

THE *GENE* ***REGULATION***

The control of gene expression

- Each cell in the human contains all the genetic material for the growth and development of a human
- Some of these genes will be need to be expressed all the time
- These are the genes that are involved in of vital biochemical processes such as respiration
- Other genes are not expressed all the time
- They are switched on an off at need.

Operons

- An operon is a group of genes that are **transcribed at the same time**.
- They usually control an important biochemical process.
- They are **only found in prokaryotes**.

The Nobel Prize in Physiology or Medicine 1965



François Jacob
Prize share: 1/3



André Lwoff
Prize share: 1/3



Jacques Monod
Prize share: 1/3

The *lac* Operon

- The *lac* operon consists of **three genes** each involved in processing the sugar lactose
- One of them is the gene for the enzyme **β -galactosidase**
- This enzyme hydrolyses lactose into glucose and galactose.

Adapting to the environment

- *E. coli* can use either glucose, which is a monosaccharide, or lactose, which is a disaccharide
- However, lactose needs to be hydrolysed (digested) first
- So the bacterium prefers to use glucose when it can.

Four situations are possible


1. When glucose is **present** and lactose is **absent** the E. coli does **not** produce β -galactosidase.
2. When glucose is **present** and lactose is **present** the E. coli does **not** produce β -galactosidase.
3. When glucose is **absent** and lactose is **absent** the E. coli does **not** produce β -galactosidase.
4. When glucose is **absent** and lactose is **present** the E. coli **does** produce β -galactosidase.

The control of the *lac* operon

LAC OPERON:- ?

Gene Concept by operon model → Jacob & Monod (1961)

↳ cluster of gene with related functions:



operon {
 Inducer - LAC OPERON [LACTOSE]
 Repressor - Trp OPERON [Tryptophan]

- STRUCTURAL GENE →

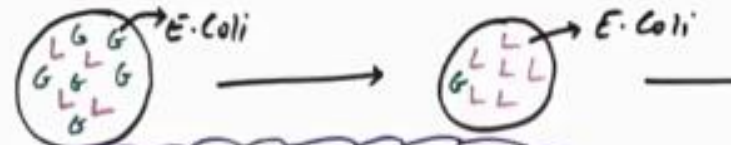
3 S.G.	→	Lac operon	} E. coli
5 S.G.	→	Trp operon	
9 S.G.	→	Histidine operon	} Salmonella typhimurium.

- Inducible operator system:- LAC OPERON

→ E. coli → food → Glucose (prefer) - over then → LACTOSE

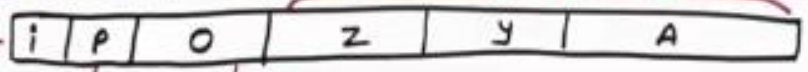
operon is not Active

operon is Active



∴ Lactose is an inducer for the operon activation

STRUCTURE OF LAC OPERON



Regulatory Gene (i)

- codes for repressor protein
- Repressor tetramer
- binds to operator

Promoter (P)

- small sequence of DNA
- provided binding site for RNA polymerase

operator (O)

- between promoter & structural gene
- Repressor protein binds

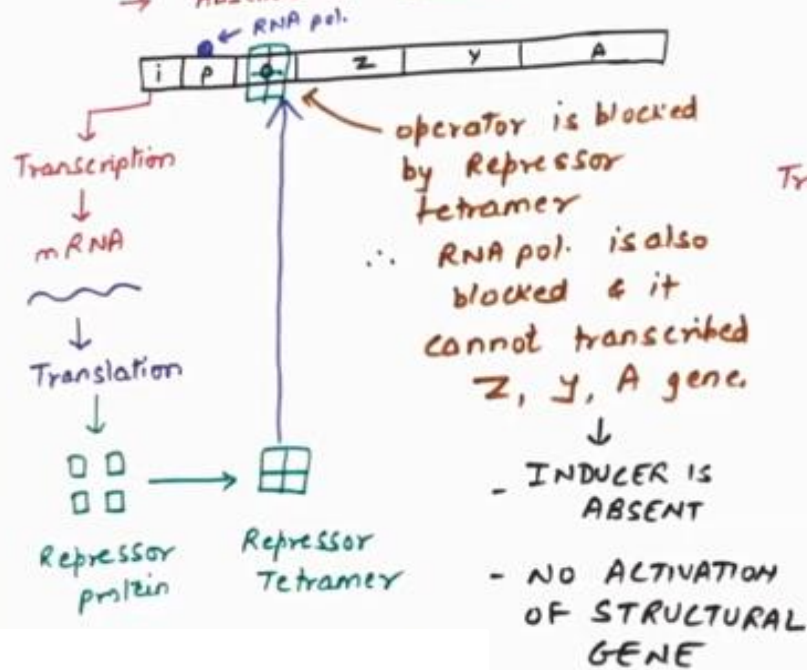
structural gene (Z, Y, A)

- gene to be transcribed of lac operon.
- Poly cistronic gene

- Z - β -galactosidase \rightarrow Breaks Lactose into glucose and galactose.
 Y - permease \rightarrow Provides entry for lactose in the cell.
 A - Transacetylase \rightarrow Adds acetyl group to β -galactosidase and activates it.

2 conditions:-

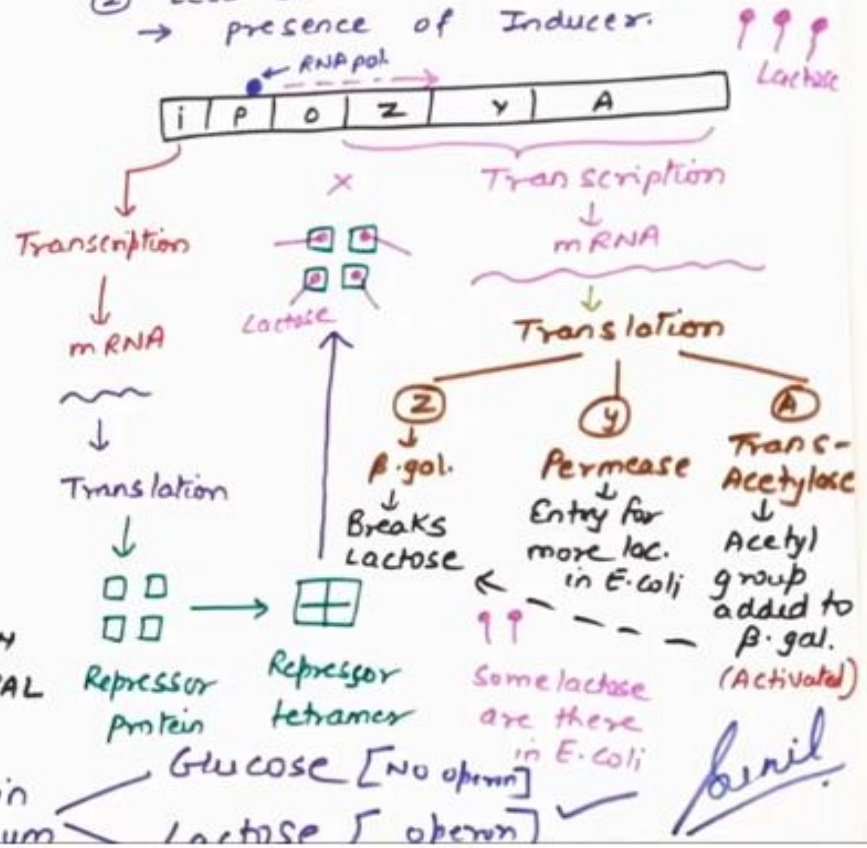
- ① more glucose & less lactose in medium
 \rightarrow Absence of Inducer



NO ACTIVATION OF STRUCTURAL GENE

Can survive in both medium

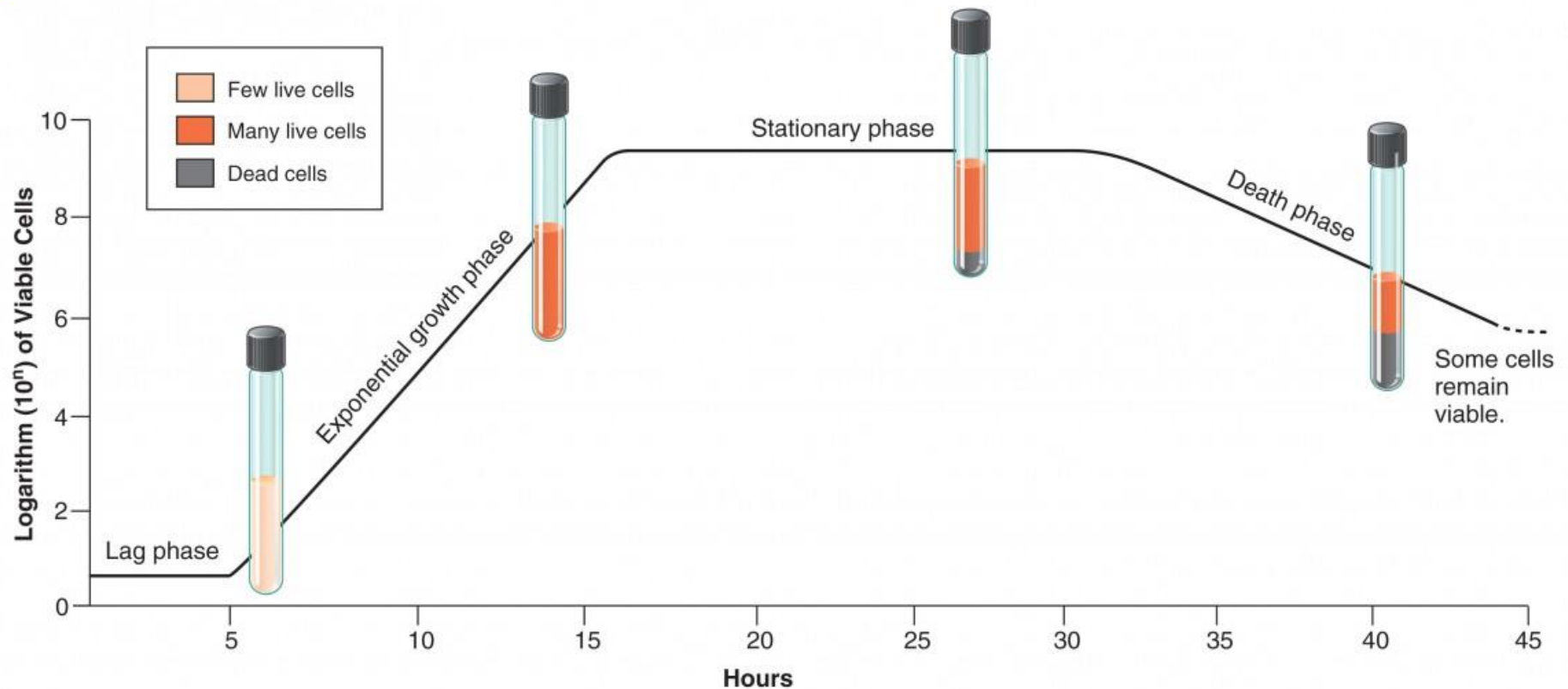
- ② Less Glucose & more lactose in medium
 \rightarrow presence of Inducer.



Benil

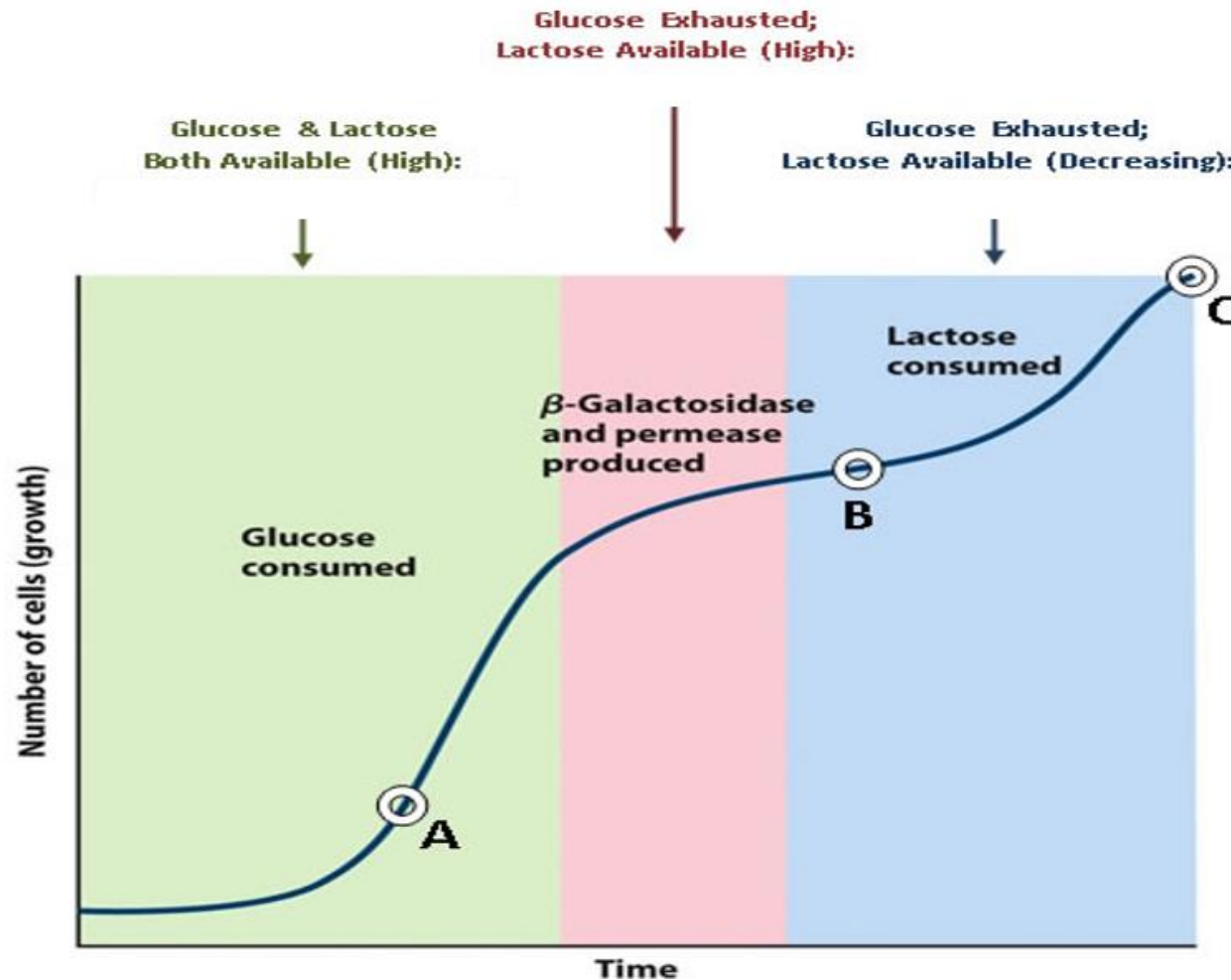
The typical model of cell growth in presence of sugar or other media source

Copyright © The McGraw-Hill Companies, Inc. Permission required for reproduction or display.



Total cells in population, live and dead, at each phase.

The change behaviour of the plot in gene regulation

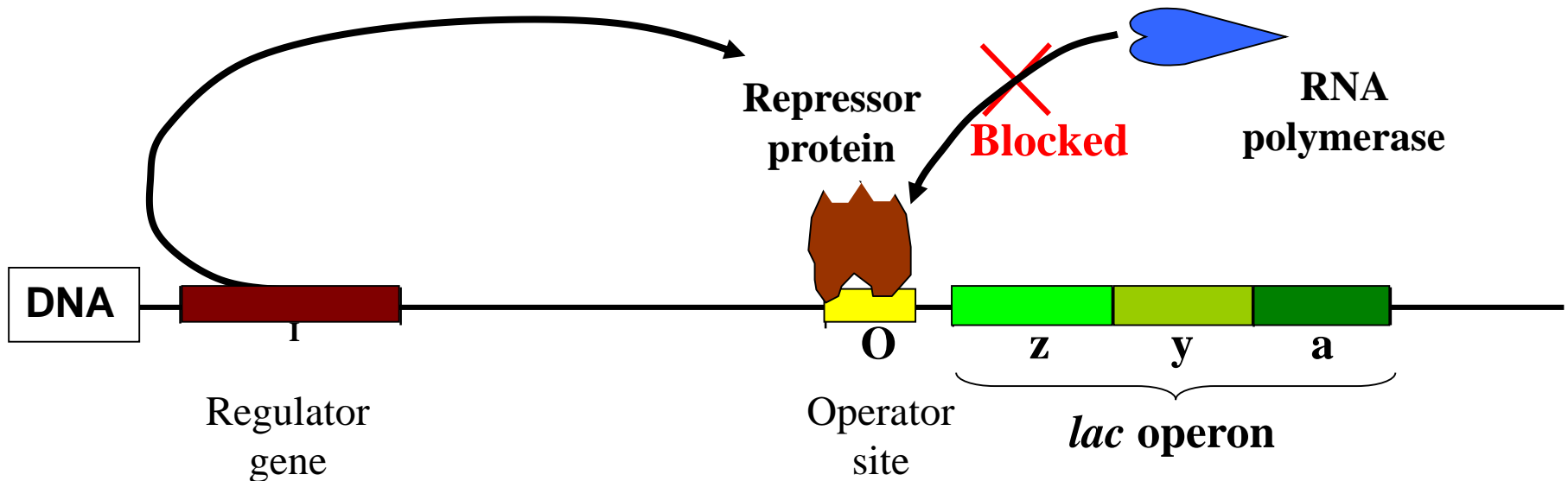


Summary

Carbohydrates	Activator protein	Repressor protein	RNA polymerase	<i>lac</i> Operon
+ GLUCOSE + LACTOSE	Not bound to DNA	Lifted off operator site	Keeps falling off promoter site	No transcription
+ GLUCOSE - LACTOSE	Not bound to DNA	Bound to operator site	Blocked by the repressor	No transcription
- GLUCOSE - LACTOSE	Bound to DNA	Bound to operator site	Blocked by the repressor	No transcription
- GLUCOSE + LACTOSE	Bound to DNA	Lifted off operator site	Sits on the promoter site	Transcription

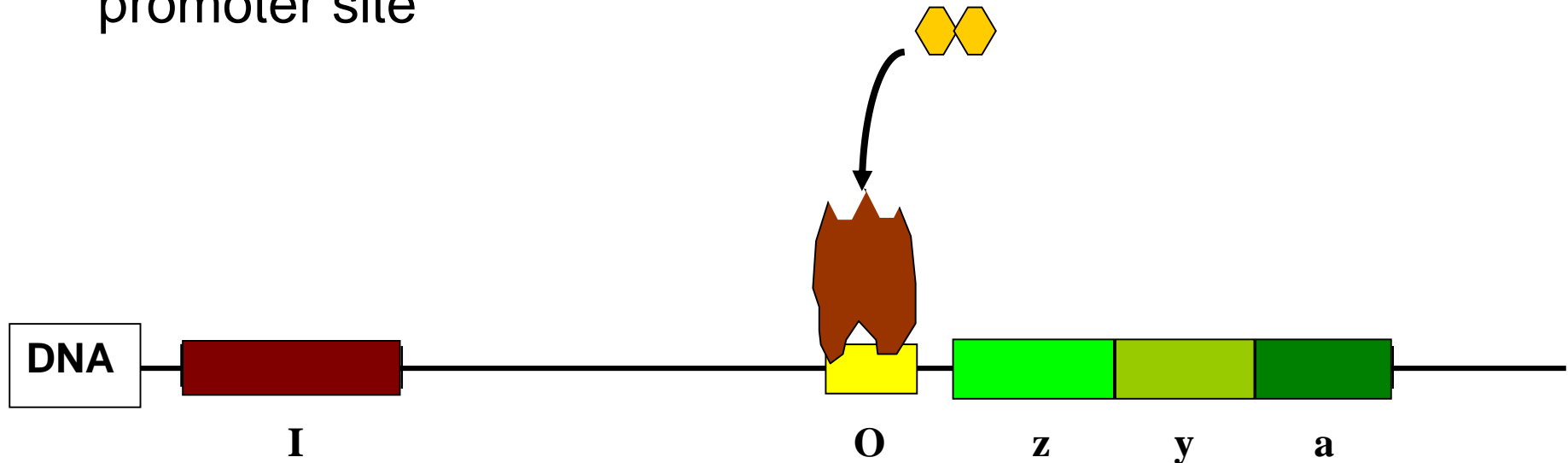
1. When lactose is absent

- A repressor protein is continuously synthesised. It sits on a sequence of DNA just in front of the *lac* operon, the **Operator site**
- The **repressor protein** blocks the **Promoter site** where the RNA polymerase settles before it starts transcribing



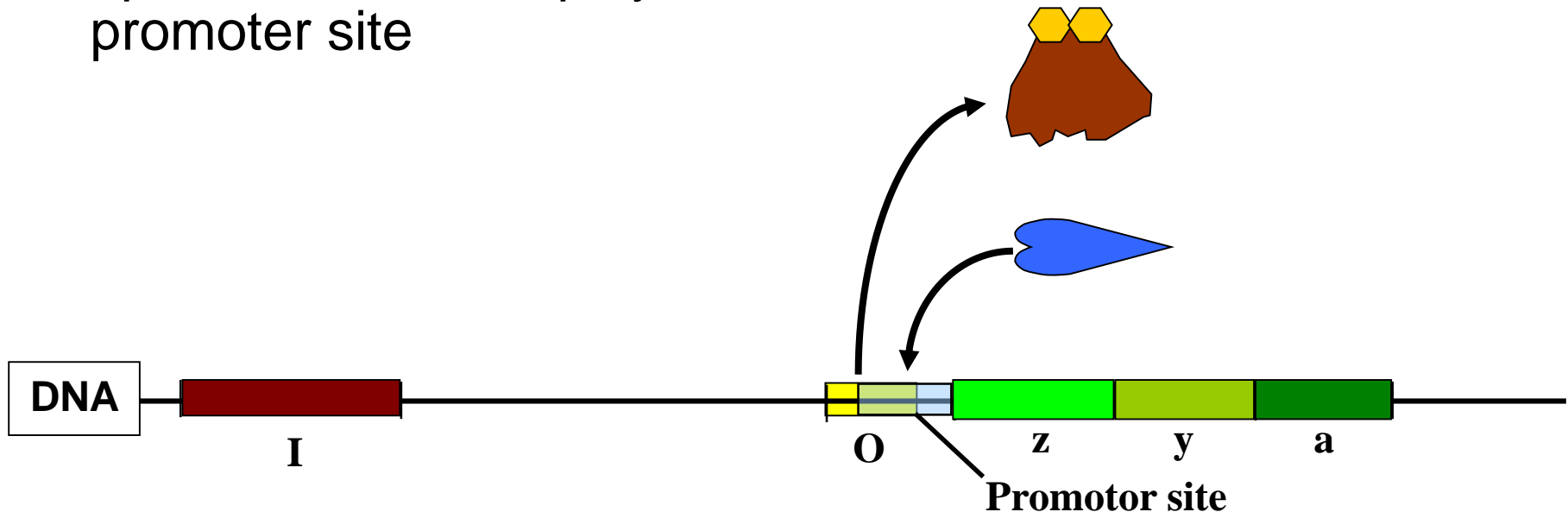
2. When lactose is present

- A small amount of a sugar allolactose is formed within the bacterial cell. This fits onto the repressor protein at another active site (**allosteric site**)
- This causes the repressor protein to change its shape (a **conformational change**). It can no longer sit on the operator site. RNA polymerase can now reach its promoter site



2. When lactose is present

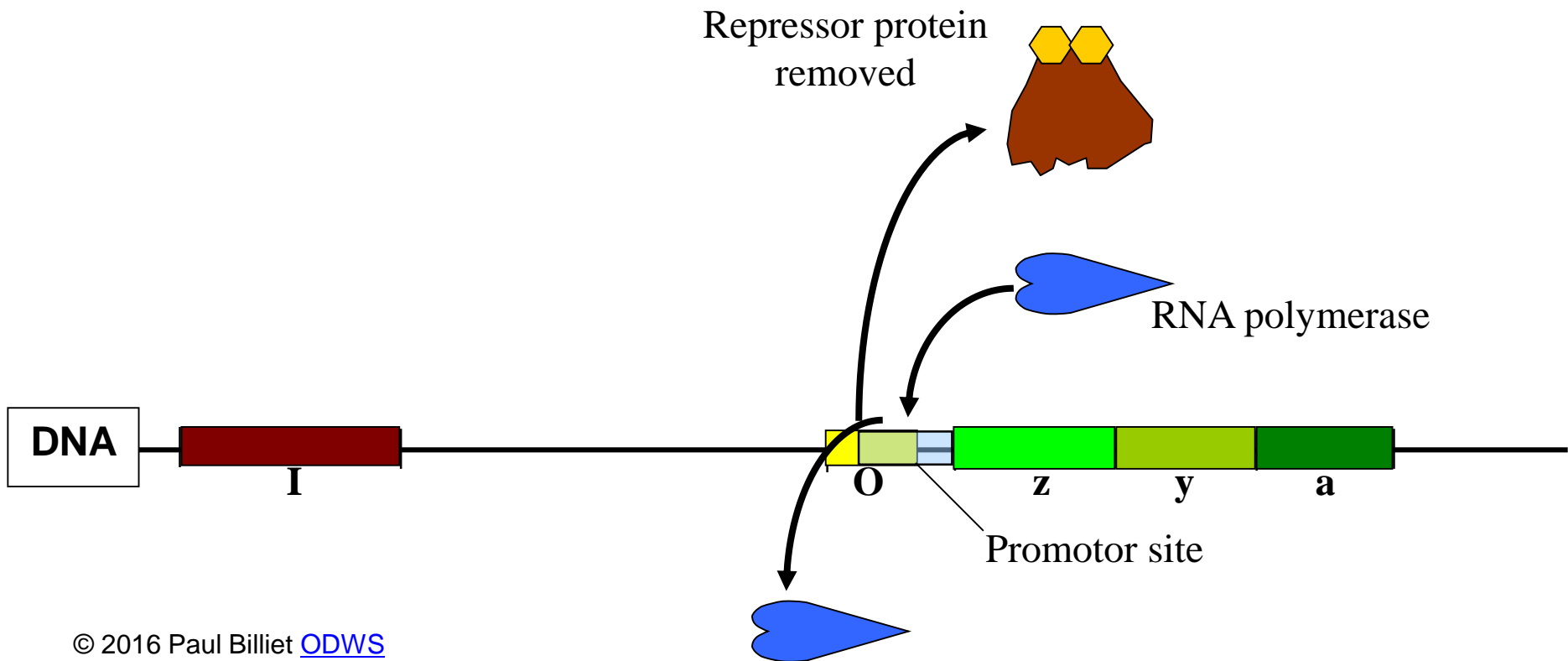
- A small amount of a sugar allolactose is formed within the bacterial cell. This fits onto the repressor protein at another active site (**allosteric site**)
- This causes the repressor protein to change its shape (a **conformational change**). It can no longer sit on the operator site. RNA polymerase can now reach its promoter site



3. When both glucose and lactose are present

- This explains how the *lac* operon is transcribed only when lactose is present
- BUT..... this does **not** explain why the operon is not transcribed when **both** glucose and lactose are present.

- When glucose and lactose are present RNA polymerase can sit on the promoter site but it is unstable and it keeps falling off



4. When glucose is absent and lactose is present

- Another protein is needed, an **activator protein**. This stabilises RNA polymerase.
- The activator protein only works when glucose is absent
- In this way *E. coli* only makes enzymes to metabolise other sugars in the absence of glucose.

