

Exercise walk-through

1.3

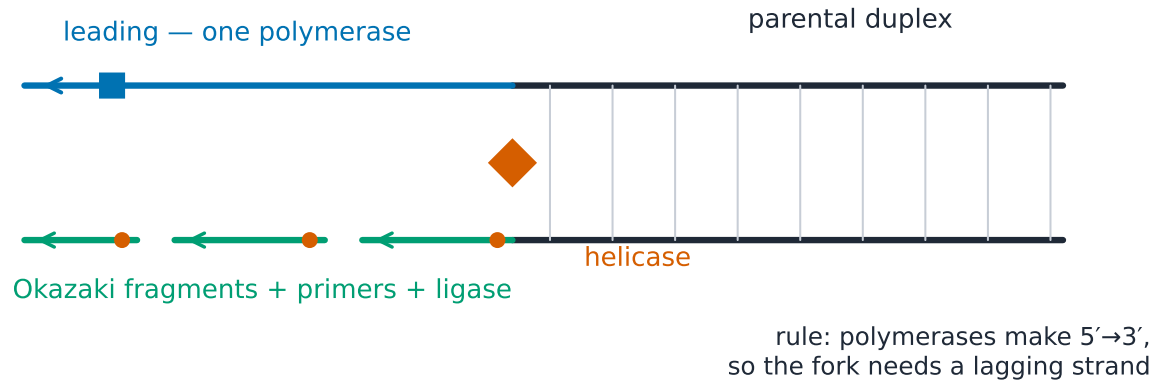
DNA replication and repair

University Medicine

Replication: copy 6.4 billion letters

- 1 Budget** $6.4 \times 10^9 \text{ bp} \times 10^{-9} \approx 6$ mutations survive per division - the number oncology and genetics both lean on.
- 2 Timing** One fork pair at 50 bp/s would need 2 years; 30 000 origins give ~35 min of pure synthesis inside an 8 h S phase.
- 3 Repair** Each repair pathway owns one lesion class: UV dimers to excision repair, mismatches to MMR - absence names a syndrome.

The fork



Antiparallel templates plus a 5'→3' enzyme force a leading and a lagging strand.

Exercises 2.1-2.3

2.1 Why is one strand made in Okazaki fragments?

[3]

2.2 E. coli (4.6 Mb) at 1000 nt/s from ONE bidirectional origin: approximate the copy time.

[3]

2.3 What lesion class does nucleotide excision repair own?

[3]

Exercises 2.1·2.3

2.1 Why is one strand made in Okazaki fragments? [3]

2.1

- Polymerases extend 5'→3' only; on the antiparallel template that means synthesising away from the fork in restarted fragments.

2.2 E. coli (4.6 Mb) at 1000 nt/s from ONE bidirectional origin: approximate the copy time. [3]

2.2

- $4.6 \times 10^6 / (2 \times 1000) = 2300 \text{ s} \approx 38 \text{ min} \checkmark$.

2.3 What lesion class does nucleotide excision repair own? [3]

2.3

- Bulky helix-distorting lesions, e.g. UV thymine dimers.

Exercise 3.1

3.1 A cell loses mismatch repair.

Compute the new mutations per division. Explain why this predisposes to early colon cancer (constant epithelial division). State which fidelity ladder layer is missing and which remain. [7]

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3.1

- $\text{Rate} \times 100 \rightarrow 6.4 \times 10^9 \times 10^{-7} \approx 640$ mutations per division ✓.
- Colon epithelium divides constantly, so the elevated rate compounds into driver mutations early.
- Missing: mismatch repair; remaining: polymerase selectivity and proofreading.

Exercise 3.2

3.2 Compare bacterial and human replication strategy.

Compute *E. coli*'s copy time (4.6 Mb, 1000 nt/s, bidirectional). Compute the human single-origin time and the 30 000-origin time. Explain why eukaryotes need many origins AND why S phase still takes 8 h. [8]

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3.2

- *E. coli*: $2300 \text{ s} \approx 38 \text{ min}$ (above).
- Human single origin: $6.4 \times 10^7 \text{ s} \approx 2.0 \text{ years}$ ✓.
- 30 000 origins: $\sim 35 \text{ min}$ synthesis ✓.
- Many origins because forks stall at damage and chromatin; 8 h because origins fire in timed clusters and chromatin must be opened and reassembled.