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.

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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_2max
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

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3 Cellular Metabolism – ATP Factory Tour

1. **Glycolysis (cytosol)**
   Glucose → 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 → Acetyl-CoA + NADH + CO_2
   • Thiamine-dependent*: patients with alcoholism—monitor for weakness.

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3. **TCA / Krebs Cycle**
   Acetyl-CoA → 3 NADH + $FADH_2$ + GTP + 2 CO_2
   • After 2 min of exercise*, this becomes core ATP provider.
4. **Electron Transport Chain & Oxidative Phosphorylation**
   NADH / $FADH_2$ donate e^- → O_2, pumping H^+ → ATP synthase yields ~ 34 ATP.
   • Clinical: Hypoxia (SpO_2 < 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.

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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.

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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).

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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.

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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	ΔΠ (osmotic pressure)	Aquaporins	Water shift in edema	Elevation + compression stockings create hydrostatic counter-pressure

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

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
Ca^{2+}-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^+/Ca^{2+} Exchanger (NCX):** Removes Ca^{2+} post-contraction—digitalis inhibits Na^+/K^+-ATPase ⇒ ↑ intracellular Ca^{2+}, ↑ inotropy; PT monitors HR in cardiac patients.

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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
• *Phagocytosis*	Actin-driven engulfing of pathogens	Neutrophil action in wound	Adequate circulation & movement speed healing
• *Pinocytosis*	“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

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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

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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 (Vmax).
2. Ouabain blocks **Na^+/K^+-ATPase** → depolarises cell (↑ Na^+ inside); in heart, raises intracellular Ca^{2+} 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.

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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.

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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

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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, IP_3-Ca^{2+}, 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 + $G\alpha\beta\gamma$	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, Ca^{2+}/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

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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 Ca^{2+} via IP_3-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 (IP_3).**
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.

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.