Biochemistry

Unit 1 · Lesson 3 · Polysaccharides and glycosaminoglycans

The notes for Lesson 3 of Unit 1: chapters 1.6 to 1.7 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 3 of 4 | 2 chapters | Chapters 1.6 to 1.7

About these notes

These are the notes for **Lesson 3 · Polysaccharides and glycosaminoglycans** of the University free n easy video lessons on Biochemistry Unit 1, Foundations: Water, pH and Carbohydrates. They are chapters 1.6 to 1.7 of the unit book, unchanged, so a page here is the same page in the full book.

1.6 Polysaccharides: starch, glycogen, cellulose and chitin

Polysaccharides are long chains of sugar units, and a small change in the glycosidic bond changes everything about them. α1→4 links make chains that coil and pack into compact, digestible fuel stores (starch and glycogen); β1→4 links make straight chains that stack into tough, insoluble fibres (cellulose and chitin).

You need: α and β glycosidic links and reducing ends (Chapter 1.5).

Starch: amylose and amylopectin

Starch is the fuel store of plants, packed into granules in the seeds, tubers and roots we eat (rice, wheat, potato, tapioca). It is a mixture of two glucose polymers. **Amylose** is unbranched: D-glucose units joined only by α1→4 links, from a few hundred to several thousand per chain. The α link puts a bend at every unit, so the chain coils into a helix with about six glucose units per turn; iodine slips inside the helix and gives the deep blue-black colour of the starch test. **Amylopectin** has the same α1→4 chains plus α1→6 branch points about every 24 to 30 units. It is much larger than amylose and gives a red-violet colour with iodine. Most starches are roughly 20 to 30% amylose; "waxy" types such as sticky rice are almost all amylopectin.

Digestion starts in the mouth with salivary α-amylase and continues with pancreatic α-amylase. Both cut internal α1→4 links, giving maltose, maltotriose and branched fragments called limit dextrins; enzymes on the intestinal lining finish the job, including the α1→6 branches. Cooking matters. Heating starch in water makes the granules swell and lose their order (gelatinisation), which makes them easy to digest. On cooling, amylose chains slowly pair up again (retrogradation), and part of the starch in cooled rice or bread then resists digestion.

Glycogen

Glycogen is the glucose store of animals, fungi and bacteria. Like amylopectin it is an α1→4 chain with α1→6 branches, but it branches more often, about every 8 to 12 units, and is more compact. It lies as granules in the cytosol, mainly of liver and skeletal muscle, and each molecule grows on a primer protein, glycogenin. Liver glycogen keeps blood glucose up between meals; muscle glycogen fuels the muscle itself.

Branching is a design for speed. A branched polymer has one reducing end but many non-reducing ends, one more than its number of branch points (Figure 1.6.1), and the enzyme glycogen phosphorylase removes glucose from the non-reducing ends. More ends mean more places to work at once, so glucose is released fast in a sprint or when a meal is late. Branching also makes glycogen more soluble. Storing glucose as one giant molecule instead of millions of free ones keeps the osmotic pressure of the cell low, as the worked example shows.

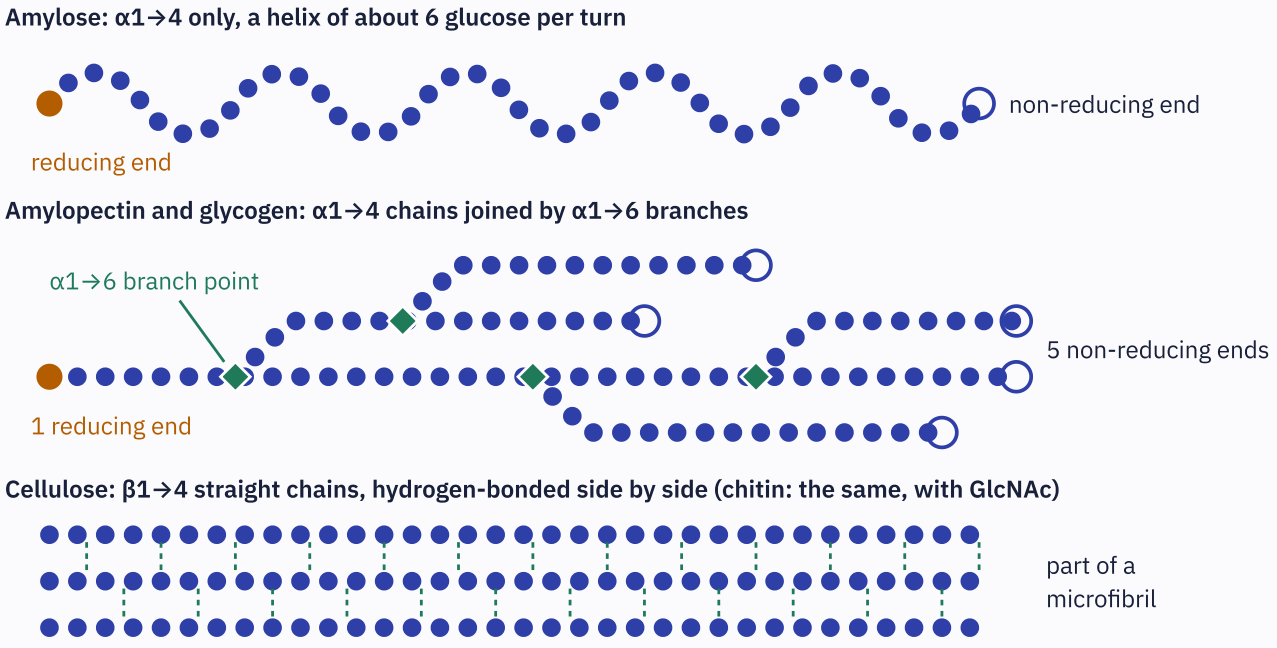


Figure 1.6.1 Each dot is one glucose unit. Amylose (top) is a single coiled chain. Amylopectin and glycogen (middle) branch through α1→6 links (diamonds); notice that four branch points give five non-reducing ends (rings) but still only one reducing end. Cellulose chains (bottom) are straight and hydrogen-bonded (dashes) into microfibrils.

Cellulose

Cellulose is the most abundant organic polymer on Earth: the main material of plant cell walls, almost all of a cotton fibre, and a large part of wood (with lignin and hemicellulose). It is an unbranched chain of 10,000 to 15,000 D-glucose units joined by β1→4 links. The β link turns each glucose 180° relative to its neighbour, so the chain is straight and flat rather than helical. Hydrogen bonds within each chain and between neighbouring chains lock parallel chains into crystalline microfibrils with great tensile strength, and water cannot get in, so cellulose is insoluble.

Humans make no enzyme that cuts the β1→4 link (cellulase). Cellulose therefore passes through us as dietary fibre, which adds bulk and feeds gut bacteria. Cows, goats and termites digest it only because microbes in their gut make cellulases. Industry uses cellulose for paper, cotton and viscose textiles, and derivatives such as carboxymethylcellulose, a thickener in food and toothpaste.

Chitin

Chitin is cellulose's counterpart in animals and fungi: unbranched β1→4 chains of N-acetyl-D-glucosamine (GlcNAc), a glucose whose C2–OH is replaced by an acetamido group (–NH–CO–CH_3). The chains pack like cellulose into hydrogen-bonded sheets that build the hard exoskeletons of insects, crabs and prawns and the cell walls of fungi. After cellulose, it is the most abundant polysaccharide in nature. Hot alkali removes most acetyl groups to give chitosan, whose free amino groups become positively charged in dilute acid, so it dissolves there. Chitosan, made from prawn and crab shell waste, is used in wound dressings, water treatment and edible coatings.

POLYMER	UNIT	LINKS	BRANCHING	IODINE COLOUR	ROLE
Amylose	glucose	α1→4	none	blue-black	plant fuel store
Amylopectin	glucose	α1→4, α1→6	every 24 to 30	red-violet	plant fuel store
Glycogen	glucose	α1→4, α1→6	every 8 to 12	red-brown	animal fuel store
Cellulose	glucose	β1→4	none	none	plant cell wall
Chitin	GlcNAc	β1→4	none	none	exoskeleton, fungal wall

WORKED EXAMPLE

Question (6 marks). A liver cell stores glycogen equivalent to 0.40 M glucose, while the glycogen molecules themselves are about 0.01 μM. (a) Using the van 't Hoff equation, find the osmotic pressure at 37 °C due to (i) 0.40 M free glucose and (ii) 0.01 μM glycogen. (b) A glycogen molecule of 6,000 glucose units branches every 10 units. How many non-reducing ends does it have, and why does that matter?

1. The van 't Hoff equation is $\Pi = icRT$, where Π is osmotic pressure, i the number of particles per molecule (1 for glucose), c the molar concentration, R = 0.08314 L·bar/(mol·K) and T the absolute temperature (37 °C = 310 K).
2. (i) $\Pi = 0.40 \times 0.08314 \times 310 =$ **10.3 bar**, about ten times atmospheric pressure: enough to pull in water and burst the cell.
3. (ii) 0.01 μM = 1.0×10^{-8} M, so $\Pi = 1.0 \times 10^{-8} \times 0.08314 \times 310 =$ **2.6×10^{-7} bar**, negligible. The osmotic load falls $0.40/10^{-8} = 4 \times 10^{7}$-fold.
4. (b) Branch points ≈ 6,000/10 = 600, so non-reducing ends = 600 + 1 = **601**, with a single reducing end.
5. Glycogen phosphorylase works at non-reducing ends, so about 600 ends can release glucose at the same time: fast mobilisation in exercise or fasting.

EXAM TRAPS

- Amylose is unbranched. Amylopectin branches every 24 to 30 units and glycogen every 8 to 12; do not swap the numbers.
- Starch and cellulose are both glucose polymers. The difference is the α or β link, not the monomer.
- Chitin's unit is N-acetylglucosamine, not glucose.
- However large, a polysaccharide has only one reducing end, so it gives a weak or negative reducing-sugar test.
- Iodine colours: amylose blue-black, amylopectin red-violet, glycogen red-brown.

CHECK YOURSELF

– REMEMBER **Give the glycosidic links in amylose, amylopectin and cellulose.** 3 marks

Amylose: α1→4 only. Amylopectin: α1→4 chains with α1→6 branches. Cellulose: β1→4 only.

– UNDERSTAND **Why is a cellulose chain straight while amylose coils into a helix?** 2 marks

In the β1→4 link each glucose is turned 180° to its neighbour, so the chain runs straight and can hydrogen bond to parallel chains. The α1→4 link puts the same bend at every unit, so the chain curls into a helix.

– UNDERSTAND **Why does chitosan dissolve in dilute acetic acid while chitin does not?** 2 marks

Chitosan has free $-NH_2$ groups that take up H^+ to become $-NH_3^+$; the charged chains repel one another and hydrate. Chitin's acetylated amides do not ionise, and its chains stay locked in hydrogen-bonded sheets.

– APPLY **An amylopectin molecule of 12,000 units branches every 25 units. Find its branch points, non-reducing ends and reducing ends.** 3 marks

Branch points = 12,000/25 = **480**; non-reducing ends = 480 + 1 = **481**; reducing ends = **1**.

– APPLY **Predict the iodine colour for potato starch, liver glycogen and filter paper.** 2 marks

Potato starch: blue-black (from its amylose). Glycogen: red-brown (short branched chains form no long helix). Filter paper is cellulose: no colour.

– ANALYZE **Glycogen branches more often than amylopectin. Relate this to the needs of animals.** 3 marks

Animals must release glucose fast (running, fasting). More branches mean more non-reducing ends for phosphorylase to act on at once, and a more soluble, compact granule. A plant seed releases its starch slowly during germination, so fewer branches suffice.

BEYOND THE SYLLABUS

Food scientists breed and process grains for more "resistant starch", which raises blood glucose more slowly. Cellulose broken into nanometre-wide fibres (nanocellulose) makes strong, transparent films, and cellulase enzymes turn crop residues such as rice straw into second-generation ethanol (see the bioenergy subject). Inherited defects in the enzymes that make or break glycogen cause the glycogen storage diseases (Unit 6). Search next for "resistant starch", "nanocellulose" and "glycogen storage disease". None of this is for the exam.

1.7 Glycosaminoglycans, proteoglycans and glycoconjugates

Glycosaminoglycans (GAGs) are long, unbranched heteropolysaccharides built from one repeating disaccharide of an amino sugar and, usually, a uronic acid, most of them carrying sulfate groups. Their dense negative charge makes them stiff, extended and water-loving, which is why cartilage is springy and joint fluid is slippery. Attached to a core protein, GAGs form proteoglycans; together with glycoproteins and glycolipids these make up the glycoconjugates, the sugar-bearing molecules that coat every cell.

You need: heteropolysaccharides (Chapter 1.3); weak interactions and osmosis (Chapter 1.2).

What a glycosaminoglycan is

Each GAG repeats one disaccharide hundreds of times. One partner is an amino sugar: N-acetylglucosamine (GlcNAc), N-acetylgalactosamine (GalNAc) or, in heparin, N-sulfated glucosamine (GlcNS). The other is usually a uronic acid: D-glucuronic acid (GlcA), which is glucose with C6 oxidised to –COOH, or its C5 epimer L-iduronic acid (IdoA). Keratan sulfate is the exception, with galactose in place of the uronic acid. Sulfate esters ($–OSO_3^-$) on many sugars, plus the carboxylates ($–COO^-$), make GAGs the most negatively charged molecules in the body. Their old name, mucopolysaccharides, comes from the slimy feel of their solutions.

Charge explains function. Neighbouring negative groups repel, so each chain stretches out and sweeps a huge volume. The charges attract cations such as Na^+, and water follows by osmosis (Chapter 1.2), so GAGs form a hydrated gel. Squeeze the gel and water is pushed out; release it and water flows back in. That is the cushioning of cartilage. Hyaluronic acid adds slipperiness: its solutions are viscous at rest but thin out when sheared, ideal for a moving joint.

GAG	REPEATING DISACCHARIDE	SULFATED?	FOUND IN	ROLE
Hyaluronic acid	`GlcA(β1→3)GlcNAc, repeats β1→4`	no	joint fluid, vitreous humour, cartilage, skin	lubricant, shock absorber
Chondroitin sulfate	`GlcA(β1→3)GalNAc-4S or -6S`	yes	cartilage, tendon, bone	resists compression
Dermatan sulfate	`IdoA(α1→3)GalNAc-4S`	yes	skin, blood vessels, heart valves	flexibility; binds collagen
Keratan sulfate	`Gal(β1→4)GlcNAc-6S, no uronic acid`	yes	cornea, cartilage	corneal transparency

GAG	REPEATING DISACCHARIDE	SULFATED?	FOUND IN	ROLE
Heparin	`IdoA-2S(α1→4)GlcNS-6S (main unit)`	most of all	granules of mast cells	anticoagulant
Heparan sulfate	`like heparin, fewer sulfates, more GlcA`	yes	cell surfaces, basement membranes	binds growth factors

Two of these stand apart. **Hyaluronic acid** (hyaluronan) is the only GAG that is not sulfated and not bound covalently to a protein. It is also the largest, reaching millions of daltons, and is made at the plasma membrane rather than in the Golgi. **Heparin** is the most heavily sulfated. Mast cells store it in granules, and as a drug it prevents clotting by helping the plasma protein antithrombin switch off clotting enzymes. Dermatan sulfate is simply chondroitin sulfate in which some GlcA has been turned into IdoA. Its list misprints keratan sulfate as "keratin sulphate", and keratin is a protein.

Proteoglycans

A **proteoglycan** is a core protein carrying one or more covalently attached GAG chains; by mass it is mostly carbohydrate. Most chains join a serine of the core through a fixed linker, the tetrasaccharide GlcA–Gal–Gal–Xyl–Ser, with xylose bonded to the serine.

In cartilage the main proteoglycan is **aggrecan**. Each aggrecan core carries many chondroitin sulfate chains and shorter keratan sulfate chains, and many aggrecans bind along one hyaluronic acid chain, held there by a small link protein. The result is a huge bottle-brush aggregate (Figure 1.7.1) trapped in a mesh of collagen fibres: collagen resists stretching, the aggregate resists compression. Loss of aggrecan is an early event in osteoarthritis. Other proteoglycans sit on cell surfaces (syndecans span the membrane) or in basement membranes (perlecan), where their heparan sulfate chains bind growth factors and guide signalling.

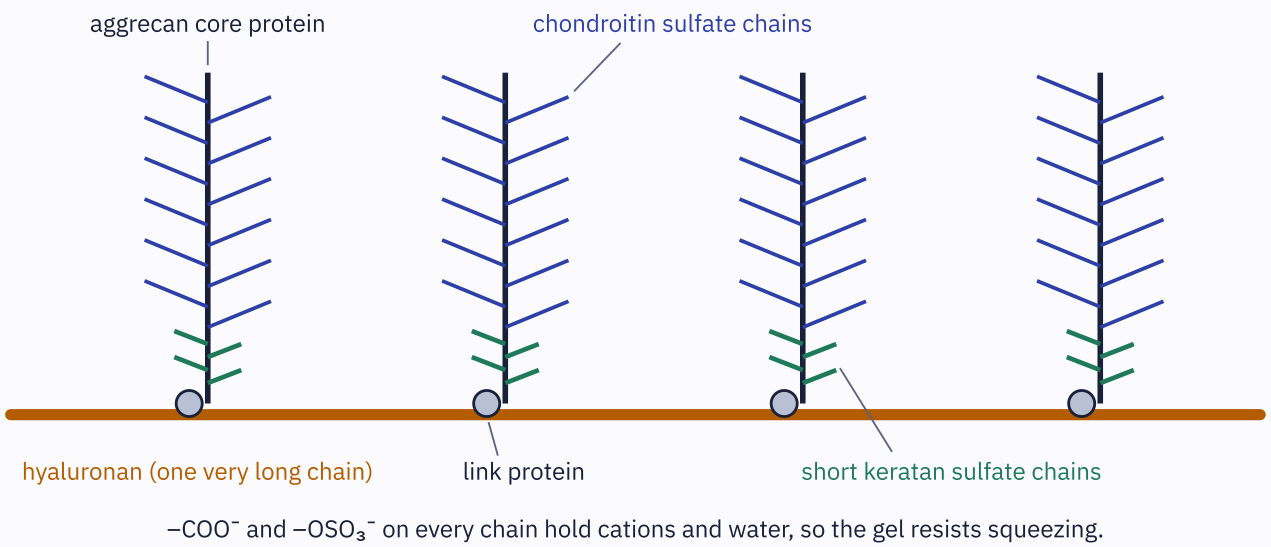


Figure 1.7.1 The proteoglycan aggregate of cartilage (not to scale, and with far fewer chains than the real thing). Aggrecan cores carry long chondroitin sulfate and short keratan sulfate chains and bind, through link proteins, along a single hyaluronan chain. Notice that the GAG chains, not the proteins, fill most of the space: that space is held open by charge and water.

Glycoconjugates: glycoproteins and glycolipids

Glycoconjugate is the umbrella term for any protein or lipid with sugars covalently attached. Proteoglycans are one kind. **Glycoproteins** are proteins carrying one or more short, often branched oligosaccharides (glycans). Most secreted and cell-surface proteins are glycoproteins, including antibodies, many hormones and the mucins of mucus, which carry so many sugars that they form a gel. Their glycans attach either to the amide nitrogen of asparagine (N-linked) or to the –OH of serine or threonine (O-linked); how cells add them is Chapter 1.9. **Glycolipids** are lipids with a sugar head: in animals mostly glycosphingolipids such as cerebrosides and gangliosides (Unit 3), and in Gram-negative bacteria the lipopolysaccharide of the outer membrane, which acts as endotoxin.

Do not mix up the two protein conjugates. A proteoglycan is mostly carbohydrate, with long, unbranched, repeating, sulfated GAG chains. A glycoprotein is mostly protein, with short, branched, non-repeating glycans. Glycans act as identity tags read by sugar-binding proteins called lectins: the ABO blood groups differ only in the last sugar of a glycan, influenza virus binds sialic acid on our airway cells, and selectins on blood-vessel walls catch the glycans of white blood cells to slow them at a site of infection. GAGs are broken down step by step in lysosomes, and an inherited lack of one of these enzymes makes them pile up in tissues, as in the mucopolysaccharidoses such as Hurler syndrome (Unit 6).

WORKED EXAMPLE

Question (6 marks). At pH 7 each carboxyl and each sulfate group carries one negative charge; N-acetyl groups are uncharged. (a) Find the charge per repeating disaccharide of hyaluronate, chondroitin 4-sulfate, keratan sulfate (one sulfate) and the main heparin unit (IdoA-2-sulfate with N-sulfated, 6-sulfated glucosamine). (b) Find the charge of a heparin chain of 20 such units. (c) Explain why protamine, a small arginine-rich protein, reverses heparin after heart surgery.

1. Hyaluronate: GlcA (−1, carboxylate) + GlcNAc (0) = **−1**.
2. Chondroitin 4-sulfate: GlcA (−1) + GalNAc-4-sulfate (−1) = **−2**.
3. Keratan sulfate: Gal (0) + GlcNAc-6-sulfate (−1) = **−1**; there is no uronic acid.
4. Heparin: IdoA-2-sulfate (−1 carboxylate, −1 sulfate) + GlcNS-6-sulfate (−1 N-sulfate, −1 O-sulfate) = **−4**.
5. (b) 20 units × (−4) = **−80** charges on one chain.
6. (c) Arginine side chains are positive at pH 7. Protamine binds heparin by ionic attraction, neutralises its charge and stops it from helping antithrombin.

Ranking by charge per unit: heparin, then chondroitin and dermatan sulfate, then hyaluronate and keratan sulfate.

EXAM TRAPS

- Keratan sulfate, not "keratin sulfate": keratin is a protein of hair and nails.
- Hyaluronic acid is the only GAG that is unsulfated and not covalently bound to a core protein.
- Heparin and heparan sulfate are different: heparin is more sulfated and stored in mast cells; heparan sulfate sits on cell surfaces.
- Proteoglycan is not glycoprotein: mostly sugar with long repeating chains, against mostly protein with short branched glycans.
- Dermatan sulfate contains L-iduronic acid, the C5 epimer of D-glucuronic acid.

CHECK YOURSELF

– REMEMBER **Name the two sugars of the hyaluronic acid repeat, and the one GAG that has no uronic acid.** 2 marks

D-glucuronic acid and N-acetyl-D-glucosamine. Keratan sulfate has galactose instead of a uronic acid.

– UNDERSTAND **Why are GAG solutions viscous and slippery?** 2 marks

The chains are long and stiffened by repelling negative charges, so they occupy a large volume and trap water, giving a viscous gel. Under shear the chains line up, so the fluid thins and lubricates.

– UNDERSTAND **Give three differences between a proteoglycan and a glycoprotein.** 3 marks

Proteoglycan: mostly carbohydrate; long unbranched GAG chains of repeating disaccharides; usually sulfated. Glycoprotein: mostly protein; short branched glycans with no repeating unit; sulfate rare.

– APPLY **What is the charge of a chondroitin 4-sulfate chain of 50 disaccharide units at pH 7?** 2 marks

Each unit is −2 (one carboxylate, one sulfate), so 50 × (−2) = **−100**.

– ANALYZE **Explain why cartilage resists compression and then recovers its shape.** 3 marks

Aggrecan aggregates pack fixed negative charges into the collagen mesh. These hold cations and water, creating a swelling pressure. Compression squeezes water out against this pressure; when the load is removed, the charges draw water back and the tissue re-swells.

– ANALYZE **Many invasive bacteria secrete hyaluronidase, called a "spreading factor". Explain the name.** 2 marks

The enzyme cuts the hyaluronan that keeps connective tissue a thick gel. As the gel thins, bacteria and their toxins move through the tissue more easily.

BEYOND THE SYLLABUS

Heparin for medicine is still extracted from pig intestine. In 2008, batches contaminated with an oversulfated chondroitin sulfate harmed patients, and regulators then added tests such as NMR to tell real heparin from look-alikes. Fondaparinux, a fully synthetic copy of the five-sugar heparin sequence that binds antithrombin, shows that chemical synthesis (Chapter 1.9) can replace an animal product. Hyaluronic acid is used in knee injections, eye surgery and cosmetic fillers. Search next for "heparin contamination 2008", "fondaparinux" and "glycocalyx". None of this is for the exam.

Key terms of this lesson

TERM	MEANING OR FORMULA	CHAPTER
Branching rule	non-reducing ends = branch points + 1; always one reducing end	1.6
Osmotic pressure	Π = icRT (van 't Hoff)	1.6
Glycosaminoglycan	repeating disaccharide of an amino sugar and a uronic acid, mostly sulfated	1.7

Glossary (terms used in this lesson)

Glycoconjugate A protein or lipid with sugars covalently attached: glycoproteins, proteoglycans and glycolipids.

Glycosidic bond The bond from the anomeric carbon of a sugar to an –OH (O-glycosidic) or an –NH (N-glycosidic) of another molecule.

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.

Proteoglycan A core protein carrying one or more covalently attached GAG chains; mostly carbohydrate by mass.

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.