www.ramauniversity.ac.in

FACULTY OF ENGINEERING & TECHNOLOGY

DEPARTMENT OF BIOTECHNOLOGY

Carbon Catabolite Repression

•Enzyme Induction is still considered a form of negative control because the effect of the regulatory molecule (the active repressor) is to decrease or downregulate the rate of transcription.

•Catabolite repression is a type of positive control of transcription, since a regulatory protein affects an increase (upregulation) in the rate of transcription of an operon. The process was discovered in *E. coli* and was originally referred to as the glucose effect because it was found that glucose repressed the synthesis of certain inducible enzymes, even though the inducer of the pathway was present in the environment.

•The discovery was made during study of the regulation of lac operon in *E. coli*. Since glucose is degraded by constitutive enzymes and lactose is initially degraded by inducible enzymes, what would happen if the bacterium was grown in limiting amounts of glucose and lactose?

•A plot of the bacterial growth rate resulted in a diauxic growth curve which showed two distinct phases of active growth (Figure). During the first phase of exponential growth, the bacteria utilize glucose as a source of energy until all the glucose is exhausted. Then, after a secondary lag phase, the lactose is utilized during a second stage of exponential growth.

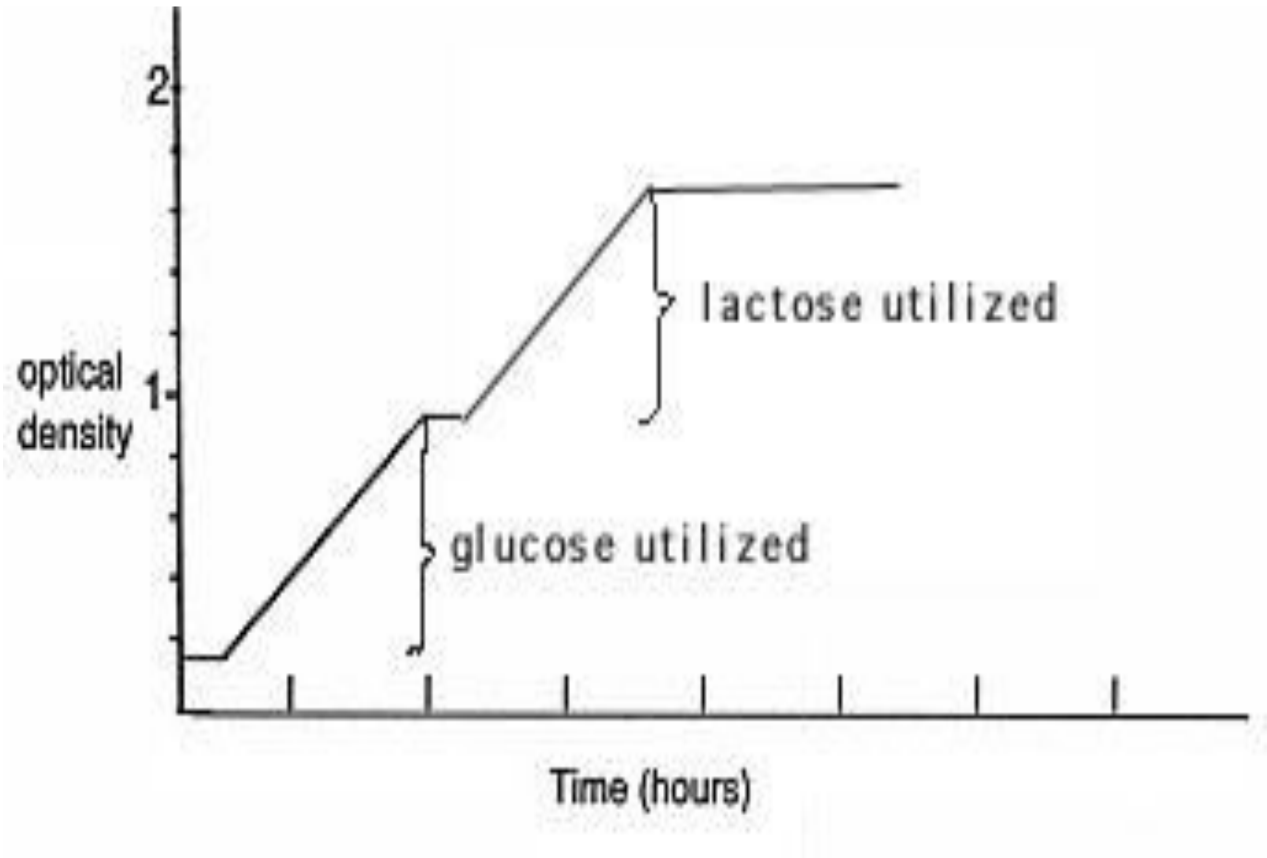

Figure :The Diauxic Growth Curve of *E. coli* grown in limiting concentrations of a mixture of glucose and lactose

•During the period of glucose utilization, lactose is not utilized because the cells are unable to transport and cleave the disaccharide lactose.

•Glucose is always metabolized first in preference to other sugars. Only after glucose is completely utilized is lactose degraded.

•The lactose operon is repressed even though lactose (the inducer) is present. The ecological rationale is that glucose is a better source of energy than lactose since its utilization requires two less enzymes.

•

•Only after glucose is exhausted are the enzymes for lactose utilization synthesized.

•The secondary lag during diauxic growth represents the time required for the complete induction of the lac operon and synthesis of the enzymes necessary for lactose utilization (lactose permease and beta-galactosidase).

•Only then does bacterial growth occur at the expense of lactose. Since the availability of **glucose represses the enzymes for lactose utilization**, this type of repression became known as **catabolite repression** or the **glucose effect**.

•Glucose is known to repress a large number of inducible enzymes in many different bacteria.

•Glucose represses the induction of inducible operons by inhibiting the synthesis of **cyclic AMP (cAMP)**, a nucleotide that is required for the initiation of transcription of a large number of inducible enzyme systems including the lac operon.

•The role of cyclic a cAMP is complicated. cAMP is required to activate an allosteric protein called **CAP (catabolite activator protein)** which binds to the promoter CAP site and stimulates the binding of RNAp polymerase to the promoter for the initiation of transcription.

•Thus, to efficiently promote gene transcription of the lac operon, not only must lactose be present to inactivate the lac repressor, but cAMP must be available to bind to CAP which binds to DNA to facilitate transcription.

•**In the presence of glucose**, adenylate cyclase (AC) activity is blocked. AC is required to synthesize cAMP from ATP. Therefore, if cAMP levels are low, CAP is inactive and **transcription does not occur**. **In the absence of glucose**, cAMP levels are high, CAP is activated by cAMP, and **transcription occurs** (in the presence of lactose).

•Many positively controlled promoters, such as the lac promoter, are not fully functional in the presence of RNAp alone and require activation by CAP. CAP is encoded by a separate Regulatory gene, and is present in constitutive levels.

•CAP is active only in the presence of cAMP. The binding of cAMP to CAP causes a conformational change in the protein allowing it to bind to the promoter near the RNAp binding site. CAP can apparently interact with RNAp to increase the rate of operon transcription about 50-fold. Positive control of the lac operon is illustrated in Figure

•As a form of catabolite repression, the glucose effect serves a useful function in bacteria: it requires the cells to use the best available source of energy. For many bacteria, glucose is the most common and readily utilizable substrate for growth. Thus, it inhibits indirectly the synthesis of enzymes that metabolize poorer sources of energy.

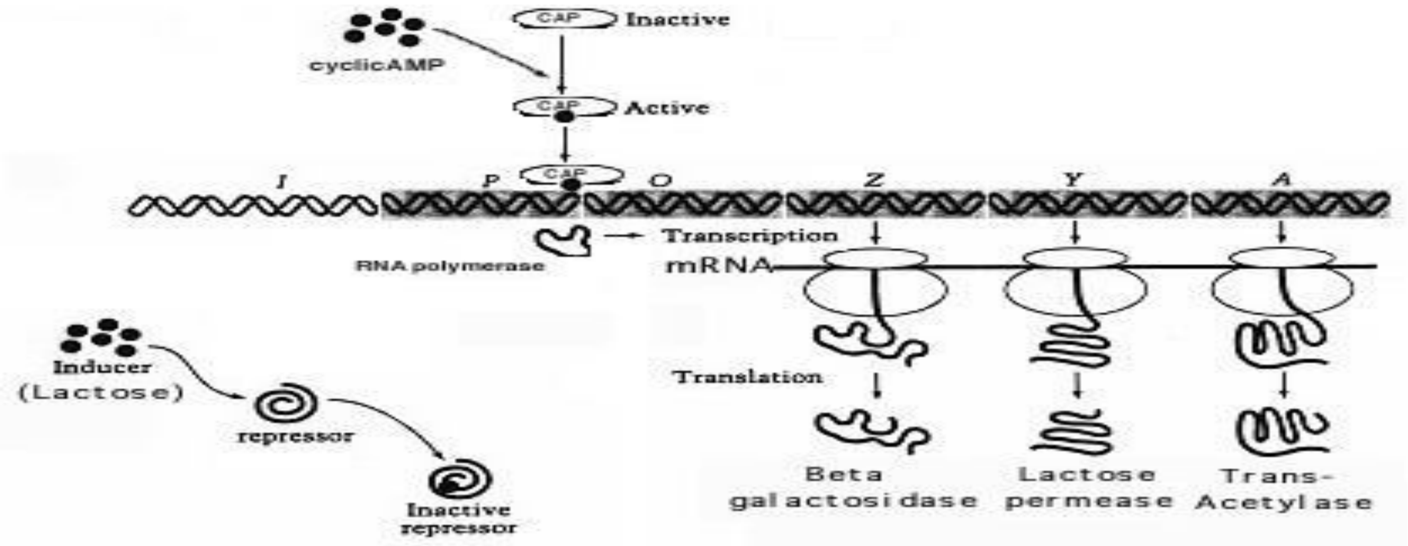

Figure . Catabolite repression is positive control of the lac operon. The effect is an increase in the rate of transcription. In this case, the CAP protein is activated by cAMP to bind to the lac operon and facilitate the binding of RNA polymerase to the promoter to transcribe the genes for lactose utilization.