Gene Regulation in Prokaryotes

Gene transcription does not occur at a constant rate. Genes can either be turned “on” (with transcription occurring at a relatively high rate) or “off” (transcription occurs at a very low rate). The problems in this unit ask you to reason about the behavior of the regulatory systems that control gene expression in bacteria.

Regulatory System Components

These regulatory systems have multiple components:

(1) A **structural** gene that codes for an enzyme. This is the gene whose activity is being controlled. For instance, in *E. coli* the LacZ gene codes for an enzyme **beta-galactosidase** that metabolizes lactose.
(2) A **regulatory** gene that codes for a **regulatory protein** that, in conjunction with an effector molecule described below, controls transcription of the structural gene. (In *E. coli*, the **LacI** gene codes for the regulatory protein **LacR**, which controls transcription of LacZ.)
(3) An **operator** gene, which is a sequence of DNA adjacent to the structural gene on the chromosome. The regulatory protein binds to the operator to control expression of the structural gene. (In *E. coli*, the LacR regulatory protein binds to the **LacO** operator site.)

(4) An **effector** is a small molecule that binds to the regulatory protein to govern the activity of the regulatory protein. For instance, lactose itself is the small molecule that binds with the regulatory protein LacR in E. coli to control transcription of the LacZ gene.

Effector Function: Inducible and Repressible Regulatory Systems

The small effector molecules essentially signal the need for a specific metabolic activity in a cell, and different effectors function in two contrasting ways.

• In **inducible systems**, the presence of effector molecules in the cell **promotes gene transcription**.

In such systems, the presence of the effector signals a need for increased metabolic activity.

In our example above, lactose itself is the effector molecule. Its presence in the cell signals the opportunity to create energy by breaking down the lactose, and it interacts with the regulatory protein LacR to promote transcription of the LacZ gene.

More generally, inducible systems are typical for genes that code for catabolic enzymes, which break down nutrients. As in our example, the nutrient serves an the effector that promotes transcription of the catabolic enzyme.

• In **repressible systems**, the presence of effector molecules in the cell **inhibits gene transcription**.

In such systems, the presence of the effector signals that a specific metabolic activity is not needed.

Repressible systems are more typical for genes that code for anabolic enzymes, which synthesize small molecule building blocks, such as amino acids. In these systems, the amino acid itself serves as the effector; the presence of the amino acid in large quantities indicates that no more synthesis is needed and the corresponding gene transcription is inhibited.

Regulatory Protein Function: Negative and Positive Regulation

There are two broad categories of gene transcription. For some genes, the default state for transcription is “on,” and for other genes, the default transcription state is “off.” Correspondingly, there are two basic types of gene regulation systems.

- In **Negative Regulation,** the default state for structural gene transcription is "on."

  Transcription of the structural gene occurs unless it is turned "off" by a regulatory protein that binds to the operator gene upstream from the transcription site.

  In negative regulation, the regulatory gene is called a **repressor gene**, which codes for a **repressor protein.**

- In **Positive Regulation.** the default state for structural gene expression is "off."
  - Transcription of the structural gene occurs when it is turned "on" by a regulatory protein that binds to the operator gene upstream form the transcription site.
  - In positive regulation, the regulatory gene is called an **activator gene**, which codes for an **activator protein.**

Four Types of Regulatory Systems

Given the two types of effector activity and regulatory protein function, there are four possible types of regulatory system, as summarized in Fig. 1, (although only three of the are observed in bacteria):

Inducible Negative Regulation
Repressible Negative Regulation
Inducible Positive Regulation
***Repressible Positive Regulation**

	Negative Regulation The Repressor binds to the Operator to **block** transcription	**Positive Regulation** The Activator binds to the Operator to **enable** transcription
Inducible Presence of the Effector **enables** transcription	Inducible Negative Regulation	Inducible Positive Regulation
Repressible Presence of the Effector **blocks** transcription	Repressible Negative Regulation	*Repressible Positive Regulation

Fig. 1. Four possible types of gene regulatory systems.

- In **inducible negative regulation,** the default state of gene transcription is "on." The regulatory protein on its own binds to the operator site to block transcription, turning it off. But when the effector is present, the regulatory protein preferentially binds with the effector, and as a consequence is unable to bind with the operator, permitting gene transcription to remain on.

- In **repressible negative regulation,** the default state of gene transcription is "on." The regulatory protein alone cannot bind to the operator site to turn it off, but when the effector is present, it binds to the regulatory protein and the resulting molecular complex binds to the operator, and turns gene transcription off.

- In **inducible positive regulation,** the default state of gene transcription is "off." The regulatory protein alone cannot bind to the operator site to turn it on, but when the effector is present, it binds to the regulatory protein and the resulting molecular complex binds to the operator, and turns gene transcription on.

- ***Repressible positive regulation** is not observed in nature**.**