Biochemistry

Unit 1 · Lesson 1 · Biomolecules and water

The notes for Lesson 1 of Unit 1: chapters 1.1 to 1.2 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 1 of 4 | 2 chapters | Chapters 1.1 to 1.2

About these notes

These are the notes for **Lesson 1 · Biomolecules and water** of the University free n easy video lessons on Biochemistry Unit 1, Foundations: Water, pH and Carbohydrates. They are chapters 1.1 to 1.2 of the unit book, unchanged, so a page here is the same page in the full book.

1.1 Biomolecules and the chemical foundations of biochemistry

Biochemistry explains life in the language of chemistry. A living cell is built from a few elements, arranged into a small set of building blocks (sugars, amino acids, nucleotides, fatty acids) that join into large molecules. The rules that govern a reaction in a test tube (covalent bonds, functional groups, shape and energy) also govern a reaction in a liver cell. Learn these rules once and every later unit becomes a set of examples.

What biochemistry studies, and why

Biochemistry has four aims: to describe the structures of the molecules of life; to explain how they recognise and bind one another; to trace how cells make and break them (metabolism, Units 5 and 6); and to find out how all of this is controlled and inherited.

The scope is wide because almost every question about living things is, at bottom, a chemical one. In **medicine**, a blood-glucose test, a lipid profile and a liver-enzyme test are biochemical measurements. In **food and agriculture**, the ripening of a mango, the setting of curd and the rising of idli batter are enzyme and carbohydrate chemistry. In **industry**, detergent enzymes, recombinant insulin, vaccines and biofuels all start from knowing which molecule does what.

Elements and building blocks

Of the roughly 90 natural elements, only about 30 are essential to living things. Four of them, carbon, hydrogen, oxygen and nitrogen, make up more than 99% of the mass of most cells. Phosphorus and sulfur come next. Ions such as Na^+, K^+, Mg^{2+}, Ca^{2+} and Cl^- are needed in bulk, and trace elements such as Fe, Zn, Cu, Se and I in small amounts, mostly inside enzymes.

Carbon is the backbone because each carbon atom forms four stable covalent bonds, single or double, to other carbons or to H, O and N. Carbon can therefore build chains, branches and rings of almost any size, and its tetrahedral bonds give these skeletons a definite three-dimensional shape. Water, the medium for all of this, makes up about 70% of the mass of most cells (Chapter 1.2).

Most biomolecules belong to four classes. Three are true polymers, made by joining many similar units through one kind of bond (Figure 1.1.1). Lipids are the exception: they are assembled from fatty acids and other parts but do not form long repeating chains (Unit 3). Cells also hold thousands of small molecules, the metabolites such as pyruvate, citrate and ATP, that are the intermediates of metabolism.

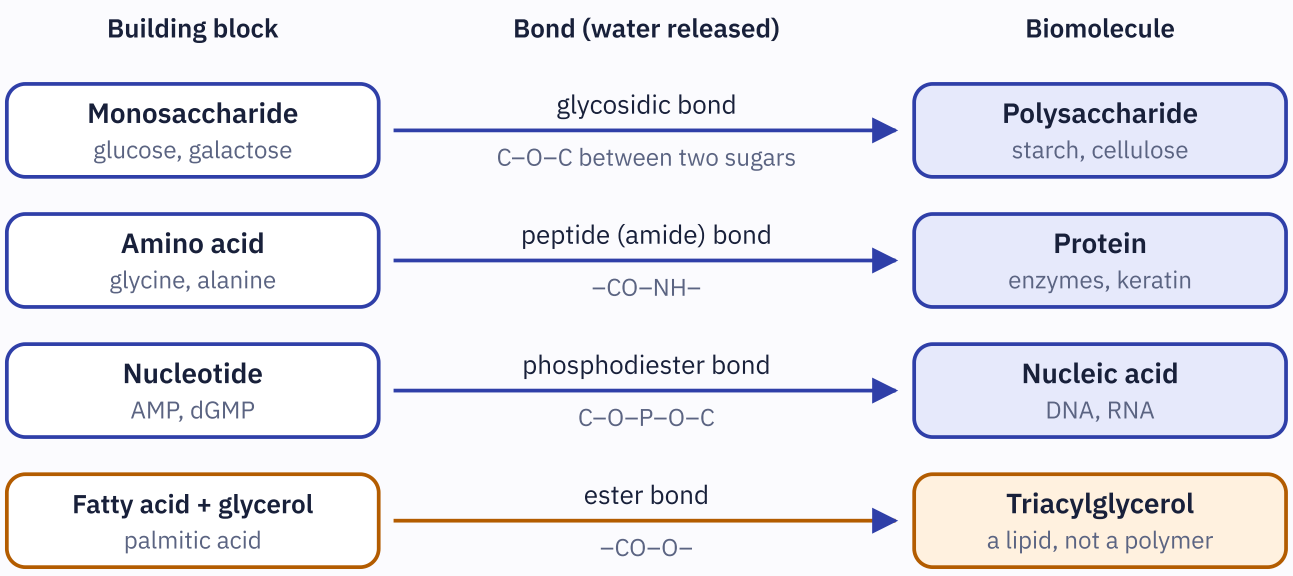


Figure 1.1.1 The three polymer classes and the lipids. Every bond shown forms when water is removed (condensation) and breaks when water is added back (hydrolysis). Notice that a triacylglycerol is made by the same kind of chemistry but is not a long chain of repeating units.

Joining two building blocks removes a molecule of water: an –OH from one partner and an –H from the other. This is a **condensation** (dehydration) reaction. The reverse, splitting the bond by adding water back, is **hydrolysis**. Digestion is hydrolysis; building a protein or a starch granule is condensation, paid for with energy from ATP or an activated donor (Chapter 1.9 and Unit 5).

Polymers also have direction. A polysaccharide has a reducing end and a non-reducing end (Chapter 1.6), a protein an amino end and a carboxyl end, and a nucleic acid a 5′ end and a 3′ end. The order of units along the chain carries information: twenty kinds of amino acid in a chain of 100 can be arranged in 20^{100} ways, far more than the number of atoms in the observable universe.

Functional groups

A functional group is a set of atoms that reacts in a characteristic way wherever it sits. Most biomolecules carry several, and their solubility, charge and reactivity follow from them. The charges shown are those at pH 7, explained in Chapter 1.2.

GROUP	STRUCTURE	WHERE YOU MEET IT
Hydroxyl	–OH	sugars, alcohols, serine
Aldehyde (carbonyl)	–CHO	open-chain aldoses such as glucose
Ketone (carbonyl)	>C=O	ketoses such as fructose; pyruvate
Carboxyl	–COOH ($–COO^-$)	amino acids, fatty acids, uronic acids
Amino	$–NH_2$ ($–NH_3^+$)	amino acids, amino sugars
Amide	–CO–NH–	peptide bond, N-acetylglucosamine
Ester	–CO–O–R	fats and oils, acetylated sugars
Ether or acetal	C–O–C	glycosidic bonds
Phosphoryl	$–O–PO_3^{2-}$	sugar phosphates, nucleotides, ATP
Thiol (sulfhydryl)	–SH	cysteine, coenzyme A
Sulfate ester	$–O–SO_3^-$	glycosaminoglycans (Chapter 1.7)

Shape: configuration, conformation and chirality

Two molecules with the same atoms and bonds can still differ in shape, and in biology shape decides function. The **configuration** of a molecule is the fixed arrangement of its atoms in space; changing it means breaking a covalent bond. Cis and trans double bonds, and the two mirror-image forms of a chiral molecule, differ in configuration. A **conformation** is any shape the molecule can take by rotating about single bonds, without breaking any. A sugar ring flexing between chair forms, or a protein chain folding, changes conformation only.

A carbon atom with four different groups attached is a **chiral centre**. It can exist as two non-superimposable mirror images (enantiomers), like a left and a right hand. Living systems are strongly one-handed: proteins are built from L-amino acids and most natural sugars are D-sugars (Chapter 1.4). Enzymes and receptors are themselves chiral, so they usually accept only one enantiomer. Even our noses tell the two forms of carvone apart: one smells of spearmint, the other of caraway seeds.

Shape is held in place by weak interactions (Chapter 1.2), and energy decides which reactions run; how cells capture and spend energy is bioenergetics (Unit 5).

WORKED EXAMPLE

Question (6 marks). (a) Ten glucose molecules ($C_6H_{12}O_6$, molar mass 180.16 g/mol) join in a straight chain. How many water molecules are released, and what is the molar mass of the chain? (b) Estimate the molar mass of a protein of 300 amino acid residues. (c) Name the bond formed in each case.

1. A straight chain of n units has n − 1 links, and each link releases one H_2O (18.02 g/mol). For n = 10: **9 water molecules**.
2. Molar mass of the chain = 10 × 180.16 − 9 × 18.02 = 1801.6 − 162.2 = **1639.4 g/mol**.
3. Check another way: each glucose inside a chain is a residue $C_6H_{10}O_5$ (162.14 g/mol), and one water's worth of atoms stays at the two ends: 10 × 162.14 + 18.02 = 1639.4 g/mol. The answers agree.
4. For proteins, the average mass of an amino acid residue (water already removed) is about 110 Da, where 1 Da corresponds to 1 g/mol. So 300 × 110 ≈ 33,000 Da, that is **about 33 kDa**.
5. The glucose chain is held by glycosidic bonds; the protein by peptide (amide) bonds.

Rule: a polymer's molar mass is never just n times the monomer's; subtract (n − 1) waters.

EXAM TRAPS

- "Biomolecule" is not the same as "macromolecule". Lipids and small metabolites such as pyruvate are biomolecules, but they are not polymers.
- Condensation and hydrolysis are often swapped. Condensation releases water and makes the bond; hydrolysis uses water and breaks it.
- Configuration or conformation? Rotation about a single bond changes conformation; a change of configuration needs a bond to break. The α to β change of glucose is a change of configuration, because the ring must open (Chapter 1.4).
- The letters D and L describe configuration, not the direction in which a sugar rotates light (Chapter 1.4).
- Structures are often drawn with –COOH and $–NH_2$, but at pH 7 these groups exist as $–COO^-$ and $–NH_3^+$. Give the charged forms when the question is about a cell.

CHECK YOURSELF

– REMEMBER **Which four elements make up more than 99% of the mass of most cells?** 2 marks

Carbon, hydrogen, oxygen and nitrogen.

– UNDERSTAND **Why are lipids called biomolecules but not polymers?** 2 marks

They are assembled from a few different parts (glycerol, fatty acids, phosphate, bases) joined mainly by ester bonds, and they do not form long chains of one repeating unit. Large lipid structures such as membranes are held by weak forces, not by a covalent chain.

– APPLY **Calculate the molar mass of a straight chain of 25 glucose residues.** 3 marks

25 × 162.14 + 18.02 = 4053.5 + 18.0 = **4071.5 g/mol** (or 25 × 180.16 − 24 × 18.02, which gives the same).

– APPLY **Name the functional groups in pyruvate ($CH_3–CO–COO^-$) and in glucose 6-phosphate.** 4 marks

Pyruvate: a ketone (carbonyl) group and a carboxylate group. Glucose 6-phosphate: several hydroxyl groups, the aldehyde (hemiacetal in the ring form) at C1, and a phosphoryl group as a phosphate ester at C6.

– ANALYZE **Twenty amino acids are enough to build millions of different proteins. Show why with a calculation.** 4 marks

Each position can hold any of 20 amino acids, so a chain of n residues has 20^n possible sequences. Even a 10-residue peptide has $20^{10} \approx 1.0 \times 10^{13}$ sequences. The order of units carries the information, just as 26 letters make every book.

– ANALYZE **Why does an enzyme usually act on only one enantiomer of its substrate?** 3 marks

The active site is built from L-amino acids and is itself chiral. The substrate must touch it at three or more points at once; its mirror image can match at most two of them, like a left hand in a right glove.

BEYOND THE SYLLABUS

Modern biochemistry measures thousands of molecules at once. Metabolomics uses mass spectrometry to profile the small molecules of a cell, and cryo-electron microscopy and AI prediction (AlphaFold) show the shapes of the large ones. Why life uses only one hand of each chiral molecule, called homochirality, is still an open question in origin-of-life chemistry. Search next for "metabolomics", "Human Metabolome Database" and "homochirality". None of this is for the exam.

1.2 Water, weak interactions, pH and biological buffers

Water is the medium of life, a reactant in every hydrolysis and a sculptor of biomolecules. Its bent, polar molecules hydrogen bond to one another and to polar groups, push nonpolar groups together, and split very slightly into H^+ and OH^-. That last property gives the pH scale, and buffers (a weak acid with its conjugate base) keep pH steady in blood, cells and the lab.

Water and the hydrogen bond

Oxygen is more electronegative than hydrogen, so in a water molecule it pulls the shared electrons towards itself: the O carries a partial negative charge (δ–) and each H a partial positive charge (δ+). The molecule is bent, with an H–O–H angle of 104.5°, so the charges do not cancel and water is a dipole. A **hydrogen bond** forms when a δ+ hydrogen, already bonded to an O or N, is attracted to a lone pair on another O or N. Each water molecule can make up to four: two through its hydrogens and two through its oxygen (Figure 1.2.1, left).

A hydrogen bond in liquid water has a dissociation energy of about 23 kJ/mol, against about 470 kJ/mol for the covalent O–H bond. Each lasts only picoseconds, but at any moment most molecules are bonded, so liquid water is a constantly reshuffling network. This explains water's high boiling point, specific heat and heat of vaporisation (sweat cools you because breaking the bonds takes heat). In ice every molecule is locked into four bonds in an open lattice, so ice is less dense than water and floats.

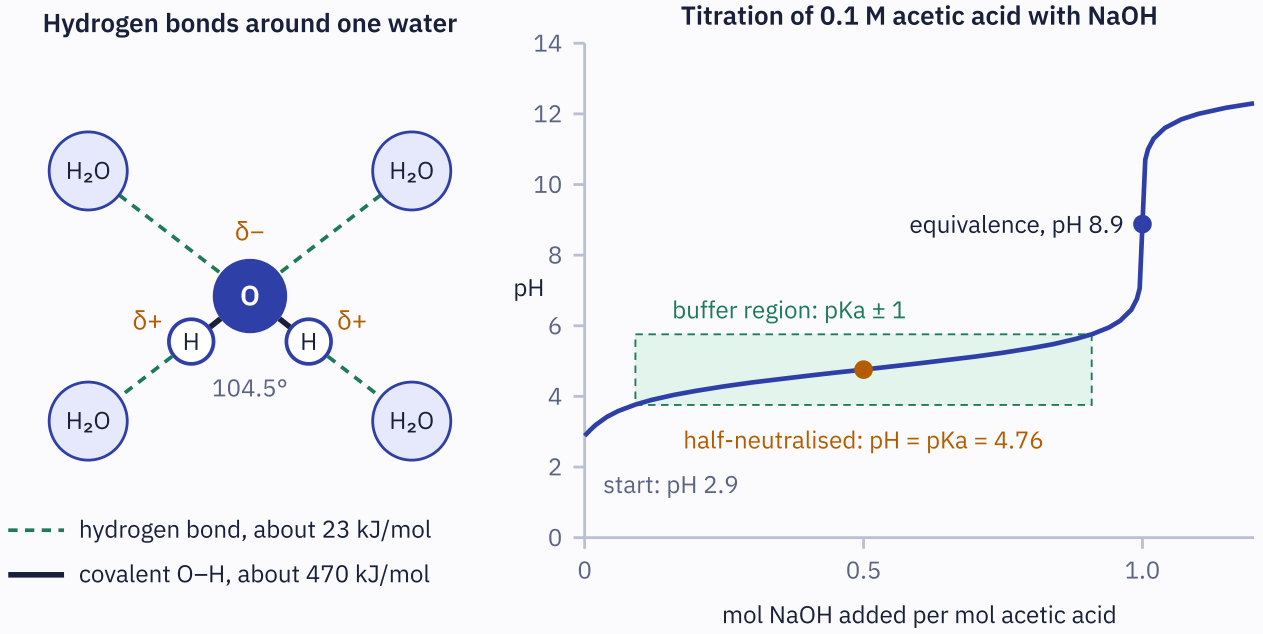


Figure 1.2.1 Left: one water molecule can donate two hydrogen bonds and accept two. Right: titration of 0.1 M acetic acid, computed point by point (volume change ignored). Notice how flat the curve is around pH 4.76, where acid and conjugate base are equal: that is the buffer region.

Weak interactions and the hydrophobic effect

Covalent bonds hold the atoms of a biomolecule together; weak (non-covalent) interactions hold its shape and let molecules recognise each other. Each is weak and breaks easily, but hundreds together are strong and specific.

INTERACTION	WHAT ATTRACTS WHAT	EXAMPLE
Hydrogen bond	δ+ H on O or N to a lone pair on O or N	DNA base pairs, protein helices, sugar–water
Ionic (electrostatic)	opposite charges, such as $–COO^-$ and $–NH_3^+$	salt bridges in proteins, Mg^{2+} with ATP
Hydrophobic effect	nonpolar groups clustering away from water	oil droplets, membranes, protein cores

INTERACTION	WHAT ATTRACTS WHAT	EXAMPLE
van der Waals	short-lived dipoles of atoms in close contact, a few kJ/mol each	tightly packed protein interiors, enzyme–substrate fit

Water weakens ionic attractions. By Coulomb's law the force between charges q_1 and q_2 at distance r is $F = q_1 q_2/(4\pi\varepsilon_0\varepsilon r^2)$, where ε_0 is the permittivity of free space and ε the dielectric constant of the medium. For water ε is about 78.5 at 25 °C, so opposite charges attract with only about 1/80 of their force in a vacuum. That is why salts dissolve: water surrounds and screens each ion (hydration). Polar and charged molecules such as sugars are hydrophilic; nonpolar ones such as oils are hydrophobic.

The **hydrophobic effect** is not a true attraction between nonpolar groups. A nonpolar molecule cannot hydrogen bond, so the water around it is forced into an ordered cage, which lowers entropy. When nonpolar groups cluster, caged water is set free and its entropy rises. Amphipathic molecules (a polar head and a nonpolar tail, as in soaps and phospholipids) therefore form micelles and bilayers, tails inside (Unit 3).

Ionisation of water, pH and pKa

Water ionises slightly: $H_2O \rightleftharpoons H^+ + OH^-$ (the H^+ is really carried as H_3O^+). The ion product of water is $K_w = [H^+][OH^-] = 1.0 \times 10^{-14}$ M² at 25 °C, where square brackets mean molar concentration; in pure water $[H^+] = [OH^-] = 10^{-7}$ M. The pH is defined as $pH = -\log_{10}[H^+]$, so neutral water at 25 °C has pH 7. The scale is logarithmic: one pH unit is a tenfold change in $[H^+]$.

A weak acid HA dissociates only partly: $HA \rightleftharpoons H^+ + A^-$, where A^- is its conjugate base. Its acid dissociation constant is $K_a = [H^+][A^-]/[HA]$, and $pK_a = -\log K_a$; the lower the pKa, the stronger the acid. Taking logarithms of Ka gives the Henderson–Hasselbalch equation:

```
Ka = [H⁺][A⁻] / [HA]
log Ka = log[H⁺] + log([A⁻]/[HA])
−log[H⁺] = −log Ka + log([A⁻]/[HA])
pH = pKa + log([A⁻]/[HA])
```

When $[A^-] = [HA]$, the log term is zero and pH = pKa: the acid is exactly half dissociated. That is the flat middle of the titration curve in Figure 1.2.1.

Biological buffers and how to prepare one

A **buffer** is a mixture of a weak acid and its conjugate base that resists a change in pH when a little acid or base is added. Added H^+ is taken up by A^- (forming HA); added OH^- takes H^+ from HA (forming A^- and water). The ratio $[A^-]/[HA]$, and so the pH, changes only a little. A buffer works best at pH = pKa, usefully within pKa ± 1, and its capacity grows with concentration.

Blood plasma (pH 7.35 to 7.45) relies on the bicarbonate system, $CO_2 + H_2O \rightleftharpoons H_2CO_3 \rightleftharpoons H^+ + HCO_3^-$, with an apparent pKa of 6.1. It works despite that pKa because it is open: the lungs remove CO_2 and the kidneys adjust HCO_3^-. Inside cells the phosphate pair $H_2PO_4^- \rightleftharpoons H^+ + HPO_4^{2-}$ (pKa 7.2 in dilute solution, about 6.9 at cellular ionic strength) does most of the work, helped by histidine side chains of proteins (pKa about 6). Blood pH below 7.35 is acidosis (as when ketone bodies pile up in uncontrolled diabetes, Unit 6); above 7.45 is alkalosis (as after hyperventilation).

Common lab buffers are phosphate, acetate (pKa 4.76), Tris (pKa about 8.1) and HEPES (pKa about 7.5). The procedure:

1. Choose a buffer with pKa within 1 unit of the pH you need, that does not interfere with the experiment.
2. Find the ratio $[A^-]/[HA] = 10^{(pH - pKa)}$.
3. From concentration and volume, work out moles, then grams (a hydrate has a different molar mass).
4. Dissolve in about 80% of the final volume, check with a calibrated pH meter at the working temperature (Tris shifts about 0.03 pH unit per °C), and adjust with dilute acid or base.
5. Make up to volume in a volumetric flask.

WORKED EXAMPLE

Question (6 marks). Prepare 1.0 L of 0.10 M sodium phosphate buffer, pH 7.4, from anhydrous NaH_2PO_4 (119.98 g/mol) and Na_2HPO_4 (141.96 g/mol). Take pKa = 7.20.

1. Ratio: $[HPO_4^{2-}]/[H_2PO_4^-] = 10^{(7.4 - 7.2)} = 10^{0.2} = 1.585$.
2. Let $[H_2PO_4^-] = x$. Then $x + 1.585x = 0.10$ M, so $x = 0.10/2.585 = 0.0387$ M, and $[HPO_4^{2-}] = 0.0613$ M. Check: 0.0387 + 0.0613 = 0.100 M.
3. In 1.0 L that is 0.0387 mol and 0.0613 mol.
4. Masses: $NaH_2PO_4 = 0.0387 \times 119.98 =$ **4.64 g**; $Na_2HPO_4 = 0.0613 \times 141.96 =$ **8.70 g**.
5. Dissolve in about 800 mL of water, check with the pH meter, adjust and make up to 1.0 L. The reading is usually a little below 7.4, because ionic strength lowers the effective pKa.

EXAM TRAPS

- pH is logarithmic: pH 6 has ten times the $[H^+]$ of pH 7, not "a little more".
- In Henderson–Hasselbalch the ratio is base over acid, $[A^-]/[HA]$. Writing it upside down flips the sign of the log term.
- A buffer has a range, pKa ± 1. Acetate cannot buffer at pH 7.4, however concentrated it is.
- Neutral pH is 7.0 only at 25 °C, because Kw changes with temperature.
- The hydrophobic effect is driven by the entropy of water, not by an attraction between nonpolar molecules; "hydrophobic bond" is a misleading name.

CHECK YOURSELF

– REMEMBER **Write the Henderson–Hasselbalch equation and define each term.** 2 marks

pH = pKa + log([A⁻]/[HA]); pKa = –log Ka of the weak acid, [A⁻] is the conjugate base concentration and [HA] the undissociated acid concentration.

– UNDERSTAND **Why does oil not mix with water?** 3 marks

Oil cannot hydrogen bond, so water forms ordered cages around it. Droplets merging frees caged water, and that gain in the water's entropy drives the separation (the hydrophobic effect).

– APPLY **A 1 L buffer has 0.10 M acetic acid and 0.10 M sodium acetate (pKa 4.76). Find the pH after adding 0.010 mol HCl, and compare with pure water.** 4 marks

H^+ converts acetate to acetic acid: [HA] = 0.11 M, $[A^-]$ = 0.09 M. pH = 4.76 + log(0.09/0.11) = 4.76 – 0.09 = **4.67**, a drop of only 0.09. The same HCl in 1 L of pure water gives $[H^+]$ = 0.01 M, so pH falls from 7 to **2**.

– APPLY **Blood has $[HCO_3^-]$ = 24 mM and pCO_2 = 40 mmHg (dissolved CO_2 = 0.03 mM per mmHg; pKa 6.1). Find the pH, and the pH if pCO_2 rises to 60 mmHg.** 4 marks

CO_2 = 1.2 mM: pH = 6.1 + log(24/1.2) = 6.1 + 1.30 = **7.40**. At 60 mmHg, CO_2 = 1.8 mM: pH = 6.1 + log 13.3 = **7.22**, a respiratory acidosis (breathing too little).

– ANALYZE **For an enzyme assay at pH 7.2, choose between acetate (pKa 4.76), phosphate (7.2) and Tris (8.1). Justify.** 3 marks

Phosphate: its pKa equals the target pH, so capacity is greatest. Tris is at the edge of its range and drifts with temperature; acetate is outside its range. If phosphate inhibits the enzyme or precipitates Ca^{2+}, use HEPES.

– ANALYZE **The bicarbonate pKa (6.1) is far from 7.4, yet it is the main buffer of blood. Explain.** 3 marks

It is an open system: the lungs adjust CO_2 within minutes and the kidneys adjust HCO_3^- over hours to days, so the ratio $[HCO_3^-]/[CO_2]$ stays near 20.

BEYOND THE SYLLABUS

Good's buffers (HEPES, MES, MOPS and others) were designed in the 1960s to suit biology: pKa near 7, little binding of metal ions, and no passage through membranes. In research, weak interactions are now known to drive liquid–liquid phase separation, in which proteins and RNA condense into membraneless droplets inside cells. Search next for "Good's buffers" and "biomolecular condensates". None of this is for the exam.

Key terms of this lesson

TERM	MEANING OR FORMULA	CHAPTER
Condensation, hydrolysis	joining two units releases H_2O; hydrolysis adds it back and breaks the bond	1.1
Polymer molar mass	n × M(monomer) − (n − 1) × 18.02 g/mol	1.1
Hydrogen bond	δ+ H on O or N attracted to a lone pair on O or N; about 23 kJ/mol in water	1.2
Hydrophobic effect	nonpolar groups cluster because freeing ordered water raises its entropy	1.2
Ion product, pH	$K_w = [H^+][OH^-] = 1.0 \times 10^{-14}$ M² at 25 °C; pH = −log[H^+]	1.2
Henderson–Hasselbalch	pH = pKa + log([A^-]/[HA]); a buffer works within pKa ± 1	1.2

Glossary (terms used in this lesson)

Buffer	A solution of a weak acid and its conjugate base that resists a change in pH; it works within pKa ± 1.
D and L	The configuration of the chiral carbon farthest from the carbonyl: –OH on the right in a Fischer projection is D.
Enantiomers	Non-superimposable mirror images, with every chiral centre inverted, such as D- and L-glucose.
Glycosidic bond	The bond from the anomeric carbon of a sugar to an –OH (O-glycosidic) or an –NH (N-glycosidic) of another molecule.
Hemiacetal	The product of an alcohol adding to an aldehyde; the ring form of an aldose is one, and a ketose ring is a hemiketal.
Hydrogen bond	The attraction of a δ+ hydrogen on O or N to a lone pair on another O or N; about 23 kJ/mol in water.
Hydrophobic effect	The clustering of nonpolar groups in water, driven by the entropy gained by the water molecules released.
pKa	–log Ka; the pH at which an acid is half dissociated.

The full unit book

Every chapter of Unit 1, the unit summary, the exam question bank with model answers and the full glossary: Biochemistry · Unit 1 · Foundations: Water, pH and Carbohydrates (one file, works offline).

Sources and further reading

Textbooks

- David L. Nelson and Michael M. Cox, *Lehninger Principles of Biochemistry*, W. H. Freeman; chapters on water and on carbohydrates and glycobiology (from memory; check). Source of the bond energies, the branching frequencies of amylopectin and glycogen and the chain length of cellulose used here.
- Jeremy M. Berg, John L. Tymoczko, Gregory J. Gatto Jr. and Lubert Stryer, *Biochemistry*, W. H. Freeman; chapter on carbohydrates (from memory; check).
- Donald Voet and Judith G. Voet, *Biochemistry*, Wiley (from memory; check).

- U. Satyanarayana and U. Chakrapani, *Biochemistry*, Elsevier India; widely prescribed in Indian universities, with the colour tests for carbohydrates (from memory; check).
- Ajit Varki and others (editors), *Essentials of Glycobiology*, Cold Spring Harbor Laboratory Press, also free on the NCBI Bookshelf; for Chapters 1.7 and 1.9 (from memory; check).

Other standard values in this book, such as the specific rotations of sucrose (+66.5°) and fructose (−92.4°), are textbook values written from memory; check them against your prescribed book.

Open resources opened for this book

- Wikipedia, "Mutarotation": en.wikipedia.org/wiki/Mutarotation. Source of the specific rotations of α- and β-D-glucose (+112.2°, +18.7°), the equilibrium value (+52.7°) and the 36 : 64 ratio of the anomers.
- NPTEL, Module 11 (Carbohydrates), Lecture 30, course 104103071: archive.nptel.ac.in. Confirms the same rotation values and the reducing and non-reducing classes by hemiacetal and acetal form.
- US Food and Drug Administration, "Aspartame and Other Sweeteners in Food": fda.gov. Source of the sweetness of the high-intensity sweeteners relative to sucrose in Chapter 1.5.

Syllabus: the University free n easy universal syllabus, built from top universities' syllabi.

Built for the University free n easy YouTube channel from the universal syllabus of Biochemistry (Oct 2026). Written with top universities' syllabi and standard textbooks; check a formula against your prescribed book before an exam, and report mistakes on the channel.