# Biochemistry

**Unit 4 · Lesson 2 · The double helix and its forms**

The notes for Lesson 2 of Unit 4: chapters 4.3 to 4.4 of the unit book, with their figures, worked examples, exam traps and quizzes, in one file. The full unit book, with every chapter, the exam question bank and the glossary, is linked at the end.

Lesson 2 of 4 | 2 chapters | Chapters 4.3 to 4.4

## About these notes

These are the notes for **Lesson 2 · The double helix and its forms** of the University free n easy video lessons on Biochemistry Unit 4, Nucleic Acids, Vitamins and Minerals. They are chapters 4.3 to 4.4 of the unit book, unchanged, so a page here is the same page in the full book.

## 4.3 DNA double helix: Watson-Crick model and Chargaff's rules

In 1953 James Watson and Francis Crick proposed that DNA is two strands wound around each other, with the bases paired inside, A with T and G with C. The model explained two sets of facts at once: Erwin Chargaff’s measurements that A equals T and G equals C, and the X-ray pictures of DNA fibres taken by Rosalind Franklin and Maurice Wilkins. Because each strand fixes the sequence of the other, the model also showed how genes can be copied, which is why it is the most examined structure in this unit.

You need: nucleotides and the 5′ → 3′ direction from Chapter 4.2.

### Chargaff’s rules

Around 1950 Chargaff hydrolysed DNA from many species, separated the bases by paper chromatography and measured each one. For double-stranded DNA he found:

1. **A = T and G = C** (as moles or mole percent).
2. So total purines equal total pyrimidines: **A + G = T + C**, and also A + C = G + T.
3. Base composition **differs between species**, usually stated as the ratio (A + T)/(G + C) or as GC content.

4. Within one species, composition is the **same in every tissue** and does not change with age, diet or environment.

The rules hold for double-stranded DNA only. Single-stranded DNA (bacteriophage φX174) and RNA do not obey A = T or G = C, because their bases are not paired.

## The Watson–Crick model, point by point

Franklin's fibre diffraction pattern (with Raymond Gosling) showed a helix with a repeat of 3.4 nm and a spacing of 0.34 nm. Watson and Crick built a model that fitted those numbers and Chargaff's ratios. Watson, Crick and Wilkins received the 1962 Nobel Prize; Franklin had died in 1958.

1. **Two strands, one axis.** Two polynucleotide chains coil around a common axis to form a right-handed double helix.
2. **Antiparallel.** One strand runs 5′ → 3′ upward and the other 5′ → 3′ downward.
3. **Backbone outside, bases inside.** The charged sugar–phosphate backbones face the water; the flat bases lie inside, nearly perpendicular to the axis.
4. **Complementary pairing.** A pairs with T through two hydrogen bonds; G pairs with C through three. Every pair is one purine plus one pyrimidine, so the helix has a constant diameter of about 2 nm.
5. **Dimensions.** Neighbouring pairs are 0.34 nm apart and the model had 10 pairs per turn, so one turn is 3.4 nm. Later measurements of DNA in solution give about 10.5 pairs per turn.
6. **Two grooves.** The sugars of a base pair are not exactly opposite each other, so the backbones leave a wide **major groove** and a narrow **minor groove**. Proteins that read DNA sequence, such as transcription factors, mostly do so in the major groove.

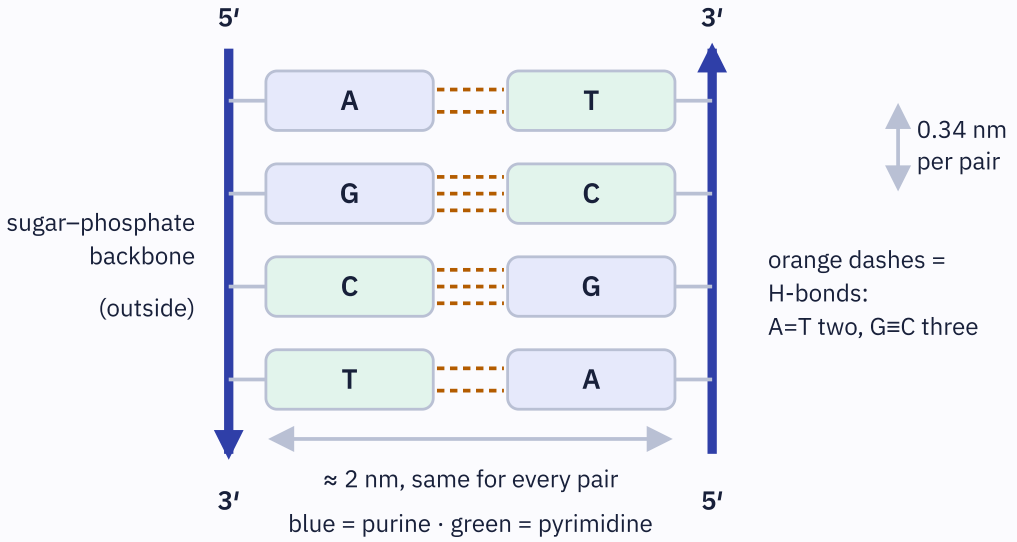



**Figure 4.3.1** The double helix unwound into a ladder. Arrows show the antiparallel strands; every rung is a purine (blue) paired with a pyrimidine (green), so all rungs have the same length. Count the dashes: two for A=T, three for G≡C.

## What holds the helix together, and how it melts

Hydrogen bonds give **specificity**: only A–T and G–C fit the geometry. Most of the **stability**, however, comes from base stacking, the van der Waals and hydrophobic contacts between neighbouring flat pairs. Positive ions ($Na^+$, $Mg^{2+}$) shield the repulsion between the negative phosphates.

Heating separates the strands. This is **denaturation** or melting, and the temperature at which half the DNA is single-stranded is the **melting temperature, Tm**. As the bases unstack, absorbance at 260 nm rises; this is the **hyperchromic effect**. DNA with more G–C pairs has a higher Tm, because G–C pairs have three hydrogen bonds and stack more strongly. On slow cooling, complementary strands find each other again (renaturation or annealing), which is the basis of PCR and of hybridisation probes.

## WORKED EXAMPLE

**Question (8 marks).** (a) A double-stranded DNA contains 22% adenine. Find the percentage of the other bases. (b) In one strand of a DNA duplex, (A + G)/(T + C) = 0.6. What is this ratio in the complementary strand and in the whole duplex? (c) The *E. coli* K-12 genome is about $4.64 \times 10^6$ base pairs of B-DNA. Find its length and the number of helical turns, using 0.34 nm per pair and 10.5 pairs per turn.

1. (a) A = T, so T = **22%**. A + T = 44%, leaving 56% for G + C. G = C = **28%** each.
2. (b) Each A in strand 1 faces a T in strand 2, and each G faces a C. So (A + G) of strand 1 = (T + C) of strand 2, and the ratio in strand 2 is the inverse: 1 ÷ 0.6 = **1.67**.
3. In the duplex, purines equal pyrimidines, so the ratio is **1.0**.
4. (c) Length = $4.64 \times 10^6 \times 0.34$ nm = $1.58 \times 10^6$ nm = **1.58 mm**, roughly a thousand times longer than the bacterium itself (about 1–2 µm).
5. Turns = $4.64 \times 10^6 \div 10.5$ = **$4.4 \times 10^5$ turns**.

## EXAM TRAPS

- Chargaff says A = T and G = C, not A = G. And (A + T)/(G + C) varies between species; it is not 1.
- The rules apply to double-stranded DNA only; do not use them for RNA or single-stranded DNA.
- Hydrogen bonds explain which bases pair; stacking explains most of the helix's stability. Examiners like this distinction.
- The strands are antiparallel, and the complementary strand of 5′-ATGC-3′ is 5′-GCAT-3′, not 5′-TACG-3′.
- Higher GC content means higher Tm; the hyperchromic effect is a rise, not a fall, in A260.

## CHECK YOURSELF

– REMEMBER **State Chargaff's rules.** 3 marks

In double-stranded DNA, A = T and G = C, so purines = pyrimidines; composition varies between species but is constant across tissues of one species and is not changed by age, diet or environment.

– REMEMBER **How many hydrogen bonds are there in an A–T pair and in a G–C pair?** 1 mark

Two in A–T; three in G–C.

– UNDERSTAND **Why is the diameter of the double helix constant along its length?** 2 marks

Each rung is one two-ring purine plus one one-ring pyrimidine, so every pair spans the same width (about 2 nm). Purine–purine pairs would be too wide and pyrimidine–pyrimidine pairs too narrow.

– UNDERSTAND **What is the hyperchromic effect?** 2 marks

The rise in UV absorbance at 260 nm when double-stranded DNA is denatured, because unstacked bases absorb more light than stacked ones.

– APPLY **A DNA sample has 35% G. Find A, T and C.** 2 marks

C = 35%; G + C = 70%; A + T = 30%, so A = T = 15%.

– APPLY **Write the complementary strand of 5′-AGGTCA-3′ in the 5′ → 3′ direction.** 2 marks

Pair each base and reverse: 3′-TCCAGT-5′ becomes **5′-TGACCT-3′**.

– ANALYZE **DNA X has Tm 72 °C and DNA Y has Tm 88 °C in the same buffer. Which has more A–T pairs, and why?** 3 marks

X. Lower Tm means the helix is less stable, which follows from fewer G–C pairs (three hydrogen bonds and stronger stacking), so X has more A–T pairs.

**BEYOND THE SYLLABUS**

The same pairing rules let engineers design DNA origami, where a long strand is folded by short “staple” strands into shapes a few nanometres across, used in drug delivery and nanoscale sensors. Not all DNA is a simple double helix: guanine-rich sequences such as telomeres can fold into four-stranded G-quadruplexes, now studied as drug targets. The history of the structure, including the role of Franklin’s Photograph 51, is retold in many accounts worth reading. Search “DNA origami” and “G-quadruplex”. This is not for the exam.

## 4.4 Forms of DNA: A, B and Z

The Watson–Crick helix is one shape DNA can take, not the only one. The same double strand can be squeezed into a shorter, wider right-handed **A form** when water is scarce, or twisted into a thin left-handed **Z form** by certain sequences.

You need: the B-form dimensions and grooves from Chapter 4.3.

### Why DNA changes shape

The backbone has several rotatable bonds, and the sugar ring can pucker in two main ways: C2′-endo (C2′ bent out of the ring plane toward C5′) or C3′-endo. The base can also turn about its glycosidic bond, into the **anti** position (base away from the sugar, the usual case) or the **syn** position (base over the sugar). Change the pucker and the base rotation, and the whole helix changes its width, rise and handedness. Water, salt, sequence and supercoiling decide which shape wins.

### The three forms compared

Values differ slightly between textbooks and crystal structures, so learn the approximate numbers and, above all, the direction of each difference.

| FEATURE | A-DNA | B-DNA | Z-DNA |
|---|---|---|---|
| Handedness | Right | Right | Left |
| Base pairs per turn | 11 | 10.5 (10 in fibres) | 12 (6 dinucleotide repeats) |
| Rise per base pair | ≈ 0.23–0.26 nm | ≈ 0.33–0.34 nm | ≈ 0.37–0.38 nm |
| Pitch (one turn) | ≈ 2.8 nm | ≈ 3.4 nm | ≈ 4.5 nm |
| Diameter | ≈ 2.3–2.6 nm (widest) | ≈ 2.0 nm | ≈ 1.8 nm (thinnest) |
| Base pairs relative to axis | Strongly tilted, pushed off the axis | Nearly perpendicular, on the axis | Slightly tilted |
| Sugar pucker | C3′-endo | C2′-endo | Alternates: C2′-endo at C, C3′-endo type at G |

| FEATURE | A-DNA | B-DNA | Z-DNA |
|---|---|---|---|
| Glycosidic bond | Anti | Anti | Anti at pyrimidines, syn at purines |
| Grooves | Major narrow and deep; minor wide and shallow | Major wide and deep; minor narrow | Major almost flat; minor narrow and deep |
| Favoured by | Low humidity (dehydrated fibres); also RNA–RNA and DNA–RNA duplexes | High humidity; normal cell conditions | Alternating purine–pyrimidine (e.g. CGCGCG), high salt, cytosine methylation, negative supercoiling |

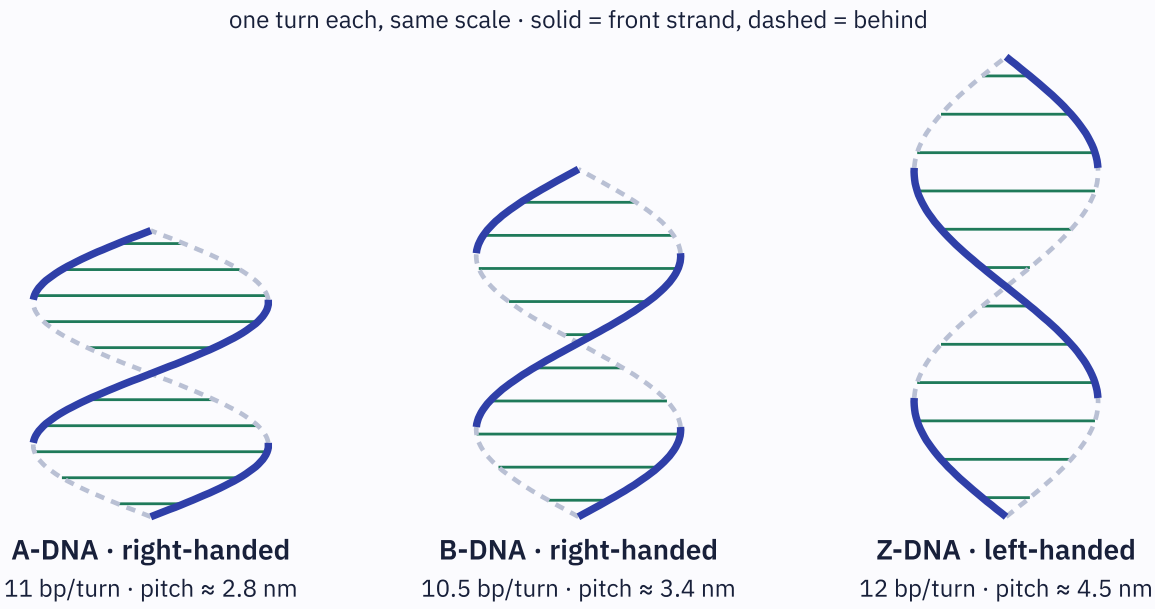



**Figure 4.4.1** One helical turn of each form drawn to the same scale from the approximate pitch and diameter in the table (green rungs are base pairs). Notice that A is short and wide, Z is long and thin, and the front strands of Z slope the opposite way because it is left-handed.

## Where each form matters

**B-DNA** is the form of almost all DNA in cells. **A-form** geometry matters mainly for RNA: double-stranded RNA and DNA–RNA hybrids cannot take the B form, because the 2′-OH of ribose favours the C3′-endo pucker, so they adopt an A-like helix. **Z-DNA** was discovered in 1979 when Alexander Rich's group solved the crystal structure of the short sequence CGCGCG. Its backbone zigzags, which gave it the name. In cells, short Z stretches form behind a moving RNA polymerase where the DNA becomes negatively supercoiled, and some proteins bind Z-DNA specifically.

### WORKED EXAMPLE

**Question (5 marks).** A 120-bp segment of DNA is converted from B to A form and, separately, to Z form. Using rises of 0.26, 0.34 and 0.37 nm and 11, 10.5 and 12 bp per turn for A, B and Z, find the length and number of turns in each form.

1. A form: length = 120 × 0.26 = **31.2 nm**; turns = 120 ÷ 11 = **10.9** (right-handed).
2. B form: length = 120 × 0.34 = **40.8 nm**; turns = 120 ÷ 10.5 = **11.4** (right-handed).
3. Z form: length = 120 × 0.37 = **44.4 nm**; turns = 120 ÷ 12 = **10** (left-handed).
4. So the same molecule is about 24% shorter in A form and about 9% longer in Z form than in B form (31.2/40.8 = 0.76; 44.4/40.8 = 1.09).

### EXAM TRAPS

- Only Z is left-handed; A and B are both right-handed.
- A-DNA is the widest and shortest per turn; Z-DNA is the thinnest. Students often swap A and Z.
- Z-DNA needs an alternating purine–pyrimidine sequence; a random sequence does not form it easily.
- In Z-DNA the purines are syn and the pyrimidines anti; in A and B every base is anti.

### CHECK YOURSELF

– REMEMBER **Which DNA form is left-handed, and who described it first?** 1 mark

Z-DNA; Alexander Rich and colleagues, 1979, from crystals of CGCGCG.

– REMEMBER **Give the sugar pucker of A- and B-DNA.** 1 mark

A: C3′-endo. B: C2′-endo.

– UNDERSTAND **Why do double-stranded RNA molecules form an A-like helix rather than a B helix?** 2 marks

The 2′-OH of ribose clashes with the C2′-endo pucker that B form needs, so ribose stays C3′-endo, which gives A-form geometry.

– APPLY **How many turns does a 360-bp Z-DNA stretch make?** 1 mark

360 ÷ 12 = **30 left-handed turns**.

– ANALYZE **A DNA fibre gives a wider, shorter helix when dried and returns to the usual shape when humid. Identify the two forms and explain the role of water.** 3 marks

Dry fibre: A form; humid: B form. Water hydrates the backbone and the grooves; removing it lets the sugars switch to C3′-endo and the pairs tilt and move off the axis, giving the shorter, wider A helix.

**BEYOND THE SYLLABUS**

Proteins with a Zα domain, such as the RNA-editing enzyme ADAR1 and the immune sensor ZBP1, bind Z-shaped DNA and RNA, and research links them to antiviral defence and inflammation. Other non-B structures, such as triplexes, cruciforms and G-quadruplexes, form at special sequences and can cause genome instability. Search “Z-DNA binding proteins” and “non-B DNA”. This is not for the exam.

## Key terms of this lesson

| TERM | MEANING OR FORMULA | CHAPTER |
|---|---|---|
| Chargaff’s rules | A = T, G = C, A + G = T + C (double-stranded DNA) | 4.3 |
| B-DNA length | length = base pairs × 0.34 nm; turns = bp ÷ 10.5 | 4.3 |
| A, B, Z DNA | Right, right, left; ≈ 11, 10.5, 12 bp per turn | 4.4 |

## Glossary (terms used in this lesson)

**Base stacking** The van der Waals and hydrophobic contacts between neighbouring flat base pairs; the main stabilising force of the double helix.

**Chargaff’s rules** In double-stranded DNA, A = T and G = C, so purines equal pyrimidines.

**Hyperchromic effect** The rise in absorbance at 260 nm when double-stranded DNA is denatured.

**Major groove** The wider of the two grooves on the B-DNA helix, where most sequence-reading proteins bind.

| | |
|---|---|
| **Nucleotide** | A nucleoside with one or more phosphate groups on the sugar. |
| **Z-DNA** | A left-handed DNA double helix with a zigzag backbone, favoured by alternating purine–pyrimidine sequences. |

## The full unit book

Every chapter of Unit 4, the unit summary, the exam question bank with model answers and the full glossary: Biochemistry · Unit 4 · Nucleic Acids, Vitamins and Minerals (one file, works offline).

## Sources and further reading

### Standard textbooks

- David L. Nelson and Michael M. Cox, *Lehninger Principles of Biochemistry*: the chapters on nucleotides and nucleic acids, and on vitamins as coenzymes (from memory; check the chapter numbers in your edition).
- U. Satyanarayana and U. Chakrapani, *Biochemistry*: the chapters on nucleic acids, vitamins and minerals; widely prescribed in Indian universities (from memory; check).
- Jeremy M. Berg, John L. Tymoczko and Lubert Stryer (later editions with Gregory Gatto), *Biochemistry* (from memory; check).
- Donald Voet and Judith G. Voet, *Biochemistry*: detailed treatment of DNA conformations A, B and Z (from memory; check).

### Open web resources

- Wikipedia, “Nucleic acid double helix”, comparison table of A-, B- and Z-DNA geometry: en.wikipedia.org/wiki/Nucleic_acid_double_helix
- NIH Office of Dietary Supplements, “Vitamin A and Carotenoids: Fact Sheet for Health Professionals”, for the IU and RAE conversion factors: ods.od.nih.gov/factsheets/VitaminA-HealthProfessional

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