

Lecture 12

Regulation of Gene Expression
Negative regulation - Lac Operon
Attenuation - Tryptophan Operon

Acknowledgement: Leninger Chapter 28

Objectives

Emergence of Life
Fundamental units of life
Cellular assemblies
Protein Folding
Protein Synthesis
Gene Regulation

1. Understanding gene re
a) Operons and regulons
2. Negative and positive regulation
3. Lac operon
4. Attenuation regulation operon

Genes are expressed when required

- ❖ Some proteins are expressed abundantly such as elongation factor and rubisco
- ❖ Others such as DNA repair enzymes are synthesized very few number
- ❖ Requirements of gene products varies in the cell-type and in the cell cycle
 - ❖ Ribosomes are synthesized rapidly during the exponential growth phase of the cell

What factors determine the cellular concentration of proteins

1. Synthesis of the primary RNA transcript (transcription)
2. Posttranscriptional modification of mRNA
3. Messenger RNA degradation
4. Protein synthesis (translation)
5. Posttranslational modification of proteins
6. Protein targeting and transport
7. Protein degradation

Gene regulation

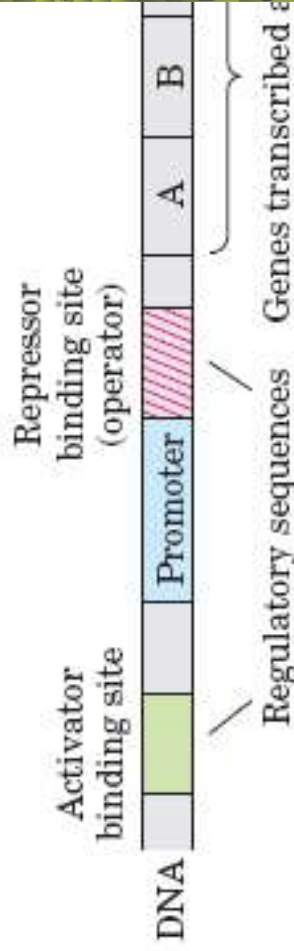
House Keeping Genes

- Constitutive gene expression

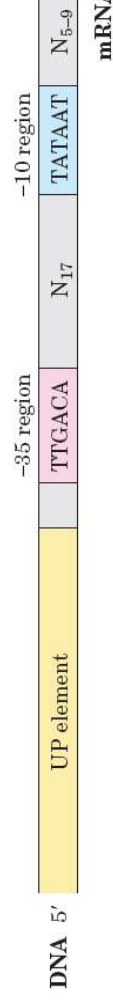
Regulated Genes

- Inducible gene expression
- Repressible gene expression

RNA polymerase

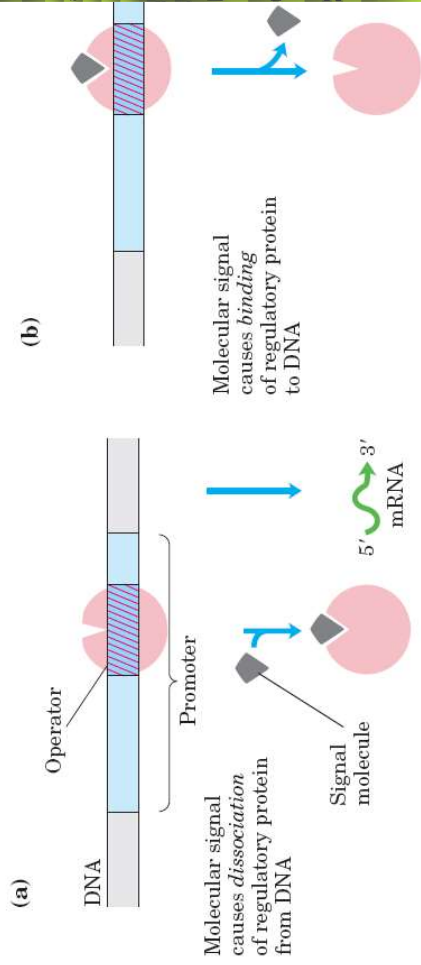


- ❖ Genes A, B, and C are transcribed on one polycistronic mRNA
- regulatory sequences include binding sites for proteins that either activate or repress transcription from the promoter

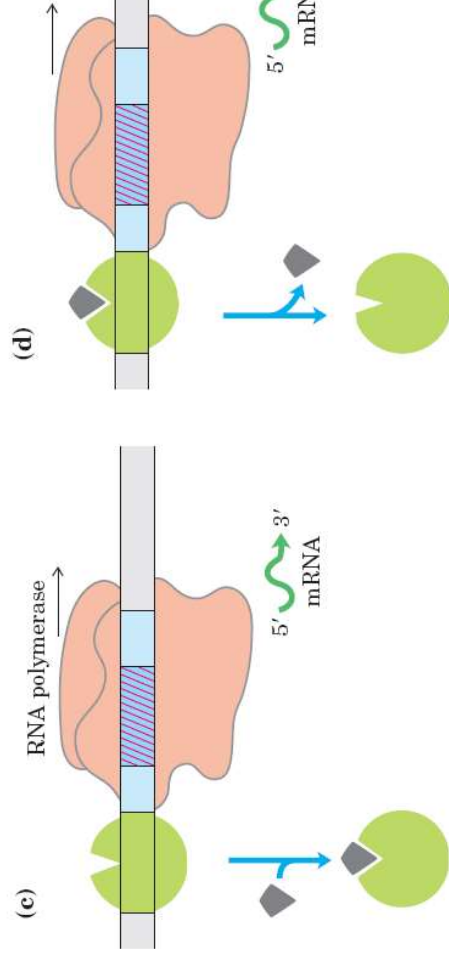


- ❖ RNA polymerases bind to DNA and initiate transcription at promoter; generally found near points at which RNA synthesis begins on the DNA
- ❖ The regulation of transcription initiation often entails changes in how polymerase interacts with a promoter

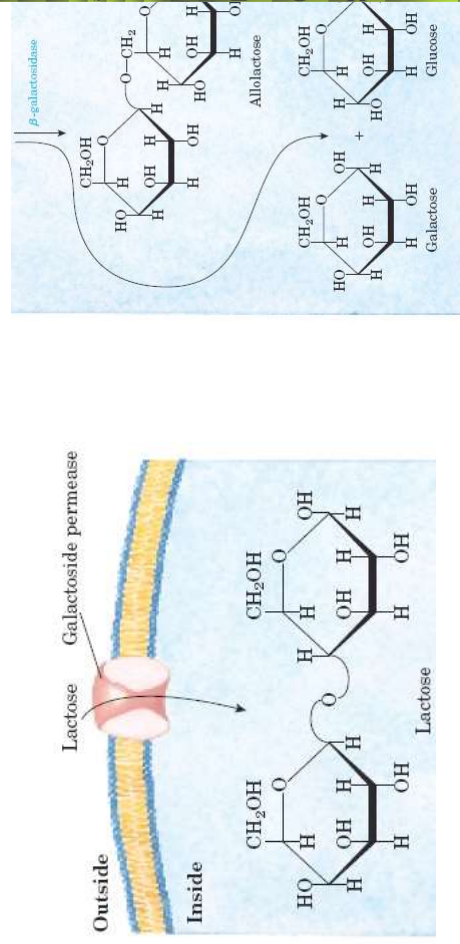
Negative Regulation of Gene Expression



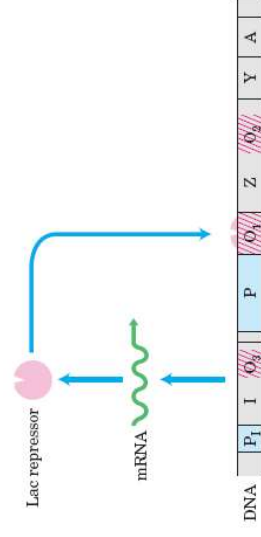
Positive Regulation of Gene Expression



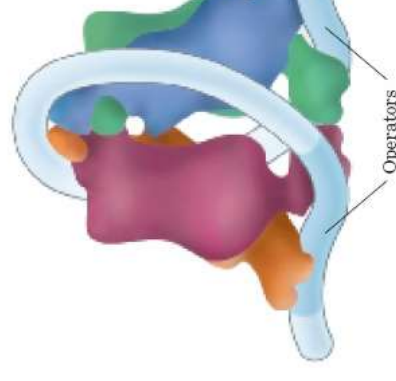
Lactose metabolism in *E. coli*



The Lac Operon

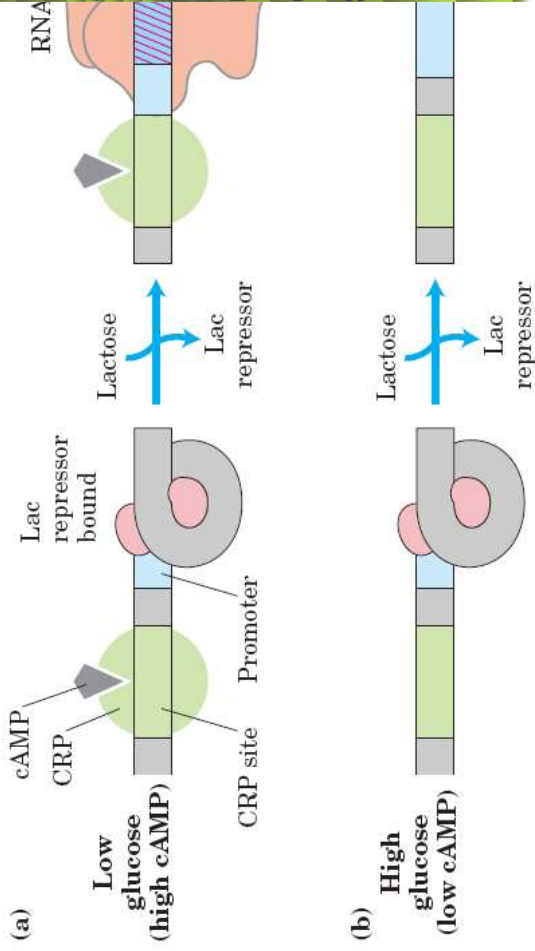


- ❖ The **I** gene encodes the **Lac repressor**.
- The **lac Z**, **Y**, and **A** genes encode **beta-galactosidase**, **galactoside permease**, and **thiogalactoside transacetylase**, respectively

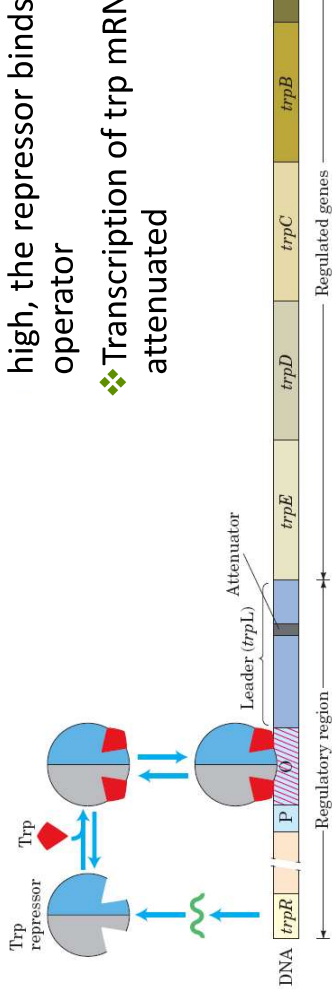


- ❖ **O₁** is the main operator for the **Lac** operon.
- ❖ The **Lac** repressor binds to the **operator** and **O₂** or **O₃**, apparently forming a loop in the DNA that wraps around the repressor.

The Lac Operon



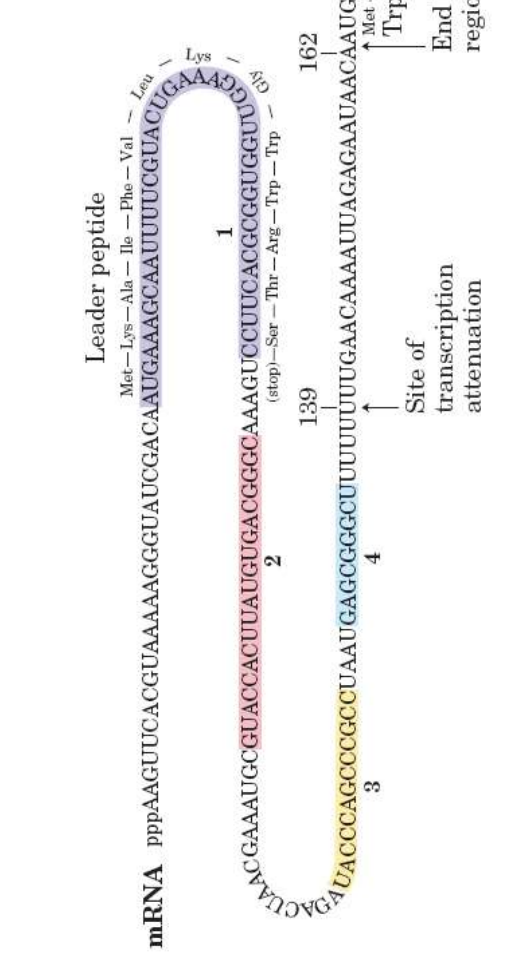
The Trp Operon



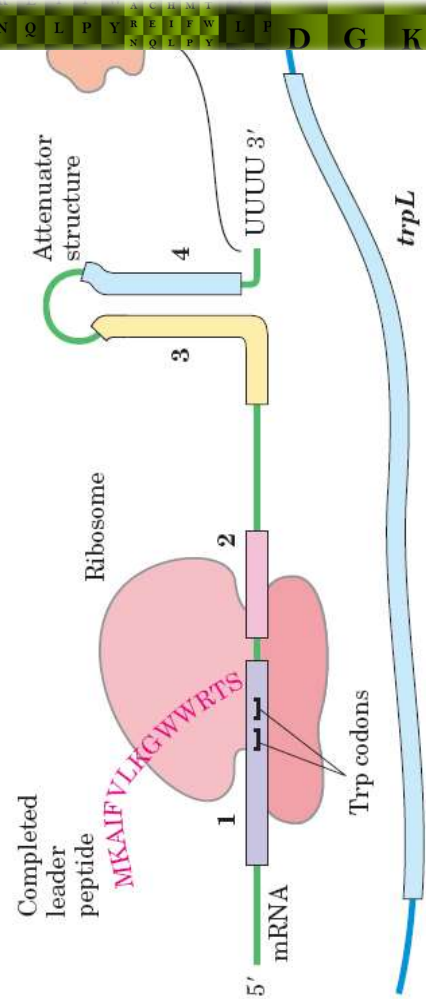
This operon is regulated by mechanisms:

- ❖ When tryptophan levels are high, the repressor binds to the operator
- ❖ Transcription of *trp* mRNA is attenuated

The Trp mRNA Sequence

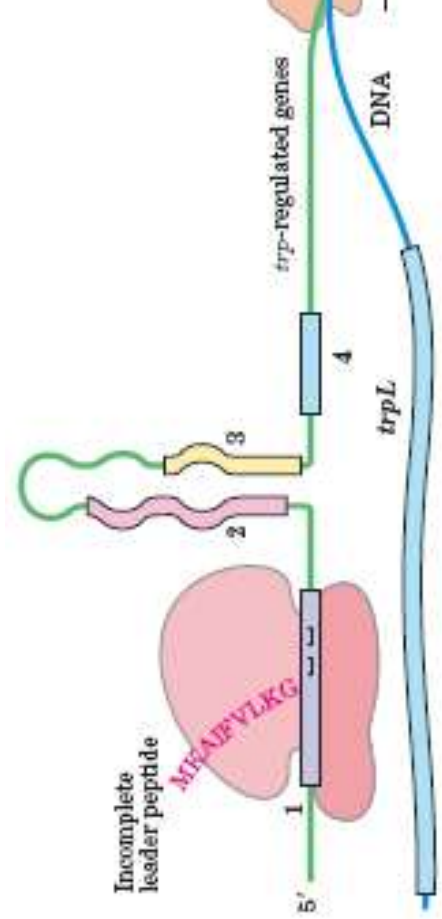


What happens at high Tryptophan levels



❖ When tryptophan levels are high, the ribosome quickly translates sequence 1 (open reading frame) and blocks sequence 2 before sequence 3 is transcribed. Continued transcription of the terminator-like attenuator structure formed by sequences 3 and 4

What happens at low Tryptophan levels



❖ When tryptophan levels are low, the ribosome pauses at the Trp codons in sequence 1. Formation of the attenuator structure between sequences 2 and 3 prevents attenuation, because sequence 3 is no longer available to form the attenuator structure with sequence 4. The 2:3 structure, unlike the 3:4 attenuator, does not prevent transcription.