What is an operon?

In genetics, an operon is a functioning unit of genomic DNA containing a cluster of genes under the control of a single regulatory signal or promoter. The genes contained in the operon are either expressed together or not at all.

Where are they found?

- Originally, operons were thought to exist solely in prokaryotes, but since the discovery of the first operons in eukaryotes they are thought to be more common in eukaryotes than previously assumed.
- In general, expression of prokaryotic operons leads to the generation of polycistronic mRNAs, while eukaryotic operons lead to monocistronic mRNAs.
  
  *** [A mRNA molecule is said to be monocistronic when it contains the genetic information to translate only a single protein chain (polypeptide). On the other hand, polycistronic mRNA carries several open reading frames (ORFs), each of which is translated into a polypeptide.]

Give some examples of operon in E.coli?

- Trp operon: It is induced by a substance (tryptophan), so it is an example of positive inducible operon.
- LAC operon: It is inhibited by a substance (lactose), so it is an example of negative inducible operon.
The LAC operon

The *lac* operon of the model bacterium *Escherichia coli* was the first operon to be discovered and provided a typical example of operon function.

Structure of the *lac* operon:

The *lac* operon consists of:

- Three structural genes,
- A promoter,
- A terminator,
- A regulator, and
- An operator.

The three structural genes are: *lacZ*, *lacY*, and *lacA*.

- *lacZ* encodes β-galactosidase, an intracellular enzyme which converts lactose into the intermediate allolactose and then hydrolyzes this into glucose and galactose.
- *lacY* encodes permease, a membrane-bound transport protein that pumps lactose into the cell.
- *lacA* encodes transacetylase, an enzyme that transfers an acetyl group from acetyl-CoA to β-galactosides, not necessary for lactose metabolism.

The general effect of lactose in the growth of E.coli in culture medium:

- If we take a culture of *E. coli* that is feeding on glucose and then transfer some of the cells to a medium contain lactose, a revealing sequence of events takes place.
At first the cells are quiescent: they do not metabolize the lactose, their other metabolic activities decline, and cell division ceases.

Soon, however, the culture begins growing rapidly again with the lactose being rapidly consumed.

Explanation of this event:

- During the quiescent interval, the cells began to produce 3 enzymes discussed above.
- The permease enzyme leads to entry of lactose into the cell.
- The β-galactosidase enzyme leads to conversion of lactose into an intermediate allolactose and finally into glucose and galactose.
- This leads to rapid growth of the organism as glucose is of nutritive importance.
Details of this event:

- The capacity to respond to the presence of lactose was always there. But until lactose was added to the culture medium, these 3 genes were not expressed completely. *(Synthesis of β-galactosidase in the quiescent cell is just as much as to be capable of producing allolactose from lactose.)*
- *In the absence of lactose, a repressor protein encoded by the regulatory gene binds to the lac operator and prevents its transcription.* This repressor protein has 2 binding sites:
  1. With the allolactose molecule,
  2. With the operator site.
- *Binding of allolactose* (which is synthesized from the lactose given in the medium by weakly expressed β-galactosidase) to the repressor causes it to leave the operator.
- *This enables RNA polymerase to transcribe the 3 genes of the operon.*
- The resulting single mRNA molecule is then translated into the three proteins, causing rapid uptake of lactose into the cell and its conversion into glucose, responsible for the rapid growth of E.coli.

CONTROLS OF THE TRANSCRIPTION

Negative control of transcription:

- As discussed above, *the negative control in LAC operon is the repressor molecule encoded by the regulatory gene.*

Positive control of transcription: CAP:

- Absence of the lac repressor is essential but not sufficient for effective transcription of the lac operon.
• The activity of RNA polymerase also depends on the presence of another DNA-binding protein called **catabolite activator protein** or CAP.

• Like the repressor molecule, CAP also has two types of binding sites:
  1. One which binds to Cyclic AMP (cAMP) and
  2. One which binds to a region upstream of the promoter. (See picture)

• **CAP can bind to DNA only when cAMP is bound to CAP.**

• **So when cAMP levels in the cell are low, CAP fails to bind DNA and thus RNA polymerase cannot begin its work, even in the absence of the repressor. (***

![Diagram]

**Explanation of the above diagram:**

1. When only glucose is present in the medium and taken by the cell, it leads to lowering of the cAMP level. So CAP is detached from the binding site of DNA and transcription of the genes ceases.

2. When only lactose is present within the medium and taken up by the cell, it leads to binding of lactose with the repressor molecule and at the same time formation of CAP-cAMP complex, resulting in full transcription of the 3 genes.
3. When none of glucose and lactose is present, repressor molecules are tightly bound to the operator region, leading to stoppage of transcription.

4. When both glucose and lactose are present within the medium, there is a 2nd mechanism of control. This control is called “inducer exclusion”, where binding of glucose to the membrane bound permease protein leads to blockage of the transport of lactose. This may also be called a “preferential transport system” as it prefers glucose to lactose as a nutritive substance in E.coli.

THE trp OPERON

- The trp operon in E. coli was the first repressible operon to be discovered.
- While the lac operon can be activated by a chemical (allolactose), the tryptophan (Trp) operon is inhibited by a chemical (tryptophan).

Structure of the operon:

- This operon contains five structural genes: trp A - E, which encodes tryptophan synthetase.
- It also contains a promoter which binds to RNA polymerase and an operator which blocks transcription when bound to the protein synthesized by the repressor gene (trp R) that binds to the operator.

A special feature: Attenuation:

- Repression by trp is not always complete, however, and so unlike the lac operon, the trp operon is also regulated by a process known as attenuation.
- With attenuation, transcription is initiated but is terminated well before completion.
Control of the transcription:

- If trp is plentiful, transcription that escaped repression by trp is attenuated (stopped) by the formation of a hairpin (stem-loop) structure at the 5′-end of the mRNA.

If trp is scarce, the operon is expressed:

- The 5′-end of the mRNA contains two adjacent codons for trp.
- The lack of trp causes ribosomes to stall at these codons, covering regions of the mRNA required for formation of the attenuation hairpin.
- This prevents attenuation and thus allows transcription to continue.
- This is an example of co-repressible model.

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