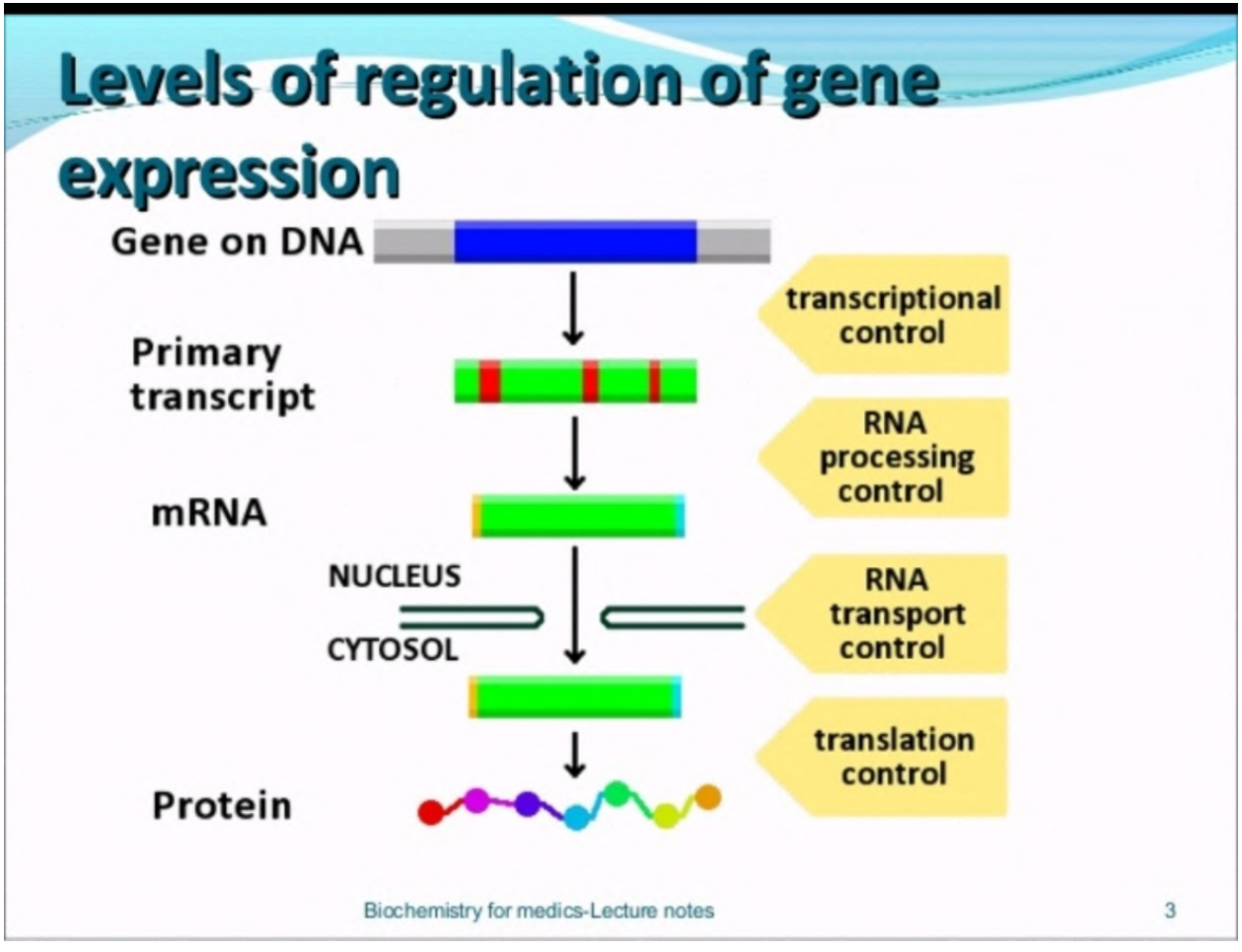


PRINCIPLES OF GENE REGULATION.

- INDUCTION AND REPRESSION. (ENHANCERS AND SILENCER).
- HOUSEKEEPING AND INVISIBLE GENES.
- DNA ORGANISATION AND GENE EXPRESSION.
- GENOMIC ORGANOSATION –SIZE AND GENE NUMBER.
- COVALENT MODIFICATION OF HISTONES CONTROL GENE EXPRESSION.
- DNA –PROTEIN INTERACTIONS----
- PROTEIN MOTIFS-
- HELIX-TURN-HELIX
- ZINC FINGER MOTIF
- LEUCINE ZIPPER MOTIF
-

DNA REGULATORY PROTEIN.

- PROTEIN that regulate the gene expression include repressors, inducers, enhancers, silencers, etc.
- They bind with specific region of DNA.
- These protein have unique structure which allow them to bind to target region.
- Some example are given below.....

REGULATION OF GENE EXPRESSION IN PROKARYOTES.

- INDUCTION AND REPRESSION- ENHANCERS AND SILENCERS---
- Gene expression involves the transcription of a gene into mRNA and the translation of the mRNA into protein.
- At any given time , only a fraction of the genome is expressed.
- Gene expression is induced by positive regulatory elements(inducers or enhancers).
- Can be decreased or blocked by negative regulations (repressors or silencers).

- There are many gene which are not subjected to regulation. e.g.- the enzymes of the Krebs cycle. Such genes are known as constitutive or housekeeping genes.

- Other group of genes are regulated by inducers or repressors as per cellular needs are called inducible genes.

- Most of the DNA is associated with specific class of proteins known as histones to form a structure called nucleosome.

- INTRONS- intervening sequence.

- EXONS---coding region.

COVALENT MODIFICATION OF HISTONES CONTROL GENE EXPRESSION.

- Histone proteins by undergoing covalent modifications (acetylation, methylation, phosphorylation) exert control over gene expression.

- Acetylation of histones promotes gene expression while deacetylation represses it.

- Methylation on some DNA sequences, blocks gene expression.

DNA-Protein interactions.

- Certain proteins bind to specific sequences on the DNA and regulate transcription.
- These are known as regulatory protein which have a high binding affinity to the control site on DNA.
- The DNA – protein are mediated by certain motifs.
- Three types of protein motifs.
- 1.Helix-turn-helix motif.
- 2.Zinc finger motif.
- 3.Leucine zipper motif.

HELIX-TURN-HELIX MOTIF

- The helix-turn-helix motif is made up of about 20 amino acids organised into two *α*-helices separated by a *β*-sheet.

- Lac repressor, tryptophan repressor and cyclic AMP catabolite activator protein (CAP) of *E* . coli and several regulatory proteins in mammalian cells act via this DNA-binding motif.

ZINC FINGER MOTIF

- Many regulatory proteins eukaryotic cells contain multiple zinc fingers (e.g. TF IIIA).

- The receptors of group l hormones (steroid and thyroids) contain zinc fingers.

- A mutation involving a single amino acid in a zinc finger of calcitriol receptor protein interferes with its function and results in rickets.

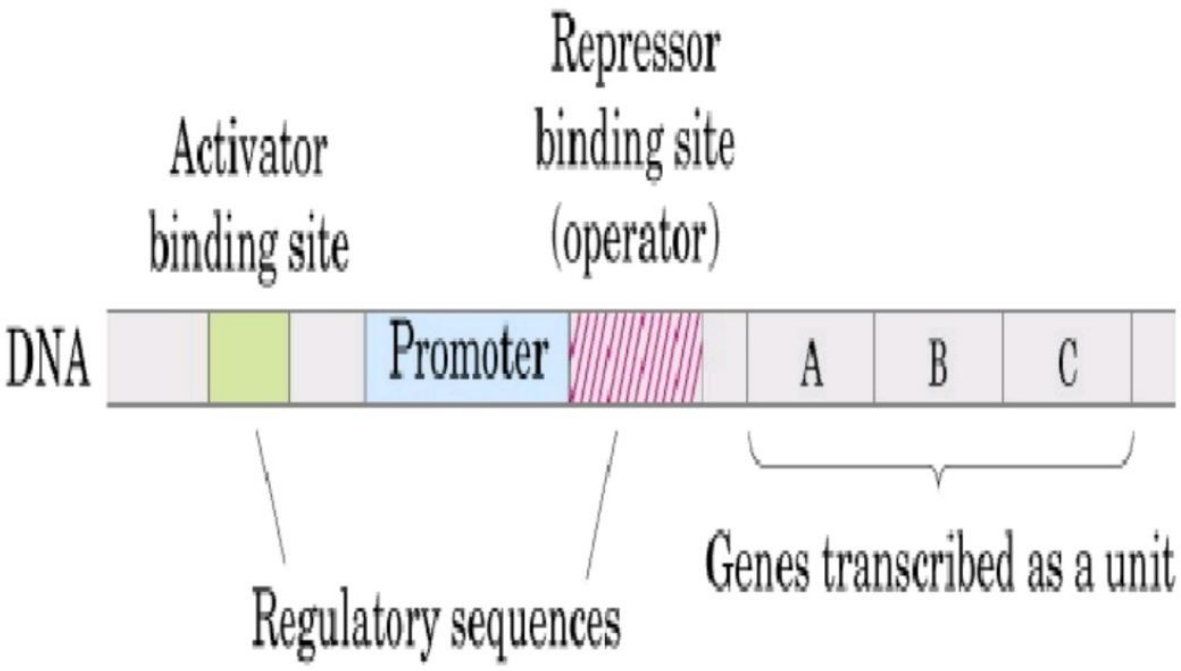
LEUCINE ZIPPER MOTIF.

- Regulatory proteins with leucine zipper motifs contain a large number of basic amino acids (Lys and Arg), which associate with the negatively phosphates of the DNA molecule.

- The a-helices of this motif contain the amino acid leucine at every seventh position.

- Many regulatory proteins contain this type of motif (e.g. The enhancer binding proteins- FOS and JUN).

Operon:



REGULATION OF GENE EXPRESSION IN PROKARYOTES.

- **Operon concept-**

  To explain how genes are regulated in prokaryotes.

The expression of structure gene encoding protein is under control of regulatory gene.

The regulatory element and and protein – encoding genes act in a well orchestrated manner and function as a single unit called **O**peron.

Operon-

Operon can be considered as a coordinated unit of gene expression in prokaryotes.

LAC OPERON.

- ***MECHANISM OF REPRESSI ON--***
- ***When glucose is available to the E. Coli bacteria , lac Z, Y and A, Genes are repressed.***
- ***They are not transcribed, This is mediated by repressor.***
- ***Repressor bind to operator, Repressor binding interferes with the RNA polymerase binding and prevent transcription of structural genes—lacA, lac Z and lac Y.***

LAC OPERON

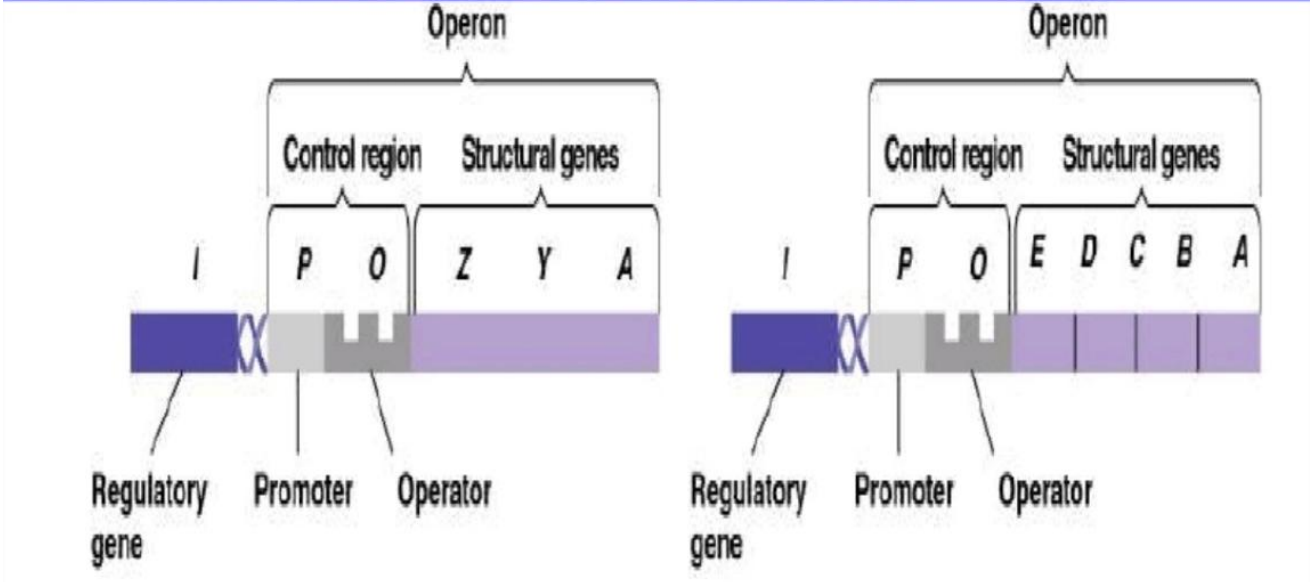
- MECHANISM OF INDUCTION
- Absence of glucose induces the lac operon to transcribe the three enzymes gene i.e.-Z , Y and A.
- The induced enzyme then act on lactose to produce allolactose, the actual inducer of lac operon.
- Inducer bind to repressor molecule , and induce a conformational change in repressor. Repressor does not bind to the operator , Now RNA polymerase can bind with DNA and initiate transcription.
- RNA polymerase requires the binding of cAMP and CAP(catabolic gene activator protein) complex.

ANABOLIC OPERON.

- TRYPTOPHAN OPERON-
- Gene of anabolic pathway such as synthesis of aminoacid are also regulated by operon.

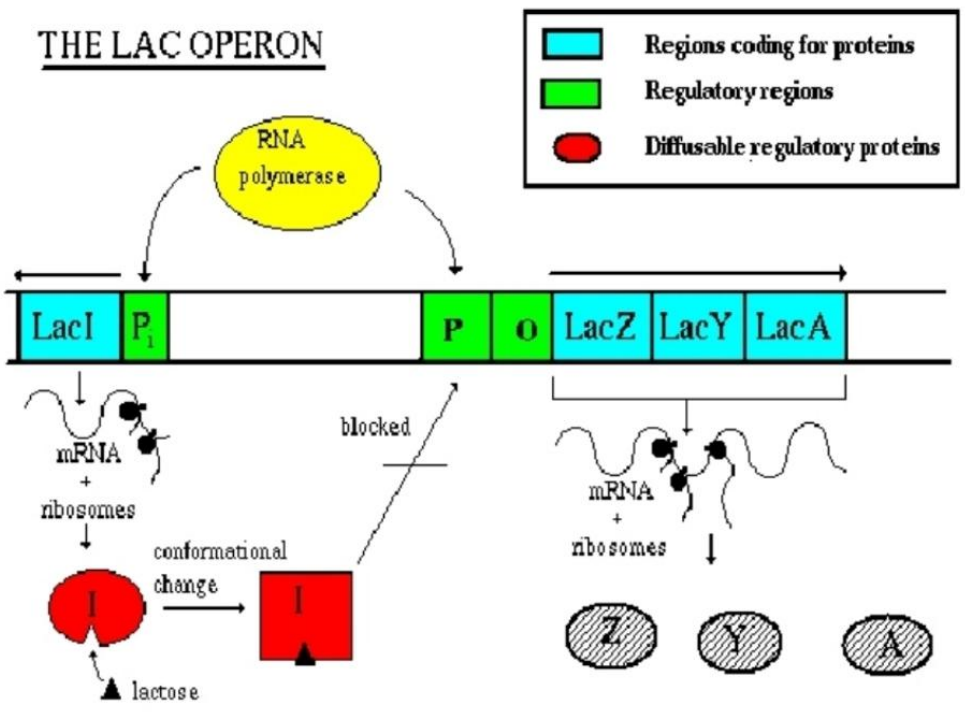
- Tryptophan operon is one such example seen in E. Coli, depending on the concentration of tryptophan in cell,and when there is deficiency , transcription is allowed.

General structure of an OPERON



1 **Structure of the operon.** The operon consists of the promoter (*P*), and operator (*O*) sites, and structural genes which code for the protein. The operon is regulated by the product of the regulatory gene (*I*).

Presence of lac preron:

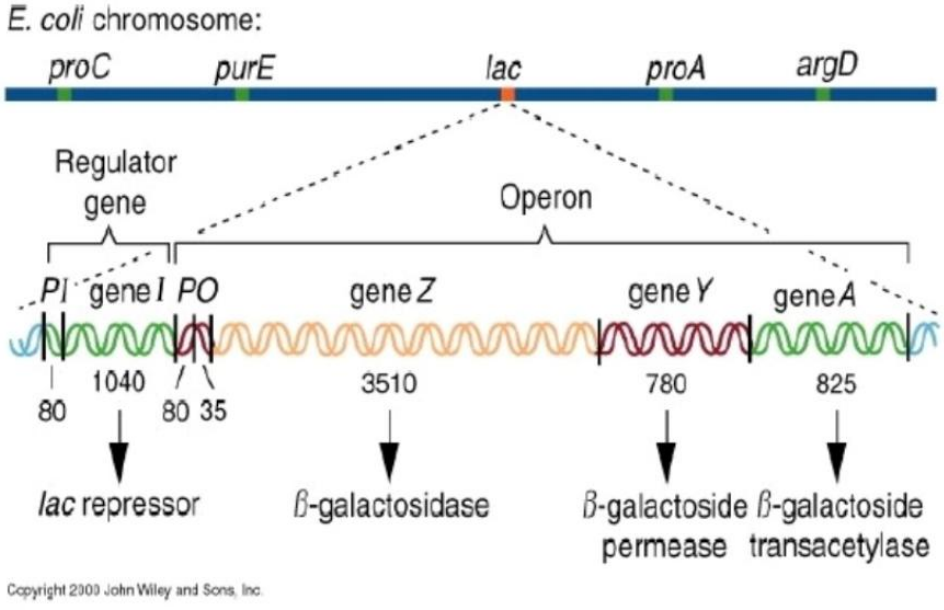


LAC OPERON.(Jacob and Monod).

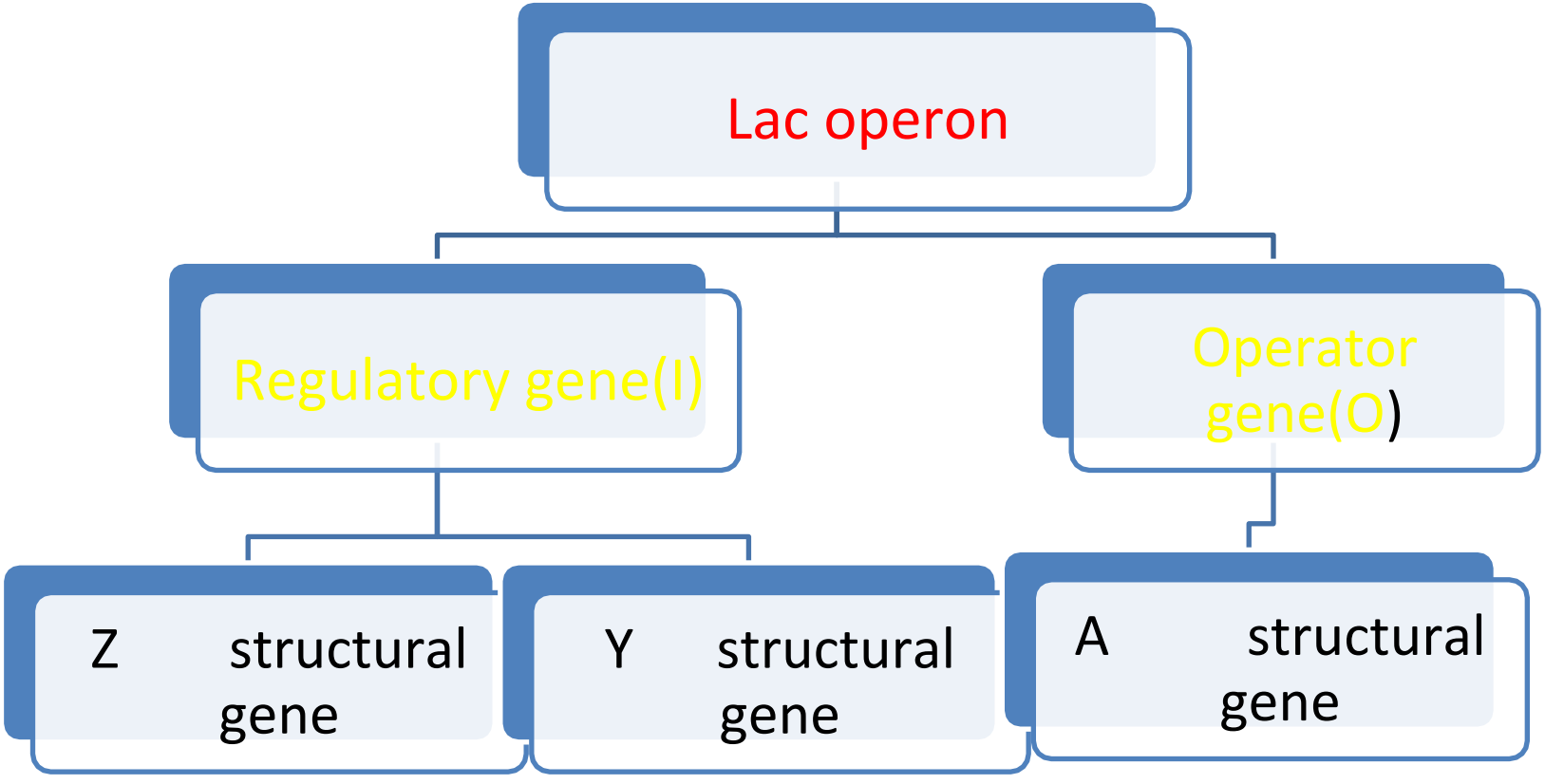
- Most bacteria, such as E.coli, utilise glucose as the fuel source . But when glucose is unavailable ,E. Coli uses lactose as the alternative fuel source.
- Regulation of lactose metabolism in E. Coli.

- Three enzymes are involved in the lactose metabolism.
- Beta galactosidase.
- Permease.
- Transacetylase.

The lac operon of E. Coli:

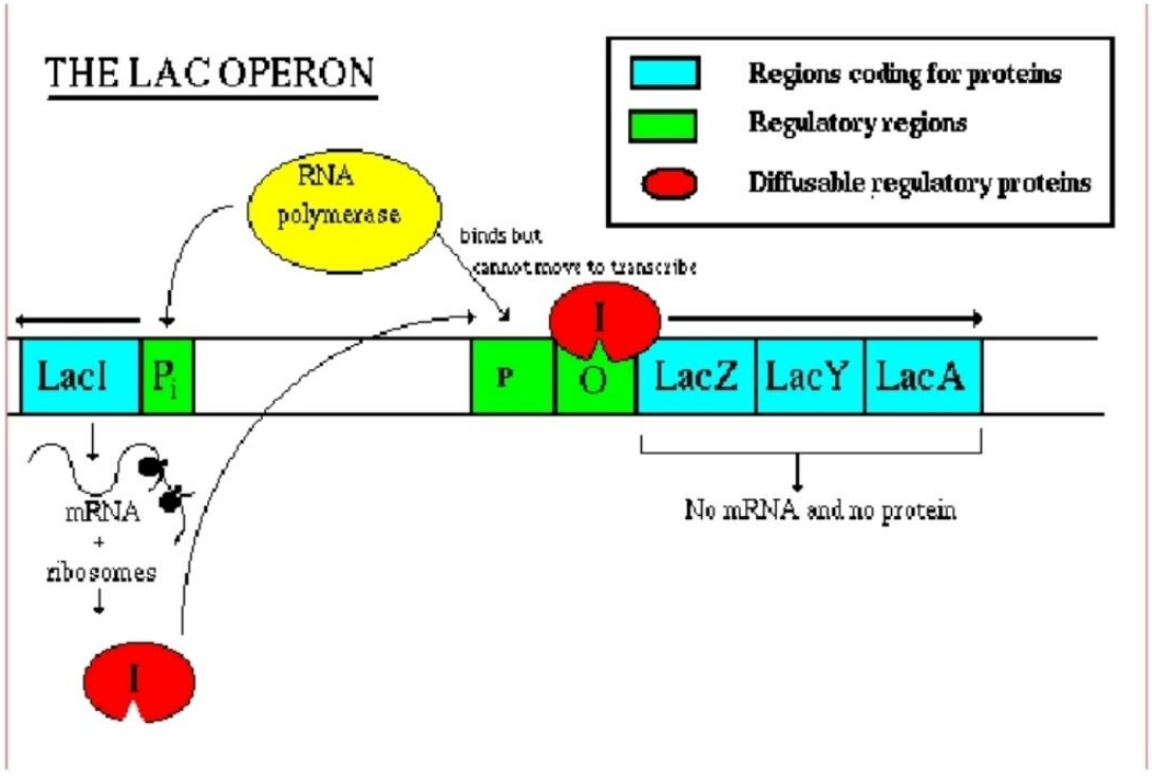


STRUCTURE OF LAC OPERON.



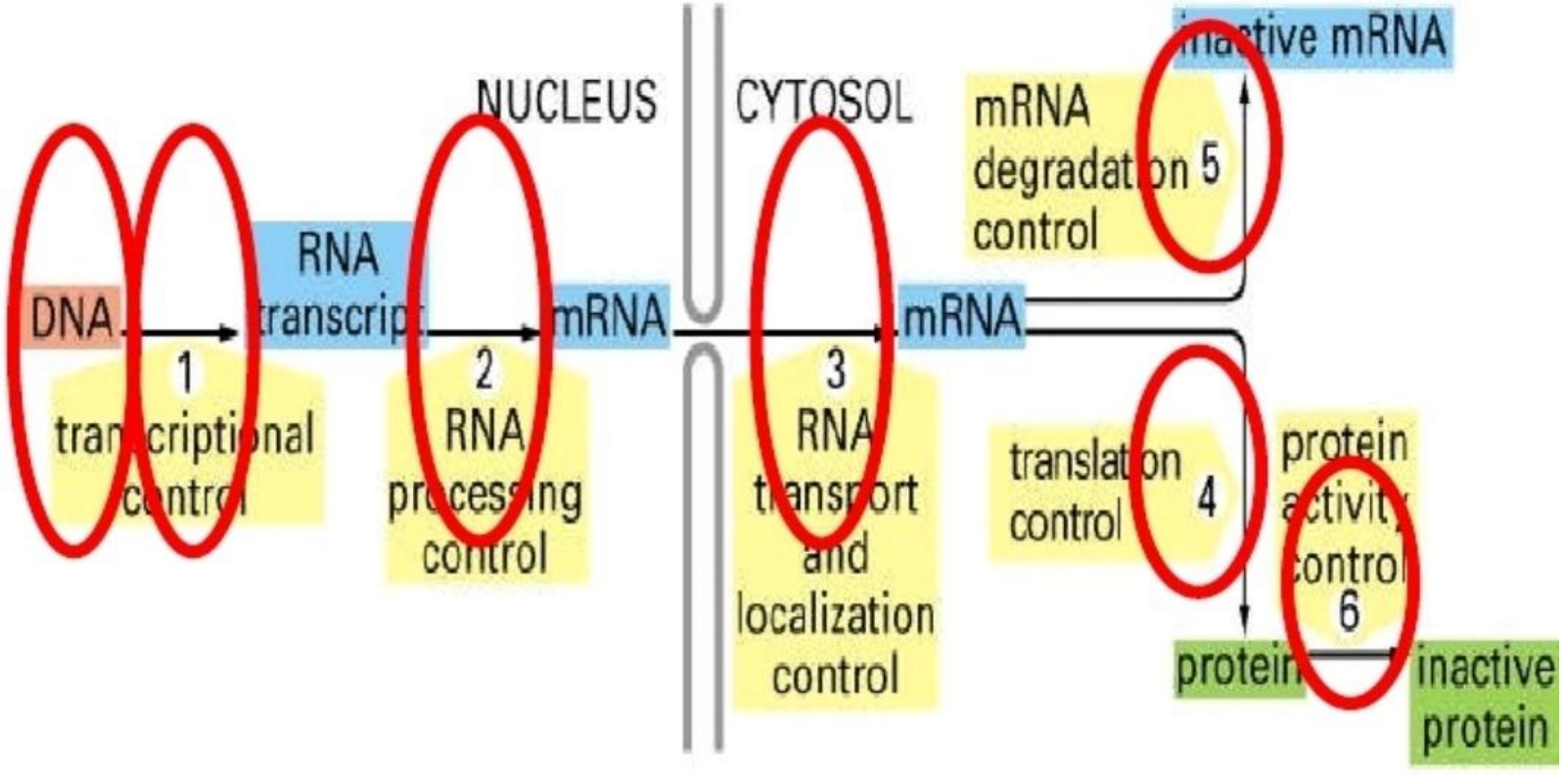
- Apart from structural gene (Z Y A) the operon also contain a promoter site (P).
- Operator site directs the RNA polymerase to the correct transcription start site.
- The Z , Y , and A genes are transcribed into a single large mRNA that encodes for the three enzymes.

Absence of lac operon:



GENE REGULATION IN EUKARYOTES.

- 1.chromatin structure.
- 2.Gene amplification.
- 3.Gene rearrangement.
- 4.Regulatory element.
  5.Transcriptional control.
- 6.RNA processing control.
- 7.RNA transport and localisation control.
- 8.Translation control.
- 9.mRNA degradation.
- 10.protein activator control/ Gene regulation at the level of translation.



- *1.Chromatin structure and gene regulation-*

  covalent modification on Histone protein remodel chromatin and make it more transcription friendly.

2. Gene amplification-

An amplification of a few pre-existing gene occurs, resulting in formation of desired proteins.

3. Gene rearrangement—synthesis of antibodies.

4. Rgulatory element—

Promoter element-role in initiating the transcription by recruiting the RNA polymerase at the correct site on the gene.

TATA box.

Hormone responsive element.

Enhancers.

Repressors.

- *5.Transcription factors-*
- *various transcription factors (TFIIA, TFIIB, TFIID, TFIIE....) assembledb in a specific sequence to form a preinitiation complex.*
- *6.RNA processing–*
- *post-transcriptional modification to form mature mRNA.*
- *7.m RNA splicing.....*
- *8.Transport of mRNA.*
- *9.Gene regulation and translation---Gene regulation can be regulated at the level of translation.*
- *The gene encoding transferrin , ferritin, and hemosiderin.*

- Regulation by RNA editing-
- ApoB100 to Apo B 48.
- Tissue specific Expression by Enhancer--
- Enhanced expression of immunoglobulin genes is seen in plasma cell produced from activated B lymphocytes but not in other cell.