

Chapter 2. Cellular Physiology

Part 1 | Cell Structure & Function

1 Learning Objectives

After this section you will be able to ...

1. **Sketch or label a typical human cell** and name the function of every major organelle.
2. **Explain how mitochondrial, endoplasmic-reticular, and cytoskeletal functions support movement, repair and energy supply**—key pillars of physiotherapy.
3. **Summarise the biochemical pathways of cellular metabolism** (glycolysis → TCA → ETC) and relate ATP yield to exercise intensity.
4. **Describe the steps of mitosis and meiosis**, linking cell-cycle control to growth, healing and oncological precautions in rehabilitation.

2 The Cell: “Functional Unit of Life - Functional Unit of Rehab”

Organelle	Structure	Core Function	PT-Centred Clinical Angle
Plasma Membrane	Phospholipid bilayer with cholesterol, proteins & glycocalyx	Selective barrier; houses receptors & ion channels	NMES depolarises membrane; fluid mosaic disrupted in burn injuries—manage edema carefully
Nucleus	Double membrane with nuclear pores; contains chromatin, nucleolus	Stores DNA; transcription & ribosome assembly	Hypertrophy training triggers gene transcription via mechanotransduction
Mitochondria	Double membrane; cristae; own mtDNA	Aerobic ATP (OXPHOS), β -oxidation, apoptosis signalling	Increased mitochondrial density after endurance training → improved VO_2 max
Rough ER	Flattened sacs studded with ribosomes	Synthesise & fold secretory/membrane proteins	Collagen type I synthesis for tendon repair requires adequate AA & vit C
Smooth ER	Tubular network; no ribosomes	Lipid synthesis; Ca^{2+} store (muscle SR)	Ca^{2+} release drives cross-bridge cycling; SR leaks in fatigue
Golgi Apparatus	Stacked cisternae	Post-translational modification & sorting	Defective glycosylation weakens cartilage proteoglycans—OA risk
Lysosomes	Single membrane vesicles with acid hydrolases	Intracellular digestion, autophagy	Eccentric-exercise micro-damage cleared via autophagy—timing recovery days
Peroxisomes	Oxidative enzymes (catalase)	Very-long-chain FA oxidation; ROS detox	Oxidative stress in chronic inflammation—antioxidant nutrition advice
Cytoskeleton	Microfilaments (actin), microtubules, intermediate filaments	Shape, transport, contraction	Actin-myosin interaction = muscle; microtubule disruption → neuropathies (vincristine)
Centrosome	Pair of centrioles + pericentriolar matrix	Spindle formation in mitosis	Rapid healing tissues (skin)—proliferation phase hinges on intact centrosomes

3 Cellular Metabolism - ATP Factory Tour

1. **Glycolysis (cytosol)**
 $Glucose \rightarrow 2 Pyruvate + 2 ATP + 2 NADH$ (anaerobic or aerobic).
 • Physiotherapy link*: HIIT relies on rapid glycolysis; lactate threshold training delays fatigue.
2. **Pyruvate Dehydrogenase Complex (mitochondrial matrix)**
 $Pyruvate \rightarrow Acetyl-CoA + NADH + CO_2$
 • Thiamine-dependent*: patients with alcoholism—monitor for weakness.

3. TCA / Krebs Cycle

Acetyl-CoA → 3 NADH + FADH₂ + GTP + 2 CO₂

- After 2 min of exercise*, this becomes core ATP provider.

4. Electron Transport Chain & Oxidative Phosphorylation

NADH / FADH₂ donate e⁻ → O₂, pumping H⁺ → ATP synthase yields ~ 34 ATP.

- Clinical: Hypoxia (SpO₂ < 90 %) impairs ETC - modify exercise intensity.

5. Anaerobic Fate

NADH + Pyruvate → Lactate via LDH—allows glycolysis to continue; lactate recycled (Cori cycle).

- Post-exercise active recovery clears lactate via oxidation in slow-twitch fibres.

4 Cell Division

Phase	Key Events	Physiotherapy Significance
Interphase	G ₁ (growth), S (DNA replication), G ₂ (prep)	Wound-healing fibroblasts proliferate—adequate protein & circulation essential
Mitosis	Prophase (chromatin condense), Metaphase (align), Anaphase (sister chromatids separate), Telophase (nuclear re-form) → Cytokinesis	Skin, GI tract & blood cells renew rapidly—consider when scheduling modalities (e.g., ultrasound) after radiotherapy
Meiosis	Two nuclear divisions → gametes (haploid)	Genetic disorders (e.g., DMD) explained by meiotic errors; informs paediatric counselling

Cell-cycle checkpoints (p53, cyclins) are disrupted in cancer → PT must adjust intensity and infection control.

5 Integration Example - Tendon Healing Timeline

1. **Inflammation (Day 0-3):** Neutrophils & macrophages—lysosomal enzymes remove debris.
2. **Proliferation (Day 3-21):** Fibroblasts (RER ↑) synthesise type III collagen → converted to type I in maturation; vitamin C-dependent hydroxylation in rough ER & Golgi.
3. **Maturation (Weeks 3-52):** Cross-linking (lysyl oxidase) strengthens fibrils; progressive mechanical loading aligns fibres (Wolff's law at cellular scale).

6 Self-Check Quiz (answers below)

1. **Which organelle is expanded in hypertrophied muscle fibres to meet increased ATP demand?**
2. **State the net ATP yield from one glucose molecule under aerobic conditions.**
3. **During which mitotic phase do centromeres split?**
4. **Name the enzyme that cross-links collagen and the cofactor it requires.**
5. **Why does mitochondrial DNA mutate faster than nuclear DNA, and what implication does this have for ageing muscle?**

Answers

1. **Mitochondria.**
2. Approximately **36-38 ATP** (depending on shuttle pathway).
3. **Anaphase.**
4. **Lysyl oxidase**; requires **copper**.
5. Mitochondria reside in an ROS-rich environment and lack protective histones → mutations accumulate, reducing oxidative capacity and contributing to sarcopenia.

7 Practical / Lab Suggestions

Lab	Activity
Histology slide session	Identify mitochondria density differences in red vs white muscle fibres.
Metabolic pathway mapping	Group builds colour-coded wall chart of glycolysis → TCA → ETC with ATP tally.
Cell-cycle bingo	Match chemotherapeutic agents to affected cell-cycle checkpoints to understand onco-PT precautions.

8 Key Take-Home Messages

- **Organelles cooperate like a factory**; damage or adaptation in any compartment directly impacts rehabilitation outcomes.
- **ATP supply pathways dictate exercise tolerance**—understand where each fits on the intensity-time continuum.
- **Cell division underlies healing and growth**; PT must match load to the tissue’s biological timetable.

Part 2 | Membrane-Transport Mechanisms

1 Learning Objectives

1. **Differentiate passive from active membrane transport** and cite one physiotherapy-relevant example of each.
2. **Describe the driving forces** (concentration, electrical and hydrostatic gradients) behind diffusion and osmosis.
3. **Explain primary- and secondary-active transport**, naming the key pumps that maintain excitability of nerves and muscles.
4. **Outline vesicular transport (endocytosis / exocytosis)** and relate it to tissue repair, inflammation and drug delivery in rehabilitation.

2 Passive Transport

Mode	Driver	Pore / Carrier?	Physiological Example	PT Significance
Simple diffusion	ΔC or ΔE	No	O ₂ & CO ₂ across alveolar membrane	Teach diaphragmatic breathing to optimise O ₂ diffusion (↑ alveolar surface, ↓ thickness)
Facilitated diffusion	ΔC	Carrier (GLUT-4) or channel (ion)	Glucose uptake into myocytes via insulin-regulated GLUT-4	Strength training ↑ GLUT-4 density → better glycaemic control in T2DM clients
Osmosis	$\Delta \Pi$ (osmotic pressure)	Aquaporins	Water shift in edema	Elevation + compression stockings create hydrostatic counter-pressure

Fick’s Law (simple diffusion) $J = -D A \frac{\Delta C}{\Delta x}$ = -D, A, \frac{\Delta C}{\Delta x} = -DA \frac{\Delta C}{\Delta x}

Greater surface (A) or smaller distance (Δx) boosts flux—reasoning behind incentive-spirometry post-surgery.

3 Active Transport

3.1 Primary-Active (ATP-driven)

Pump	Stoichiometry	Function	Rehab Connection
Na⁺/K⁺-ATPase	3 Na ⁺ out : 2 K ⁺ in + ATP	Maintains resting membrane potential (−70 mV)	Adequate K ⁺ intake critical for avoiding arrhythmia during electrotherapy
Ca²⁺-ATPase (SERCA)	2 Ca ²⁺ in SR/ER per ATP	Muscle relaxation; replenishes SR	Spasticity drugs (dantrolene) modulate Ca ²⁺ release—affects tone management
H⁺/K⁺-ATPase	Gastric acid secretion	Not directly PT relevant but explains reflux precautions in prone positioning	

3.2 Secondary-Active (Coupled-Carrier)

- **Sodium-Glucose Co-Transporter (SGLT-1/2):** Glucose reabsorption in gut & kidney—rehydration drinks exploit Na⁺-glucose co-transport.
- **Na⁺/Ca²⁺ Exchanger (NCX):** Removes Ca²⁺ post-contraction—digitalis inhibits Na⁺/K⁺-ATPase ⇒ ↑ intracellular Ca²⁺, ↑ inotropy; PT monitors HR in cardiac patients.

4 Vesicular Transport (Bulk)

Process	Mechanism	Example	Clinical Angle
Endocytosis	Plasma-membrane invagination	Receptor-mediated LDL uptake	Statin-treated clients: monitor myalgia due to altered lipid endocytosis
• <i>Phagocytosis</i>	Actin-driven engulfing of pathogens	Neutrophil action in wound	Adequate circulation & movement speed healing
• <i>Pinocytosis</i>	“Cell drinking” small vesicles	Synovial A-cells sampling fluid	Joint mobilisation may aid nutrient exchange
Exocytosis	Vesicle fusion (SNARE proteins)	ACh release at NMJ	Botulinum toxin blocks SNARE → focal spasticity management

5 Integrated Clinical Examples

Pathology	Transport Defect	Manifestation	PT Strategy
Cystic Fibrosis	Mutant CFTR Cl ⁻ channel (facilitated diffusion)	Thick mucus, ↓ ciliary clearance	Percussion, PEP devices, Autogenic drainage
Exercise-Associated Hyponatremia	Excessive water intake, osmosis shifts	Confusion, seizures	Educate on isotonic hydration; monitor weight change ±3 %
Edema in CHF	↑ Venous hydrostatic P > oncotic P	Peripheral swelling	Elevation, calf-pump activation, intermittent pneumatic compression

6 Self-Check Quiz (answers below)

1. Why does simple diffusion rate plateau with membrane thickness but facilitated diffusion shows saturation?
2. State the effect of ouabain on resting membrane potential and muscle contractility.
3. Which vesicular transport process is up-regulated during macrophage activity in acute inflammation?
4. Explain how Na⁺/glucose co-transport enables oral rehydration therapy.
5. During NMES, why is extracellular K⁺ concentration critical for avoiding fatigue?

Answers

1. Simple diffusion is limited only by ΔC and distance; carriers in facilitated diffusion become **saturated** at high

substrate concentration (V_{max}).

2. Ouabain blocks **Na⁺/K⁺-ATPase** → depolarises cell (↑ Na⁺ inside); in heart, raises intracellular Ca²⁺ via NCX, increasing contractility.
3. **Phagocytosis**—a form of endocytosis mediated by actin.
4. Na⁺ pumped out by basolateral Na⁺/K⁺-ATPase keeps luminal [Na⁺] low; SGLT couples **Na⁺ influx with glucose**, pulling water osmotically into enterocytes, hydrating the body.
5. High extracellular K⁺ diminishes K⁺ gradient, delaying repolarisation → impulse failure. Adequate K⁺ prevents rapid fatigue during repetitive stimulation.

7 Key Take-Home Points

- **Passive transport** relies on gradients; **active transport** spends ATP or stored ion energy to move substances against gradients.
- Clinicians manipulate these mechanisms—**breathing control, hydration, NMES, compression**—to optimise patient outcomes.
- Understanding membrane dynamics prevents adverse events (e.g., hyponatremia, hyperkalemia) and explains therapeutic effects (muscle relaxation, airway clearance).

Part 3 | Cell Communication & Signalling

(focus: hormonal signalling & receptor types)

1 • Learning Objectives

After this part you will be able to ...

1. **Outline the basic routes of inter-cell communication** (autocrine, paracrine, endocrine, neurocrine, juxtacrine).
2. **Explain endocrine (hormonal) signalling** from hormone synthesis to target-cell response, including feedback loops.
3. **Classify receptors into four major families**—ion-channel, G-protein-coupled, enzyme-linked, intracellular—and match each to representative ligands and second-messenger systems.
4. **Relate signalling concepts to physiotherapy practice**, such as exercise-induced hormonal changes, pharmacological precautions, and tissue-healing cascades.

2 • Communication Pathways Cheat-Sheet

Mode	Range	Signal Molecule	Speed / Duration	Rehab Relevance
Autocrine	Same cell	IL-6 from exercising muscle (myokine)	Fast / short	Explains local hypertrophy signalling during resistance training
Paracrine	Neighbour cells	Nitric oxide from endothelium	Fast / brief	Warm-up ↑ NO → vasodilation, ↓ vascular resistance
Endocrine (Hormonal)	Bloodstream to distant organs	Insulin, cortisol, GH	Slower / long (min → hrs)	Glycaemic control, stress response to exercise
Neurocrine	Synapse	Acetylcholine, NA	Milliseconds	NMES & spasticity management
Juxtacrine	Contact-dependent	Integrins, notch ligands	Continuous	Cell adhesion in wound healing

3 • Hormonal Signalling - From Gland to Effect

1. Synthesis & Storage

Peptide hormones (e.g., insulin) synthesised on RER, stored in vesicles;
Steroid hormones (e.g., cortisol) synthesised from cholesterol on demand.

2. Release & Transport

Stimuli (neural, humoral, hormonal) trigger exocytosis or diffusion.
Carriers bind lipophilic hormones (cortisol-CBG) → longer half-life.

3. Reception

Hormone binds specific receptor (cell-surface or intracellular).

4. Signal Transduction & Amplification

Second messengers (cAMP, IP₃-Ca²⁺, cGMP) or direct gene activation.

5. Physiological Response

Metabolic change, membrane transport, gene transcription, mitosis.

6. Feedback Regulation

Negative feedback is most common (↑ cortisol → ↓ ACTH).
Positive feedback rare (oxytocin in labour).

Example	Trigger	Effector Pathway	PT Angle
Insulin	↑ Blood glucose	Insulin-R (RTK) → GLUT-4 translocation	Monitor BG before/after exercise; exercise ↑ GLUT-4 independent of insulin
Parathyroid Hormone	↓ Serum Ca ²⁺	cAMP pathway ↑ osteoclast activity	Weight-bearing exercise stimulates bone, synergising with PTH
Catecholamines	Sympathetic drive	β ₁ heart (Gs → cAMP ↑ HR), β ₂ bronchi (Gs → bronchodilation)	Beta-blocker blunts HR rise; adjust aerobic intensity using RPE

4 • Receptor Families & Key Features

Family	Structure	Typical Ligands	Transduction	Time-course	Clinical / PT Notes
Ligand-Gated Ion Channels (Ionotropic)	5-subunit pore	ACh (nicotinic), GABA, ATP	Opens ion channel directly	Milliseconds	Botulinum toxin blocks ACh release → ↓ spasms
G-Protein-Coupled Receptors (GPCR)	7-TM helix + Gαβγ	Adrenaline, glucagon, endorphins	Gs/Gi → cAMP; Gq → IP ₃ /Ca ²⁺	Seconds	β ₂ agonist inhaler pre-exercise ↑ FEV ₁ in asthma
Enzyme-Linked Receptors (Receptor Tyrosine Kinase, Ser/Thr, Guanylyl)	Single TM; intrinsic catalytic domain	Insulin, IGF-1, growth factors	Autophosphorylation → MAPK, PI3K	Minutes-hours	IGF-1 surge after resistance training supports hypertrophy
Intracellular (Nuclear) Receptors	Cytosolic / nuclear	Steroids, thyroid hormone, vitamin D	Hormone-receptor binds DNA (HRE)	Hours-days	Glucocorticoids delay collagen synthesis; dose-timing affects rehab

Second-Messenger Mnemonic “CAMP-PI3-DAG-Ca”:

cAMP, PI3K-Akt, DAG/PKC, Ca²⁺/calmodulin—know which pathways your patient’s drugs or diseases influence.

5 • Applied Mini-Scenarios

Scenario	Underlying Signalling	PT Adjustment
Post-menopausal Osteoporosis - low oestrogen	↓ Oestrogen-ER gene activation → ↑ osteoclast	↑ WBV, resistance train to mechanical-load bones; ensure vit D



Scenario	Underlying Signalling	PT Adjustment
Delayed-onset Muscle Soreness	IL-6 & IGF-1 autocrine signalling from damaged fibres	Schedule lighter session 48-72 h later; adequate protein
Parkinson's Bradykinesia	Dopamine loss at D1/D2 GPCR	Cue external pacing; monitor for on-off medication periods
β-Blocker Use in Cardiac Rehab	Blocks β ₁ GPCR → ↓ cAMP → ↓ HR	Use Borg RPE 11-13 instead of HR zone

6 • Self-Check Quiz (answers below)

1. Which receptor type is directly linked to rapid synaptic transmission in skeletal muscle?
2. Name the second messenger that increases intracellular Ca²⁺ via IP₃-mediated SR release.
3. Why can long-term glucocorticoid therapy impede tendon healing?
4. Exercise induces translocation of which glucose transporter to the sarcolemma?
5. Describe one positive-feedback hormonal loop relevant to childbirth.

Answers

1. **Nicotinic acetylcholine receptor (ligand-gated ion channel).**
 2. **Inositol-1,4,5-trisphosphate (IP₃).**
 3. Steroids bind intracellular GR → down-regulate collagen gene expression and inhibit fibroblast proliferation.
 4. **GLUT-4.**
 5. Uterine stretch → hypothalamus → posterior pituitary releases **oxytocin**, which intensifies contractions and further stretch.
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7 • Key Take-Home Points

- **Hormones are long-range messengers; receptors are the language translators.**
 - Understanding receptor families lets PTs predict **drug interactions, exercise responses, and healing timelines.**
 - **Exercise is a potent endocrine stimulus**—myokines, catecholamines, IGF-1—harness them through programme design.
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