

Chapter 6. Biochemical Principles and Metabolism

Part 1 | Basic Biochemical Concepts

1 Learning Objectives

By the end of this unit you will be able to ...

- 1. **Sketch or recognise** the core chemical structures of amino-acids, monosaccharides, fatty-acids / glycerol, and nucleotides.
- 2. **Explain how monomers assemble into macromolecules** (proteins, carbohydrates, lipids, nucleic-acids) and relate each class to human-movement physiology.
- 3. **Describe enzyme architecture, active-site specificity, and catalytic mechanisms**, including Michaelis-Menten kinetics and common forms of regulation.
- 4. **Apply biochemical concepts to physiotherapy practice**—e.g. muscle-protein synthesis, glycogen loading, lipid-mediated inflammation control, and genetic considerations in exercise responses.

2 Major Biomolecule Classes

Class	Building Block → Bond	Key Functions	Physiotherapy Relevance
Proteins	Amino-acids (20) → peptide bond (-CONH-)	Enzymes, structural fibres (collagen), contractile filaments (actin-myosin), transporters (Hb)	↑ dietary protein (1.2–1.6 g·kg ⁻¹) accelerates muscle repair; collagen- rich supplements aid tendon rehab
Carbohydrates	Monosaccharides (glucose) → glycosidic bond	Quick ATP via glycolysis, glycogen storage, cell recognition	Glycogen re-synthesis critical in multi- session rehab; monitor blood glucose in diabetics during exercise
Lipids	Fatty-acids + glycerol → ester bonds (triacylglycerol); phospholipids; cholesterol	Energy-dense fuel, membrane fluidity, eicosanoid signalling	Omega-3 FAs reduce chronic inflammation; β-oxidation dominates low-intensity endurance prescriptions
Nucleic acids	Nucleotides (adenine-ribose-P) → phosphodiester bonds	Genetic code (DNA/RNA); energy currency (ATP); cell signalling (cAMP)	Satellite-cell DNA replication underpins hypertrophy; ATP hydrolysis powers every rehab exercise

3 Protein Structure Hierarchy

- 1. Primary amino-acid sequence (genetic code).
- 2. **Secondary** α-helix, β-sheet (H-bonds).
- 3. **Tertiary** 3-D folding via hydrophobic, ionic, disulfide interactions.
- 4. **Quaternary** multi-polypeptide assembly (e.g., $Hb = \alpha_2\beta_2$).

Clinical link: Mutations altering primary structure of collagen cause Ehlers-Danlos \rightarrow joint instability; tailor proprioceptive training accordingly.

4 Enzyme Structure & Function

Feature Explanation

Active site 3-D pocket; binds substrate via induced-fit.

 $\textbf{Cofactors / Co-enzymes} \text{ Metal ions } (Zn^{2+}, Mg^{2+}) \text{ or vitamin-derived (NAD+ from niacin) essential for catalysis.}$

Catalytic speed Lowers activation energy (E_a) \rightarrow accelerates reactions up to 10^6 -fold.

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Feature Explanation

Specificity Lock-and-key or induced-fit ensures metabolic order.

RegulationAllosteric modulators, covalent phosphorylation, enzyme quantity (gene expression),

compartmentalisation.

Michaelis-Menten Snapshot

 $v=Vmax[S]Km+[S]v=\{v_{max}[S]\}\{K_m+[S]\}$

- **Vmax** maximal velocity (enzyme saturation).
- **Km** substrate concentration at ½ Vmax; lower Km = higher affinity.

Competitive inhibition: ↑ Km, same Vmax (statins vs HMG-CoA reductase). **Non-competitive:** ↓ Vmax, same Km (cyanide vs cytochrome oxidase).

5 Integrated Examples for Physiotherapists

Scenario	Biochemical Basis	Action Point
DOMS recovery	Micro-tear → protease & collagenase activation	20-30 g whey (rich in EAA & leucine) within 1 h supports MPS via mTOR
Glycogen-depleted patient on consecutive rehab days	Liver & muscle glycogen < 60 %	1.2 g·kg ⁻¹ h ⁻¹ carbohydrate + 0.3 g·kg ⁻¹ protein immediately post-session
Anti-inflammatory dietary advice for tendinopathy	Ω -3 FAs compete with arachidonic acid in COX pathway \rightarrow fewer prostaglandins	Encourage fish oil or flaxseed; monitor clotting if on anticoagulants
Pharmacology: ACE inhibitors	Competitive enzyme inhibition blocks angiotensin-II formation	Check for hypotension during early standing or aquatic sessions

6 Self-Check Quiz (answers below)

- 1. Which amino-acid contains a sulfur group critical for disulfide bond formation?
- 2. Name the high-energy bond in ATP responsible for energy release during hydrolysis.
- 3. In competitive inhibition, what happens to Vmax and Km?
- 4. Why are unsaturated fatty-acids liquid at room temperature while saturated fats are solid?
- 5. Give one example of a nucleotide second messenger and its producing enzyme.
- 1. Cysteine (-SH side chain).
- 2. The **terminal phosphoanhydride bond** between β- and γ-phosphate.
- 3. Vmax unchanged, Km increases (need more substrate).
- 4. Double bonds create kinks preventing tight packing, lowering melting point.
- 5. **cAMP** produced by **adenylyl cyclase** from ATP.

7 Key Take-Home Points

- **Biomolecules are the hardware; enzymes are the software** driving every physiologic reaction in movement and repair.
- Proteins build and move us, carbohydrates fuel bursts, lipids fuel distance, nucleic-acids script adaptation.
- Enzyme regulation underlies drug actions, metabolic diseases and training responses—knowledge here empowers safer, more effective physiotherapy plans.

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Part 2 | Major Metabolic Pathways

1 Learning Objectives

On completing this part, you should be able to ...

- 1. Trace the key reactions, cellular locations and ATP yields of glycolysis, gluconeogenesis, β -oxidation, lipogenesis, transamination and the urea cycle.
- 2. Identify rate-limiting enzymes and major regulators (allosteric, hormonal, covalent) of each pathway.
- 3. **Predict metabolic shifts** during fed/fasted states, high-intensity vs endurance exercise, and clinical conditions such as diabetes or liver disease.
- 4. **Translate biochemical knowledge into physiotherapy practice,** e.g., nutritional timing, monitoring catabolic states, and designing energy-appropriate exercise programmes.

2 Carbohydrate Metabolism

Pathway	Location	Net Equation & Yield	Key Control Point(s)	Clinical / PT Angle
Glycolysis	Cytosol (all cells)	Glucose + 2 ADP + 2 Pi + 2 NAD+ → 2 Pyruvate + 2 ATP + 2 NADH	PFK-1 (+ AMP, ADP, F-2,6-BP; – ATP, citrate); Hexokinase/Glucokinase ; Pyruvate kinase	Dominant in high- intensity bursts; lactate export buffers H+—teach active recovery
Anaerobic fate	Cytosol	Pyruvate + NADH → Lactate + NAD+ (LDH)	↓ O₂ availability	Pursed-lip breathing aids CO2 clearance; HIIT raises lactate threshold
Gluconeogenesis	Liver (90 s %), kidney cortex	2 Pyruvate + 4 ATP + 2 GTP + 2 NADH → Glucose + 4 ADP + 2 GDP	Pyruvate carboxylase (needs biotin & acetyl-CoA) & PEP carboxykinase; Fructose-1,6-bisphosphatase (- AMP, F-2,6-BP)	Cori cycle recycles exercise lactate → glucose; caution prolonged low-CHO diets in heavy training

3 Lipid Metabolism

Pathway	Location	Net Outcome	Key Enzymes / Regulators	PT Relevance
β-Oxidation (fatty-acid catabolism)	Mitochondrial matrix (liver, muscle)	Each cycle: $FA(n) \rightarrow$ FA(n-2) + Acetyl-CoA + $FADH_2 + NADH (\approx 14$ ATP/2C)	Carnitine shuttle (CPT-I) rate-limiting (-malonyl-CoA); activated by glucagon, epinephrine	Supplies > 70 % ATP in long, moderate-intensity sessions—fat-max training improves utilisation
Lipogenesis (fatty-acid synthesis)	Cytosol (liver, adipose)	Acetyl-CoA + ATP + NADPH → Palmitate (16 C)	Acetyl-CoA carboxylase (ACC) (+ citrate, insulin; - AMP-PK, palmitoyl-CoA)	Excess post-exercise carbs convert to TAG; AMPK activation by endurance work inhibits ACC (↓ fat synth)
TAG mobilization	Adipose cytosol to plasma	Hormone-sensitive lipase (HSL) releases FFA + glycerol	↑ by catecholamines, ↓ by insulin	Fasted cardio elevates FFA; diabetics on insulin risk blunted lypolysis—monitor hypoglycaemia

4 Protein & Nitrogen Metabolism

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Process	Location	Highlight Steps	Key Enzymes / Vitamins	Rehab Implications
Amino-acid transamination	Cytosol & mito (liver, muscle)	AA + α- ketoglutarate ⇌ α- ketoacid + Glutamate	ALT, AST (need vitamin B_6)	Elevated serum AST/ALT signals muscle or liver damage post-exercise
Oxidative de- amination	Hepatic mitochondria	Glutamate \rightarrow NH ₃ + α -KG + NADH (GDH)		Produces NH ₃ for urea cycle; ammonia build-up causes fatigue in ultra-endurance events
Urea cycle	Liver mitochondria (1) & cytosol (2-5)	2 NH ₃ + CO ₂ + 3 ATP \rightarrow Urea + 2 ADP + AMP	CPS-I (rate limit, needs N-acetyl-glutamate)	Liver impairment elevates blood NH₃ → encephalopathy—dose exercise cautiously
Muscle protein synthesis (MPS)	Ribosomes; mTORC1- regulated	Leucine triggers; requires ATP + tRNA	Adequate EAA + resistance load (≥ 65 % 1-RM) doubles MPS for 24 h	

5 Fed-Fasted & Exercise Integration

State	Hormonal Milieu	Dominant Pathways	What PT Should Know
Fed (high insulin)	↑ Insulin, ↓ glucagon	Glycolysis, glycogen & lipid synthesis	Schedule skill sessions; energy plentiful for neural focus
Early fast / moderate exercise	↓ Insulin, ↑ glucagon, catecholamines	Glycogenolysis, β -oxidation rising	Keep carbs handy if diabetic; monitor RPE
Prolonged fast / endurance (> 90 min)	↑ Cortisol, GH; very low insulin	Gluconeogenesis, full β- oxidation, some ketogenesis	Hitting the wall = glycogen exhausted; teach CHO periodisation
Post-strength bout	Transient ↑ GH, T, IGF-1; AMPK ↓	MPS > breakdown (if protein supplied)	25 g whey + 40 g carbs within 1 h enhances hypertrophy

6 Self-Check Quiz (answers below)

- Name the enzyme that converts pyruvate to oxaloacetate in gluconeogenesis and its required cofactor.
- 2. How many ATP equivalents are produced from complete oxidation of one palmitate (16 C) molecule? (Hint: 7 β-oxidation cycles + TCA)
- 3. Which metabolite allosterically inhibits carnitine palmitoyltransferase-I (CPT-I)?
- 4. True/False: The urea cycle directly consumes two molecules of ATP per one molecule of urea synthesized.
- 5. During high-intensity 30-second sprinting, which metabolic pathway supplies the majority of ATP?

Answers:

- 1. Pyruvate carboxylase; co-factor biotin (vit B₇) and requires acetyl-CoA as allosteric activator.
- 2. About **106 ATP** (gross) 2 ATP for activation yields ~**104 net**.
- 3. Malonyl-CoA.
- 4. **False.** It consumes **three** ATP equivalents (two ATP → 2 ADP + PP_i at CPS-I, one ATP → AMP at argininosuccinate synthase).
- 5. **Anaerobic glycolysis** (fast glycolytic breakdown of muscle glycogen).

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7 Key Take-Home Points

- Pathway dominance shifts with intensity, duration, nutrition and disease—recognise and leverage these shifts in rehab programming.
- Rate-limiting enzymes are the "gear-shifters" of metabolism—hormones, allosteric metabolites and exercise stimuli move the gears.
- Matching **protein, carbohydrate and fat availability** to pathway demands accelerates recovery and adaptation.

Part 3 | Biochemical Aspects of Nutrition

1 Learning Objectives

When you finish this part you should be able to ...

- 1. **Identify all essential macro- and micronutrients,** state their biochemical roles, and quote recommended intakes relevant to active adults.
- 2. **Explain nutrient fate in the fed, post-absorptive and exercise states,** highlighting hormonal regulation and substrate switching.
- 3. **Discuss metabolic adaptations to popular dietary patterns** (high-carbohydrate, low-carbohydrate/ketogenic, intermittent fasting, high-protein) and the implications for physiotherapy.
- 4. **Integrate evidence-based nutrition advice** into rehabilitation plans to optimise recovery, body-composition and performance.

2 Nutrients at a Glance

Category	Key Molecules	Core Biochemical Functions	Practical PT Angle
Carbohydrates (4 kcal g ⁻¹)	Glucose, fructose, glycogen	Quick ATP via glycolysis; replenish muscle & liver glycogen; spare protein	5–7 g kg $^{-1}$ d $^{-1}$ for moderate training; 1.2 g kg $^{-1}$ h $^{-1}$ in first 2 h postsession for rapid re-loading
Proteins (4 kcal g ⁻¹)	20 amino-acids (9 essential)	Tissue synthesis; enzymes, transporters, buffers	1.2 – 1.6 g kg $^{-1}$ d $^{-1}$ in rehab or older adults; distribute 20–40 g high-leucine doses per meal
Lipids (9 kcal g ⁻¹)	TAGs, phospholipids, cholesterol, ω -3 & ω -6 FAs	Dense fuel; cell membranes; steroid and eicosanoid precursors	\leq 30 % kcal; emphasise ω -3 (EPA/DHA 1–2 g d ⁻¹) to modulate inflammation
Water & Electrolytes	H ₂ O, Na ⁺ , K ⁺ , Cl ⁻ , Mg ²⁺	Solvent, temperature control, action-potential conduction	Replace 150 % of exercise fluid loss; add 0.5–0.7 g $\rm L^{-1}$ Na+ for >2 h sessions
Vitamins	Fat-soluble (A D E K), Water-soluble (B- complex, C)	Co-enzymes ($B_{1,2,3}$), antioxidants (C, E), Ca^{2+} homeostasis (D)	B_6/B_{12} support energy metabolism; vit $D \ge 30$ ng mL ⁻¹ for bone and muscle
Minerals & Trace	Ca, Fe, Zn, Se, Cu, Mn, I, Cr	Bone matrix, Hb O ₂ -carriage, antioxidant enzymes, insulin potentiation	Female athlete triad: assess Fe & Ca; Zn/Se support wound healing

3 Fed-Fasted-Exercise Continuum

Phase	Dominant Hormones	Primary Fuel & Pathways	Biochemical Highlights
Fed (0-2 h)	↑ Insulin, ↓ Glucagon	Blood glucose → glycolysis + glycogenesis; lipogenesis in liver	ACC active \rightarrow malonyl-CoA inhibits CPT-I (blocks β -oxidation)

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Phase	Dominant Hormones	Primary Fuel & Pathways	Biochemical Highlights
Post-absorptive (2-12 h)	↓ Insulin, baseline glucagon	Hepatic glycogenolysis, early β -oxidation	HSL in adipose releases FFA; RQ drops from 1.0→0.85
Fasted (>12 h)/Overnight	↑ Glucagon, ↑ Cortisol	Gluconeogenesis (alanine, lactate), β-oxidation, ketone genesis	Brain begins to utilise β- hydroxybutyrate
Moderate exercise (40-60 % VO₂max)	↑ Epinephrine, ↑ SNS	Mix FFA + muscle glycogen	AMPK phosphorylates ACC, lifts β -oxidation block
High-intensity (≥85 % VO₂max)	Peak catecholamines	Anaerobic glycolysis → lactate	PFK-1 activated by AMP; intracellular pH drop drives ventilatory threshold

4 Dietary Patterns & Metabolic Adaptation

Pattern	Core Change	Metabolic Shift	Suitability in Rehab
High-CHO (55-65 % kcal)	Ample glycogen	↑ Insulin, ↓ fat oxidation	Endurance blocks; caution in insulin- resistance
Low-CHO / Ketogenic (< 50 g CHO)	Chronic ketosis	↑ β-oxidation, ↑ ketones, ↓ insulin	May aid weight loss; risk low glycogen → limited HIIT capacity; monitor BP during transition
High-Protein (≥ 2 g kg ⁻¹)	Elevated AA pool	↑ MPS (mTOR), ↑ urea cycle load	Post-operative, sarcopenia; ensure renal function
Intermittent fasting (16:8, 5:2)	Extended fasting windows	↑ Fat oxidation, ↑ GH, improved insulin sensitivity	Useful in weight management; schedule rehab around feeding window to fuel workouts

5 Practical Applications for Physiotherapists

- Early post-injury: emphasise protein (0.3 g kg^{-1} per meal) & $\omega\text{--}3$ to curb catabolism.
- **Glycogen-depleted cardiac rehab:** begin at lower workloads; post-session carb/protein shake prevents hypoglycaemia.
- Chronic inflammation (OA, tendinopathy): suggest Mediterranean-style diet rich in antioxidants, polyphenols,
- Edema control with compression: ensure albumin adequacy (≥ 3.5 g dL⁻¹) for oncotic pressure; address malnutrition.

6 Self-Check Quiz (answers below)

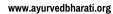
- 1. Which vitamin deficiency impairs collagen hydroxylation during wound healing?
- 2. Name the rate-limiting enzyme for fatty-acid synthesis and one activator.
- 3. What respiratory quotient (RQ) value indicates pure fat oxidation?
- 4. During a 90-min moderate run, what hormone shift facilitates hepatic glucose output?
- 5. True/False: Ketone bodies can be used by skeletal muscle during prolonged exercise when glycogen is low.

Answers:

- 1. Vitamin C (ascorbic acid).
- 2. Acetyl-CoA carboxylase; activated by citrate (and insulin).
- 3. **0.70.**
- 4. Rising glucagon: insulin ratio plus catecholamines mobilise hepatic glycogen.
- 5. **True.**

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7 Key Take-Home Points

- Macronutrient balance steers which metabolic pathways predominate; align intake with session goals.
- Micronutrients and water are co-factors and solvents; deficiencies stall rehabilitation progress.
- A physiotherapist armed with basic nutrition biochemistry can **fine-tune recovery, reduce complications and improve adherence**.

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