19.8: Enzyme Regulation

Skills to Develop

1. Briefly compare the genetic control of enzyme activity in bacteria with control of enzyme activity through feedback inhibition.
2. Briefly compare an inducible operon with a repressible operon.

In living cells, there are hundreds of different enzymes working together in a coordinated manner. Living cells neither synthesize nor breakdown more material than is required for normal metabolism and growth. All of this necessitates precise control mechanisms for turning metabolic reactions on and off. Enzymes can be controlled or regulated in two ways: controlling the synthesis of the enzyme (genetic control) and controlling the activity of the enzyme (feedback inhibition).

Genetic Control

Genetic control of enzyme activity refers to controlling transcription of the mRNA needed for an enzyme's synthesis. In prokaryotic cells, this involves the induction or repression of enzyme synthesis by regulatory proteins that can bind to DNA and either block or enhance the function of RNA polymerase, the enzyme required for transcription. The regulatory proteins are part of either an operon or a regulon. An operon is a set of genes transcribed as a polycistronic message that is collectively controlled by a regulatory protein. A regulon is a set of related genes controlled by the same regulatory protein but transcribed as monocistronic units. Regulatory proteins may function either as repressors or activators.
Genetic Control: Repressors

Repressors are regulatory proteins that block transcription of mRNA. They do this by binding to a portion of DNA called the operator that lies downstream of a promoter. The binding of the regulatory protein to the operator prevents RNA polymerase from passing the operator and transcribing the coding sequence for the enzymes. This is called negative control. Repressors are allosteric proteins that have a binding site for a specific molecule. Binding of that molecule to the allosteric site of the repressor can alter the repressor’s shape that, in turn affects its ability to bind to DNA. This can work in one of two ways:

Some repressors are synthesized in a form that cannot by itself bind to the operator. The binding of a molecule called a corepressor, however, alters the shape of the regulatory protein to a form that can bind to the operator and block transcription.

![Diagram of a repressible operon with steps and labels for genetic control](https://bio.libretexts.org/Bookshelves/Microbiology/Book%3A_Microbiology_(Kaiser)/Unit_7%3A_Microbial_Genetics_and_Mi...)

**Figure (PageIndex(1)):** A Repressible Operon in the Absence of a Corepressor (The Tryptophan Operon).

Step 1: The regulator gene codes for an inactive repressor protein. Step 2: The inactivated repressor protein is unable to bind to the operator region of the operon.

An example of this type of repression is the *trp* operon in *E. coli* that encodes the five enzymes in the pathway for the biosynthesis of the amino acid tryptophan. In this case, the repressor protein, coded for by a regulatory gene, normally does not bind to the operator region of the *trp* operon and the five enzymes needed to synthesize the amino acid tryptophan are made (Figure (PageIndex(1)) and Figure (PageIndex(2))).

![Diagram of a repressible operon with steps and labels for genetic control](https://bio.libretexts.org/Bookshelves/Microbiology/Book%3A_Microbiology_(Kaiser)/Unit_7%3A_Microbial_Genetics_and_Mi...)

**Figure (PageIndex(2)):** A Repressible Operon in the Absence of a Corepressor (The Tryptophan Operon).

Step 3: Since the inactive repressor protein is unable to bind to the operator region, RNA polymerase (the enzyme responsible for transcription) can transcribe the genes coding for the five enzymes needed to synthesize tryptophan. Step 4: The enzymes are synthesized.
for the transcription of genes) is now able to bind to the promoter region of the operon. Step 4: RNA polymerase is now able to transcribe the five enzyme genes into mRNA. Step 5: With the transcription of these genes, the five enzymes needed for the bacterium to synthesize the amino acid tryptophan are now made.

Tryptophan, the end product of these enzyme reactions, however, functions as a corepressor. The tryptophan is able to bind to a site on the allosteric repressor protein, changing its shape and enabling it to interact with the operator region. Once the repressor binds to the operator, RNA polymerase is unable to get beyond the operator and transcribe the genes for tryptophan biosynthesis. Therefore, when sufficient tryptophan is present, transcription of the enzymes that allows for its biosynthesis are turned off (Figure \(\PageIndex{3}\) and Figure \(\PageIndex{4}\)).

![Figure \(\PageIndex{3}\): A Repressible Operon in the Presence of a Corepressor (The Tryptophan Operon). Step 1: The regulator gene codes for an inactive repressor protein. Step 2: If the corepressor, tryptophan, is present it binds to the inactive repressor protein. Step 3: The binding of the corepressor causes inactive repressor protein to become activated. Step 4: The activated repressor protein then binds to the operator region of the operon.]

![Figure \(\PageIndex{4}\): A Repressible Operon in the Presence of a Corepressor (The Tryptophan Operon). Step 5: With the active repressor protein bound to the operator region, RNA polymerase (the enzyme responsible for the transcription of genes) is unable to bind to the promoter region of the operon. Step 6: If RNA polymerase does not bind to the promoter region, the five enzyme genes are not transcribed into mRNA. Step 5: Without the transcription of the five genes, the five enzymes needed for the bacterium to synthesize the amino acid tryptophan are not made.]

Other repressors are synthesized in a form that readily binds to the operator and blocks transcription. However, the binding of a molecule called an inducer alters the shape of the regulatory protein in a way that now blocks its binding to the operator and thus permits transcription.
An example of this is the ***lac*** operon that encodes for the three enzymes needed for the degradation of lactose by *E. coli*. *E. coli* will only synthesize the three enzymes it requires to utilize lactose if that sugar is present in the surrounding environment. In this case, lactose functions as an inducer. In the absence of lactose, the repressor protein binds to the operator and RNA polymerase is unable to get beyond the operator and transcribe the genes for utilization of lactose and the three enzymes for degradation of lactose are not synthesized (Figure \(\PageIndex{5}\) and Figure \(\PageIndex{6}\)).

When lactose, the inducer, is present, it binds to the allosteric repressor protein and causes it to change shape in such a way that it is no longer able to bind to the operator. Now RNA polymerase can transcribe the three genes required for the degradation of lactose and the bacterium is able to synthesize the enzymes needed for its utilization (Figure \(\PageIndex{7}\) and Figure \(\PageIndex{8}\)).

![Diagram of the lac operon](https://bio.libretexts.org/Bookshelves/Microbiology/Book%3A_Microbiology_(Kaiser)/Unit_7%3A_Microbial_Genetics_and_Mi…)

**Figure \(\PageIndex{5}\)**: An Inducible Operon in the Absence of an Inducer (The Lactose Operon). Step 1: The regulator gene codes for an active repressor protein. Step 2: The repressor protein then binds to the operator region of the operon.

**Figure \(\PageIndex{6}\)**: An Inducible Operon in the Absence of an Inducer (The Lactose Operon). Step 3: With the active repressor protein bound to the operator region, RNA polymerase (the enzyme responsible for the transcription of genes) is unable to bind to the promoter region of the operon. Step 4: If RNA polymerase does not bind to the promoter region, the three enzyme genes (Z, Y, and A) are not transcribed into mRNA. Step 5: Without the transcription of the three enzyme genes, the three enzymes needed for the utilization of the sugar lactose by the bacterium are not synthesized.
**Figure 7**: An Inducible Operon in the Presence of an Inducer (The Lactose Operon)

Step 1: The regulator gene codes for an active repressor protein. Step 2: Lactose, the inducer molecule binds to the active repressor protein. Step 3: The binding of the inducer inactivates the repressor protein. Step 4: The inactivated repressor protein is then unable to bind to the operator region of the operon.

Step 5: Since the inactive repressor protein is unable to bind to the operator region, RNA polymerase (the enzyme responsible for the transcription of genes) is now able to bind to the promoter region of the operon. Step 6: RNA polymerase is now able to transcribe the three enzyme genes (Z, Y, and A) into mRNA. Step 7: With the transcription of these genes, the three enzymes needed for the bacterium to utilize the sugar lactose are now synthesized. (The Z gene codes for beta-galactosidase, an enzyme that breaks down lactose into glucose and galactose. The Y gene codes for permease, an enzyme which transports lactose into the bacterium. The A gene codes for transacetylase, an enzyme which is thought to aid in the release of galactosides.)

**Figure 8**: An Inducible Operon in the Absence of an Inducer (The Lactose Operon)

Animation: An Inducible Operon in the Absence of an Inducer (The Lactose Operon)
• The regulator gene codes for an active repressor protein.
• The repressor protein then binds to the operator region of the operon.
• With the active repressor protein bound to the operator region, RNA polymerase (the enzyme responsible for the transcription of genes) is unable to bind to the promoter region of the operon.
• If RNA polymerase does not bind to the promoter region, the three enzyme genes (Z, Y, and A) are not transcribed into mRNA.
• Without the transcription of the three enzyme genes, the three enzymes needed for the utilization of the sugar lactose by the bacterium are not synthesized.

Animation: An Inducible Operon in the Presence of an Inducer (The Lactose Operon)

• The regulator gene codes for an active repressor protein.
• Lactose, the inducer molecule binds to the active repressor protein.
• The binding of the inducer alters the shape of the allosteric repressor causing it to become inactivated.
• The inactivated repressor protein is then unable to bind to the operator region of the operon.
• Since the inactive repressor protein is unable to bind to the operator region, RNA polymerase (the enzyme responsible for the transcription of genes) is now able to bind to the promoter region of the operon.
• RNA polymerase is now able to transcribe the three enzyme genes (Z, Y, and A) into mRNA.
• With the transcription of these genes, the three enzymes needed for the bacterium to utilize the sugar lactose are now synthesized. (The Z gene codes for beta-galactosidase, an enzyme that breaks down lactose into glucose and galactose. The Y gene codes for permease, an enzyme which transports lactose into the bacterium. The A gene codes for transacetylase, an enzyme which is thought to aid in the release of galactosides.)

Genetic Control: Activators

Activators are regulatory proteins that promote transcription of mRNA. Activators control genes that have a promoter to which RNA polymerase cannot bind. The promoter lies adjacent to a segment of DNA called the activator-binding site. The activator is an allosteric protein synthesized in a form that cannot normally bind to the activator-binding site. As a result, RNA polymerase is unable to bind to the promoter and transcribe the genes (Figure \( \PageIndex{9} \)).
However, binding of a molecule called an inducer to the activator alters the shape of the activator in a way that now allows it to bind to the activator-binding site. The binding of the activator to the activator-binding site, in turn, enables RNA polymerase to bind to the promotor and initiate transcription (Figure \(\PageIndex{1}\))0 and Figure \(\PageIndex{1}\)). This is called positive control.

Animation: An Activator Protein in the Absence of an Inducer

**Figure \(\PageIndex{9}\):** An Activator Protein in the Absence of an Inducer

**Figure \(\PageIndex{10}\):** An Activator Protein in the Presence of an Inducer, Step-1

**Figure \(\PageIndex{11}\):** An Activator Protein in the Presence of an Inducer, Step-2

Animation: An Activator Protein in the **Absence** of an Inducer

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Bacteria also use **translational control** of enzyme synthesis. In this case, the bacteria produce antisense RNA that is complementary to the mRNA coding for the enzyme. When the antisense RNA binds to the mRNA by complementary base pairing, the mRNA cannot be translated into protein and the enzyme is not made (Figure \(\PageIndex{12}\)).

**Figure \(\PageIndex{12}\):** Antisense RNA. During translational control of enzyme synthesis, bacteria produce antisense RNA that is complementary to the mRNA coding for the enzyme. When the antisense RNA binds to the mRNA by complementary base pairing, the mRNA cannot be translated into protein and the enzyme is not made.

**Animation: Antisense RNA**

During translational control of enzyme synthesis, bacteria produce antisense RNA that is complementary to the mRNA coding for the enzyme. When the antisense RNA binds to the mRNA by complementary base pairing, the mRNA cannot be translated into protein and the enzyme is not made.
Feedback Inhibition

Enzyme activity can be controlled by competitive inhibition and non-competitive inhibition. With noncompetitive inhibition, the inhibitor is the end product of a metabolic pathway that is able to bind to a second site (the allosteric site) on the enzyme. Binding of the inhibitor to the allosteric site alters the shape of the enzyme's active site thus preventing binding of the first substrate in the metabolic pathway. In this way, the pathway is turned off (Figure \(\PageIndex{13}\)).

**Figure \(\PageIndex{13}\):** Noncompetitive Inhibition with Allosteric Enzymes. When the end product (inhibitor) of a pathway combines with the allosteric site of the enzyme, this alters the enzyme's active site so it can no longer bind to the starting substrate of the pathway. This blocks production of the end product.

Animation: Noncompetitive Inhibition with Allosteric Enzymes.

When the end product (inhibitor) of a pathway combines with the allosteric site of the enzyme, this alters the enzyme's active site so it can no longer bind to the starting substrate of the pathway. This blocks production of the end product.
With competitive inhibition, the inhibitor is the end product of an enzymatic reaction. That end product is also capable of reacting with the enzyme's active site and prevents the enzyme from binding its normal substrate. As a result, the end product is no longer synthesized (Figure \(\PageIndex{14}\)).

**Figure \(\PageIndex{14}\):** Competitive Inhibition of Enzyme Activity. The end product (inhibitor) of a pathway binds to the active site of the first enzyme in the pathway. As a result, the enzyme can no longer bind to the starting substrate of the pathway.

**Contributors**

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