Exercise walk-through

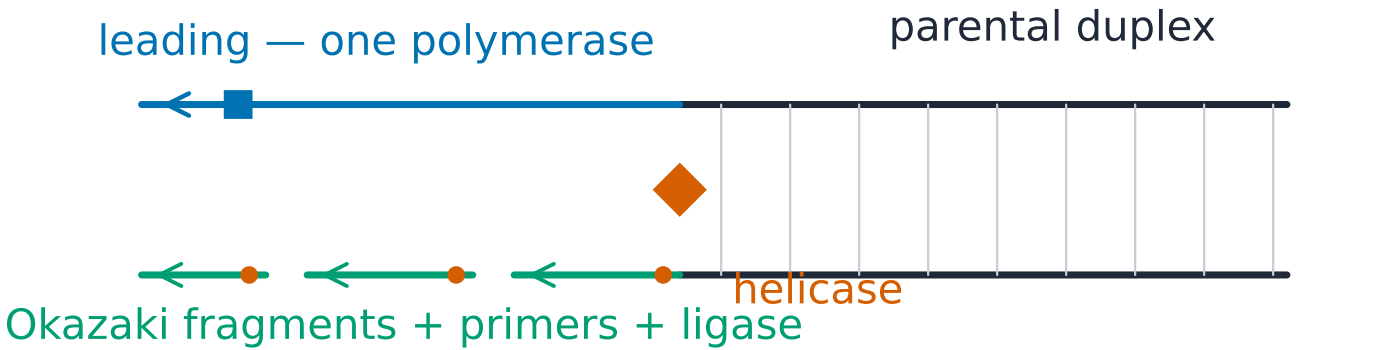
1.3
DNA replication and repair

University Medicine

Replication: copy 6.4 billion letters

1. **Budget** 6.4×10^{9} 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



rule: polymerases make 5′→3′,
so the fork needs a lagging strand

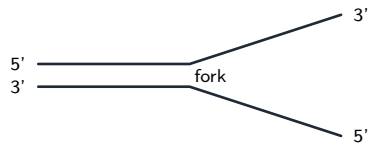
Antiparallel templates plus a $5' \to 3'$ enzyme force a leading and a **lagging strand**.

Exercises 2.1·2.2

2.1 Write the strand that pairs with `5′-AATGCCGT-3′`, from its 5′ end. [2]

5' | A | A | T | G | C | C | G | T | 3'

2.2 Explain why one new strand is made continuously and the other in pieces. [2]



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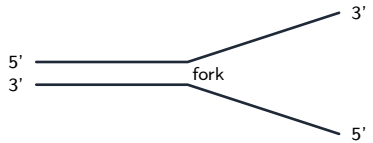
5′ | A | A | T | G | C | C | G | T | 3′

2.1

pairs: TTACGGCA, read 3′ → 5′ under the strand

written 5′ → 3′: `5′-ACGGCATT-3′`

2.2 Explain why one new strand is made continuously and the other in pieces. [2]



2.2

polymerase can only add to a 3′ end, so new DNA grows 5′ → 3′

on one template that is towards the fork (continuous); on the other it is away from the fork, so short fragments are made and joined

Exercises 2.3·2.4

2.3 Use the fidelity ladder to find the new mutations per division at each stage, for 6.4×10^9 bases. [3]



2.4 Show that one origin with two forks at 50 bases per second could not copy 6.4×10^9 bases in an 8-hour S phase, and that 30 000 origins can. [3]



Exercises 2.3·2.4

2.3 Use the fidelity ladder to find the new mutations per division at each stage, for 6.4×10^9 bases. [3]



2.3

polymerase alone: $\mathbf{6.4 \times 10^4}$

with proofreading: **640**

with mismatch repair: about **6**

2.4 Show that one origin with two forks at 50 bases per second could not copy 6.4×10^9 bases in an 8-hour S phase, and that 30 000 origins can. [3]



2.4

one origin: $6.4 \times 10^9 / 100 = 6.4 \times 10^7$ s $\approx$ 2 years

30 000 origins: $\approx$ 2100 s, about 36 min, well inside 8 h

exercises.lol exercises.com.cn

Exercise 3.1 (a)

3.1 A laboratory copies a gene by the **polymerase chain reaction** (PCR), as shown.

(a) How many copies of one molecule are made after 30 cycles? [1]

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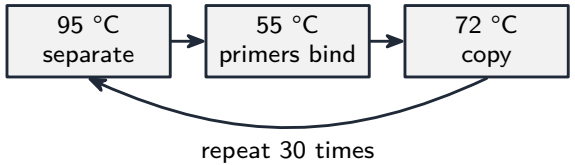
(a) How many copies of one molecule are made after 30 cycles? [1]

(a) $2^{30} \approx \mathbf{1.07 \times 10^9}$

Exercise 3.1 (b)

3.1 A laboratory copies a gene by the **polymerase chain reaction** (PCR), as shown.

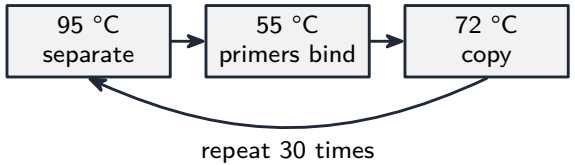
(b) Give the job of the primers, of a heat-stable polymerase, and of each temperature. [3]



Exercise 3.1 (b)

3.1 A laboratory copies a gene by the **polymerase chain reaction** (PCR), as shown.

(b) Give the job of the primers, of a heat-stable polymerase, and of each temperature. [3]



(b) primers give a 3′ end to start from and mark the region to copy; a heat-stable polymerase survives 95 °C in every cycle; 95 °C separates the strands, 55 °C lets primers bind, 72 °C is for copying

Exercise 3.1 (c)

3.1 A laboratory copies a gene by the **polymerase chain reaction** (PCR), as shown.

(c) A polymerase without proofreading makes about 10^{-4} errors per base. Find the expected errors in one new copy of a 1000-base gene. [2]

Exercise 3.1 (c)

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(c) $1000 \times 10^{-4} = \mathbf{0.1}$: about 1 copy in 10 has an error

Exercise 3.1 (d)

3.1 A laboratory copies a gene by the **polymerase chain reaction** (PCR), as shown.

(d) Why do labs that clone a gene choose a proofreading polymerase? [1]

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3.1 A laboratory copies a gene by the **polymerase chain reaction** (PCR), as shown.

(d) Why do labs that clone a gene choose a proofreading polymerase? [1]

(d) a cloned gene must have exactly the right sequence, and proofreading cuts errors about 100 times

Exercise 3.2 (a)

3.2 A (fictional) child gets severe sunburn after a few minutes outdoors, and skin cancers by age 20. Cells from the child cannot remove UV damage.

(a) Name the damage that UV light causes. [1]

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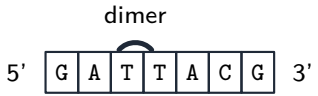
(a) Name the damage that UV light causes. [1]

(a) thymine dimers: two neighbouring T bases joined together

Exercise 3.2 (b)

3.2 A (fictional) child gets severe sunburn after a few minutes outdoors, and skin cancers by age 20. Cells from the child cannot remove UV damage.

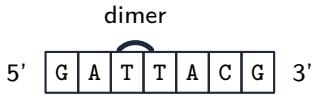
(b) Describe how nucleotide excision repair removes it. [2]



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(b) Describe how nucleotide excision repair removes it. [2]



(b) proteins cut the damaged strand on both sides and remove a short piece; polymerase fills the gap using the other strand, and ligase seals it

Exercise 3.2 (c)

3.2 A (fictional) child gets severe sunburn after a few minutes outdoors, and skin cancers by age 20. Cells from the child cannot remove UV damage.

(c) Explain why the child gets skin cancers so young. [2]

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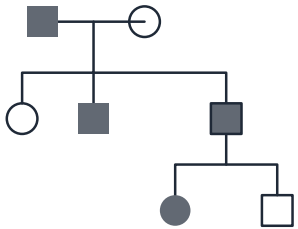
(c) Explain why the child gets skin cancers so young. [2]

(c) every sun exposure leaves unrepaired dimers that become mutations when copied; mutations soon hit the genes that control division, such as p53

Exercise 3.3 (a)

3.3 In a (fictional) family, several members had bowel cancer before age 50. They carry one faulty copy of a mismatch repair gene.

(a) If mismatch repair fails completely, the error rate stays at 10^{-7} per base. Find the mutations per division, and compare with normal. [2]

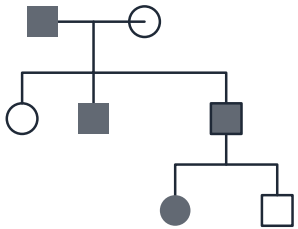


shaded: bowel cancer before 50

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shaded: bowel cancer before 50

(a) $6.4 \times 10^9 \times 10^{-7} = \mathbf{640}$: 100 times the normal 6

Exercise 3.3 (b)

3.3 In a (fictional) family, several members had bowel cancer before age 50. They carry one faulty copy of a mismatch repair gene.

(b) Why is the bowel lining often affected first? [2]

Exercise 3.3 (b)

3.3 In a (fictional) family, several members had bowel cancer before age 50. They carry one faulty copy of a mismatch repair gene.

(b) Why is the bowel lining often affected first? [2]

(b) the lining is renewed every few days, so its stem cells divide very many times and gather mutations fast

Exercise 3.3 (c)

3.3 In a (fictional) family, several members had bowel cancer before age 50. They carry one faulty copy of a mismatch repair gene.

(c) The family members have one working copy. Explain why cancer still starts early. [2]

Exercise 3.3 (c)

3.3 In a (fictional) family, several members had bowel cancer before age 50. They carry one faulty copy of a mismatch repair gene.

(c) The family members have one working copy. Explain why cancer still starts early. [2]

(c) in any one cell, a single new hit on the working copy is enough; with billions of dividing cells this second hit happens early in life

Exercise 3.3 (d)

3.3 In a (fictional) family, several members had bowel cancer before age 50. They carry one faulty copy of a mismatch repair gene.

(d) Recommend what the family should be offered. [2]

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(d) Recommend what the family should be offered. [2]

(d) genetic testing for relatives, so carriers are known; regular colonoscopy from an early age for carriers, which finds and removes growths before they become cancer