are joined by one peptide bond. How many different dipeptides could they make?

C Two: A's carboxyl to B's amine, or B's carboxyl to A's amine, and these are different molecules

Two. A peptide bond always joins a carboxyl group to an amine group, so every dipeptide has an amine end and a carboxyl end. In A-B, A keeps its free amine group; in B-A, B does. The same amino acids make different molecules, which is why the order of amino acids matters (chapter 4). Try both ways round in the bond builder.

03 You eat plenty of protein, but it lacks one essential amino acid. What happens to the proteins that need it?

A They cannot be completed, because no other amino acid can take its place in the sequence

They cannot be completed. Your cells cannot make an essential amino acid, and the gene sets the sequence, so no other amino acid can take its place. Every protein that needs it stalls at that point. That is why the total amount of protein is not the whole story: the mix matters.

04 How many different dipeptides can be made from the 20 amino acids?

D 400, because there are twenty choices at each of the two positions

400. There are 20 choices for the first amino acid and 20 for the second. Order matters (one way round is a different molecule from the other), and the same amino acid can appear twice. Move the slider to 2 to check, then try 3.

05 When an egg sets in a hot pan, which bonds break?

C The weak bonds that hold the fold, while the peptide bonds stay intact

Only the weak bonds that hold the fold. The chain of amino acids is still whole: a cooked egg is digested into exactly the same amino acids as a raw one. What heat destroys is the shape, and with it the job.

06 An R group contains a carboxyl group. Inside a cell, at about pH 7, it is:

B Negatively charged, because it has lost a hydrogen ion

Negatively charged. A carboxyl group gives up its hydrogen ion and is left negative: an acidic R group. An amine group does the opposite, gaining a hydrogen ion to become positive: a basic R group. Both are hydrophilic.

07 Two people make insulin from the same gene sequence. Do their insulin molecules have the same shape?

A Yes, exactly: the same sequence folds the same way every time

Yes. Proteins have precise, repeatable shapes. The sequence of R groups decides which bonds can form and where, so the same sequence folds the same way every time. That is why one hormone fits the same receptor in every cell, and why a protein's shape can be predicted from its sequence.

08 Which groups form the hydrogen bonds that hold an alpha helix?

D The C=O and N-H groups of the peptide bonds in the backbone

The backbone's own C=O and N-H groups, in regular positions four amino acids apart. That is why almost any stretch of chain can coil or pleat: the groups that bond are in every amino acid. The R groups decide which stretches do.

09 An ionic bond holds two parts of a protein together. The pH falls to 2. Why might the bond break?

B The negative carboxyl R group gains a hydrogen ion and loses its charge

In acid, a -COO^- picks up a hydrogen ion and becomes -COOH , with no charge, so nothing attracts it to the positive R group. Press Lower the pH to watch it. In strong alkali the opposite happens: -NH_3^+ loses its hydrogen ion.

10 A protein dissolves in blood plasma. Where are most of its hydrophobic R groups?

C Clustered in the core of the protein, away from the water

In the core. Hydrophobic R groups are not attracted to water, so in the folded protein they end up together inside, while hydrophilic ones cover the surface and keep it in solution. Fold a protein below and watch a chain do the same as it folds.

11 A haemoglobin molecule is about 5 to 6 nm across. Could you see one with the best light microscope?

B No: it is far smaller than the smallest thing light can resolve, about 200 nm

No. A light microscope cannot separate details closer than about 200 nm, some 40 times the size of a haemoglobin molecule. Electron microscopes, and now cryo-EM, image single molecules: technology extends our senses.

12 A protein is long and thin, has a repeating sequence and does not dissolve in water. What is its most likely job?

D A structural protein, as found in tendons, skin and blood vessel walls

A structural one. Long, repetitive and insoluble are the marks of a fibrous protein: strength, not binding. Hormones, enzymes and antibodies have to dissolve and fit specific molecules, which needs a compact, globular shape.

How this was made. The course structure, the activities and the teaching choices come from my own classroom, my presentations and my years of teaching IB and AP Biology. I use Claude, an AI, to help write and build the interactive guides, lesson plans, slides and practice questions, and to draw the diagrams and code the interactives. I direct the work and review it against the IB and AP specifications before it goes live.

Written and drawn for Biology by Bradford, biologybybradford.com. Free to print and share with a class.