GENERAL BIOLOGY · STUDY GUIDE

Exam 2 Study Guide

This guide covers chapters 3 and 4. First you follow energy: how cells use free energy and ATP, how enzymes control every reaction, how glucose is taken apart and how light builds it back. Then you follow information: how cells read signals, decide to divide or to die, and make gametes. Work one chapter at a time. Read the "what to know" paragraphs, copy the tables out by hand, then try each worked case with the steps covered. Finish each chapter with its ten self-test items. The cram sheet at the end holds every count and rule.

WHAT THIS GUIDE COVERS

- Chapter 3 · the laws of thermodynamics, ΔG, ATP and coupling, redox and NAD^+, enzymes and inhibitors, glycolysis, the citric acid cycle, oxidative phosphorylation, fermentation, the light reactions, the Calvin cycle, and C3, C4 and CAM plants.
- Chapter 4 · signaling distances, the three stages of signaling, receptor types, cascades and second messengers, apoptosis versus necrosis, the cell cycle and mitosis, cyclins and checkpoints, oncogenes and tumor suppressors, meiosis and genetic variation.

CHAPTER 3

Energy, Enzymes, Cellular Respiration and Photosynthesis

Read it in full: **Chapter 3 in the textbook**. See it in motion: **Energy and Enzymes Lab** and **Cellular Respiration Lab** and **Photosynthesis Lab**.

What to know

Metabolism is all of an organism's reactions. Catabolic pathways break molecules down and release energy, as respiration does. Anabolic pathways spend energy to build, as protein synthesis does. The **first law** of thermodynamics says energy is transformed but never created or destroyed. The **second law** says every transfer increases the entropy of the universe, so some energy always leaves as heat.

Free energy change is $\Delta G = \Delta H - T\Delta S$. A negative ΔG marks an **exergonic**, spontaneous reaction. A positive ΔG marks an **endergonic** one that needs an energy input. Spontaneous says nothing about speed. Glucose oxidation has a ΔG of about −686 kcal/mol, yet sugar sits on a table for years. At equilibrium ΔG is zero and no work can be done, so a living cell keeps its pathways away from equilibrium.

ATP is adenine, ribose and three phosphates. Hydrolysis of the end phosphate releases about 7.3 kcal/mol under standard conditions. The energy comes from the products being more stable, not from one magic bond. In **energy coupling**, an enzyme moves the phosphate onto another molecule (phosphorylation), making it reactive. The ΔG values add: glutamine synthesis at +3.4 plus ATP at −7.3 gives −3.9 kcal/mol overall.

In redox reactions, oxidation is loss of electrons and reduction is gain (OIL RIG). Electrons often travel as hydrogen atoms. **NAD^+** accepts two electrons and a proton to become NADH. FAD becomes $FADH_2$. Photosynthesis uses $NADP^+$ and NADPH for building.

Enzymes lower the activation energy. They never change ΔG or the equilibrium. The substrate binds the active site, and the enzyme tightens around it by induced fit. Rate rises with substrate until the enzyme is saturated at Vmax. Each enzyme has an optimal temperature and pH: pepsin near pH 2, trypsin near pH 8, most human enzymes near 37 °C. Many need cofactors (metal ions) or coenzymes (often from vitamins, such as niacin for NAD^+).

A **competitive inhibitor** takes the active site; more substrate can overcome it, so Vmax is unchanged but the apparent Km rises (statins work this way). A **noncompetitive inhibitor** binds elsewhere and lowers Vmax. Irreversible inhibitors bond covalently, like sarin or penicillin. In **allosteric regulation**, a molecule at a separate site stabilizes the active or inactive form. In **feedback inhibition**, a pathway's end product shuts down an early enzyme.

Respiration has three stages. **Glycolysis** in the cytosol splits glucose into 2 pyruvate, with a net 2 ATP and 2 NADH and no CO_2. **Pyruvate oxidation** in the matrix makes 2 acetyl CoA, 2 CO_2 and 2 NADH. The **citric acid cycle** turns twice per glucose: 4 CO_2, 6 NADH, 2 $FADH_2$ and 2 ATP. All six carbons leave as CO_2. The cycle uses no oxygen directly but stops without it, because NAD^+ runs out.

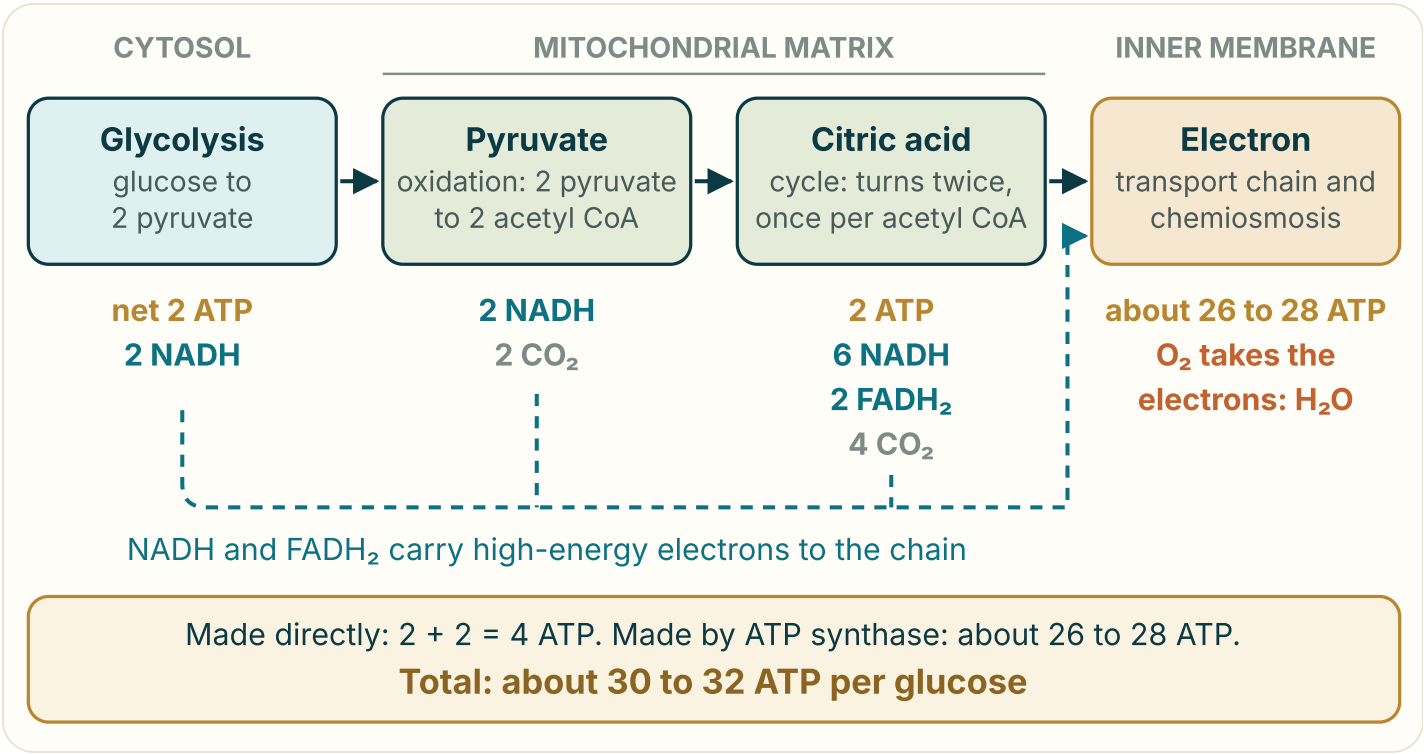
The **electron transport chain** on the inner membrane passes electrons from NADH (complex I) and $FADH_2$ (complex II) through Q, complex III, cytochrome c and complex IV to oxygen, the final acceptor, which becomes water. Complexes I, III and IV pump protons. **ATP synthase** lets them flow back and makes ATP: this is chemiosmosis. Each NADH gives about 2.5 ATP and each $FADH_2$ about 1.5. The total is about 30 to 32 ATP per glucose, about 34 percent of the energy; the rest is heat. Cyanide blocks complex IV, and uncouplers let protons leak back.

Fermentation is glycolysis plus steps that hand NADH's electrons to an organic molecule, regenerating NAD^+. It makes no extra ATP. Lactic acid fermentation (muscle, yogurt bacteria) makes lactate with no CO_2. Alcohol fermentation (yeast) makes ethanol and CO_2. Fats enter as acetyl CoA by beta oxidation and as glycerol; amino acids are deaminated first. **PFK** is the main control point: ATP and citrate inhibit it, AMP activates it.

Photosynthesis: $6\ CO_2 + 6\ H_2O$ + light gives $C_6H_{12}O_6 + 6\ O_2$. The O_2 comes from water. The **light reactions** in the thylakoids use photosystem II (P680) and photosystem I (P700). Water is split at PS II, electrons flow to PS I and then to $NADP^+$, and protons pile up in the thylakoid space to drive ATP synthase. Cyclic flow uses only PS I and makes ATP without NADPH or O_2. Chlorophyll absorbs blue and red light and reflects green.

The **Calvin cycle** in the stroma has three phases: rubisco fixes CO_2 onto RuBP, ATP and NADPH reduce 3-PGA to G3P, and ATP regenerates RuBP. One net G3P needs 3 CO_2, 9 ATP and 6 NADPH. One glucose needs 6 turns, 18 ATP and 12 NADPH.

Rubisco also binds O_2, causing wasteful **photorespiration**, worst on hot, dry days when stomata close. C3 plants (rice, wheat) suffer most. **C4 plants** (corn, sugarcane) fix CO_2 with PEP carboxylase in mesophyll cells and release it in bundle sheath cells: separation in space. **CAM plants** (pineapple, cacti) open stomata at night and store acids: separation in time.



Where the ATP comes from. The first three stages make only 4 ATP directly. Their real product is loaded electron carriers, which the chain cashes in for most of the ATP.

LOCK THESE IN

- ΔG negative: exergonic, spontaneous. ΔG positive: endergonic. ΔG zero: equilibrium.
- Enzymes change only the rate, by lowering activation energy.
- Competitive: overcome by substrate, Vmax unchanged. Noncompetitive: Vmax lowered.
- Per glucose: 10 NADH, 2 $FADH_2$, 4 ATP by substrate level, 6 CO_2, about 30 to 32 ATP total.
- NADH about 2.5 ATP; $FADH_2$ about 1.5 ATP. Oxygen is the final electron acceptor.
- Fermentation recycles NAD^+ and makes only the 2 ATP of glycolysis.
- Light reactions in thylakoids make ATP, NADPH and O_2; the Calvin cycle in the stroma spends them.
- Calvin cycle per G3P: 3 CO_2, 9 ATP, 6 NADPH. C4 separates in space, CAM in time.

Key terms and comparisons: respiration by stage (per glucose)

Stage	Where	Main outputs	ATP made directly
Glycolysis	Cytosol	2 pyruvate, 2 NADH	Net 2 (substrate level)
Pyruvate oxidation	Matrix	2 acetyl CoA, 2 CO_2, 2 NADH	0
Citric acid cycle (2 turns)	Matrix	4 CO_2, 6 NADH, 2 $FADH_2$	2 (substrate level)
Oxidative phosphorylation	Inner membrane	6 H_2O; NAD^+ and FAD returned	About 26 to 28
Total		6 CO_2, 6 H_2O	About 30 to 32

Key terms and comparisons: energy, enzymes and plants

Item	Value or meaning	Use it for
Free energy	$\Delta G = \Delta H - T\Delta S$	Predicting spontaneity
Glucose oxidation	ΔG about −686 kcal/mol	Photosynthesis is +686
ATP hydrolysis	About −7.3 kcal/mol (standard)	Coupling: add the ΔG values
Competitive inhibitor	Active site; Km up, Vmax same	Statins; ethanol versus methanol
Noncompetitive inhibitor	Other site; Vmax down	Mercury on sulfhydryl groups
PFK control	ATP and citrate inhibit; AMP activates	Committed step of glycolysis
Fermentation	2 ATP; lactate, or ethanol plus CO_2	About 16 times less ATP than aerobic
Photosystems	PS II = P680; PS I = P700	Water split at PS II
C3, C4, CAM	Rubisco; PEP carboxylase in space; PEP carboxylase at night	Limiting photorespiration

Worked cases

WORKED CASE 1 · ADDING UP THE ATP

Count the ATP from one glucose using about 2.5 ATP per NADH and 1.5 per $FADH_2$. Then find the total if the two glycolytic NADH use the shuttle that delivers their electrons to FAD.

STEP 1 · COUNT THE CARRIERS

NADH: 2 (glycolysis) + 2 (pyruvate oxidation) + 6 (cycle) = 10. $FADH_2$: 2.

STEP 2 · CONVERT

10 × 2.5 = 25 and 2 × 1.5 = 3, so 28 ATP from oxidative phosphorylation.

STEP 3 · ADD SUBSTRATE LEVEL ATP

2 from glycolysis + 2 from the cycle = 4. Total **32 ATP**.

STEP 4 · THE OTHER SHUTTLE

Now 8 NADH × 2.5 = 20, and the 2 shuttled carriers plus 2 $FADH_2$ give 4 × 1.5 = 6. 20 + 6 + 4 = **30 ATP**. That is why books give 30 to 32.

EFFICIENCY CHECK

32 × 7.3 = 233.6 kcal, and 233.6 ÷ 686 = 0.34, about 34 percent captured as ATP.

WORKED CASE 2 · COUPLING A REACTION TO ATP

A reaction has ΔG = +5.0 kcal/mol. Can coupling it to one ATP hydrolysis (−7.3 kcal/mol) make it go? What about a reaction at +9.0?

STEP 1 · ADD THE FIRST PAIR

+5.0 + (−7.3) = **−2.3 kcal/mol**. Negative, so the coupled pair proceeds.

STEP 2 · ADD THE SECOND PAIR

+9.0 + (−7.3) = +1.7 kcal/mol. Still positive, so one ATP is **not enough**.

THE RULE

Coupled reactions go when the sum of ΔG is negative. The cell does this by phosphorylating an intermediate, not by letting the energy escape as heat.

WORKED CASE 3 · READING AN INHIBITOR EXPERIMENT

Drug X lowers an enzyme's rate, but at very high substrate the rate climbs back to the original Vmax. Drug Y lowers the rate at every substrate level, and Vmax stays low. Classify each.

STEP 1 · LOOK AT VMAX WITH DRUG X

Vmax recovers, so substrate outcompetes the drug. X is a **competitive inhibitor** in the active site; its apparent Km is higher.

STEP 2 · LOOK AT VMAX WITH DRUG Y

Extra substrate does not help. Y is a **noncompetitive inhibitor** that binds another site and changes the enzyme's shape.

LINK IT

Fomepizole treats methanol poisoning as a competitive inhibitor of alcohol dehydrogenase.

WORKED CASE 4 · CALVIN CYCLE BOOKKEEPING

How many turns, ATP and NADPH does a leaf need to make one sucrose (12 carbons, built from 4 G3P)?

STEP 1 · TURNS

Each turn fixes 1 CO_2. 12 carbons need **12 turns**.

STEP 2 · ATP

9 ATP per G3P × 4 G3P = **36 ATP**.

STEP 3 · NADPH

6 NADPH per G3P × 4 = **24 NADPH**.

WHY CYCLIC FLOW MATTERS

The ratio is 36 to 24, or 3 to 2. Linear flow alone does not make enough ATP, so cyclic flow around PS I makes up the extra.

TRAPS PEOPLE FALL INTO

- **Saying an enzyme makes a reaction more exergonic.** Enzymes change only the rate. ΔG and equilibrium stay the same.
- **Reading "spontaneous" as "fast."** A negative ΔG can still react slowly because of activation energy.
- **Thinking fermentation makes ATP after glycolysis.** Its extra steps only recycle NAD^+.
- **Saying the citric acid cycle uses oxygen.** It does not, but it stops without oxygen because NADH cannot be reoxidized.
- **Believing the O_2 from photosynthesis comes from CO_2.** It comes from water split at PS II.
- **Calling the Calvin cycle the "dark reactions."** It stops in the dark within minutes because it needs ATP and NADPH from light.
- **Blaming lactate for next day soreness.** Soreness reflects small injuries to muscle fibers.
- **Mixing up C4 and CAM.** C4 separates steps in space (two cell types); CAM separates them in time (night and day).

Chapter 3 self-test · ten items

1. A reaction has a ΔG of −12 kcal/mol. Which statement is true?

A. It has reached chemical equilibrium
B. It can proceed without an energy input
C. It will proceed rapidly at room temperature
D. It needs ATP coupling to proceed at all

B. It can proceed without an energy input A negative ΔG means exergonic and spontaneous. Speed depends on activation energy, and equilibrium means ΔG is zero.

2. What does an enzyme change about the reaction it catalyzes?

A. The ΔG of the reaction
B. The final equilibrium point
C. The activation energy
D. The identity of the products

C. The activation energy Enzymes lower the energy barrier so more molecules reach the transition state. They leave ΔG and equilibrium alone.

3. In a liver cell, plenty of ATP and citrate are present. What happens at phosphofructokinase?

A. It is inhibited and glycolysis slows
B. It is activated and glycolysis speeds
C. It is denatured and destroyed
D. It switches to making fructose

A. It is inhibited and glycolysis slows ATP and citrate are allosteric inhibitors of PFK, so the cell slows glycolysis when energy is plentiful.

4. How many CO_2 molecules are released by the citric acid cycle alone per glucose?

A. 0
B. 6
C. 2
D. 4

D. 4 Two per turn, and the cycle turns twice. The other 2 CO_2 come from pyruvate oxidation.

5. Cyanide blocks complex IV. Why does ATP production collapse?

A. Glycolysis can no longer split glucose
B. Electrons stall, so proton pumping stops
C. ATP synthase is destroyed outright
D. Oxygen is cleared from the blood plasma

B. Electrons stall, so proton pumping stops With complex IV blocked, the chain stalls, protons are not pumped and ATP synthase has no gradient to use.

6. A muscle in a sprint runs short of oxygen. What does lactic acid fermentation accomplish?

A. It regenerates NAD^+ for glycolysis
B. It releases CO_2 from pyruvate
C. It sends electrons into complex I
D. It makes 30 more ATP per glucose

A. It regenerates NAD^+ for glycolysis Pyruvate takes NADH's electrons and becomes lactate, so glycolysis can keep making its 2 ATP.

7. Water labeled with heavy oxygen is given to a plant. Where does the label show up first?

A. In the RuBP of the Calvin cycle
B. In the CO_2 the leaf takes up
C. In the glucose that is made
D. In the O_2 that is released

D. In the O_2 that is released Water is split at photosystem II, and its oxygen atoms form O_2.

8. What does cyclic electron flow produce?

A. ATP, NADPH and O_2 together
B. NADPH, but no ATP and no O_2
C. ATP, but no NADPH and no O_2
D. O_2 only, with no ATP or NADPH

C. ATP, but no NADPH and no O_2 Cyclic flow uses only PS I and returns electrons to it while pumping protons.

9. How much ATP and NADPH does the Calvin cycle use for one net G3P?

A. 3 ATP and 3 NADPH
B. 6 ATP and 9 NADPH
C. 18 ATP and 12 NADPH
D. 9 ATP and 6 NADPH

D. 9 ATP and 6 NADPH Three turns fix 3 CO_2. Reduction uses 6 ATP and 6 NADPH, and regenerating RuBP uses 3 more ATP.

10. A desert succulent opens its stomata only at night. Which kind of plant is it?

A. A CAM plant
B. A plant with no rubisco
C. A C3 plant
D. A C4 plant

A. A CAM plant CAM plants fix CO_2 into acids at night and feed it to the Calvin cycle by day, separating the steps in time.

CHAPTER 4

Cell Communication and Cell Division

Read it in full: **Chapter 4 in the textbook**. See it in motion: **Cell Communication Lab** and **Cell Cycle Lab** and **Meiosis Lab**.

What to know

Cells signal over different distances. Direct contact uses gap junctions, plasmodesmata or surface molecules. **Paracrine** signals, such as growth factors, act on nearby cells. **Synaptic** signals cross a narrow gap from a nerve cell. **Autocrine** signals act on the cell that released them. **Endocrine** hormones travel in the blood. A cell responds only if it has the right receptor. Bacteria use quorum sensing to read their own population density.

Signaling has three stages: **reception** (a ligand binds a receptor and changes its shape), **transduction** (a relay of changes inside the cell) and **response** (an enzyme is switched on, the cytoskeleton moves or genes turn on). Epinephrine never enters the liver cell, yet it makes the cell break down glycogen.

Four receptor types matter most. A **GPCR** crosses the membrane seven times and swaps GDP for GTP on a G protein, which then switches on an enzyme such as adenylyl cyclase; the G protein turns itself off by hydrolyzing GTP. A **receptor tyrosine kinase** pairs up into a dimer and phosphorylates tyrosines on its partner, which can trigger ten or more pathways at once (insulin,

growth factors). A **ligand-gated ion channel** opens for ions, as acetylcholine does at muscle. **Intracellular receptors** bind steroid and thyroid hormones and act as transcription factors, so their effects are slower but longer lasting.

In a **phosphorylation cascade**, each kinase phosphorylates and switches on the next. Phosphatases remove the phosphates to switch them off. **Second messengers** are small molecules inside the cell: cAMP (made by adenylyl cyclase, read by protein kinase A, broken down by phosphodiesterase), Ca^{2+}, IP_3 and DAG. Each step **amplifies** the signal, so one epinephrine molecule can release hundreds of millions of glucose units. Cholera toxin locks a G protein on, so cAMP stays high.

Responses happen in the nucleus (gene expression) or in the cytoplasm (an enzyme, channel or cytoskeleton change). The same signal can do different things in different cells, because cells carry different receptors and relay proteins.

Apoptosis is programmed, orderly cell death run by caspases. The cell shrinks, forms blebs and breaks into apoptotic bodies that phagocytes eat, so there is no inflammation. It sculpts fingers, removes damaged cells and turns over tissues. In the **intrinsic** pathway, damage (often sensed by p53) lets Bax and Bak open the outer mitochondrial membrane, cytochrome c leaks out, joins Apaf-1 in the apoptosome and activates caspase-9. Bcl-2 is the brake. In the **extrinsic** pathway, Fas ligand or TNF binds death receptors and activates caspase-8. **Necrosis** is uncontrolled death from injury: the cell swells, bursts and causes inflammation.

The **cell cycle** is interphase (G1, S, G2) plus the M phase. DNA is copied in S, making two sister chromatids joined at the centromere. Attached sisters count as one chromosome. A human cell in culture cycles in about 24 hours, with M under an hour. Cells that stop dividing enter G0. Mitosis runs prophase, prometaphase (envelope breaks, kinetochores attach), metaphase (chromosomes on the plate), anaphase (separase cuts cohesins, sisters part) and telophase. Cytokinesis uses an actin and myosin cleavage furrow in animals and a cell plate from Golgi vesicles in plants. Prokaryotes divide by binary fission.

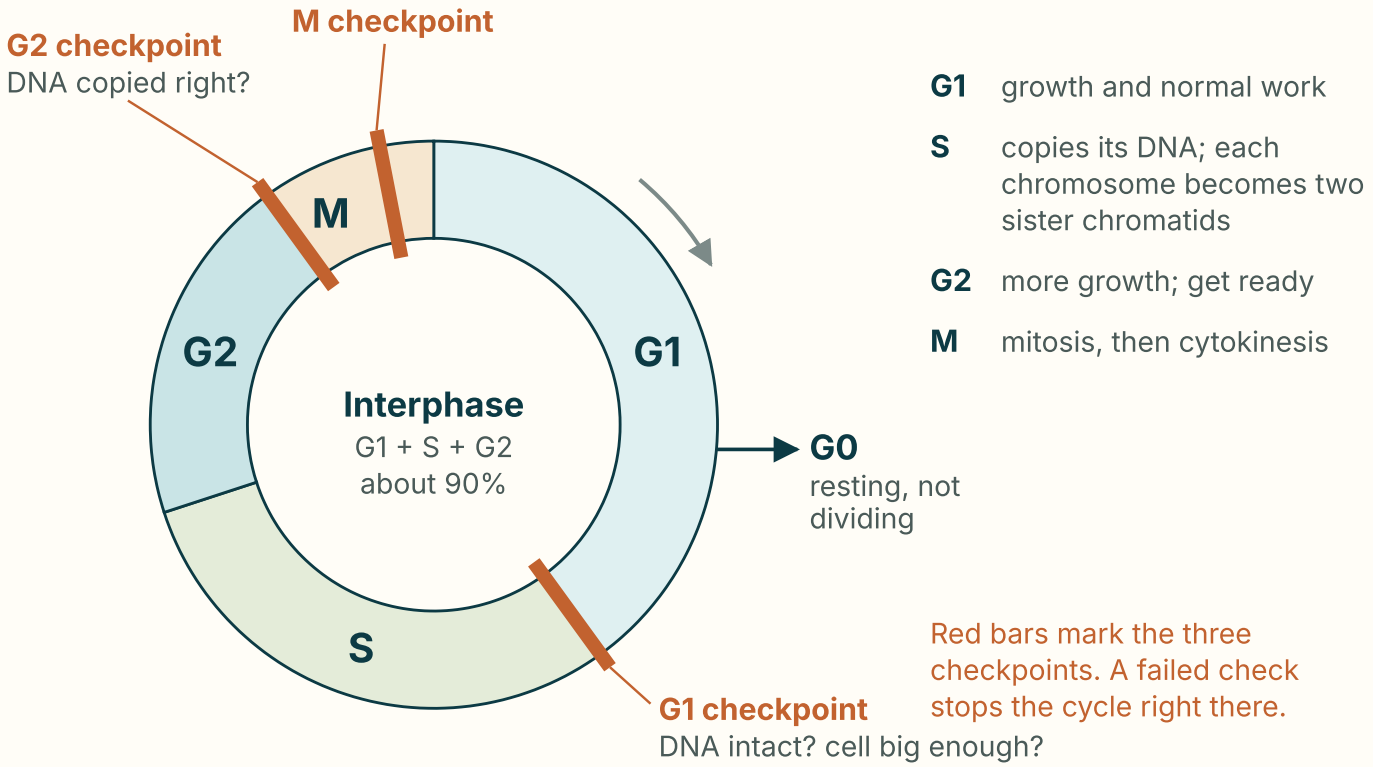
The cycle is run by **cyclins**, whose levels rise and fall, and **Cdks**, which work only when bound to cyclin. MPF (cyclin B with its Cdk) starts mitosis and then triggers destruction of its own cyclin.

Three **checkpoints**: G1 (the restriction point, the most important), G2 (DNA copied and repaired) and M (all kinetochores attached to both poles before anaphase). At G1, cyclin D-Cdk phosphorylates Rb, which releases E2F. p53 halts the cycle when DNA is damaged. Normal cells show density-dependent inhibition and anchorage dependence.

Cancer cells ignore those controls. A malignant tumor invades and can metastasize. **Proto-oncogenes** code for proteins that push division; a gain of function mutation in one copy makes an **oncogene** (ras, HER2, BCR-ABL). **Tumor suppressor genes** brake division or repair DNA; both copies must usually be lost (TP53, RB, BRCA1, BRCA2, APC). Several mutations are needed, which is why risk rises with age. About 5 to 10 percent of cancers involve an inherited predisposition.

Meiosis makes haploid cells. Humans have 2n = 46 and n = 23. Homologs carry the same genes at the same loci, one from each parent. Meiosis I separates homologs after synapsis and crossing over in prophase I; meiosis II separates sister chromatids. The result is four unique haploid cells. Life cycles differ: animals make gametes by meiosis; plants alternate a diploid sporophyte with a haploid gametophyte; most fungi have only a diploid zygote.

Variation comes from **independent assortment** (2^n combinations, about 8.4 million for humans), **crossing over** and **random fertilization** (about 70 trillion combinations for one couple, before crossing over). **Nondisjunction** gives gametes with an extra or missing chromosome, causing aneuploidy such as trisomy 21. Its risk rises with maternal age.



The cell cycle and its checkpoints. Most of a cell's life is interphase. The three checkpoints are the brakes that cancer cells lose.

LOCK THESE IN

- Reception, transduction, response. The cell needs the matching receptor.
- GPCR: G protein and GTP. RTK: dimer and autophosphorylation. Steroids: intracellular receptor and transcription factor.
- Second messengers: cAMP, Ca^{2+}, IP_3, DAG. Each relay step amplifies.
- Apoptosis: shrinks, no inflammation, caspases. Necrosis: swells, bursts, inflammation.
- G1, S, G2, M. Sister chromatids joined at the centromere count as one chromosome.
- MPF = cyclin B plus Cdk. Checkpoints at G1, G2 and M.
- Oncogene: gain of function, one copy. Tumor suppressor: loss of function, both copies.
- Meiosis I separates homologs; meiosis II separates sisters. 2^n assortment combinations.

Key terms and comparisons: receptors

Receptor	Where	How it relays	Example ligands
GPCR	Membrane; 7 passes	G protein swaps GDP for GTP; switches on an enzyme	Epinephrine, glucagon, odorants, light
Receptor tyrosine kinase	Membrane; one helix per monomer	Dimerizes, autophosphorylates, docks relay proteins	Insulin, EGF, PDGF
Ligand-gated ion channel	Membrane	Opens for ions; voltage changes	Acetylcholine, GABA, glutamate
Intracellular receptor	Cytoplasm or nucleus	Acts as a transcription factor	Steroids, thyroid hormone, NO

Key terms and comparisons: mitosis and meiosis

Feature	Mitosis	Meiosis
Divisions	One	Two
Synapsis and crossing over	No	Yes, prophase I
At the metaphase plate	Single duplicated chromosomes	Homolog pairs (I); single chromosomes (II)
What separates	Sister chromatids	Homologs (I); sister chromatids (II)
Products	Two identical cells, 2n if parent is 2n	Four unique cells, n
Role in animals	Growth, repair	Gametes

Counting through the cycle (human cell)

Stage	Chromosomes	Chromatids or DNA molecules
G1	46	46
G2 to metaphase	46	92
Anaphase of mitosis	92	92
Each daughter cell	46	46
After meiosis I (each cell)	23	46
After meiosis II (each cell)	23	23

Worked cases

WORKED CASE 1 · COUNTING CHROMOSOMES IN MEIOSIS

An animal has 2n = 6. Give the chromosome and chromatid counts in a cell in G2, after meiosis I and after meiosis II. How many gamete types can independent assortment alone give?

STEP 1 · G2

DNA is copied: **6 chromosomes, 12 chromatids**.

STEP 2 · AFTER MEIOSIS I

Homologs separate: **3 chromosomes, 6 chromatids** in each cell. The cell is now haploid.

STEP 3 · AFTER MEIOSIS II

Sisters separate: **3 chromosomes, 3 chromatids** in each of four cells.

STEP 4 · ASSORTMENT

n = 3, so 2^3 = **8** combinations.

SCALE IT UP

For humans, 2^{23} = 8,388,608, about 8.4 million. Two parents give about 8.4 million × 8.4 million, about 70 trillion.

WORKED CASE 2 · TRACING A HORMONE SIGNAL

Epinephrine reaches a liver cell. Trace it from the surface to glucose release, and say how it is switched off.

STEP 1 · RECEPTION

Epinephrine binds a GPCR. The receptor makes its G protein swap GDP for GTP.

STEP 2 · TRANSDUCTION

The G protein activates adenylyl cyclase, which turns ATP into cAMP. cAMP activates protein kinase A, which starts a kinase cascade.

STEP 3 · RESPONSE

The last kinase switches on glycogen phosphorylase, which releases glucose 1-phosphate from glycogen.

STEP 4 · SHUT OFF

The G protein hydrolyzes its GTP, phosphodiesterase breaks down cAMP, and phosphatases remove phosphates.

AMPLIFICATION

If each of three steps made 100 active molecules from one, the gain would be $100 \times 100 \times 100 = 1{,}000{,}000$. That is how a tiny dose of hormone has a large effect.

WORKED CASE 3 · GAS OR BRAKE?

Classify each mutation and say how many copies must be hit: (a) ras locked in its active form; (b) both copies of TP53 deleted; (c) extra copies of the HER2 gene; (d) one mutant RB allele inherited from a parent.

STEP 1 · RAS

Ras normally pushes division. A locked-on form is a gain of function: an **oncogene**, one copy is enough.

STEP 2 · TP53

p53 brakes the cycle and triggers repair or apoptosis. Losing it is loss of function: a **tumor suppressor**, both copies lost.

STEP 3 · HER2

Gene amplification makes too much of a growth receptor: an **oncogene**.

STEP 4 · RB INHERITED

Every cell starts with one hit. One more mutation in any cell removes the brake, which raises **risk**, not certainty.

TRAPS PEOPLE FALL INTO

- **Thinking steroids need a second messenger.** They cross the membrane and bind an intracellular receptor directly.
- **Counting chromatids as chromosomes.** Count centromeres. Attached sisters are one chromosome.

- **Separating sister chromatids in meiosis I.** Meiosis I separates homologs. Sisters part in meiosis II.
- **Calling apoptosis the same as necrosis.** Apoptosis is neat with no inflammation; necrosis bursts and inflames.
- **Thinking Cdk levels rise and fall.** Cyclin levels swing. Cdk stays fairly constant and works only with cyclin.
- **Saying one hit to a tumor suppressor causes cancer.** Usually both copies must be lost, and several genes must change.
- **Thinking haploid cells can do meiosis.** Meiosis needs homologous pairs. A gametophyte makes gametes by mitosis.
- **Forgetting that interphase is busy.** The "gap" names are historical. The cell grows and copies DNA throughout.

Chapter 4 self-test · ten items

1. A growth factor released by one cell acts on its near neighbors. What kind of signaling is this?

A. Endocrine signaling
B. Synaptic signaling
C. Paracrine signaling
D. Autocrine signaling

C. Paracrine signaling Local regulators that act on nearby cells are paracrine. Endocrine signals travel in the blood.

2. Which receptor type works by pairing into a dimer and phosphorylating its partner?

A. A G protein-coupled receptor
B. A receptor tyrosine kinase
C. A ligand-gated ion channel
D. An intracellular steroid receptor

B. A receptor tyrosine kinase RTKs dimerize when ligand binds, then each tail phosphorylates tyrosines on the other.

3. Caffeine blocks phosphodiesterase. What happens to cAMP signals?

A. They switch to Ca^{2+}
B. They are never made
C. They stop at once
D. They last longer

D. They last longer Phosphodiesterase normally turns cAMP into AMP. Blocking it keeps cAMP high.

4. Which feature marks apoptosis rather than necrosis?

A. The cell shrinks without inflammation
B. The cell swells and its membrane bursts
C. It runs with no ATP and no program
D. Its contents spill and inflame tissue

A. The cell shrinks without inflammation Apoptosis is a tidy, energy-using program. Necrosis is uncontrolled swelling and rupture.

5. In the intrinsic pathway, what leaks from mitochondria to start the caspase cascade?

A. Fas ligand
B. Cytochrome c
C. ATP synthase
D. Bcl-2 protein

B. Cytochrome c Cytochrome c joins Apaf-1 to form the apoptosome, which activates caspase-9.

6. A human cell is in metaphase of mitosis. How many chromatids does it hold?

A. 92
B. 184
C. 23
D. 46

A. 92 The cell has 46 duplicated chromosomes, each with two sister chromatids.

7. A drug keeps the anaphase promoting complex inactive. Where will the cells stop?

A. At S phase
B. At G1
C. At metaphase
D. At telophase

C. At metaphase Without the complex, separase stays inhibited and cohesins are not cut, so sisters cannot separate.

8. Unphosphorylated Rb holds E2F. What lets the cell pass the G1 checkpoint?

A. Separase cuts Rb in half
B. p53 binds and activates E2F
C. MPF destroys the Rb protein
D. Cyclin D-Cdk phosphorylates Rb

D. Cyclin D-Cdk phosphorylates Rb Phosphorylated Rb releases E2F, which switches on S phase genes.

9. Which statement fits a tumor suppressor gene?

A. It is made by amplifying a gene
B. One overactive copy is usually enough
C. It codes for a growth factor receptor
D. Both copies usually must be inactivated

D. Both copies usually must be inactivated Tumor suppressors are brakes. One working copy still brakes, so both must usually be lost.

10. Which event happens in meiosis but never in mitosis?

A. Homologs pair up and cross over
B. A spindle forms from microtubules
C. Sister chromatids separate
D. DNA is copied before division

A. Homologs pair up and cross over Synapsis and crossing over happen in prophase I only.

ONE PAGE

Cram sheet

Everything from chapters 3 and 4 in one place. Cover the right column and see if you can rebuild each row.

Numbers to know

Item	Value	Note
Glucose oxidation	ΔG about −686 kcal/mol	Photosynthesis +686
ATP hydrolysis	About −7.3 kcal/mol	About 13 in the cell
Carriers per glucose	10 NADH, 2 $FADH_2$	2.5 and 1.5 ATP each
ATP per glucose	About 30 to 32	4 by substrate level
CO_2 per glucose	6	0 glycolysis, 2 link step, 4 cycle
Efficiency	About 34%	Rest is heat
Fermentation	2 ATP per glucose	About 16 times less
Calvin cycle	Per G3P: 3 CO_2, 9 ATP, 6 NADPH	Per glucose: 18 ATP, 12 NADPH
Photosystems	P680 (PS II), P700 (PS I)	Visible light about 380 to 750 nm
Human chromosomes	2n = 46, n = 23	22 autosomes + 1 sex chromosome per gamete
Assortment	2^{23} about 8.4 million	Couple: about 70 trillion
Cell cycle	About 24 h; M under 1 h	Interphase about 90%
Cancer genes	ras in about 30%; TP53 in about half	5 to 10% inherited predisposition

Key terms and comparisons

Pair	How to tell them apart
Exergonic vs endergonic	ΔG negative, releases; ΔG positive, absorbs.
Competitive vs noncompetitive	Active site, beaten by substrate; other site, lowers Vmax.
Substrate level vs oxidative	Direct phosphate transfer; chemiosmosis through ATP synthase.
Lactic vs alcohol fermentation	Lactate, no CO_2; ethanol plus CO_2.
Linear vs cyclic flow	ATP, NADPH and O_2; ATP only.
First vs second messenger	Outside, binds receptor; inside, relays the signal.
Intrinsic vs extrinsic apoptosis	Mitochondria and cytochrome c; death receptors.
Oncogene vs tumor suppressor	Gas stuck, one copy; brakes cut, both copies.
Meiosis I vs II	Homologs separate (reductional); sisters separate (equational).

Rules that win points

Topic	The rule
Coupling	Add ΔG values; the sum must be negative.
ATP count	Count carriers first, then convert.
Enzymes	Only the rate changes.
Chromosome count	Count centromeres.
Meiosis check	Four cells, half the number, no two alike.
Life cycles	Only diploid cells do meiosis; either ploidy can do mitosis.

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