Regulation and Control of Metabolism in Bacteria

- Most bacteria are exposed to a constantly changing physical and chemical environment.
- Within limits, bacteria can react to changes in their environment through changes in patterns of structural proteins,
- transport proteins,
- toxins,
- enzymes, etc.
- which adapt them to a particular ecological situation.

- Bacteria have developed sophisticated mechanisms for the regulation of both catabolic and anabolic pathways.
- However, in real bacterial life, the control mechanisms for all these metabolic pathways must be reversible, since the environment can change quickly and drastically.
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Conditions Affecting Enzyme Formation in Bacteria

- Bacterial cells can change patterns of enzymes, in order to adapt them to their specific environment.
- Often the concentration of an enzyme in a bacterial cell depends on the presence of the substrate for the enzyme.
- Constitutive enzymes are always produced by cells independently of the composition of the medium in which the cells are grown.
- The enzymes that operate during glycolysis and the TCA cycle are generally constitutive: they are present at more or less the same concentration in cells at all times.

Enzyme Repression

- Enzyme repression is a form of negative control (down-regulation) of bacterial transcription.
- This process is called negative control because a regulatory protein brings about inhibition of mRNA synthesis which leads to decreased synthesis of enzymes.

Enzyme Induction

- Enzymes that are synthesized as a result of genes being turned on are called inducible enzymes and the substance that activates gene transcription is called the inducer.

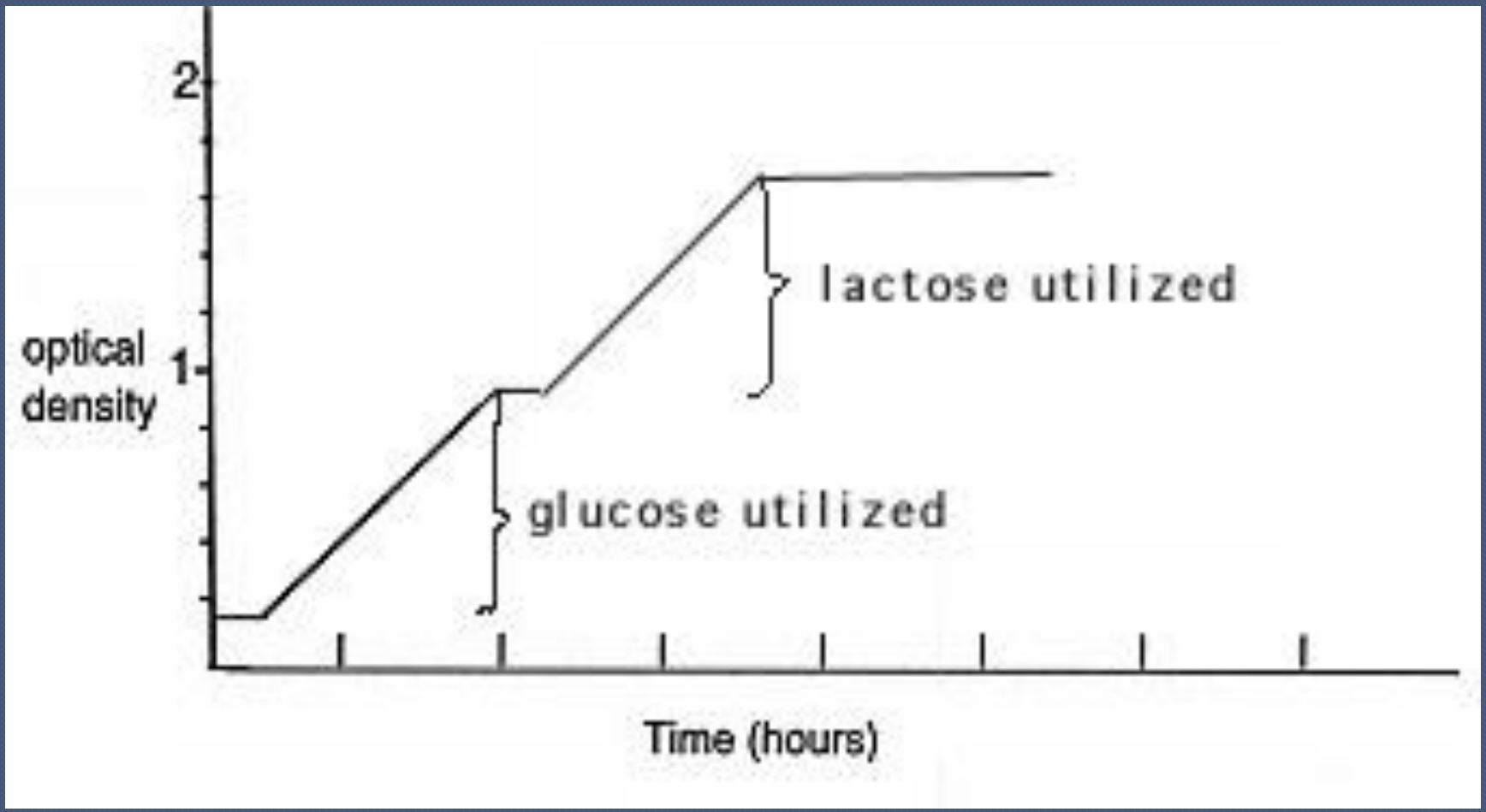
- Inducible enzymes are produced only in response to the presence of a their substrate and, in a sense, are produced only when needed.
- In this way the cell does not waste energy synthesizing unneeded enzymes.

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 ecological rationale is that glucose is a better source of energy than lactose since its utilization requires two less enzymes

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

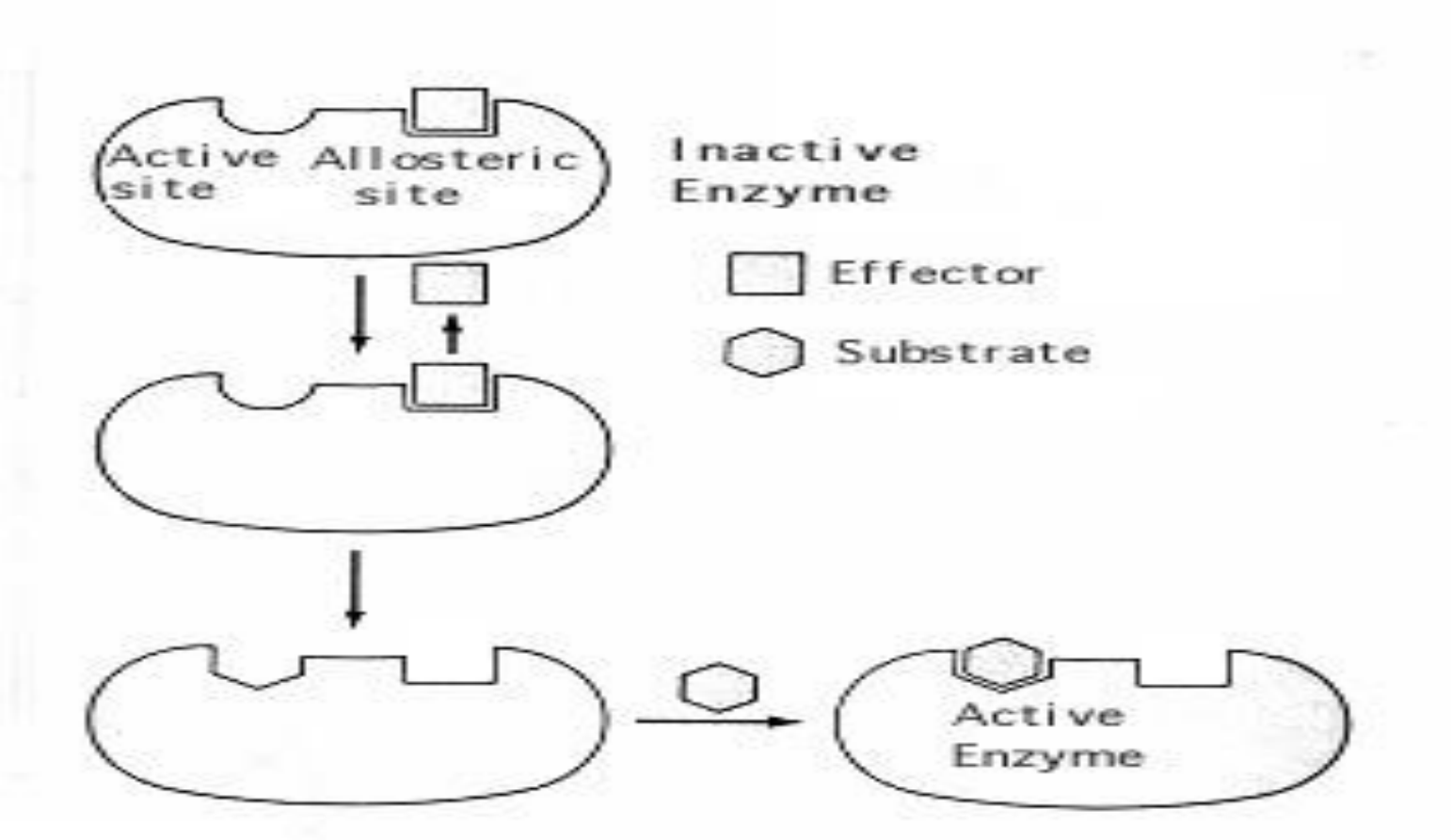


Allosteric Proteins

- These levels of control are usually modulated by proteins with the property of allostery.
- An allosteric protein is one which has an active (catalytic) site and an allosteric (effector) site.
- In an allosteric enzyme, the active site binds to the substrate of the enzyme and converts it to a product.
- The allosteric site is occupied by some small molecule which is not a substrate.

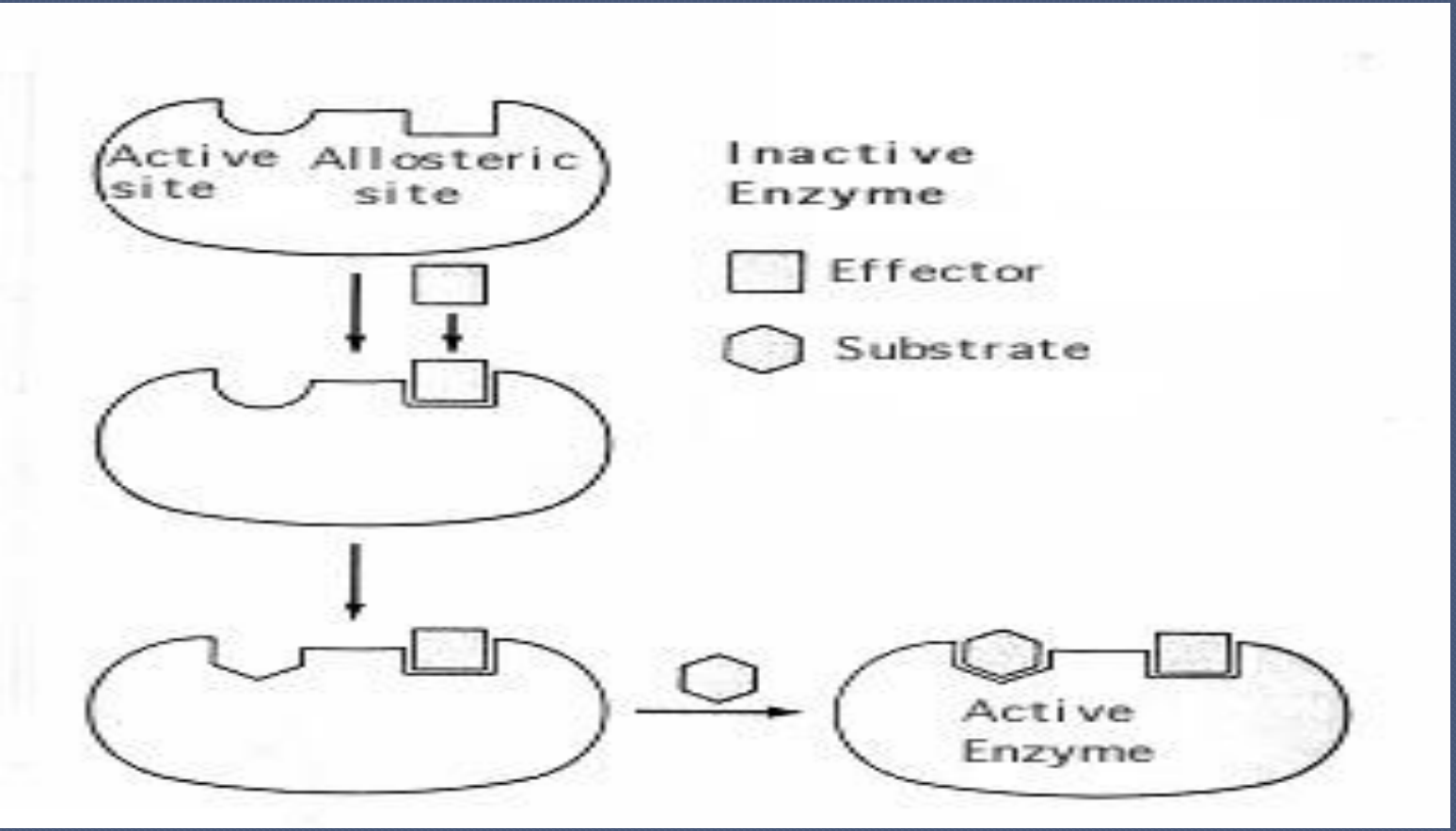
- However, when the allosteric site is occupied by the effector molecule, the configuration of the active site is changed so that it is now unable to recognize and bind to its substrate (Figure 1).
- If the protein is an enzyme, when the allosteric site is occupied, the enzyme is inactive, i.e., the effector molecule decreases the activity of the enzyme.

Example of an allosteric enzyme with a negative effector site



- There is an alternative situation, however the effector molecule of certain allosteric enzymes binds to its allosteric site and consequently transforms the enzyme from an inactive to an active state
- (Figure 2).

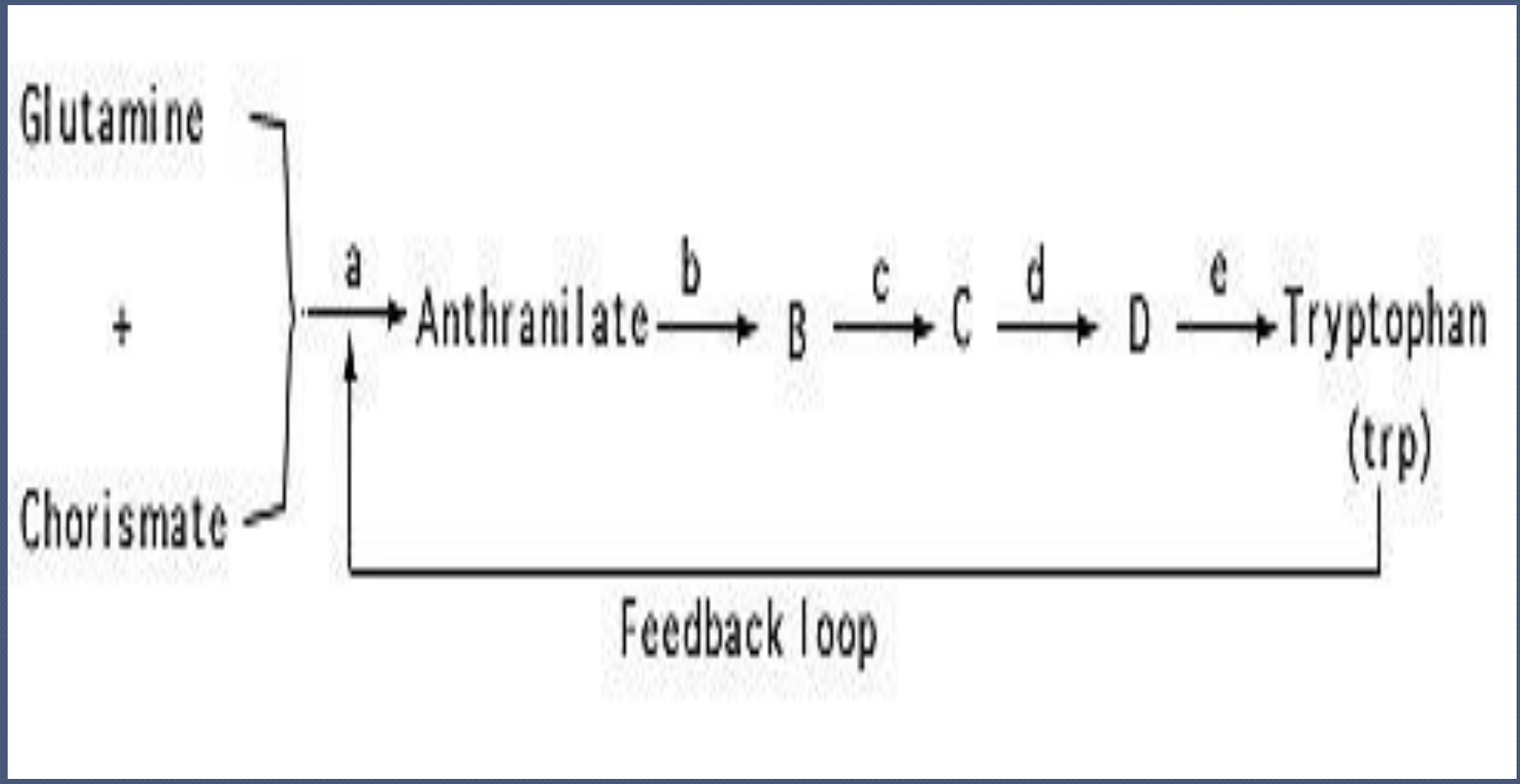
an allosteric enzyme with a positive effector site



Feedback Inhibition

- In feedback inhibition, the end product of a biosynthetic pathway inhibits the activity of the first enzyme that is unique to the pathway, thus controlling production of the end product.
- Other enzymes in the pathway remain active, but they do not see their substrates.
- The pathway is shut down as long as adequate amounts of the end product are present.
- If the end product is used up or disappears, the inhibition is relieved, the enzyme regains its activity, and the organism can resume synthesis of the end product.

The pathway of tryptophan biosynthesis in *E. coli*



- If a metabolic pathway branches, leading to the synthesis of two amino acids, each end product (amino acid) can control its own synthesis without affecting the other (Figure 4).
- For example, the amino acids proline and arginine are both synthesized from glutamic acid.
- Each amino acid can regulate the first enzyme unique to its own synthesis without affecting the other, so that a surplus of arginine will not shut off the synthesis of proline and vice versa.

Generalized scheme for regulation of a branched metabolic pathway by the process of feedback inhibition