Regulation of Gene Expression in Prokaryotes

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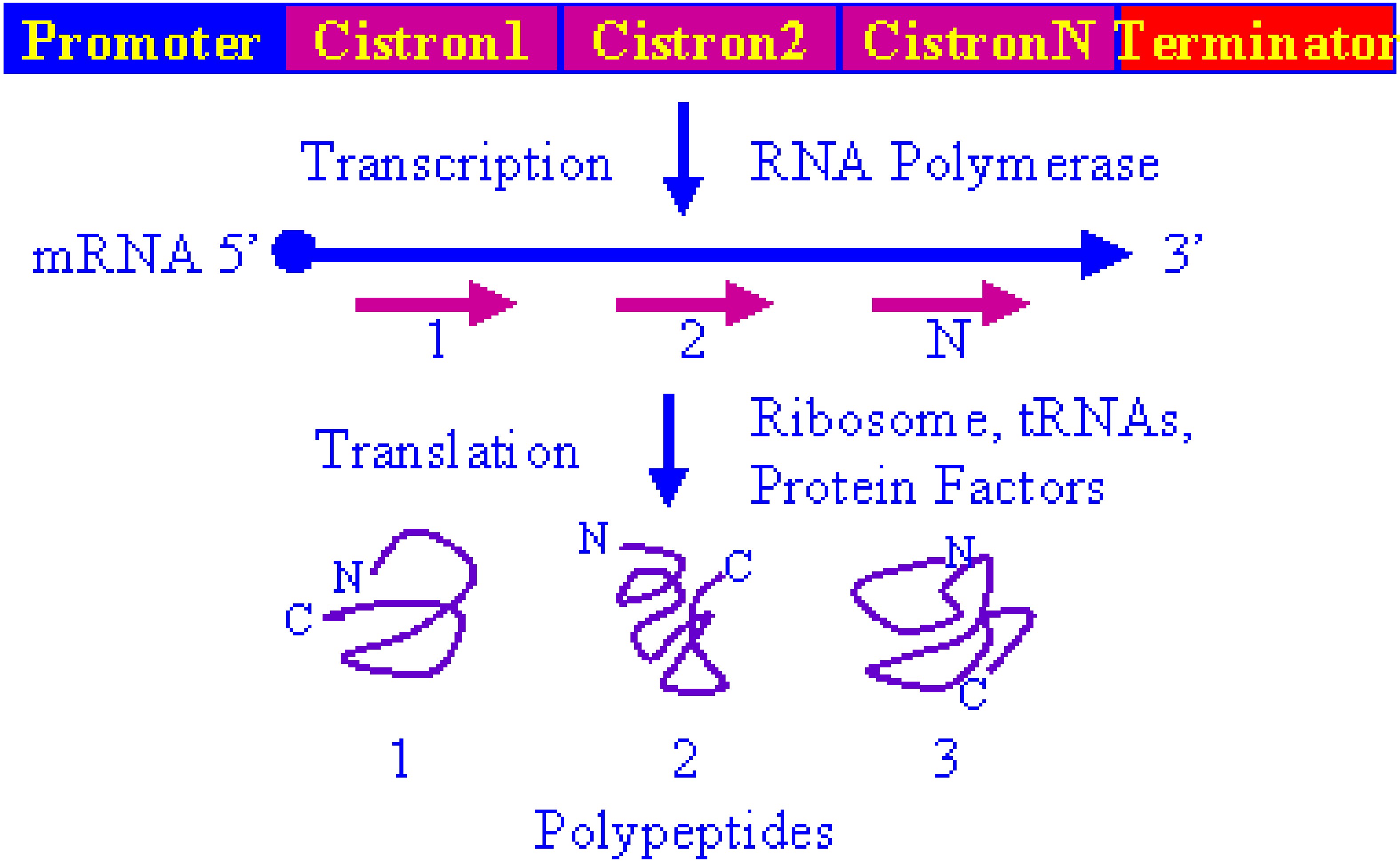
Introduction

- Control of gene expression is at the level of **transcription.**
- If a gene is not transcribed then the gene product and ultimately the phenotype will not be expressed.
- We are now going to consider two systems of control of gene expression in the *E. coli* cell.
- Both of these systems are concerned with the production of enzymes involved in cell metabolism, but each exhibits a different type of control.
- **Induction** - the production of a specific enzyme (or set of enzymes) in response to the presence of a substrate.
- **Repression** - the cessation of production of a specific enzyme (or set of enzymes) in response to an increased level of a substrate.

Introduction

- All of the genes which encode the enzymes necessary for the pathway are found next to each other on the *E. coli* chromosome.
- One key feature of both systems to be discussed is that a single mRNA is transcribed with multiple translation stop codons.
- The proteins that can be translated from the mRNA are the enzymes required for a specific pathway.
- This type of mRNA is called a **Polycistronic mRNA (code for the enzymes and are translated from a single mRNA)** and is totally unique to prokaryotes.

Prokaryotic Gene Expression



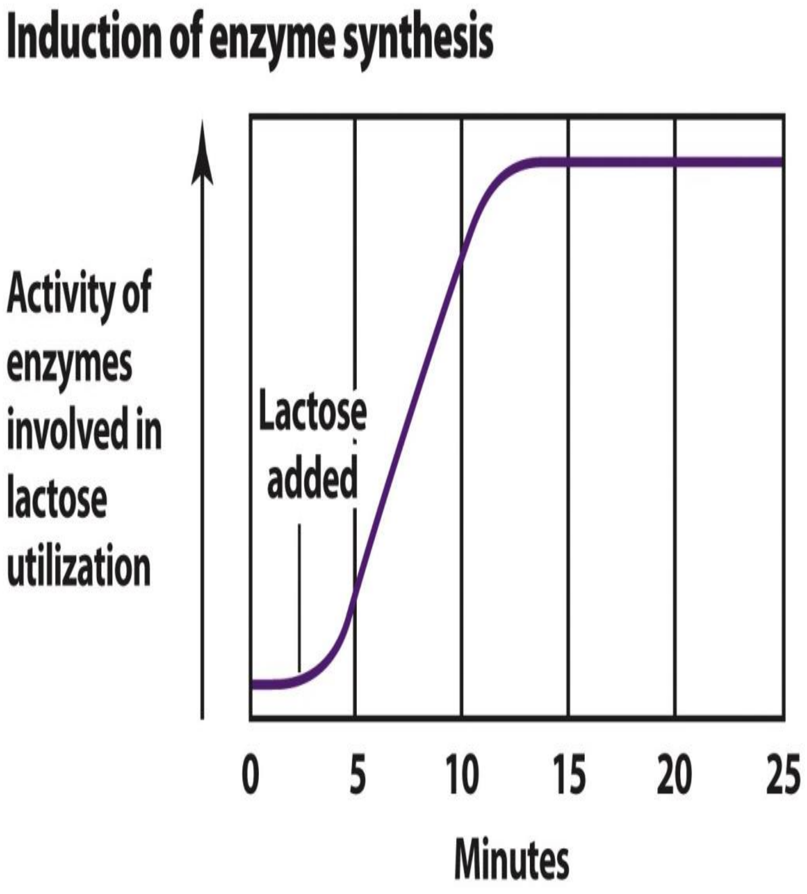
Gene Expression

- Constitutive
- Non - Constitutive
- Inducible
- Repressible
- Positive and Negative Control

Constitutive and Non-Constitutive gene expression

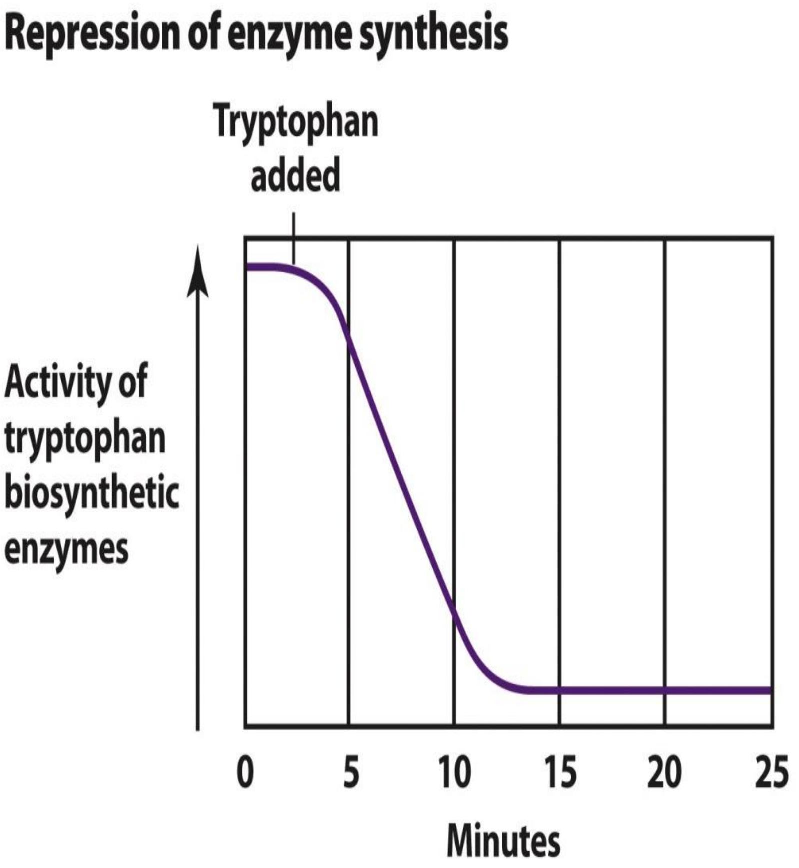
- **Constitutive:** Genes that specify cellular components that perform housekeeping functions— for example, the ribosomal RNAs and proteins involved in protein synthesis are expressed **constitutively.**
- **Non-Constitutive:** Other genes often are expressed only when their products are required for growth.

Inducible (Induction of Genes)
Example : Lactose Utilization



- Gene expression is induced when <u>glucose is absent and lactose is present.</u>
- Induction occurs at the <u>level of transcription</u> and alters the rate of enzyme synthesis.
- Enzymes involved in <u>catabolic pathways</u> are often inducible.

Repressible (Repression of Genes) Example :Tryptophan Biosynthesis



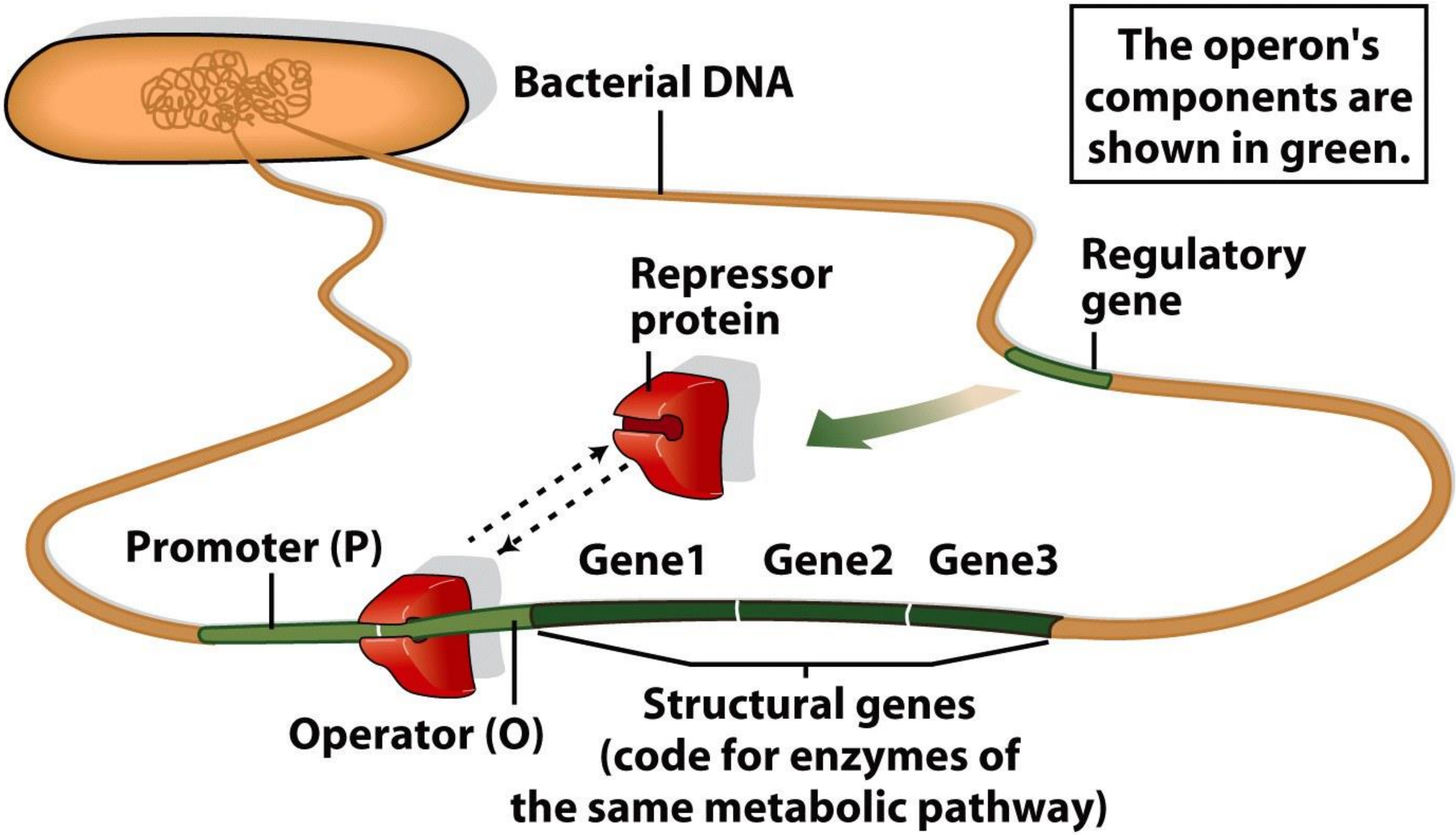
- Genes are turned on (depressed) in the absence of tryptophan and turned off (repressed) when tryptophan is available.
- Repression occurs at the level of transcription.
- Enzymes involved in anabolic pathways are often repressible.

Regulatory gene

- The product of a **regulatory gene** is required to **initiate (turn on)** the expression of one or more genes.

- The product of a **regulatory gene** is required to **turn off** the expression of one or more genes.

Regulatory gene: Organization of a bacterial operon



Positive and Negative Control Mechanisms

- **Regulator genes** encode products that regulate the expression of other genes.

- In **positive control mechanisms**, the product of the regulator gene is required to **turn on** the expression of structural genes.

- In **negative control mechanisms**, the product of the regulator gene is necessary to **shut off** the expression of structural genes.

Regulatory Mechanisms

- In a **positive control mechanism**, the activator is involved in **turning on** gene expression.

- In a **negative control mechanism**, the co-repressor is involved in **turning off** gene expression.

Operons

- Units required for Gene Expression

Sequence of DNA

- In prokaryotes, the **operon** includes structural genes, the operator and the promoter.

Components of the Operon Model

- The repressor gene encodes a **repressor**.

- The repressor binds (under appropriate conditions) to the **operator**. Binding is regulated by the presence or absence of the **effector molecule** (inducer or co-repressor).

- The **promoter** is the site of transcription initiation for the structural gene(s).

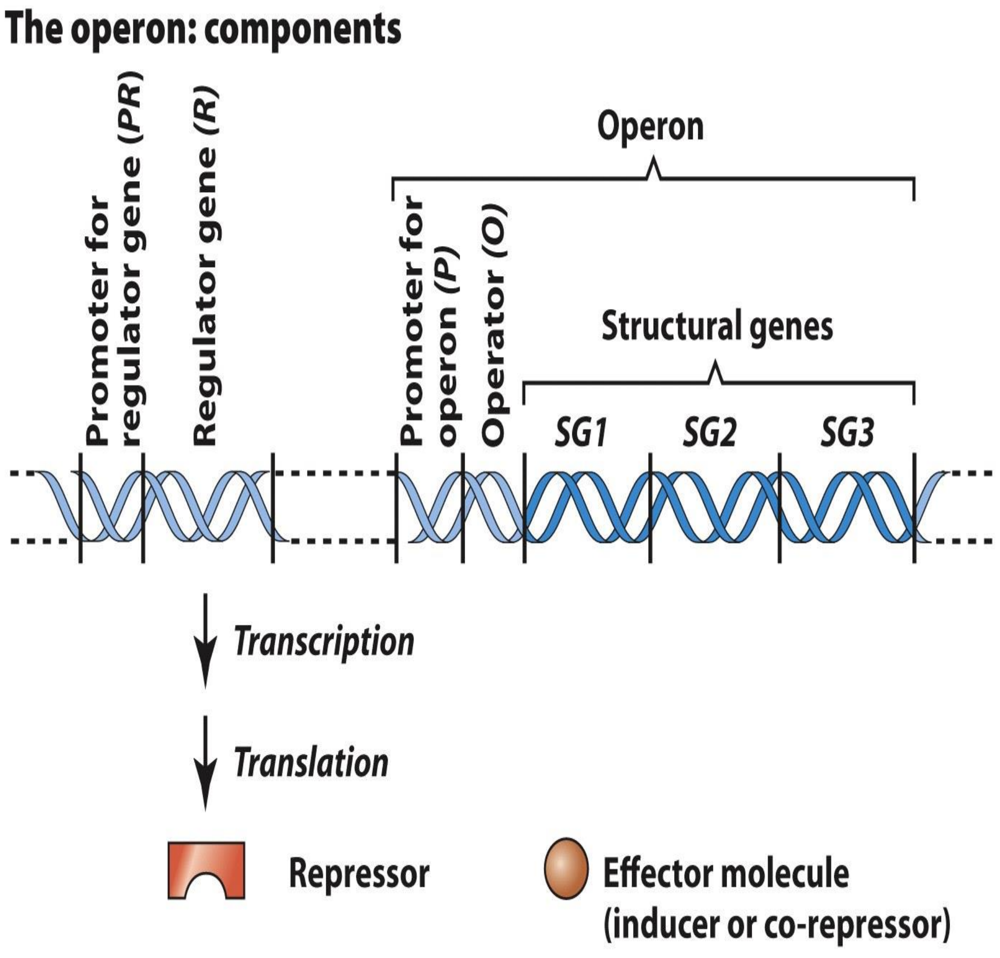
- Transcription of the **structural gene(s)** is regulated by binding of the repressor to the operator.

Control of Gene Expression in Bacteria (The Bacterial Operon)

An **operon** is a functional complex of genes containing the information for enzymes of a metabolic pathway. It includes:

- **Structural genes** – code for the enzymes and are translated from a single mRNA (**Polycistronic**).
- **Promoter** – where the RNA polymerase binds.
- **Operator** – site next to the promoter , where the regulatory protein can bind.
- A **repressor** (proteins) which binds to a specific DNA sequence to determine whether or not a particular gene is transcribed.
- The **regulatory gene** encodes the repressor protein.

The Operon Model



Each operon contains

- *several contiguous structural genes*
- *a promoter*
- *an operator*

The Structural Genes of an Operon

- A **single mRNA transcript** carries the coding information of an entire operon.
- **Operons** containing more than one structural gene are **multigenic.**
- **All structural genes** in an operon are **co-transcribed** and therefore are coordinately expressed.

The Lactose (lac) Operon in *E. coli:* **Induction and Catabolite Repression**

The structural genes in the ***lac* operon** are transcribed only when lactose is present and glucose is absent.

The *lac* Operon - an inducible system

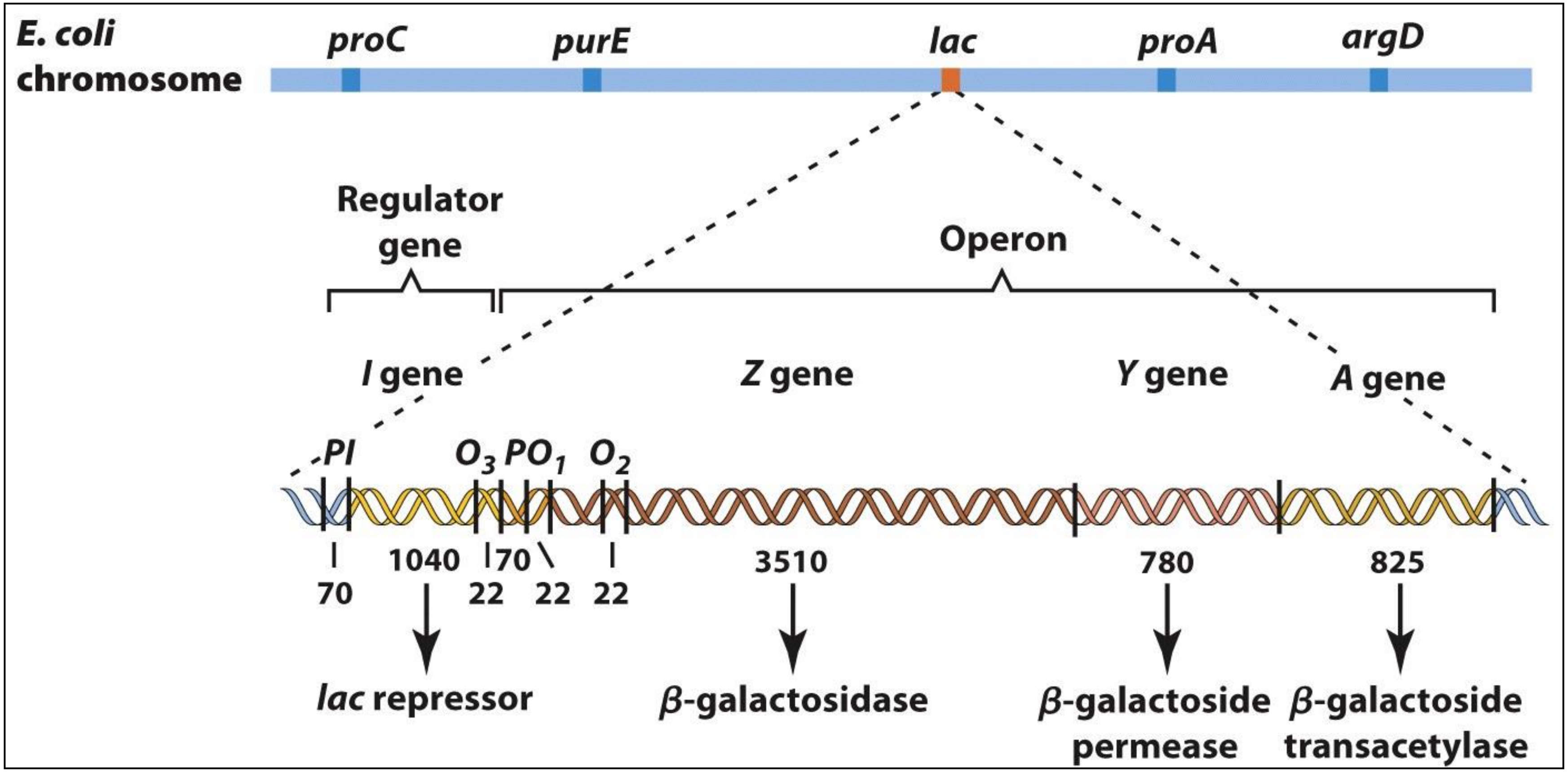
- The first control system for enzyme production worked out at the molecular level described the control of enzymes that are produced in response to the presence of the sugar lactose in *E. coli* cell.
- The work was performed by Jacob and Monod for which they were awarded the Nobel Prize.
- Pathway for production of glucose from lactose.

The *lac* Operon - an inducible system

Several proteins involved in lactose metabolism in the *E. coli* cell. They are:

- ß-galactosidase - converts lactose into glucose and galactose.
- ß-galactoside permease - transports lactose into the cell.
- ß-galactoside transacetylase – an enzyme that transfers an acetyl group from acetyl-CoA to β-galactosides.

The *lac* Operon of *E. coli*



Structural genes

The *lac* Operon of *E. coli*

lac Operon Gene	Gene Function
I	Gene for repressor protein
P	Promoter
O	Operator
lac Z	Gene for ß-galactosidase
lac Y	Gene for ß-galactoside permease
lac A	Gene for ß-galactoside transacetylase

Induction of the *lac* Operon

- <u>In the absence of inducer</u>, the repressor binds to the *lac* operator and represses transcription of the structural genes.
- When the repressor binds to <u>inducer</u>, it is released from the operator, and transcription of the structural genes is turned on.
- The inducer, <u>allolactose</u>, is derived from lactose in a reaction catalyzed by β-galactosidase.
- The ***lac I*** gene encodes a repressor.

Catabolite Repression (**Glucose effect**)

High glucose… low induction of lac operator

- The *lac* promoter has two components
  - The RNA polymerase binding site
  - A binding site for catabolite activator protein (CAP)

- Binding of CAP to the promoter activates transcription of the *lac* operon from being induced when glucose is absent.
- CAP binds to the promoter only when cyclic AMP (cAMP) is present at sufficient concentrations.

CAP Exerts Positive Control of the *lac* Operon; cAMP is the Effector

- When glucose is present
  - Adenylcyclase is inactive.
  - cAMP levels are low.
  - CAP cannot bind to the *lac* operon.
  - The *lac* structural genes cannot be induced at high levels.
- When glucose is absent
  - Adenylcyclase is active.
  - cAMP levels are high.
  - CAP/cAMP binds to the *lac* operon.
  - The *lac* structural genes can be induced.

Video link

The Lac operon | Regulation of gene expression

- https://www.youtube.com/watch?v=sc9pAk0blgo

- trp operon
- https://www.youtube.com/watch?v=Ay7OhRqYNvM

Trp operon

- Assignment