

BRIGHT SCHOLARS

BIOLOGY SERIES • BOOK 3

ADVANCED
BIOLOGY

BOOK 3 Grades 11–12

Applications in Gene Regulation, Biotechnology, Genetics, Evolution, Human
Physiology, Immunity, Ecology, and Scientific Inquiry

Learn it. Practice it. Prove it.

GENE REGULATION • BIOTECHNOLOGY • GENETICS • EVOLUTION • PHYSIOLOGY • IMMUNITY •
ECOLOGY • INQUIRY

THIS BOOK BELONGS TO

Name _____

Class / Period _____

Teacher _____

School Year _____

Contents

GETTING STARTED

How to Use This Workbook	5
Standards Alignment	6
18-Week Pacing Guide	7
Biology Skills Tracker	8
Vocabulary Tracker.....	9
Study Tips for Advanced Biology	10

UNITS

1	Gene Expression and Regulation	11
1.1	Regulating Genes in Bacteria: Operons	12
1.2	Eukaryotic Gene Regulation: Chromatin and Transcription Factors.....	14
1.3	Regulation After Transcription.....	16
1.4	Epigenetics, Imprinting, and Development	17
2	Biotechnology and Genetic Engineering.....	30
2.1	PCR and Quantitative PCR	31
2.2	Restriction Enzymes, Gels, and DNA Profiling.....	32
2.3	Cloning Genes and Making Proteins.....	34
2.4	Genome Editing with CRISPR.....	35
3	Advanced Genetics	48
3.1	Beyond Mendel: Gene Interactions	49
3.2	Polygenic Traits and Heritability.....	50
3.3	Linkage, Gene Mapping, and Chi-Square	52
3.4	Chromosome Changes and Genetic Testing	53
4	Population Genetics and Evolution.....	66
4.1	The Hardy-Weinberg Equilibrium	67
4.2	Forces That Change Allele Frequencies.....	69
4.3	Phylogenetics and Molecular Clocks.....	70
4.4	Speciation and Macroevolution.....	72
☒	Mid-Book Exam	84
5	Human Body Systems	94
5.1	The Nervous System: Neurons and Signals	95
5.2	The Endocrine System	97
5.3	The Circulatory System	99
5.4	Gas Exchange and Oxygen Transport	101
5.5	Digestion, Absorption, and the Kidney.....	103

Gene Expression and Regulation

? BIG QUESTION

Every cell in your body carries the same genome, yet a neuron and a liver cell make very different proteins. How does a cell decide which genes to use, when, and how much?

BY THE END OF THIS UNIT, I CAN

- ☐ predict lac and trp operon activity from the levels of lactose, glucose, and tryptophan.
- ☐ explain how chromatin structure, transcription factors, and enhancers control eukaryotic transcription.
- ☐ describe regulation after transcription by RNA processing, microRNAs, translation control, and protein degradation.
- ☐ explain DNA methylation, histone modification, X-inactivation, and genomic imprinting.
- ☐ connect gene regulation to cell differentiation, cancer, and evolution.

UNIT ROADMAP

- 1.1 Regulating Genes in Bacteria: Operons..... p. 12
- 1.2 Eukaryotic Gene Regulation: Chromatin and Transcription Factors p. 14
- 1.3 Regulation After Transcription..... p. 16
- 1.4 Epigenetics, Imprinting, and Development.... p. 17

Suggested time: 2 weeks

Standards: HS-LS1-1; HS-LS3-1; HS-LS3-2; SEP 2, 4, 6

KEY VOCABULARY

gene expression	operon	promoter	
operator	repressor	inducer	corepressor
CAP	cAMP	chromatin	histone acetylation
transcription factor	enhancer	silencer	
mediator	microRNA	RISC	ubiquitin
proteasome	epigenetics	DNA methylation	
CpG island	X-inactivation	genomic imprinting	

Regulating Genes in Bacteria: Operons

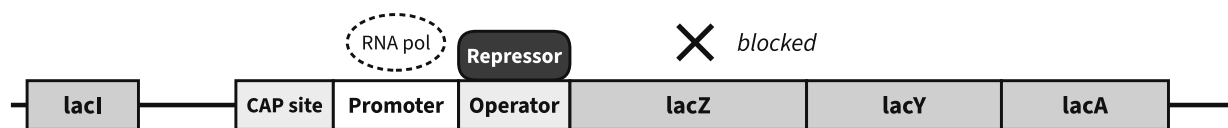
KEY TERMS operon • promoter • operator • repressor • inducer • inducible operon • repressible operon • corepressor • CAP • cAMP • negative and positive control

Bacteria live in changing environments, so they switch genes on only when the products are useful. In bacteria, genes for one pathway are often grouped into an **operon**: a single **promoter** (where RNA polymerase binds), an **operator** (a switch where a regulatory protein can bind), and the structural genes, all transcribed together into one mRNA. Book 2 showed how a promoter starts transcription; here you will see how cells decide whether it starts at all.

The lac operon is inducible. *E. coli* prefers glucose, but it can use the milk sugar lactose. The *lac* operon carries three genes, including *lacZ*, which codes for β -galactosidase, the enzyme that splits lactose. A separate gene, *lacI*, makes the **lac repressor**. With no lactose, the repressor binds the operator and blocks RNA polymerase (**negative control**). When lactose is present, some is converted to **allolactose**, the **inducer**, which binds the repressor, changes its shape, and releases it from the operator.

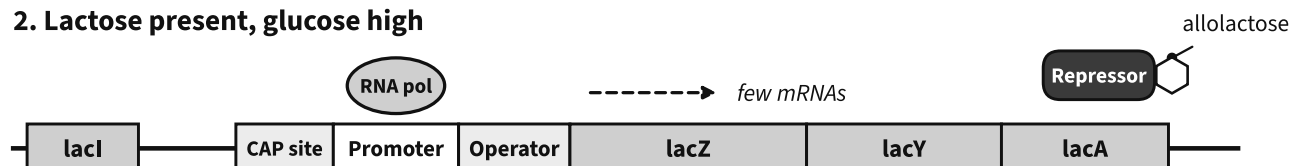
Removing the repressor allows only weak transcription, because the *lac* promoter binds RNA polymerase poorly. Strong transcription also needs an activator (**positive control**). When glucose is scarce, the cell's level of **cAMP** rises; cAMP binds the **catabolite activator protein (CAP)**, and the CAP–cAMP complex binds next to the promoter and helps RNA polymerase bind. The result: the operon is fully on only when **lactose is present and glucose is absent**. When both sugars are present, the cell uses glucose first.

1. Lactose absent



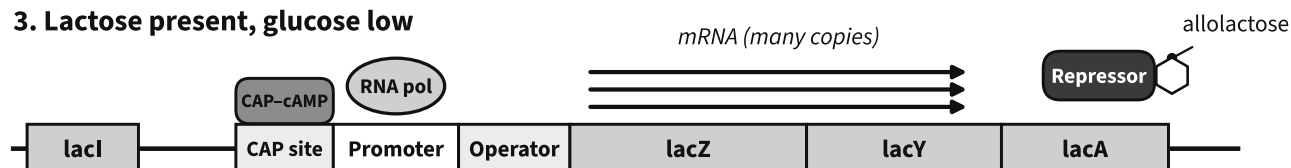
Repressor bound to the operator: no transcription

2. Lactose present, glucose high



Repressor released; no CAP-cAMP: low transcription

3. Lactose present, glucose low



Repressor released; CAP-cAMP bound: high transcription

FIGURE 1.1 The lac operon in three conditions. The repressor blocks transcription unless allolactose removes it; CAP-cAMP boosts transcription only when glucose is low.

The trp operon is repressible. The *trp* operon codes for the enzymes that make the amino acid tryptophan. It is normally on. When tryptophan is plentiful, tryptophan acts as a **corepressor**: it binds the inactive trp repressor and activates it, so the repressor binds the operator and shuts the operon off. The cell stops making an amino acid it already has.

Feature	lac operon	trp operon
Pathway	Breaks down lactose (catabolic)	Builds tryptophan (anabolic)
Normal state	Off (inducible)	On (repressible)
Repressor as made	Active; binds operator	Inactive; cannot bind operator
Small molecule	Allolactose (inducer) inactivates the repressor	Tryptophan (corepressor) activates the repressor
Fully on when	Lactose present and glucose absent	Tryptophan scarce

Unit 1 Practice



MULTIPLE CHOICE

Fill in the bubble for the best answer.

- 1 In the lac operon, the inducer allolactose
 - (A) binds the operator.
 - (B) inactivates the repressor.
 - (C) activates CAP.
 - (D) blocks RNA polymerase.
- 2 The lac operon is transcribed at its highest rate when
 - (A) glucose is high and lactose is absent.
 - (B) glucose is high and lactose is present.
 - (C) glucose is low and lactose is present.
 - (D) glucose is low and lactose is absent.
- 3 In the trp operon, tryptophan acts as a
 - (A) corepressor that activates the repressor.
 - (B) inducer that removes the repressor.
 - (C) activator that binds the enhancer.
 - (D) promoter sequence.
- 4 Which change would most directly open chromatin and increase transcription?
 - (A) DNA methylation of a promoter
 - (B) Removing acetyl groups from histones
 - (C) Condensing the region into heterochromatin
 - (D) Adding acetyl groups to histones
- 5 An enhancer is best described as a
 - (A) DNA sequence, sometimes far from the gene, that binds activators.
 - (B) protein that unwinds DNA.
 - (C) sequence where translation starts.
 - (D) region removed during splicing.

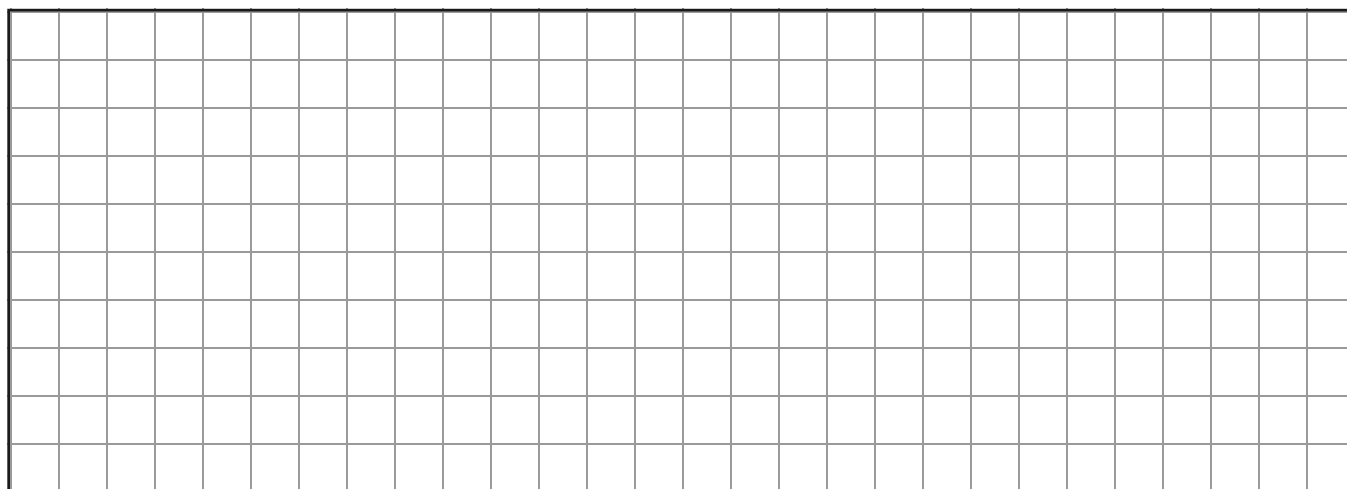
Data Lab: Measuring Gene Regulation

Researchers grew *E. coli* strains in different media and measured β -galactosidase activity, which reflects *lac* operon transcription.

DATA SET A: B-GALACTOSIDASE ACTIVITY IN *E. COLI*

Row	Strain	Glucose	Lactose	Activity (units)
1	Wild type	+	–	2
2	Wild type	+	+	60
3	Wild type	–	+	1,200
4	Wild type	–	–	3
5	<i>lacI</i> [–] (no repressor)	+	–	70
6	<i>lacI</i> [–] (no repressor)	–	–	1,150
7	<i>CAP</i> [–] (no CAP)	–	+	55

Make a bar graph of activity (y-axis) for rows 1 to 7. Choose a scale that shows both small and large values.



- 1 Compare rows 1 and 2, then rows 2 and 3. What does each comparison show about how lactose and glucose control the operon?

6 Does the DNA sequence of the tumor-suppressor gene in Tumor C change after treatment? Explain.

CASE STUDY

Case Study: Lactase Persistence, a Regulatory Mutation

 CASE STUDY

All infant mammals make **lactase**, the enzyme that digests the milk sugar lactose. In most mammals, including most humans, the lactase gene (*LCT*) is switched off after weaning. Adults who no longer make lactase can have bloating and discomfort after drinking milk. This is the ancestral, original human condition, not a disease. About one-third of adults worldwide keep making lactase for life, a trait called **lactase persistence**. In Europe, it is caused mainly by a single base change, a C-to-T substitution about 14,000 base pairs upstream of *LCT*, inside an intron of a neighboring gene. The *LCT* coding sequence is unchanged. The region acts as an enhancer, and the T version binds a transcription factor more strongly, keeping *LCT* transcribed in adult intestinal cells. One copy of the T allele is enough for persistence. The trait is common in northern Europe and in herding peoples of East Africa and the Middle East, and rare in many East Asian and Native American populations. In East Africa, the same trait is caused by different single-base changes in the same enhancer. Ancient DNA shows that the European allele became common only within the last few thousand years, after people began herding animals for milk; it is one of the most strongly selected traits known in humans.

1 The lactase persistence mutation does not change a single amino acid of lactase. Explain how it changes adult lactase levels.

2 Why is lactase persistence inherited as a dominant trait?

Linkage, Gene Mapping, and Chi-Square

KEY TERMS linked genes • parental type • recombinant type • recombination frequency • map unit (centimorgan) • three-point cross • double crossover • interference • chi-square (χ^2) • null hypothesis • degrees of freedom

Genes on the same chromosome are **linked**. They tend to be inherited together unless crossing over in prophase I separates them. In a test cross, offspring that look like the parents are **parental types**; offspring with new combinations are **recombinant types**. The **recombination frequency** is:

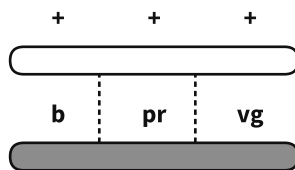
RECOMBINATION FREQUENCY

Recombination frequency = (number of recombinant offspring ÷ total offspring) × 100% 1 percent recombination = 1 **map unit**, or 1 **centimorgan (cM)**.

The farther apart two genes are, the more often a crossover falls between them, so recombination frequency measures relative distance. Genes 50 cM or more apart recombine 50 percent of the time and appear to assort independently, even if they are on the same chromosome.

Three-point crosses. Mapping three genes at once shows their order. In a test cross of a triple heterozygote, the two largest classes are parental types, and the two **smallest** classes are **double crossovers**. In a double crossover, only the **middle** gene switches relative to the other two. Compare a double crossover with the parental types: whichever gene is "out of place" is the middle gene. Then calculate each distance, counting the double crossovers in both intervals. The distance between the outer genes measured directly is a little smaller than the sum of the two intervals, because a double crossover between the outer genes leaves them in their parental combination and hides two crossovers.

Parental chromosomes



Double crossover between them switches only the middle gene:



Map from the test-cross data

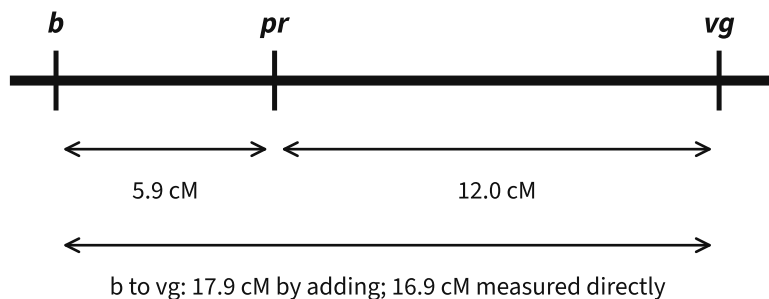


FIGURE 3.3 A three-point cross. Single crossovers in each interval and a double crossover that switches only the middle gene; the map shows the distances calculated from the data.

Final Exam

Units 1–9 • Suggested time: 2 hours

Name _____ Date _____ Score _____

A Multiple Choice	B Short Answer	C Data Analysis	D Case-Based	E Essay	Total
____ / 40	____ / 30	____ / 30	____ / 30	____ / 20	____ / 150

? EXAM DIRECTIONS

This exam covers all nine units. Show your work for every calculation and use scientific vocabulary in written answers. A chi-square critical value table is in Lesson 3.3.

Section A: Multiple Choice (40 points, 1 point each)

- In the trp operon, tryptophan
 - inactivates the repressor.
 - activates CAP.
 - binds the promoter.
 - activates the repressor so it binds the operator.
- Histone deacetylation is expected to
 - close chromatin and reduce transcription.
 - open chromatin and increase transcription.
 - change the DNA sequence.
 - add methyl groups to DNA.
- An activator protein bound 30,000 base pairs upstream of a gene increases its transcription. The site it binds is

☐ (A) a promoter.	☐ (B) an operator.
☐ (C) an enhancer.	☐ (D) an intron splice site.
- A short RNA that pairs with the 3' UTR of many mRNAs and reduces their translation is a

☐ (A) tRNA.	☐ (B) microRNA.
☐ (C) ribosomal RNA.	☐ (D) guide RNA for Cas9.

Answer Key

Accept any scientifically accurate wording. Model answers show the key ideas a complete response should include. Multiple-choice answers are in bold.

Unit 1: Gene Expression and Regulation

Lesson 1.1 Regulating Genes in Bacteria: Operons (p. 12)

1. Low. Allolactose removes the repressor, but high glucose keeps cAMP low, so CAP cannot activate the promoter; only weak transcription occurs.
2. The cell needs lactose-digesting enzymes only when lactose is available, so the operon turns on in its presence. Tryptophan is always needed, so the cell makes it by default and turns production off only when enough is already present.

Lesson 1.2 Eukaryotic Gene Regulation: Chromatin and Transcription Factors (p. 14)

1. Acetyl groups neutralize the positive charges on histone tails, so histones hold the negatively charged DNA less tightly. The chromatin opens and transcription factors and RNA polymerase can reach the promoter.
2. Each cell type has a different combination of specific transcription factors. Liver cells have the activators that bind the albumin enhancers; lens cells have the activators for the crystallin enhancers. Without the matching activators, a gene stays off.

Lesson 1.3 Regulation After Transcription (p. 16)

1. Animal miRNAs need only a partial match, mostly in a short seed region, so one miRNA can pair with the 3' UTRs of many different mRNAs and reduce the translation of all of them.
2. Stopping production leaves existing protein working until it breaks down on its own. Tagging it with ubiquitin for the proteasome removes it quickly, allowing a sharp switch, as when cyclins must disappear for the cell cycle to move on.

Lesson 1.4 Epigenetics, Imprinting, and Development (p. 17)

1. The orange and black alleles are on the X chromosome. A female can carry both, one on each X, and random X-inactivation produces patches of each color. A typical male has one X and so only one coat-color allele.
2. Silent genes carry methylation and histone marks. After replication, maintenance methyltransferases copy

methylation onto the new DNA strand, so daughter cells inherit the same pattern of silent and active genes.

Unit 1 Practice (p. 20)

MULTIPLE CHOICE

1. **B**
2. **C**
3. **A**
4. **D**
5. **A**
6. **B**
7. **C**
8. **D**
9. **A**
10. **C**

TRUE OR FALSE

1. **T**
2. **F**. Eukaryotic genes usually have their own promoters; genes in a pathway are coordinated by shared enhancer sequences, not operons.
3. **F**. Enhancers can work from thousands of base pairs away because DNA loops bring them close to the promoter.
4. **F**. Epigenetic changes alter gene expression through marks on DNA and histones without changing the sequence.
5. **T**
6. **T**

FILL IN THE BLANK

1. operator
2. cAMP
3. corepressor
4. mediator
5. RISC
6. proteasome
7. CpG
8. imprinting

SHORT ANSWER

1. In negative control, a regulatory protein turns transcription off when bound: the lac repressor binds the operator and blocks RNA polymerase. In positive control, a regulatory protein turns transcription up when bound: CAP–cAMP binds near the lac promoter and helps RNA polymerase bind.