

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 = α₂β₂).

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

4 Enzyme Structure & Function

Feature	Explanation
Active site	3-D pocket; binds substrate via induced-fit.
Cofactors / Co-enzymes	Metal ions (Zn ²⁺ , Mg ²⁺) or vitamin-derived (NAD ⁺ from niacin) essential for catalysis.
Catalytic speed	Lowers activation energy (E _a) → accelerates reactions up to 10 ⁶ -fold.

Feature	Explanation
Specificity	Lock-and-key or induced-fit ensures metabolic order.
Regulation	Allosteric modulators, covalent phosphorylation, enzyme quantity (gene expression), compartmentalisation.

Michaelis-Menten Snapshot

$$v = \frac{V_{max}[S]}{K_m + [S]}$$

- **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 → 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.

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)	↓ O ₂ availability	Pursed-lip breathing aids CO ₂ clearance; HIIT raises lactate threshold
Gluconeogenesis	Liver (90%), 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) → FA(n-2) + Acetyl-CoA + FADH ₂ + NADH (≈ 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 lipolysis—monitor hypoglycaemia

4 Protein & Nitrogen Metabolism

Process	Location	Highlight Steps	Key Enzymes / Vitamins	Rehab Implications
Amino-acid transamination	Cytosol & mito (liver, muscle)	AA + α -ketoglutarate \rightleftharpoons 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 NH ₃ \rightarrow encephalopathy—dose exercise cautiously
Muscle protein synthesis (MPS)	Ribosomes; mTORC1-regulated	Leucine triggers; requires ATP + tRNA	Adequate EAA + resistance load (\geq 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)	\uparrow Insulin, \downarrow glucagon	Glycolysis, glycogen & lipid synthesis	Schedule skill sessions; energy plentiful for neural focus
Early fast / moderate exercise	\downarrow Insulin, \uparrow glucagon, catecholamines	Glycogenolysis, β -oxidation rising	Keep carbs handy if diabetic; monitor RPE
Prolonged fast / endurance (> 90 min)	\uparrow Cortisol, GH; very low insulin	Gluconeogenesis, full β -oxidation, some ketogenesis	Hitting the wall = glycogen exhausted; teach CHO periodisation
Post-strength bout	Transient \uparrow GH, T, IGF-1; AMPK \downarrow	MPS > breakdown (if protein supplied)	25 g whey + 40 g carbs within 1 h enhances hypertrophy

6 Self-Check Quiz (answers below)

1. Name the enzyme that converts pyruvate to oxaloacetate in gluconeogenesis and its required co-factor.
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 \rightarrow 2 ADP + PP_i at CPS-I, one ATP \rightarrow AMP at argininosuccinate synthase).
5. **Anaerobic glycolysis** (fast glycolytic breakdown of muscle glycogen).

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 post-session 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	≤ 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 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 ≥ 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 → malonyl-CoA inhibits CPT-I (blocks β-oxidation)

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 % VO_2max)	↑ Epinephrine, ↑ SNS	Mix FFA + muscle glycogen	AMPK phosphorylates ACC, lifts β -oxidation block
High-intensity (≥ 85 % VO_2max)	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) & ω -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, ω -3.
- **Edema control with compression:** ensure albumin adequacy ($\geq 3.5 \text{ g dL}^{-1}$) 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.**



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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