Gene Regulation (Part-II)

(BIOT 4006: Genetics and Molecular Biology)

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Gene Regulation in Prokaryotes

- Prokaryotes dwell in a variety of environments and obtain nutrition from their surroundings in an opportunistic way.

- If prokaryotes (particularly bacteria) have to synthesize the compounds needed for their functions then they have to spend a lot of energy to manufacture enzymes necessary for the biosynthetic pathways.

- They synthesize particular compounds only on unavailability from the surrounding environment.

- For the sake of saving energy, bacteria have evolved a strategy by coupling the expression of gene products to sensor systems. These evolved regulatory systems help to detect the required compounds in the surrounding medium and regulate the gene expression.

- Regulation of enzymes involved in the sugar metabolism can be a good example of differential gene expression in bacteria.

- Bacteria can utilize a range of different sugar molecules like lactose, glucose, galactose, xylose etc. and use them as a source of energy as well as building blocks for other compounds.

- Different import proteins are required for the uptake of different sugar molecules and metabolism of each type of sugar requires a set of enzymes that are unique for that sugar.

- Simultaneous production of all the possibly required proteins and enzyme would be a high energy and resources demanding possibility for the cell.

- Therefore, cellular mechanisms have evolved to ‘switch on’ or ‘switch off’ the particular genes for specific enzymes required.

- The regulated transcription needs two types of interactions between DNA and protein which happen near the transcription start site.

- The components of one of the DNA-protein interactions are the promoter site at DNA and the RNA polymerase enzyme. This DNA-protein interaction guides the transcription initiation.

- After RNA polymerase's binding with the promoter site on DNA, transcription is initiated a few bases distant from the promoter site.

- The second DNA-protein interaction has a role in the decision of whether promoter driven transcription is allowed or not.

- The second type of DNA-protein interaction takes place through the regulatory proteins: activators and repressors.

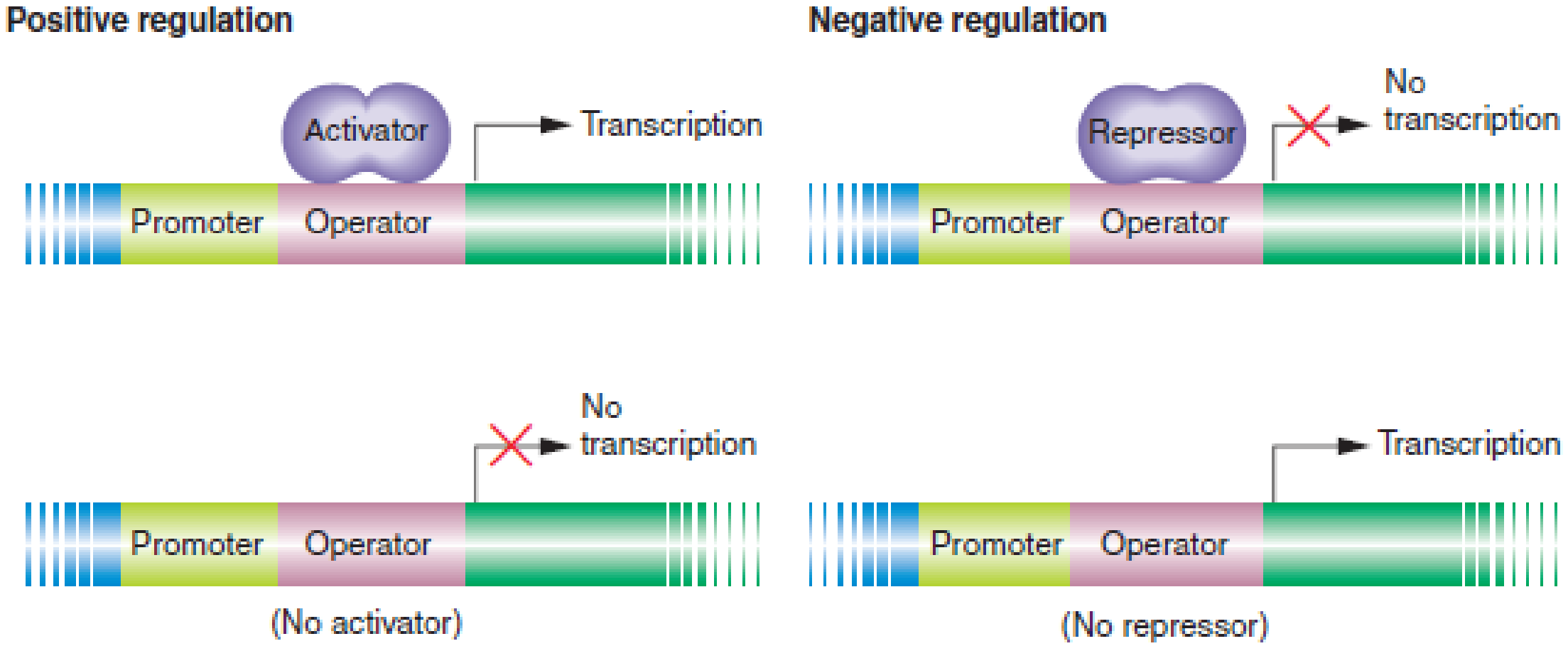
- Activators and repressors can bind to the DNA segments present near the promoter site. These binding sites are called operators.

- Transcriptional regulation occurs through these activators, repressors and operators by the following two mechanisms:

1. Positive Regulation: Presence of activator bound to operator site is a must for beginning of transcription. (presence of regulatory protein is needed)
2. Negative Regulation: Prevention of repressor binding to operator site is a must for beginning of transcription. (absence of regulatory protein is needed)

- Now a question arises of the exactly how the regulatory proteins work. Activators physically facilitate attachment of the RNA polymerase to the promoter and repressors either physically prevents RNA polymerase binding to promoter or slows down the movement of the transcribing enzyme along the DNA chain.

The activation and blocking of transcription by regulatory proteins.



Reference: Introduction to Genetic Analysis, Ninth Edition, Anthony Griffiths et al., Chapter 10

- For successfully regulating the transcription, the activity of the activator and repressor proteins must be triggered by appropriate environmental conditions.

- Both activator and repressor proteins are found in two forms: DNA binding and non-binding.

- Both the existing states must be tuned to different sets of prevailing extracellular/intracellular environmental conditions.

- That means, a particular environmental condition will favor a specific state of the regulatory protein and ultimately its effect on transcription control.

- Most of the times, there are two different sites in the three dimensional protein structure that have binding interactions with the DNA.

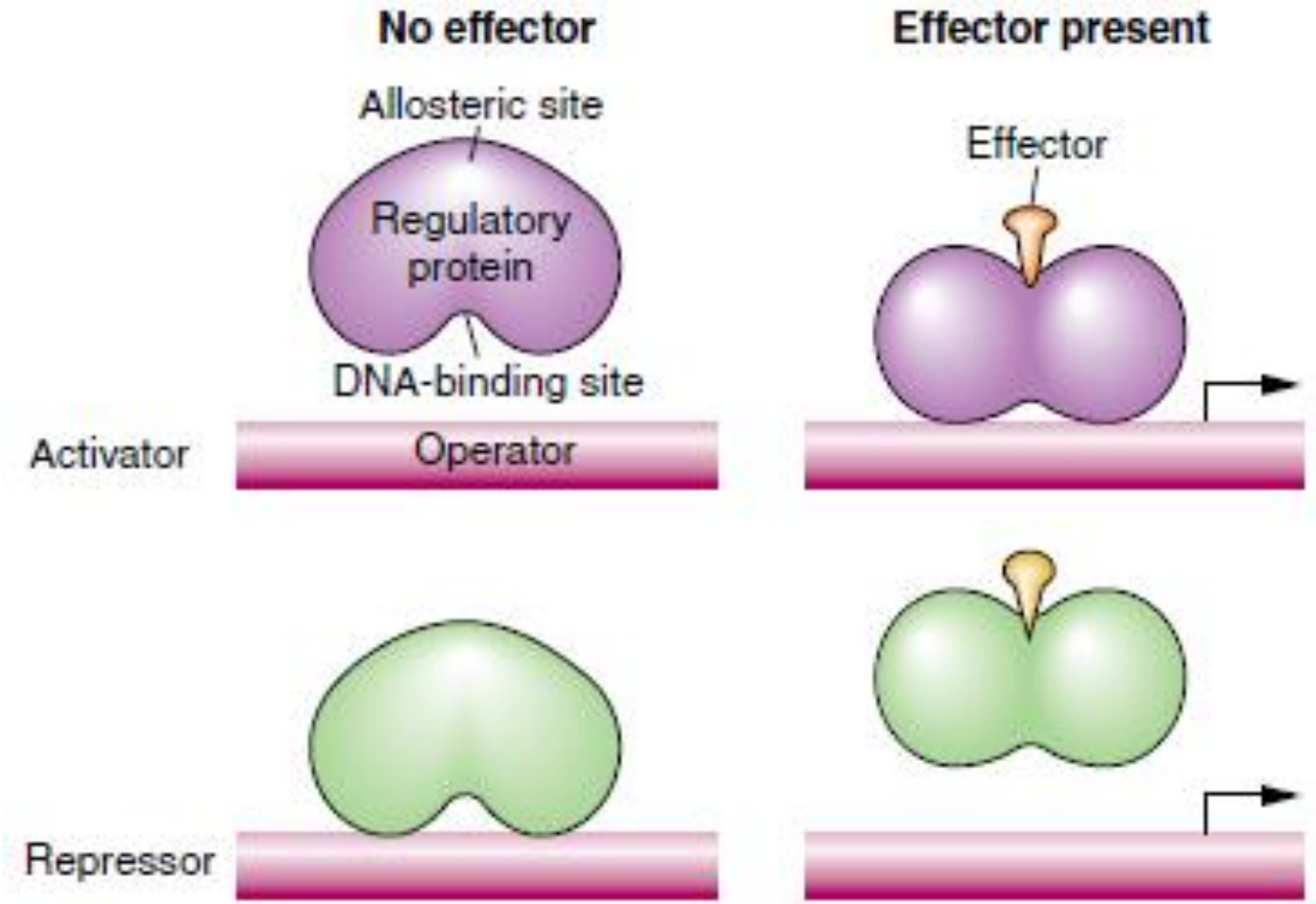
- The first site is the DNA binding domain and the second is an allosteric site.

- The DNA binding domain is responsible for tethering of the regulatory protein on the operator site and the allosteric site can change the functional/non-functional states of the DNA binding domain like a toggle switch.

- Allosteric effectors are small molecules that interact with the allosteric site in such a manner that their binding with each other changes the structure of the DNA binding domain.

- Allosteric effectors too can function in two ways. In one method, they must bind with the regulatory protein for its binding to the DNA. The other way is that the effectors must remain absent for the regulatory proteins to bind with the DNA.

DNA binding activators and repressors under the influence of effectors



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