CELL BIOLOGY

Cell Cycle

The G1-S-G2-M circuit, its checkpoints, and what happens when control fails, with a 10-question practice set and full solutions.

SUBJECT	LEVEL	INCLUDES
Biology	High school and early college	Practice set, answer key, revision sheet

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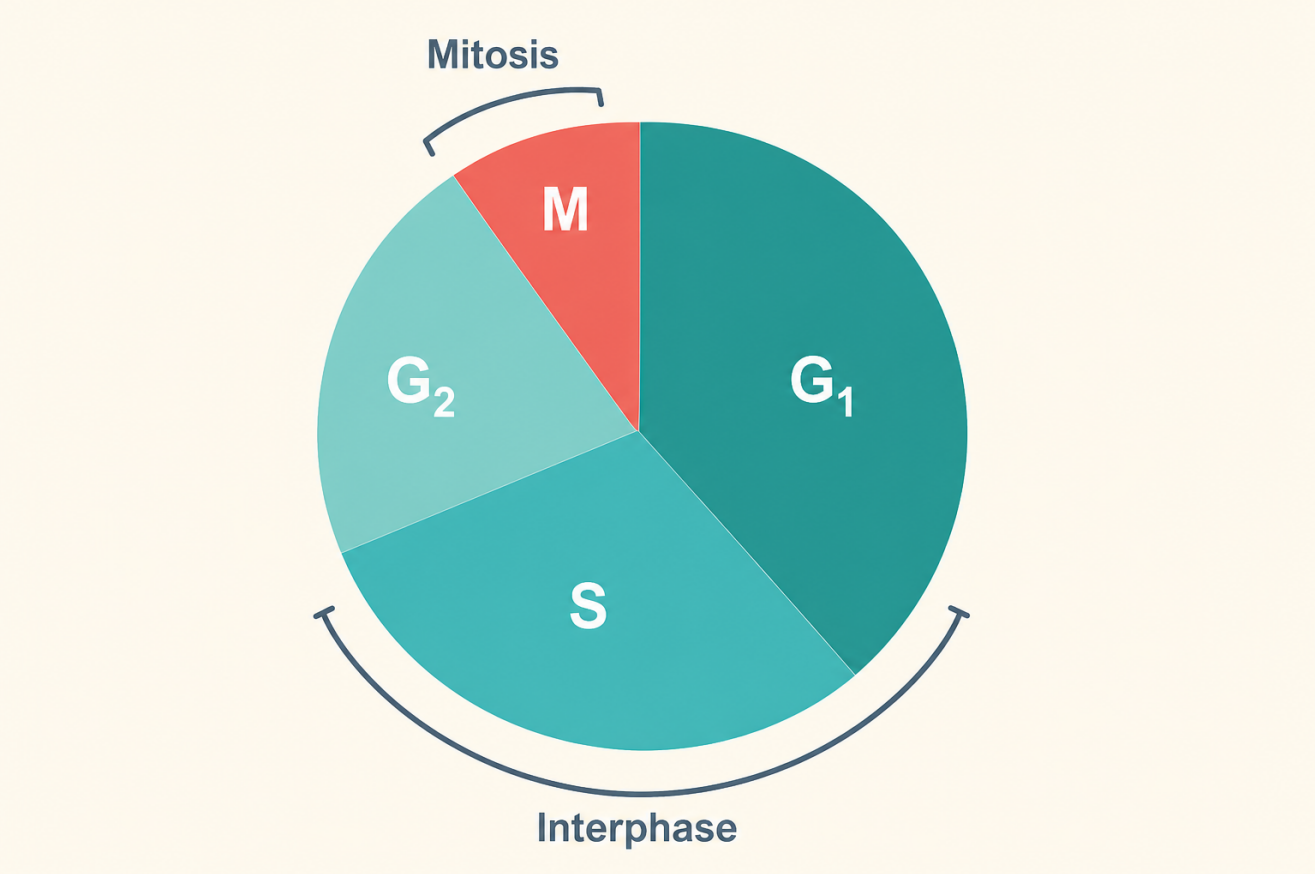
INSIDE

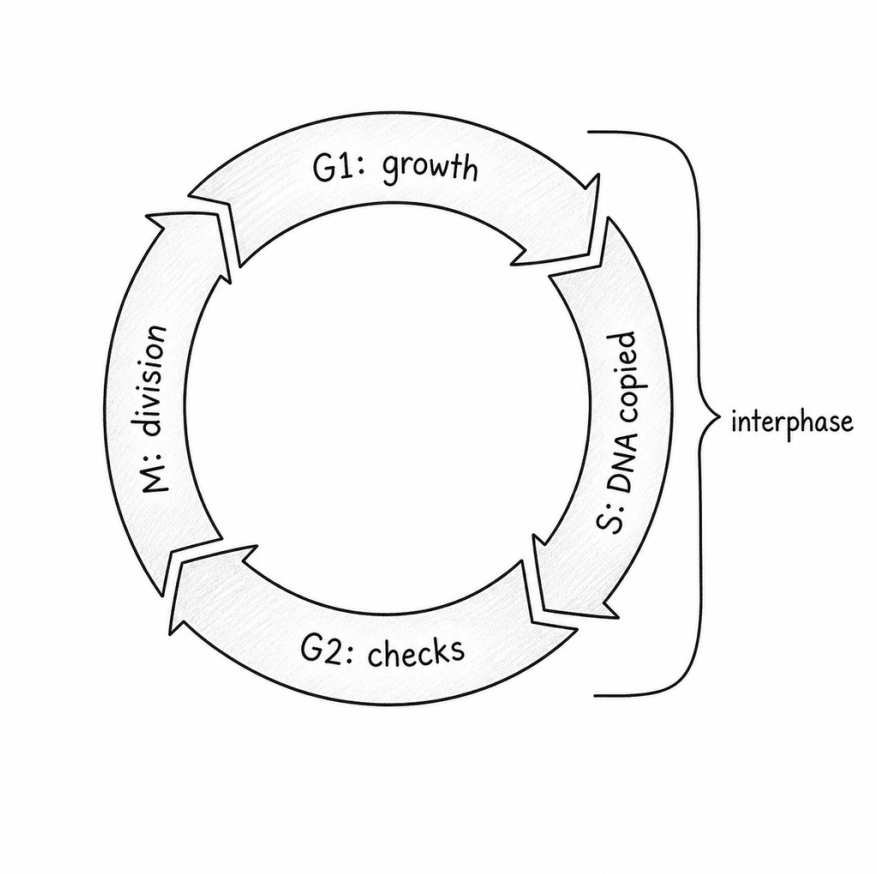
The cell cycle is the ordered sequence of events that a eukaryotic cell goes through from its birth to its division into two daughter cells. It is divided into two major periods: interphase (G1, S, G2), where the cell grows, replicates its DNA, and prepares to divide, and the M phase (mitosis plus cytokinesis), where the cell actually divides. A typical actively-dividing human cell completes one full cycle in about 24 hours. Cell-cycle control is one of the most important regulatory systems in biology, and its breakdown is the central problem in cancer.



The cell cycle, G1, S, G2 (together called Interphase) and the M phase (mitosis plus cytokinesis), with M taking only about 5% of the total cycle.

The Phases of the Cell Cycle

The cell cycle has four main phases. Three of them belong to interphase; the fourth is M phase.



The full cycle: 3 growth-and-check phases (interphase) followed by division (M).

G1 phase (Gap 1)

The cell grows in size. Organelles duplicate (more mitochondria, more ribosomes, more endoplasmic reticulum). Protein synthesis ramps up. The cell prepares for DNA replication. G1 is the longest phase in most cells, typically 11 hours in a 24-hour cycle. G1 is also the most variable phase. Cells that decide not to divide (most neurons, for example) exit G1 into a resting state called G0 and can stay there for decades.

S phase (Synthesis)

DNA replication. Each chromosome's single chromatid is duplicated into two identical sister chromatids joined at the centromere. The cell's DNA content doubles from 2C to 4C, while the chromosome number stays the same (each chromosome now consists of two chromatids instead of one). S phase typically lasts 6-8 hours in a human cell.

G2 phase (Gap 2)

Final preparation for mitosis. The cell continues growing, manufactures the proteins needed for chromosome segregation (tubulin for the spindle, condensin for chromosome compaction), and checks the

replicated DNA for damage. G2 typically lasts 3-4 hours.

M phase (Mitosis + Cytokinesis)

The cell physically divides. Mitosis (nuclear division) goes through prophase, metaphase, anaphase, and telophase, after which cytokinesis pinches the cytoplasm into two daughter cells. M phase is the shortest, typically just 1 hour, only about 5% of the total cycle.

Interphase vs M Phase Proportions

A typical 24-hour human cell cycle breaks down approximately as:

PHASE	DURATION	% OF CYCLE	MAIN ACTIVITY
G1	~11 hours	~46%	Growth, organelle duplication
S	~8 hours	~33%	DNA replication
G2	~4 hours	~17%	Final prep, damage checks
M	~1 hour	~4%	Mitosis + cytokinesis

The picture you typically see in textbooks shows mitosis as a dramatic main event, but in reality cells spend about 95% of their time in interphase quietly growing and replicating. M phase is the brief spectacular finale.

Checkpoints, The Cell Cycle's Quality Control

Three major checkpoints monitor the cell cycle, halting progression if conditions are wrong. The checkpoints are the cell's quality-control system. Their failure is the central problem in cancer.

G1/S Checkpoint (Restriction Point)

Located at the end of G1, just before entering S phase. The cell checks: is it large enough? Are nutrients available? Is the DNA undamaged? Is there a growth-factor signal telling the cell to proliferate? If any answer is no, the cell pauses in G1 (or exits to G0). The G1/S checkpoint is the main commit point, once a cell passes it, it is committed to completing the cycle.

The tumor suppressor p53 is the central player at this checkpoint. p53 senses DNA damage, halts the cycle, and either gives the cell time to repair or triggers apoptosis if the damage is irreparable. Mutations in p53 are found in over 50% of human cancers, the most commonly mutated gene in all of oncology.

G2/M Checkpoint

Located at the end of G2, just before mitosis begins. The cell checks: was DNA replication complete and correct? Is the cell ready for the physical demands of mitosis? Errors here stop the cycle until repair is complete.

Spindle Assembly Checkpoint (M Checkpoint)

Located during metaphase. The cell will not begin anaphase until every chromosome's kinetochore is properly attached to spindle microtubules from both poles. This prevents chromosome mis-segregation. When the checkpoint fails, daughter cells end up with the wrong chromosome number (aneuploidy), which is both a cause and a consequence of cancer.

Cyclins and CDKs, The Cell-Cycle Engine

The cell cycle is driven by a family of proteins called cyclin-dependent kinases (CDKs) bound to regulatory proteins called cyclins. CDKs are kinases, they add phosphate groups to other proteins, modifying their activity. Cyclins are not themselves enzymes, but they bind to CDKs to activate them.

Different cyclin-CDK combinations drive different phases:

- **Cyclin D** + **CDK4/6**: drives early G1 progression
- **Cyclin E** + **CDK2**: drives the G1/S transition
- **Cyclin A** + **CDK2**: drives S phase progression
- **Cyclin B** + **CDK1**: drives entry into mitosis

Cyclin levels rise and fall through the cycle (the periodic synthesis and destruction is what gave them the name). CDK levels stay relatively constant, but their activity follows the cyclin levels. Leland Hartwell, Tim Hunt, and Paul Nurse won the 2001 Nobel Prize in Physiology or Medicine for working out this regulatory system.

Cell Cycle and Cancer

Every cancer is, at heart, a cell-cycle disorder. Cancer cells acquire mutations that override the normal stop signals and let them divide whenever they want. The two main mutation categories:

- **Oncogenes** are activated forms of normal cell-cycle drivers. Mutations in Ras (a growth-signal transducer) lock the protein in 'on' state, telling the cell to divide constantly. Ras mutations are found in ~30% of human cancers.
- **Tumor suppressors** are normal cell-cycle brakes. Mutations that knock them out remove the safety system. p53 mutations (most common) prevent the G1/S checkpoint from halting damaged cells. Retinoblastoma (Rb) mutations prevent control of the G1/S transition. BRCA1/BRCA2 mutations impair DNA-damage response.

Modern cancer therapy increasingly targets cell-cycle proteins directly. Palbociclib, ribociclib, and abemaciclib are CDK4/6 inhibitors approved for breast cancer treatment since 2015, they halt cancer cells at the G1/S transition. PARP inhibitors exploit DNA damage repair deficiencies. The whole field of targeted oncology builds on cell-cycle biology.

Related study notes: Mitosis, Meiosis, Nucleic Acid, Enzyme.

Practice Questions

Work each question before reading its solution. The set runs from direct recall and substitution to the applied questions that exams actually use to separate grades.

Q1. Name the phases of the cell cycle and the job of each.

SOLUTION

Interphase comprises G1 (growth and normal function), S (DNA replication), and G2 (further growth and pre-division checks); M phase then divides the nucleus (mitosis) and cytoplasm (cytokinesis). A cultured human cell completes the loop in roughly 24 hours, spending about 90% of it in interphase, not division.

Q2. What happens in S phase, and what is the chromosome bookkeeping before and after?

SOLUTION

Every chromosome is replicated, converting each from 1 DNA molecule to 2 identical sister chromatids joined at the centromere. The chromosome COUNT stays 46 in humans; the DNA content doubles from 2C to 4C. Counting chromosomes by centromeres while tracking DNA mass separately untangles most exam confusion here.

Q3. What is G0, and which human cells live there?

SOLUTION

A withdrawal from the cycle into a non-dividing working state. Mature neurons and cardiac muscle cells reside there essentially permanently, which is why their losses are so hard to repair; liver cells sit in G0 but re-enter the cycle on demand, powering the liver's famous regeneration. G0 is retirement, sometimes with a recall clause.

Q4. Describe the G1/S checkpoint and the question it asks.

SOLUTION

The restriction point asks: is the cell big enough, nourished, undamaged, and instructed by growth signals to commit? Passing it commits the cell to replicating its genome. Damaged DNA halts progress here, chiefly through p53 stabilizing p21 to block the cyclin-CDK engines. It is the most consequential no-return decision in the cycle.

Q5. What do the G2/M and spindle checkpoints verify?

SOLUTION

G2/M: was the genome copied completely and without damage, before mitosis is allowed to start. The spindle (metaphase) checkpoint: is every chromosome's kinetochore attached to spindle fibers from both poles, before the sisters are pulled apart. Skipping the second one missegregates chromosomes, producing aneuploid daughters.

Q6. How do cyclins and CDKs drive the cycle forward?

SOLUTION

Cyclin-dependent kinases are engines present throughout the cycle but inert alone; cyclins are their activating keys, synthesized and destroyed in waves. Each cyclin-CDK pair phosphorylates the substrates of its phase, then the cyclin's degradation makes the step irreversible. The cycle is a ratchet of build-activate-destroy, discovered in sea urchins and yeast, honored with the 2001 Nobel.

Q7. Explain p53's title "guardian of the genome" and the consequence of losing it.

SOLUTION

On DNA damage, p53 accumulates and halts the cycle for repair; if damage is irreparable it triggers apoptosis, deleting the dangerous cell. Lose p53 and damaged cells keep dividing, stacking mutations. TP53 is mutated in roughly half of all human cancers, and inheriting one faulty copy (Li-Fraumeni syndrome) brings early, multiple tumors.

Q8. Frame cancer as a cell-cycle disease using proto-oncogenes and tumor suppressors.

SOLUTION

Proto-oncogenes are accelerators (growth-signal relays like RAS); a gain-of-function mutation jams them on. Tumor suppressors are brakes (p53, RB); loss-of-function cuts them. Cancer typically needs both: a stuck accelerator plus failed brakes, accumulated over years, which is why risk climbs with age and why oncology drugs target cycle machinery such as CDK4/6.

Q9. Contrast cytokinesis in animal and plant cells.

SOLUTION

Animal cells pinch: an actin-myosin contractile ring tightens a cleavage furrow until 2 cells separate. Plant cells cannot pinch inside rigid walls; vesicles assemble a cell plate across the middle that grows outward into a new wall. Same goal, opposite geometry: constriction from outside in, versus construction from

inside out.

Q10. A tissue biopsy shows an unusually high mitotic index. What does that measure, and what might it mean?

SOLUTION

The fraction of cells visibly in mitosis, a direct readout of proliferation rate. High values are normal in renewing tissues, bone marrow, gut lining, and in healing wounds, but in a fixed tissue they flag uncontrolled division and factor into tumor grading. Context decides whether fast cycling is health or disease.

Answer Key

QUICK ANSWERS

Q1 G1 grow, S copy, G2 check, M divide **Q2** each chromosome becomes 2 sister chromatids; 46 stays 46 **Q3** the non-dividing state; neurons, cardiac muscle, resting liver **Q4** commit-to-replication decision; p53 guards it **Q5** complete undamaged DNA; full spindle attachment

Q6 cyclin waves switch CDK engines on and off **Q7** damage arrest or apoptosis; lost in ~50% of cancers **Q8** stuck accelerators + broken brakes **Q9** cleavage furrow vs cell plate **Q10** fraction of cells in M; proliferation gauge

Revision Sheet

The loop

G1 → S → G2 → M, ~24 h in culture; interphase is ~90% of it. G0 = exit.

The engine

Cyclin waves activate CDKs; degradation ratchets each phase irreversible.

S-phase bookkeeping

Chromosome count unchanged; each becomes 2 sister chromatids (2C → 4C DNA).

The guardian

p53: arrest, repair, or apoptosis. Mutated in about half of cancers.

3 checkpoints

G1/S commit (restriction point), G2/M integrity, spindle attachment at metaphase.

Cancer formula

Oncogene accelerators stuck on + tumor-suppressor brakes lost.

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