Exercise walk-through

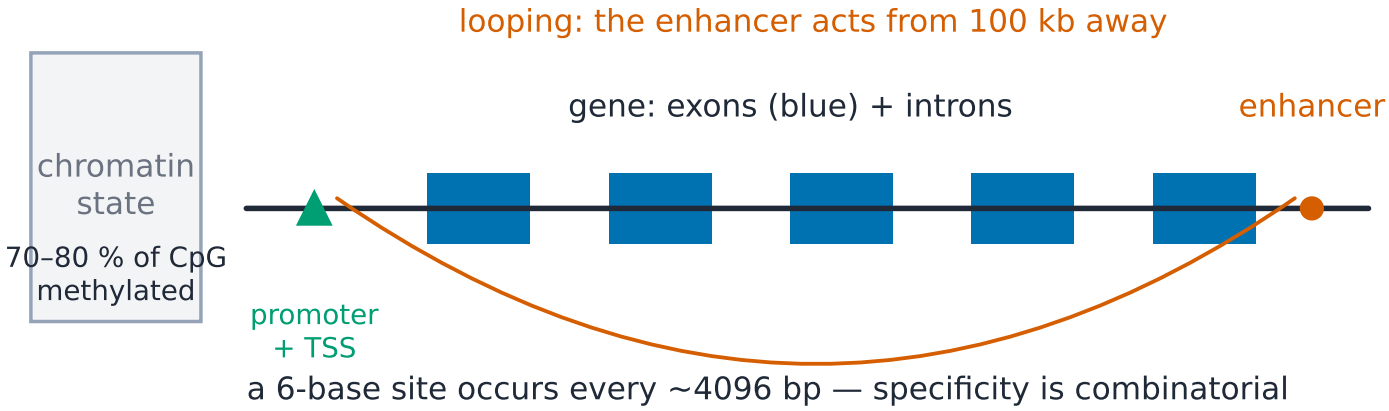
1.5
Regulation of gene expression

University Medicine

Regulation: the gene is a switch

1. **Enhancer** Lactase persistence: one base 14 kb upstream strengthens an **enhancer**, LCT stays on into adulthood - a zero-protein-change continental trait.
2. **Epigenetic** Fictional twins, identical genotypes, different severity: promoter methylation silences one copy - access, not letters.
3. **Packing** 2.2 m of DNA wraps ~200 bp nucleosomes into a ~30 nm fibre - compaction near 10^4-fold.

Regulatory regions



Enhancer, promoter, **transcription** start, exons - with the chromatin gate in front and looping from 100 kb away.

Exercises 2.1·2.3

2.1 How often does a random 8-base motif occur per strand (6.4×10^{9} bp)? [3]

2.2 Distinguish promoter from enhancer in one sentence each. [3]

2.3 Why is “epigenetic” not “permanent”? [3]

Exercises 2.1·2.3

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2.1

- $6.4 \times 10^9 / 4^8 = 6.4 \times 10^9 / 65\,536 \approx 98\,000$ ✓.

2.2 Distinguish promoter from enhancer in one sentence each. [3]

2.2

- Promoter: fixed position at the transcription start, assembles Pol II. Enhancer: distance and orientation-independent, boosts via looping.

2.3 Why is “epigenetic” not “permanent”? [3]

2.3

- Marks are copied through cell divisions but are reprogrammable (development, some therapies target writers/erasers).

Exercise 3.1

3.1 A transcription factor binds a 6-base motif.

Compute the expected genome-wide hit count. Explain why cooperating factors binding adjacent sites restore specificity, quantitatively. State one consequence for interpreting non-coding disease variants. [7]

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3.1

- $6.4 \times 10^9/4096 \approx 1.6 \times 10^6$ ✓.
- Two cooperating 6-base sites: expected joint hits divide by ~4096 again → ~380 – specificity returns multiplicatively.
- Consequence: most disease-relevant non-coding variants sit in regulatory logic, not code.

Exercise 3.2

3.2 Fictional monozygotic twins, same variant, different severity; one has promoter methylation silencing that allele.

Explain why sequence identity does not guarantee phenotype identity. State what methylation (70–80 % of CpG) does to enhancer/promoter access. Explain why methylation assays sit next to sequencers diagnostically. [7]

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3.2

- Access differs: methylation compacts chromatin, silencing the allele without changing letters.
- Methylated CpG recruits repressors/compact histone marks → enhancer and promoter inaccessible.
- Diagnostics: severity modifiers live in the access layer, so assays of methylation complement sequencing.