Non-specific regulators

REGULATION THROUGH CHANGES IN AMOUNT OF ENZYME

A. Regulated Enzyme Synthesis

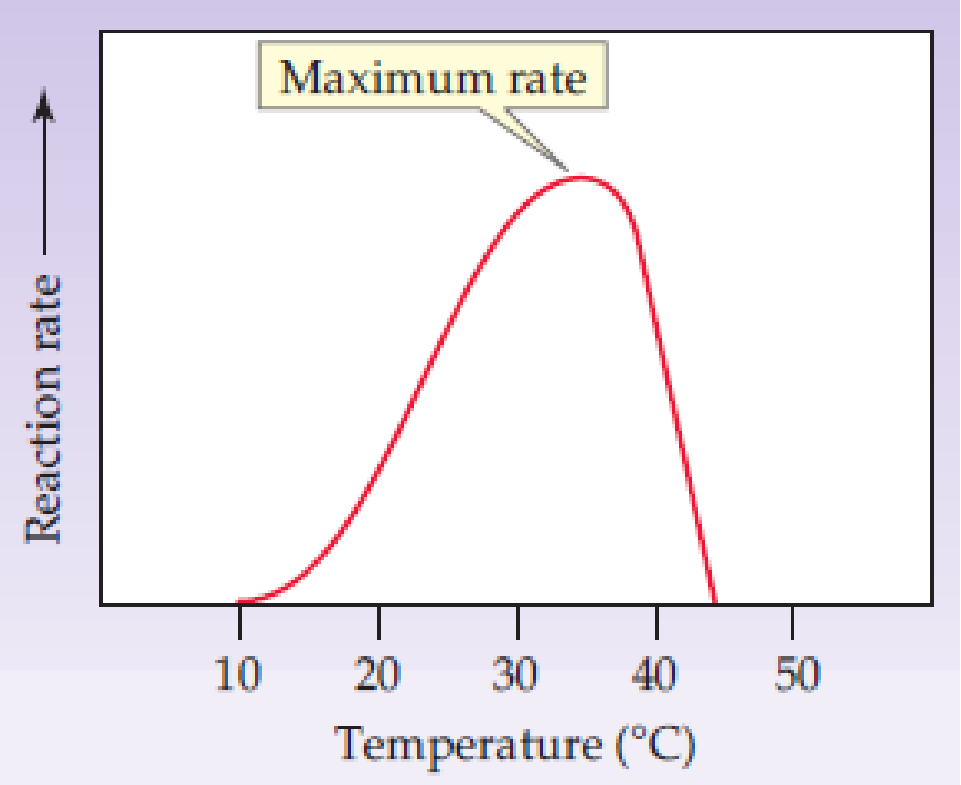
- **Regulated by increasing or decreasing the rate of gene transcription (induction & repression)**
  - **Usually slow in humans (hours to days)**
- **Sometimes through stabilization of the messenger RNA**

B. Regulated Protein Degradation

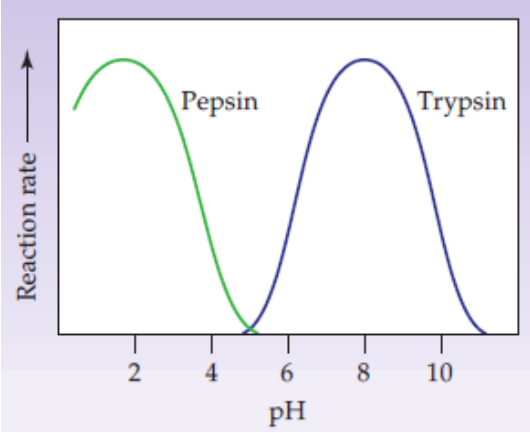
- **Can be degraded with a characteristic half-life within lysosomes**
  - **During fasting or infective stress: gluconeogenesis increase & synthesis of antibodies (protein degradation increases)**
  - **Increased synthesis of ubiquitin**

Effect of Temperature

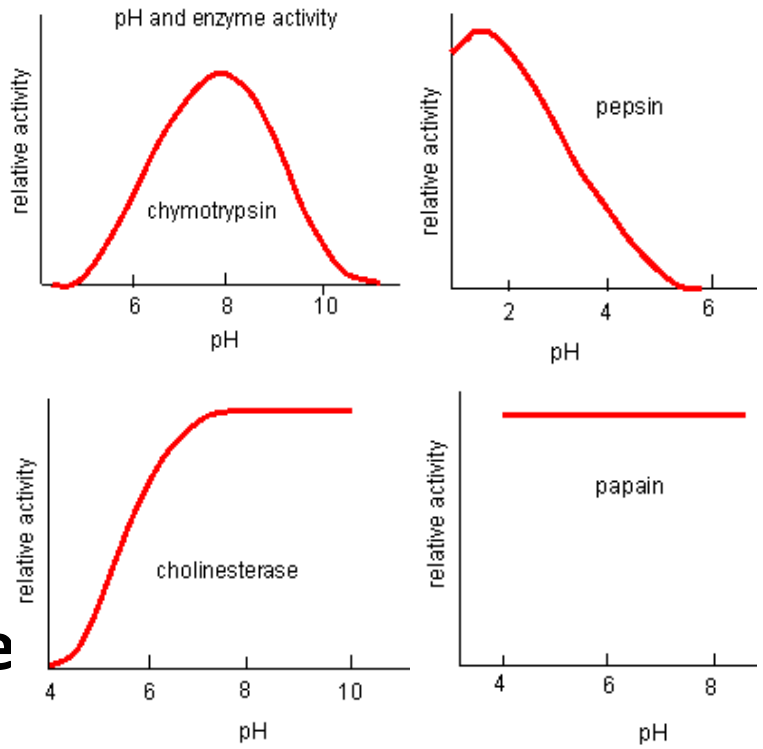
- **Increase in T° increases the rate until reaches a max (≈ 50°): the optimal temperature of each enzyme is its' denaturation**
- **Autoclave steam heating**
- **Hypothermia, metabolic reactions, cardiac surgery**



Effect of pH



- **Usually a well defined optimum point**
- **Most enzymes have their max. activity between (5-9)**
- **Extremes of pH denatures protein**
- **pH can alter binding of substrate to enzyme (K_M) by altering the protonation state of the substrate, or altering the conformation of the enzyme**



The effect of pH is enzyme-dependent

Extremozymes

Taq polymerase and PCR

Thermophiles (heat lovers)

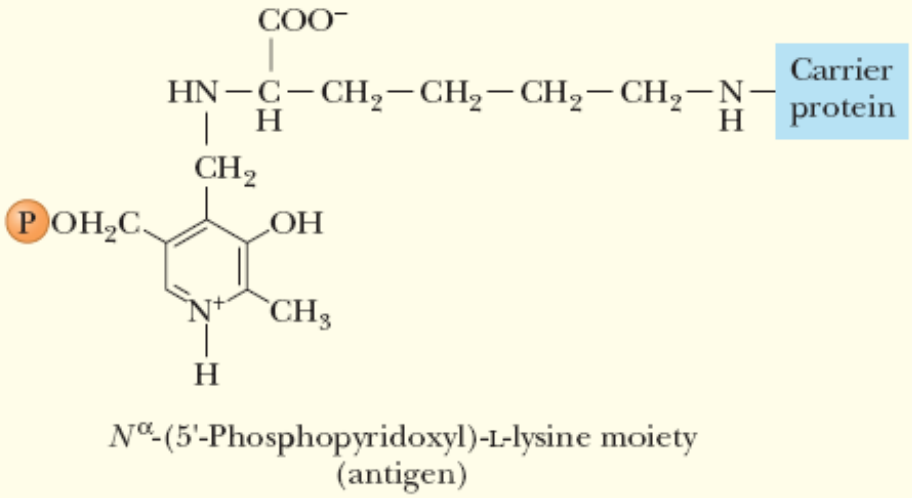
Psychrophiles (cold lovers)

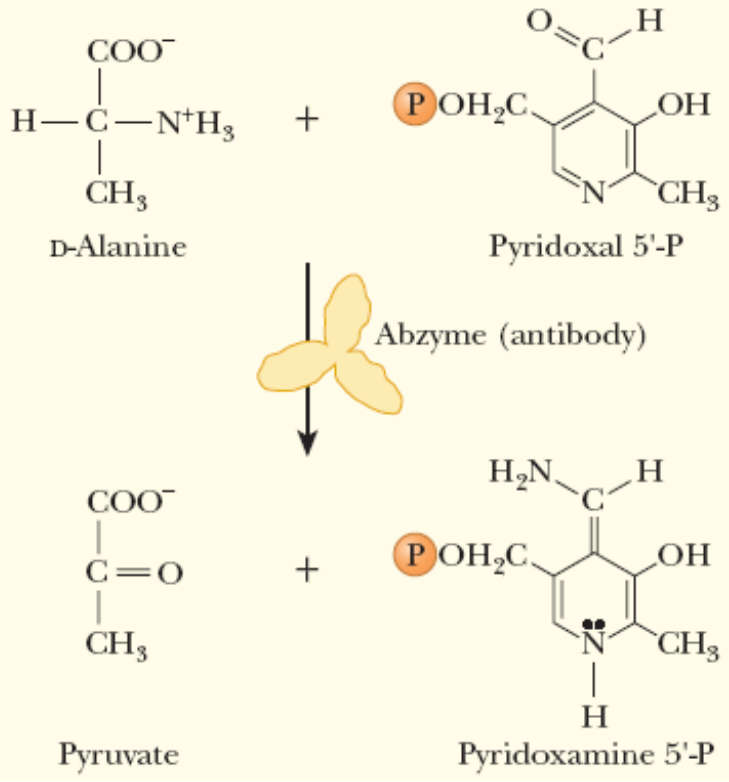
lipases and proteases

Biobleaching of paper pulp using heat-stable xylanases

Abzymes – cutting edge science

- **An antibody that is produced against a transition-state analog (active)**
- **An abzyme is created in animals**





An exception to protein enzymes
Ribozymes

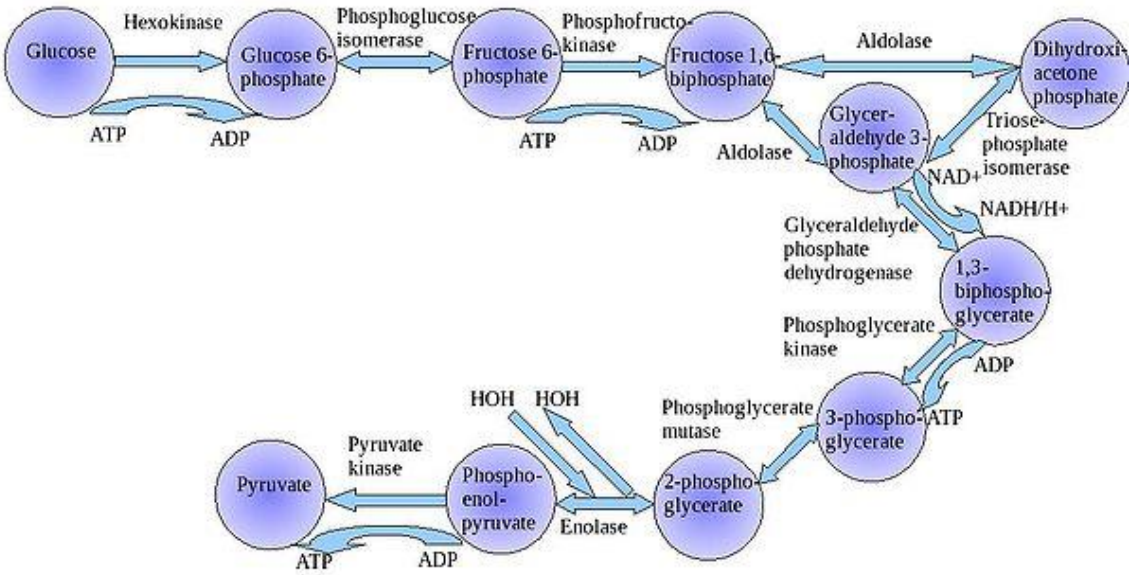
- RNA molecules
- Examples: telomerase & RNase P
- Catalyze splicing reactions and are involved in protein synthesis
- The catalytic efficiency of catalytic RNAs is less than that of protein enzymes, but can greatly be enhanced by the presence of protein subunits

REGULATION OF METABOLIC PATHWAYS

Principles of Pathway Regulation

- ***1. COUNTERREGULATION OF OPPOSING PATHWAYS***
- **Synthesis vs. degradation (a different regulatory enzyme)**
- ***2. TISSUE ISOZYMES OF REGULATORY PROTEINS***
- ***3. REGULATION AT THE RATE-LIMITING STEP***
- **Pathways are principally regulated at their rate-limiting step**
- **The slowest step & is usually not readily reversible**
  - **Changes in this step can influence flux through the rest of the pathway**

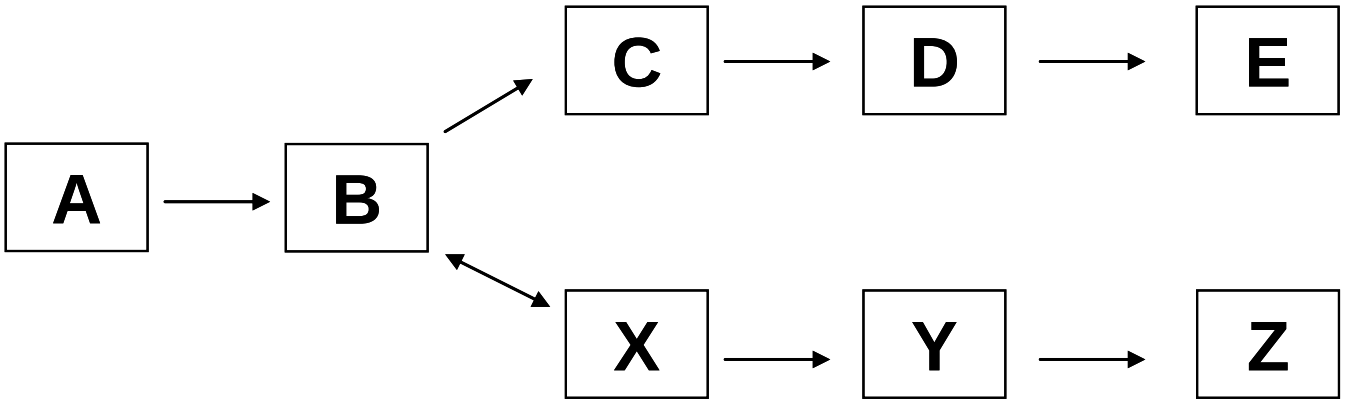
- **Usually the first committed step in a pathway**
- **Requirement for high amount of energy**
- **High K_M values of enzyme towards its substrate**



Principles of Pathway Regulation

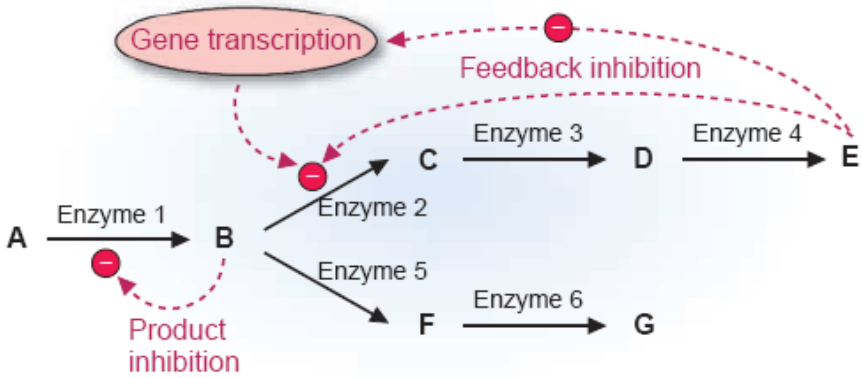
- ***4. The committed step***

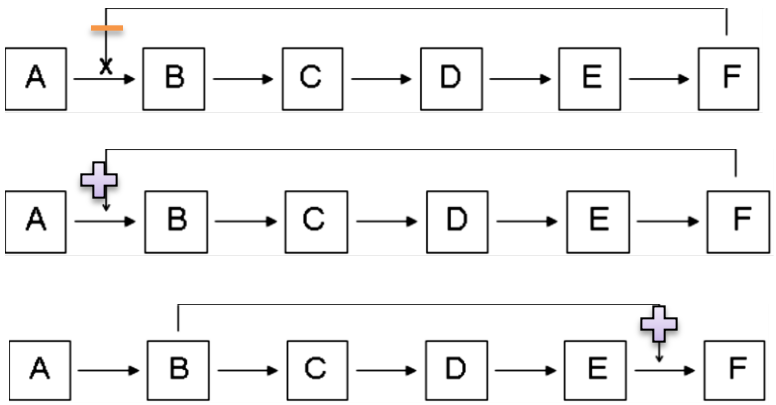
- **A committed step in a metabolic pathway is the first irreversible reaction that is unique to a pathway and that, once occurs, leads to the formation of the final substrate with no point of return**
- **Committed steps are exergonic reaction**
- **For example, the committed step for making product E is (B → C), not (A → B)**

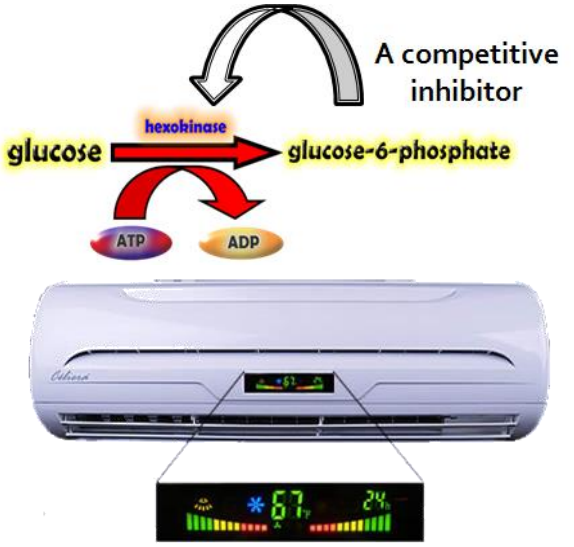


Principles of Pathway Regulation

- ***5. FEEDBACK REGULATION***
- **This type of regulation is much slower to respond to changing conditions than allosteric regulation**
  - **Negative feedback regulation (feedback inhibition)**
  - **Positive feedback regulation**
  - **Feed-forward regulation**
    - **Disposal of toxic compounds**





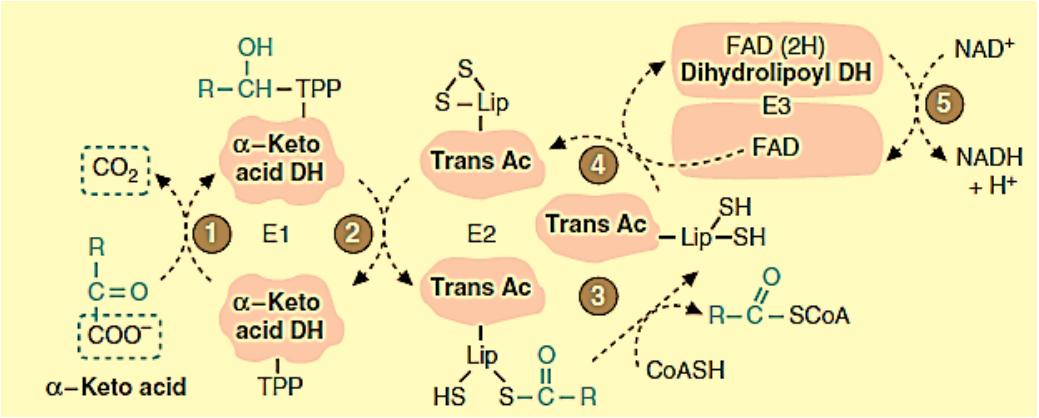


Principles of Pathway Regulation

- ***6. Enzyme compartmentalization***
- **Both enzymes and their substrates are present in relatively small amount in a cell**
- **A mechanism by which rate of reactions become faster is their compartmentalization; reducing area of diffusion**
- **In this way, enzymes are sequestered inside compartments where access to their substrates is limited**
- **Lysosomes; proteins get transported to lysozymes**
- **Mitochondria; energy metabolic pathways**
- **Metabolism of fatty acids; synthesis (cytosol) vs. degradation (mitochondria)**

Principles of Pathway Regulation

- ***7. Enzyme complexing (A multienzyme complex)***



- **Complexing various enzymes that share one process**
- **Product of enzyme A pass directly to enzyme B**
- **Pyruvate dehydrogenase (mitochondria) 3 enzymes: decarboxylation, oxidation, & transfer of the resultant acyl group to CoA**