คม 524 สารออกฤทธิ์ทางชีวภาพ

(CH 524 Bioactive compounds)

เนื้อหา หลักการเมตาบอลิซึม ส่วนที่ 2

โดย อ.ดร. เอกวิทย์ ตรีเนตร

ภาควิชาเคมี คณะวิทยาศาสตร์

Study of metabolic pathway

1. ***Major metabolic pathway***
   (เทอม ที่ 2 ในรายวิชา คม 325)

2. ***Specific metabolic pathway***
   (ในบาง pathways ที่น่าสนใจ)

Main pathways (all living organisms)

- Glycolysis
- Aerobic respiration and/or Anaerobic respiration
- Citric acid cycle / Krebs cycle
- Oxidative phosphorylation

Other pathways (most) :

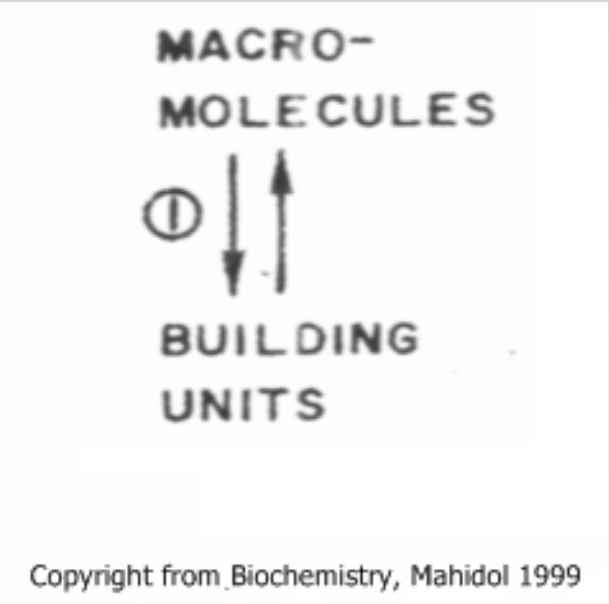
- Fatty acid oxidation (β-oxidation)
- Gluconeogenesis
- Amino acid metabolism
- Urea cycle / Nitrogen metabolism
- Nucleotide metabolism
- Glycogen synthesis / Glycogen storage
- Pentose phosphate pathway (hexose monophosphate shunt)
- Porphyrin synthesis (or heme synthesis) pathway
- Lipogenesis
- HMG-CoA reductase pathway
  (isoprene prenylation chains, see cholesterol)

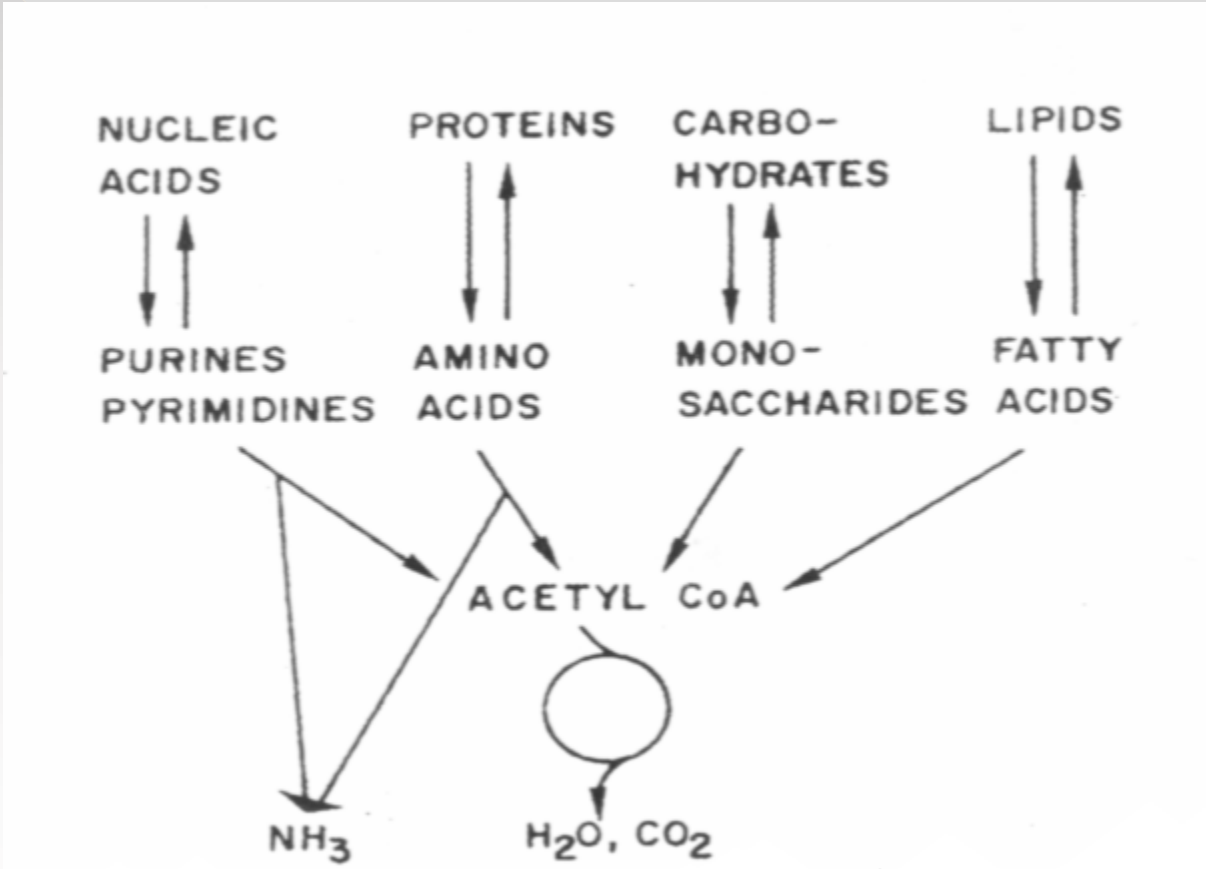
Synthesis of energetic compounds from non-living matter:

- Photosynthesis (plants, algae, cyanobacteria)
- Chemosynthesis (some bacteria)

Steps of Major Metabolic Pathway

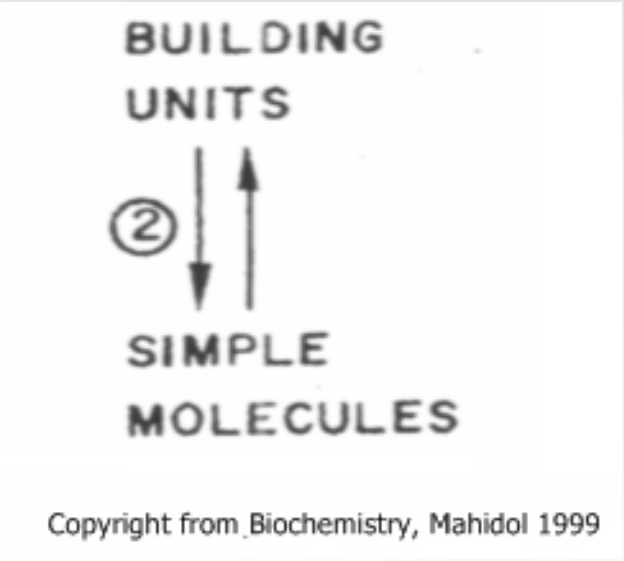
Step 1. Change between biomolecule and building units

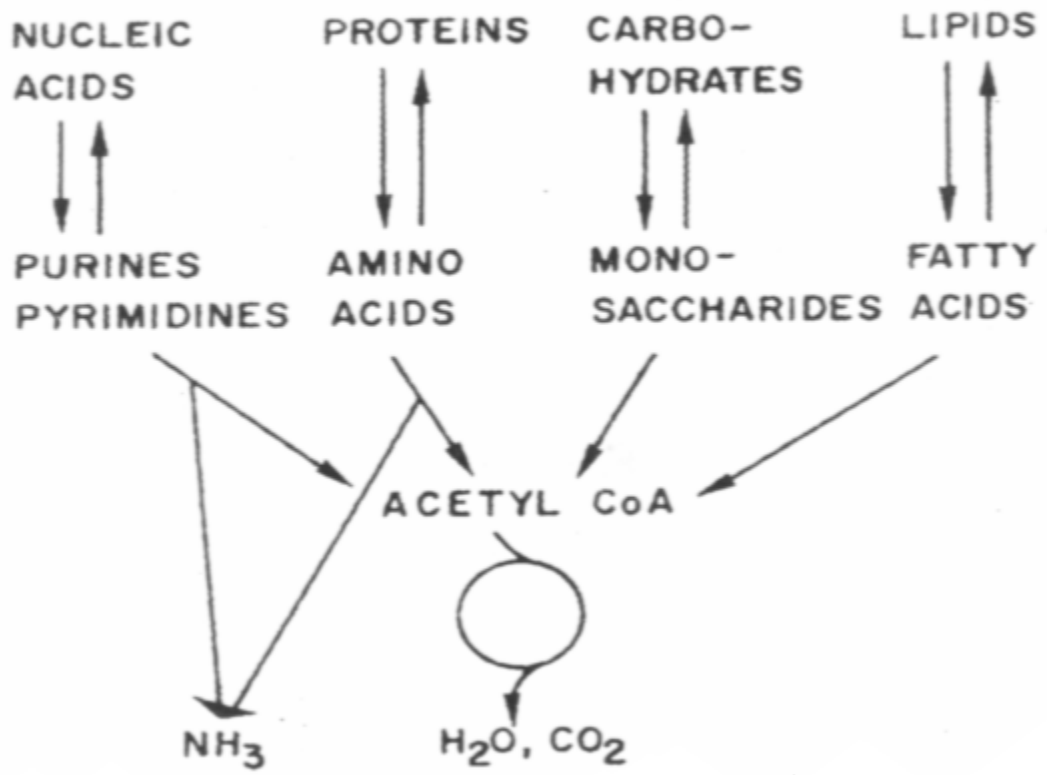




Steps of Major Metabolic Pathway

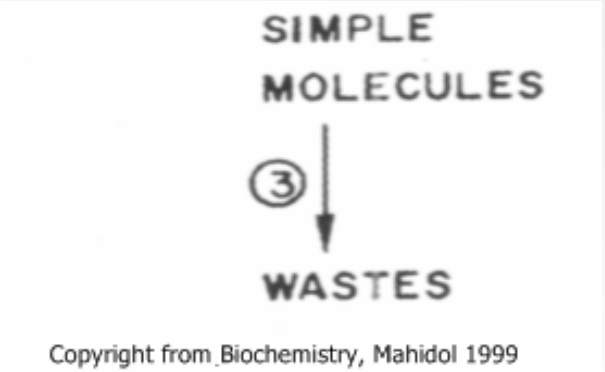
Step 2. Change between building units and simple molecules

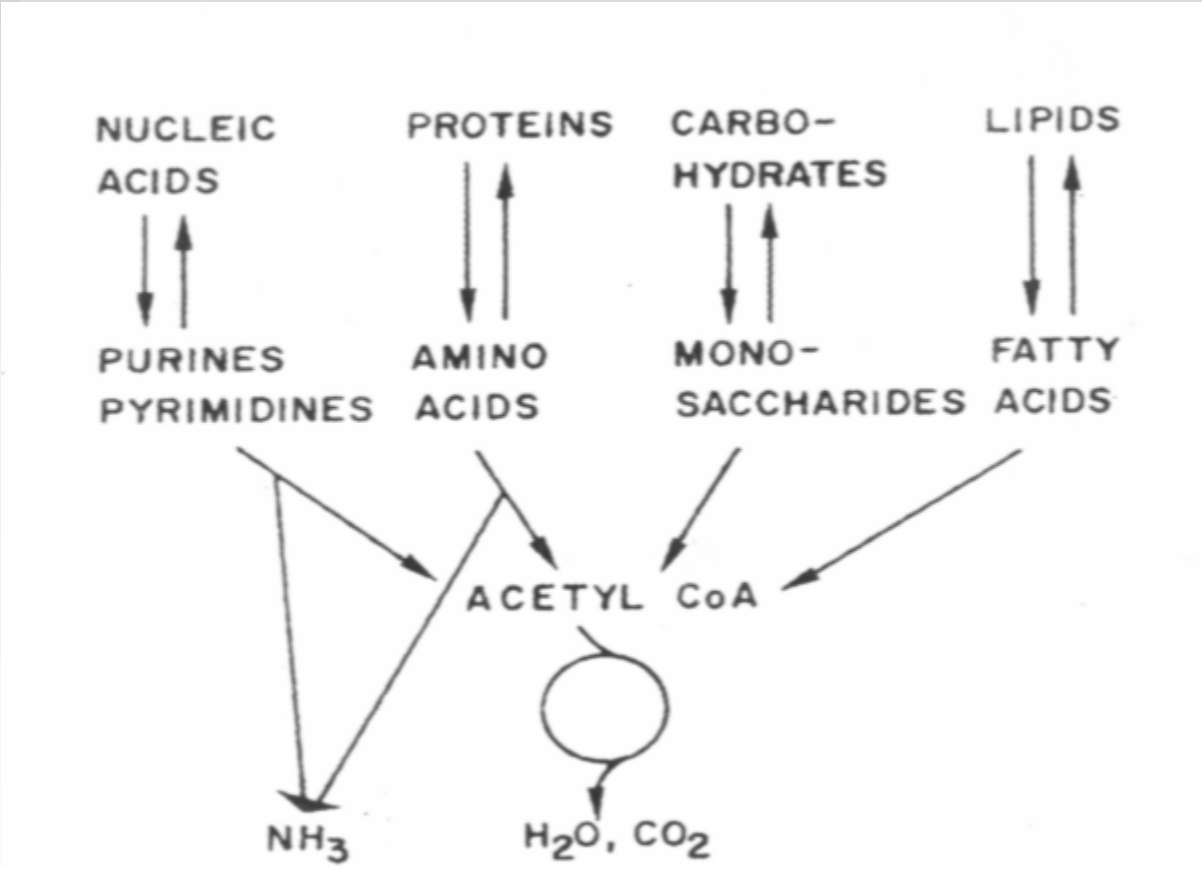




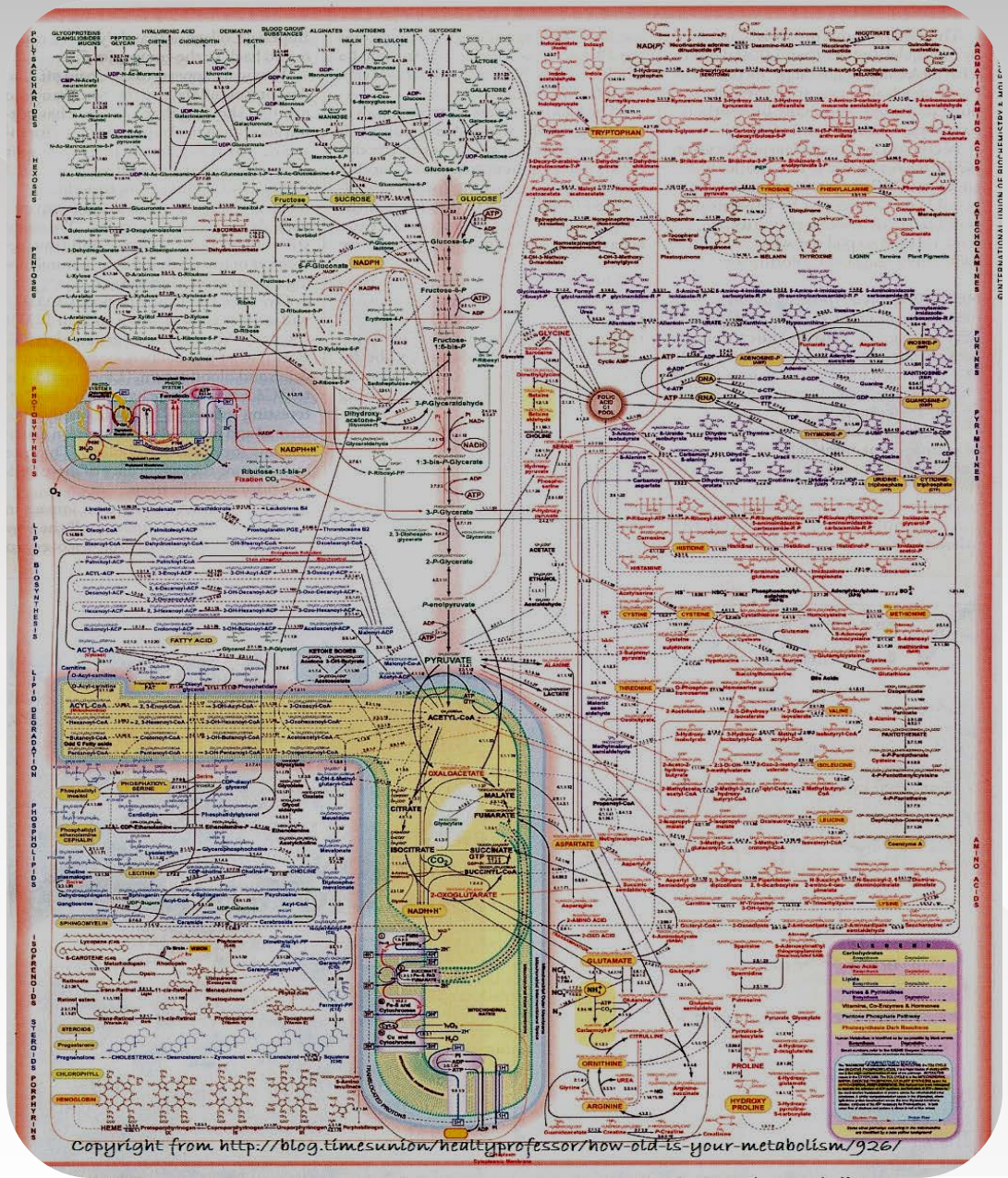
Steps of Major Metabolic Pathway

Step 3. Change between simple molecules and wastes





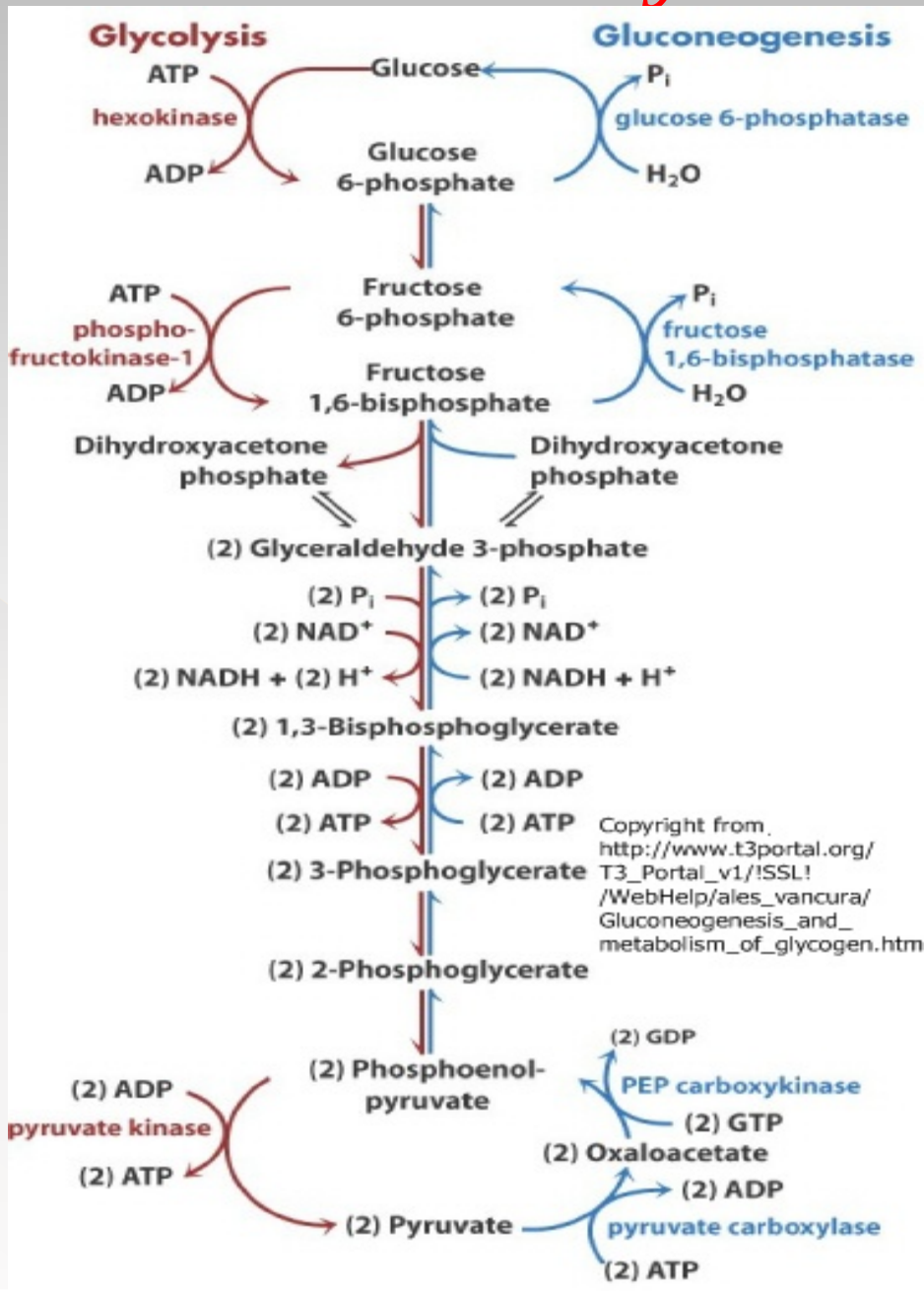
Network of Major Metabolic Pathway



Types of Major Metabolic Pathway

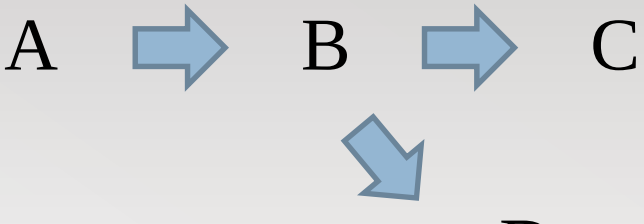
Type 1.
Linear sequence

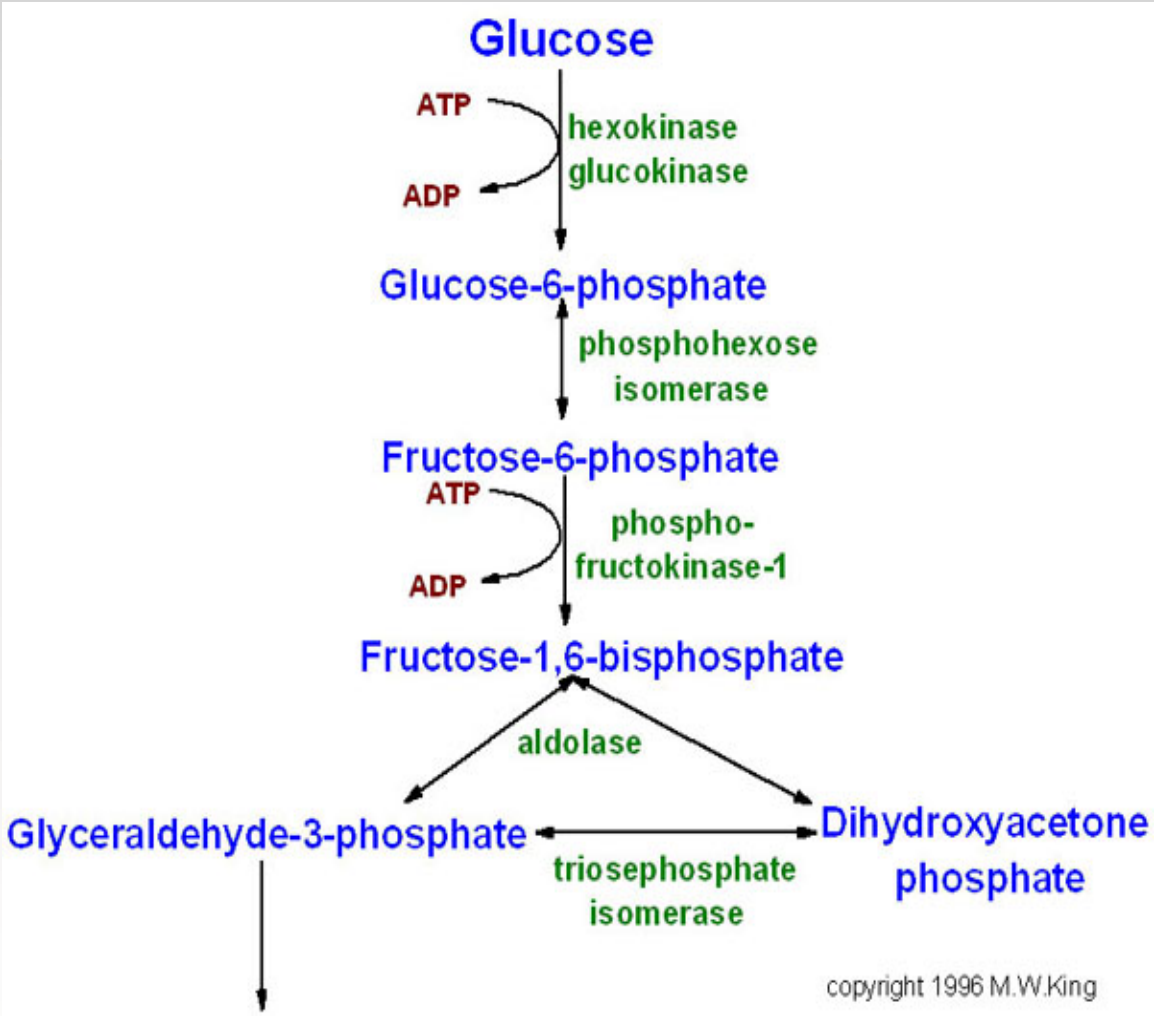
A ⇨ B ⇨ C ⇨ D



Types of Major Metabolic Pathway

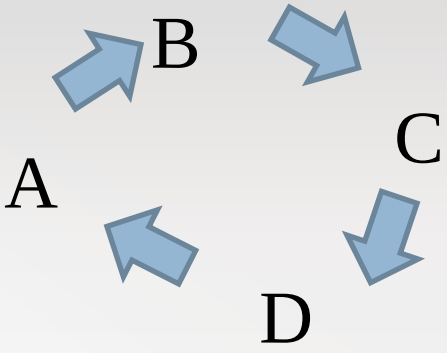
Type 2.
Branched sequence

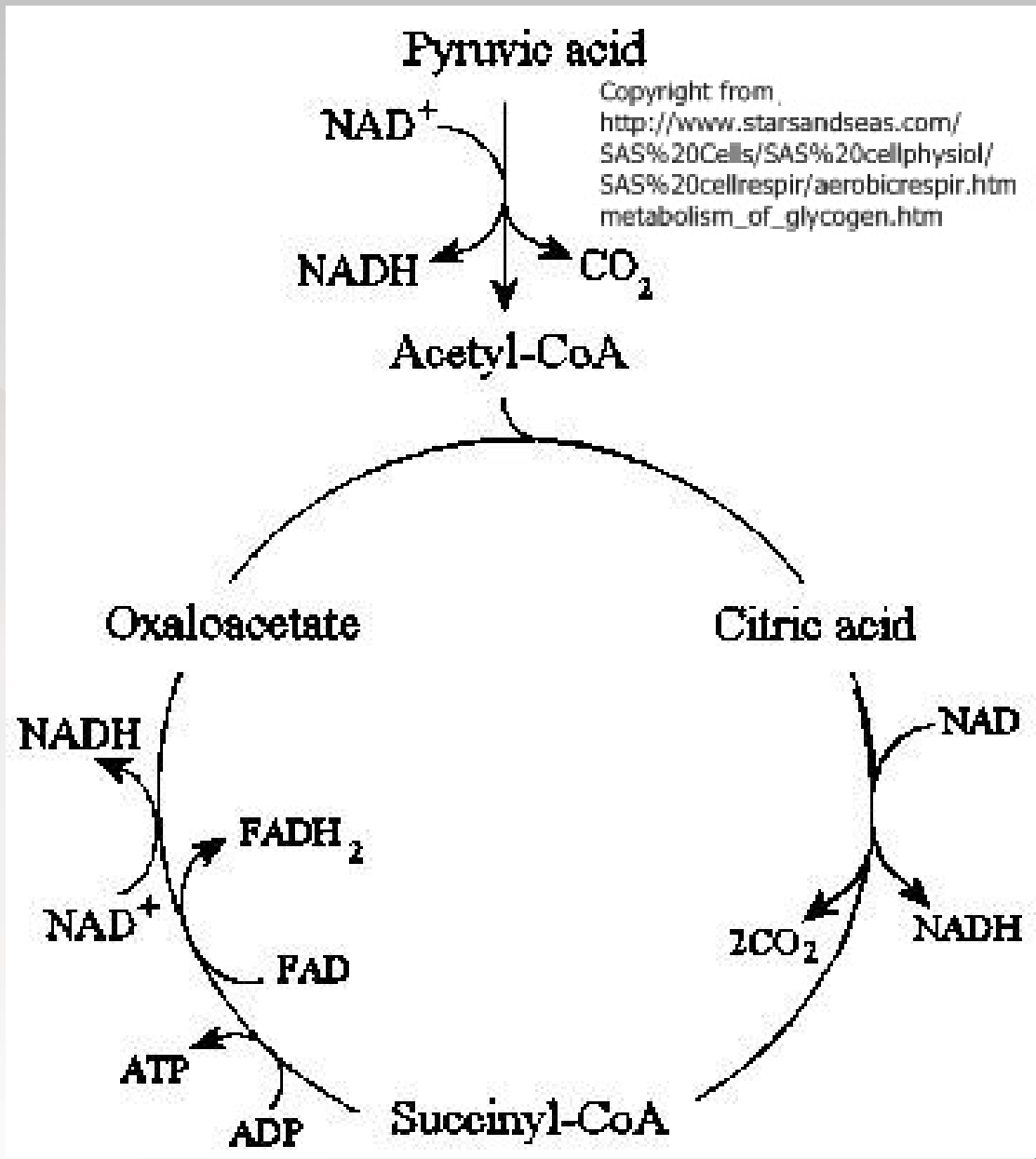




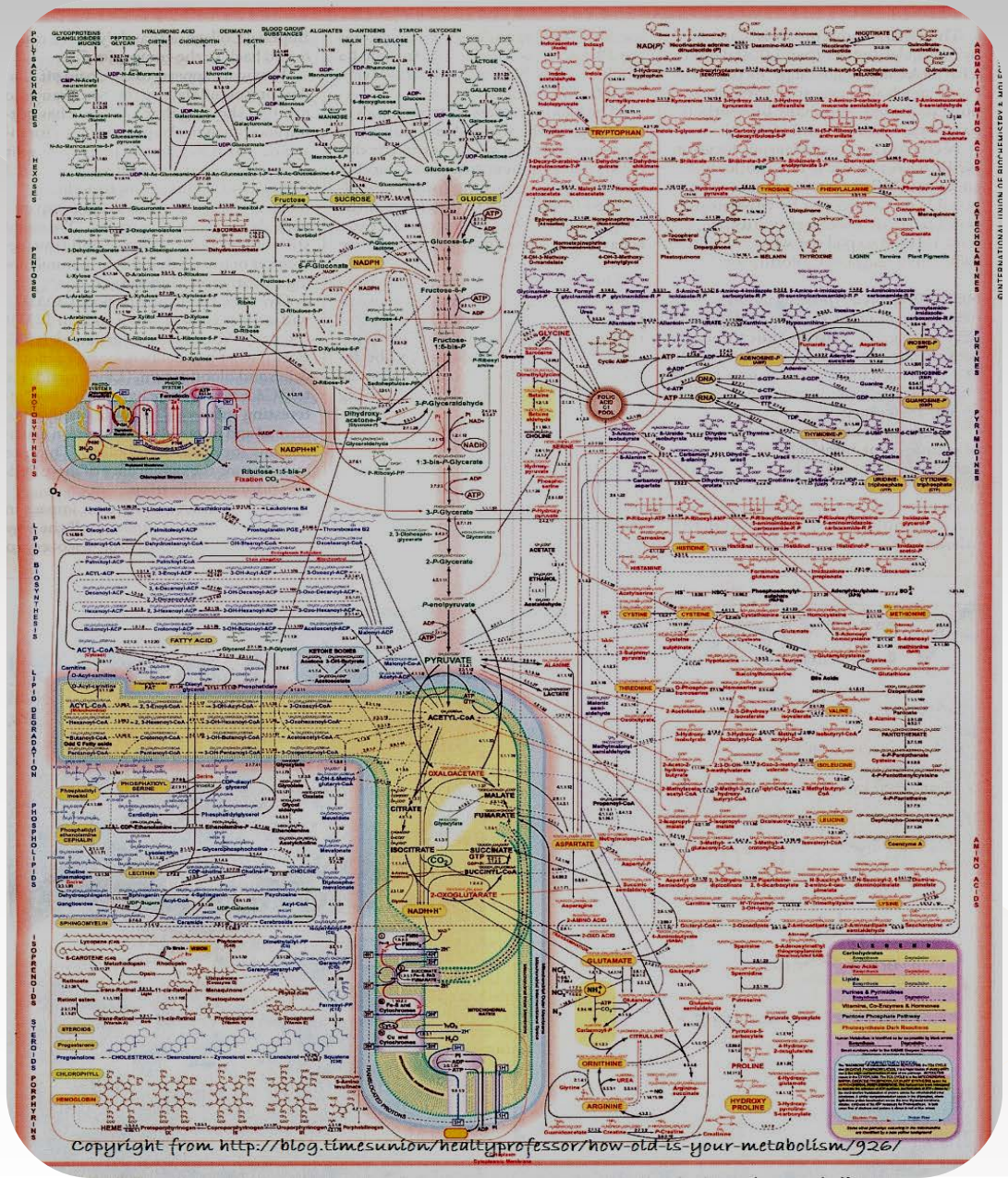
Types of Major Metabolic Pathway

Type 3. Cycle





Network of Major Metabolic Pathway



สภาวะสมดุล (Homeostasis)

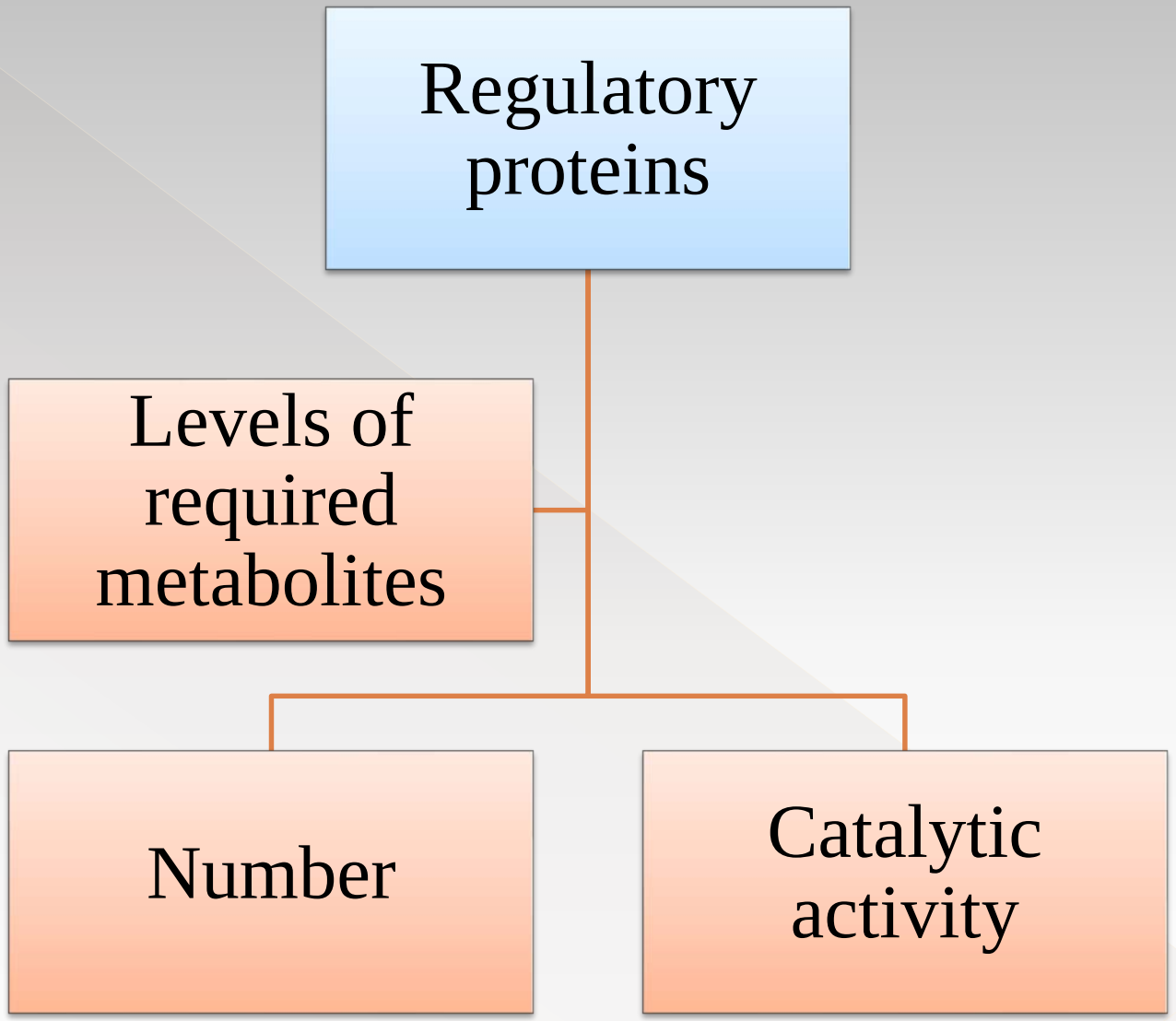
- ทุกสิ่งมีชีวิตจะรักษาสภาวะสมดุล ด้วยการรักษาระดับปริมาณของสารเมทาบอไลท์ให้อยู่ในระดับที่คงที่

(การสร้างเมทาบอไลท์ = การสลายเมทาบอไลท์)

$$S \xrightarrow[v1]{} M \xrightarrow[v2]{} P$$

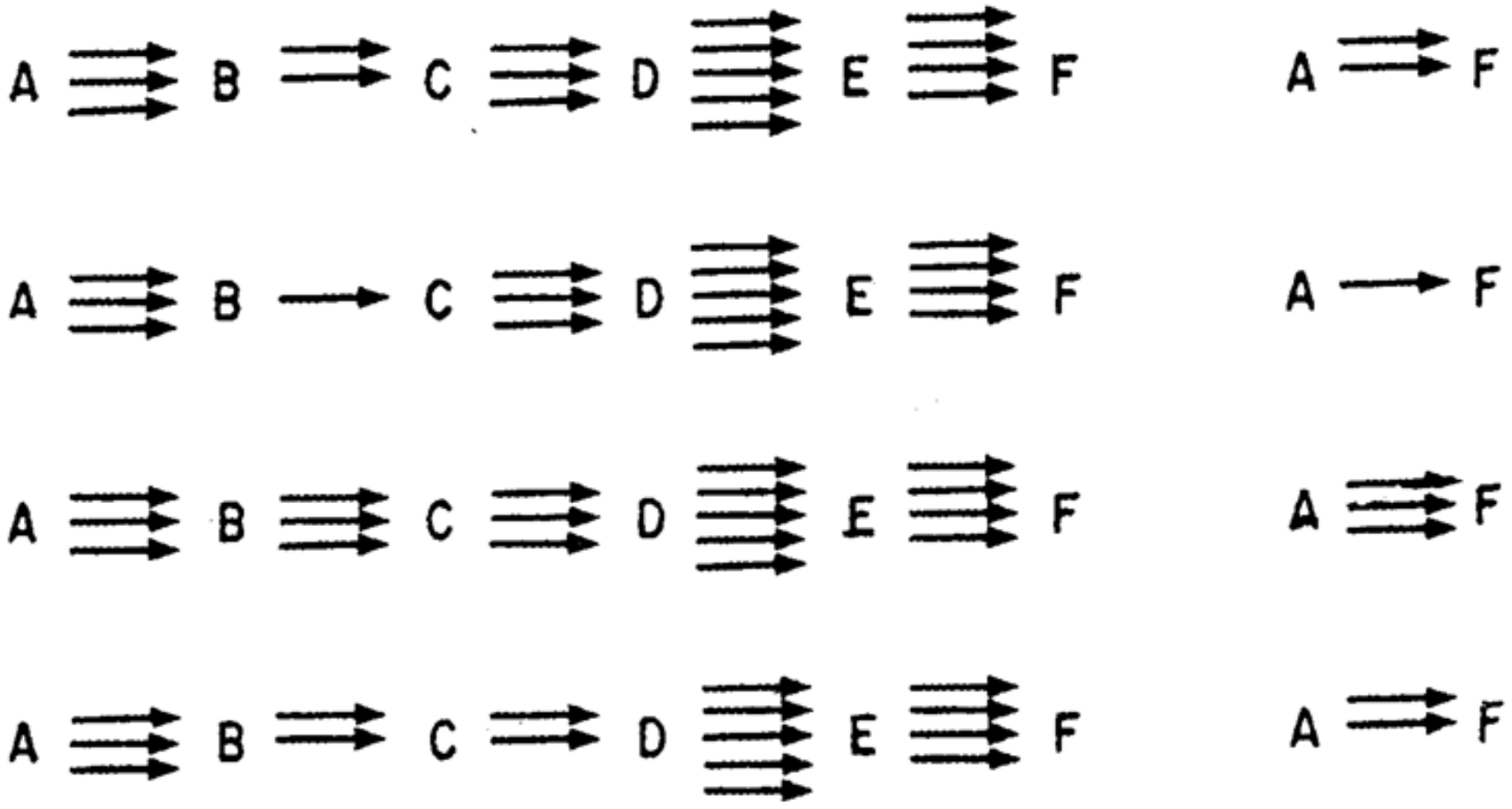
- ระดับที่คงที่ ถูกรบกวน → การเกิดโรค

- **Regulatory protein** (4000 ยีนส์ ประมาณ 12% ของยีนส์ในมนุษย์ → เป็นตัวควบคุมหลักให้เกิดสภาวะสมดุล


Regulatory proteins
Levels of required metabolites
Number
Catalytic activity

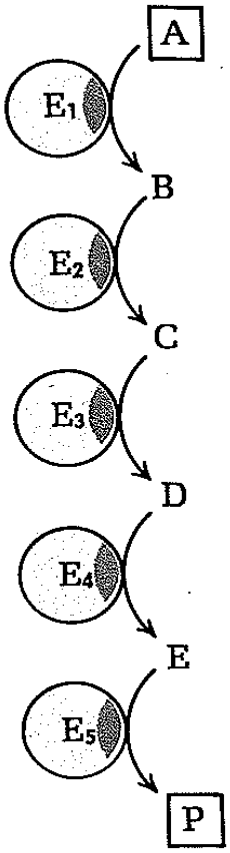
Control models of Major Metabolic Pathway

Model 1. Rate-limiting reaction

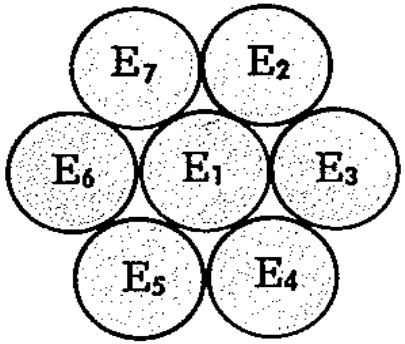


Model 2. Modulation at enzyme

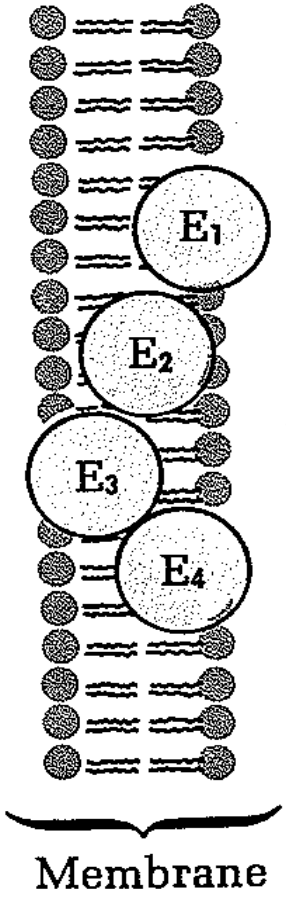
ENZYMES THAT WORK TOGETHER IN A PATHWAY CAN BE



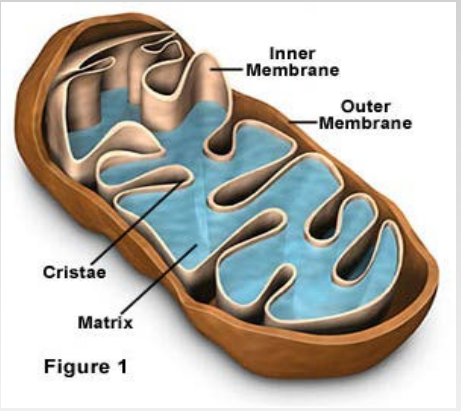
Soluble with free floating intermediates



Covalently bound in complex



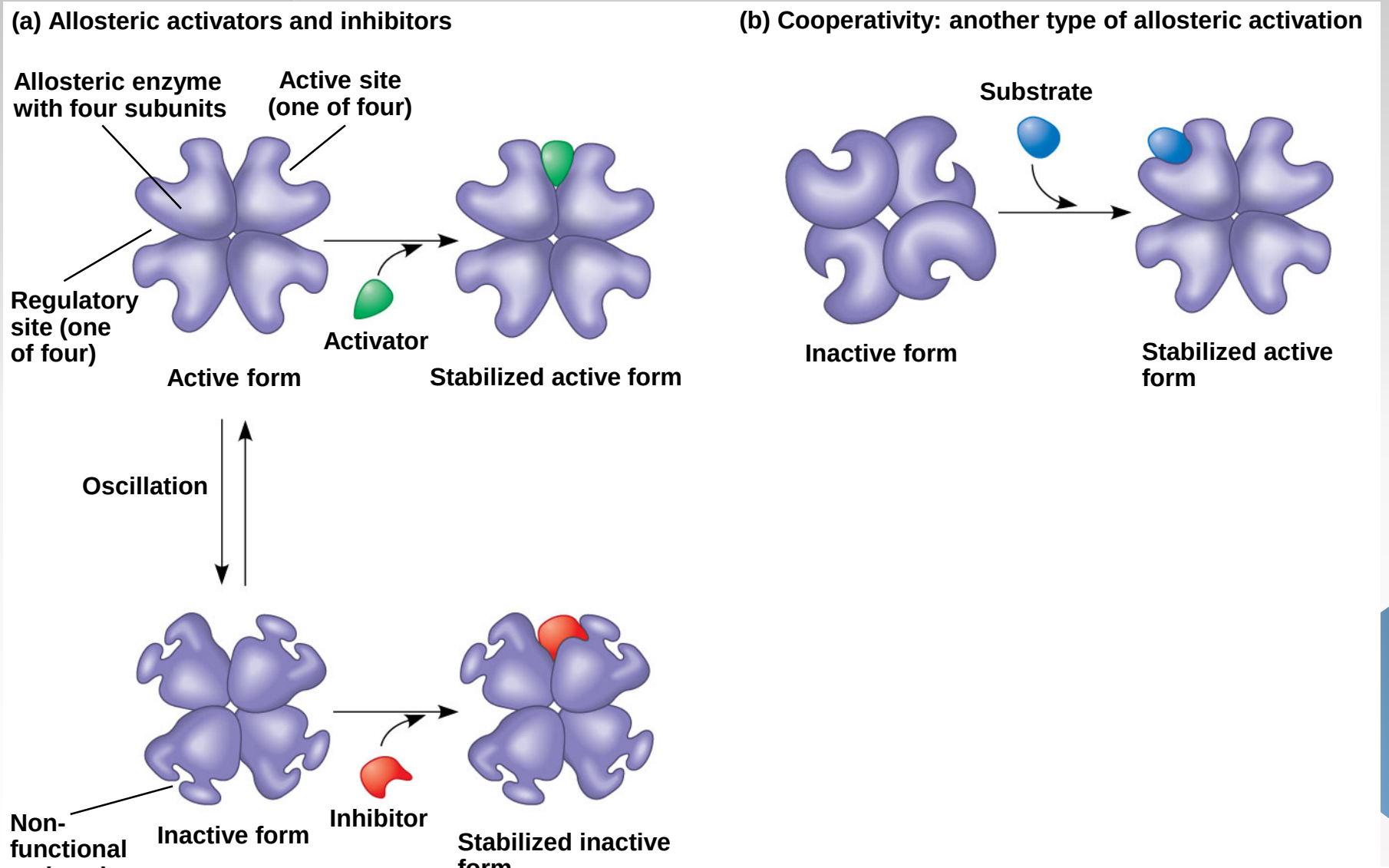
Attached to a membrane in sequence



Concentrated in specific location

Model 2. Modulation at enzyme

Model 2.1. Modulation at enzyme site

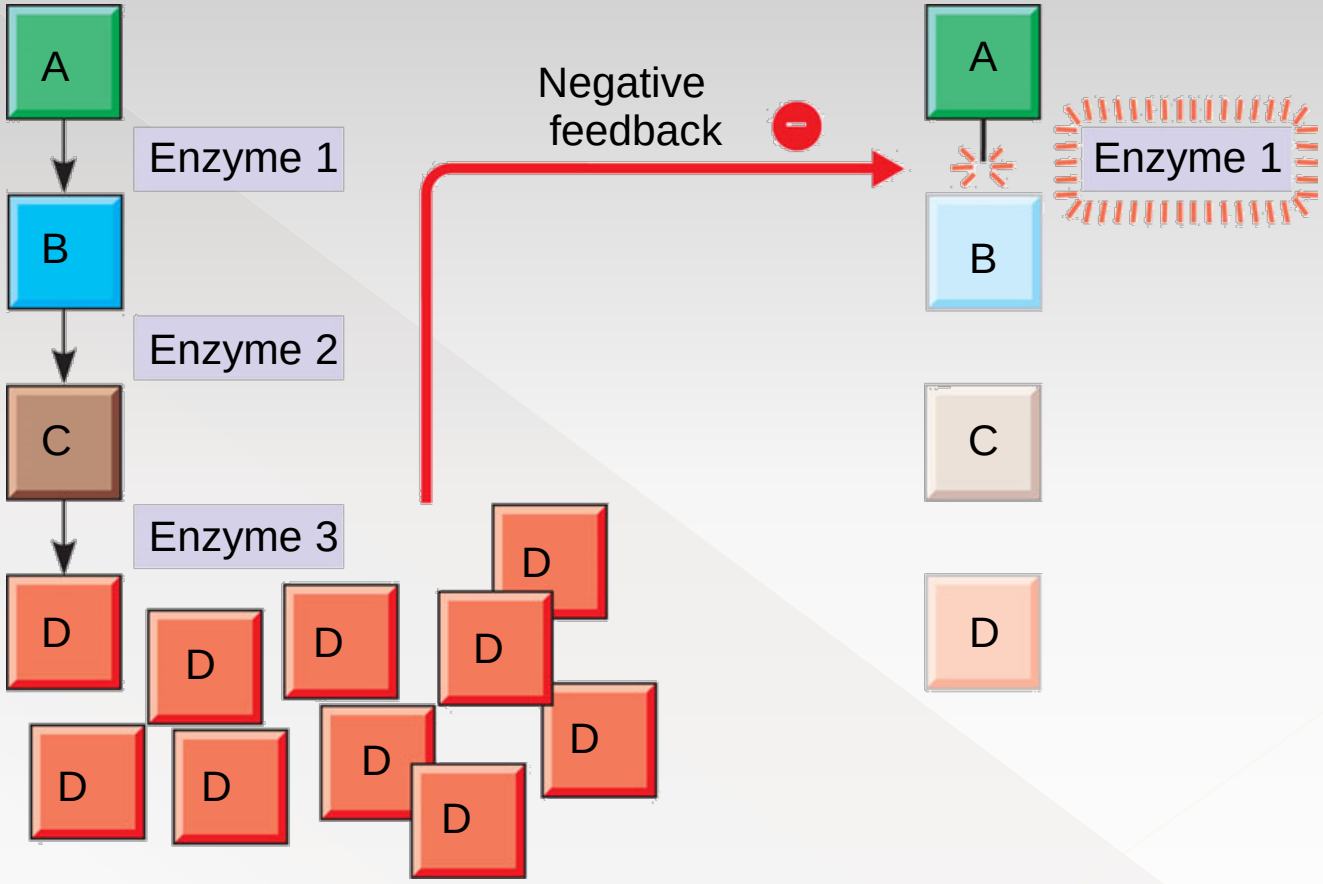


Feedback Inhibition

- In **feedback inhibition**, the end product of a metabolic pathway shuts down the pathway
- Feedback inhibition prevents a cell from wasting chemical resources by synthesizing more product than is needed

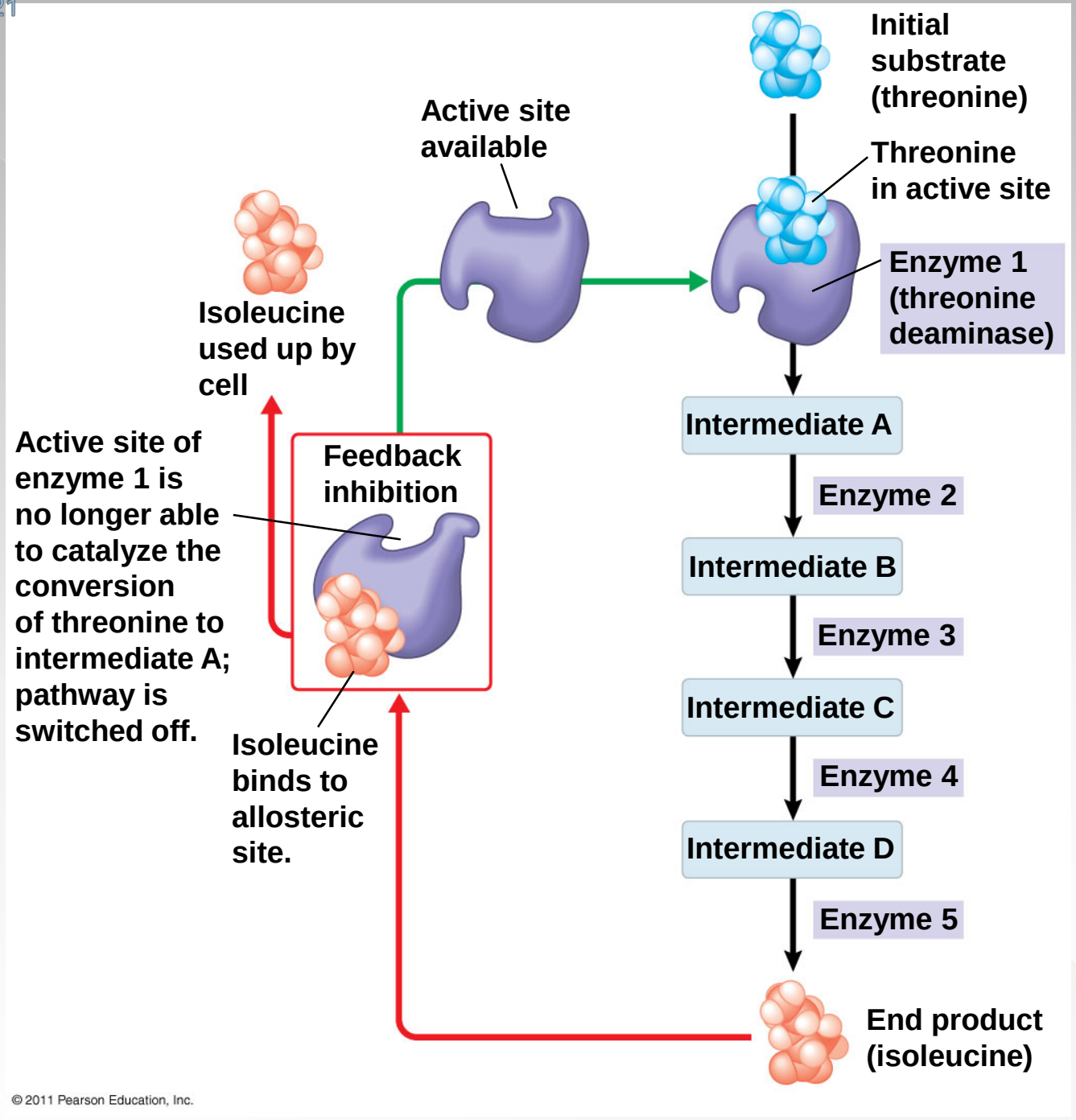
NEGATIVE FEEDBACK

- An accumulation of an end product slows the process that produces that product



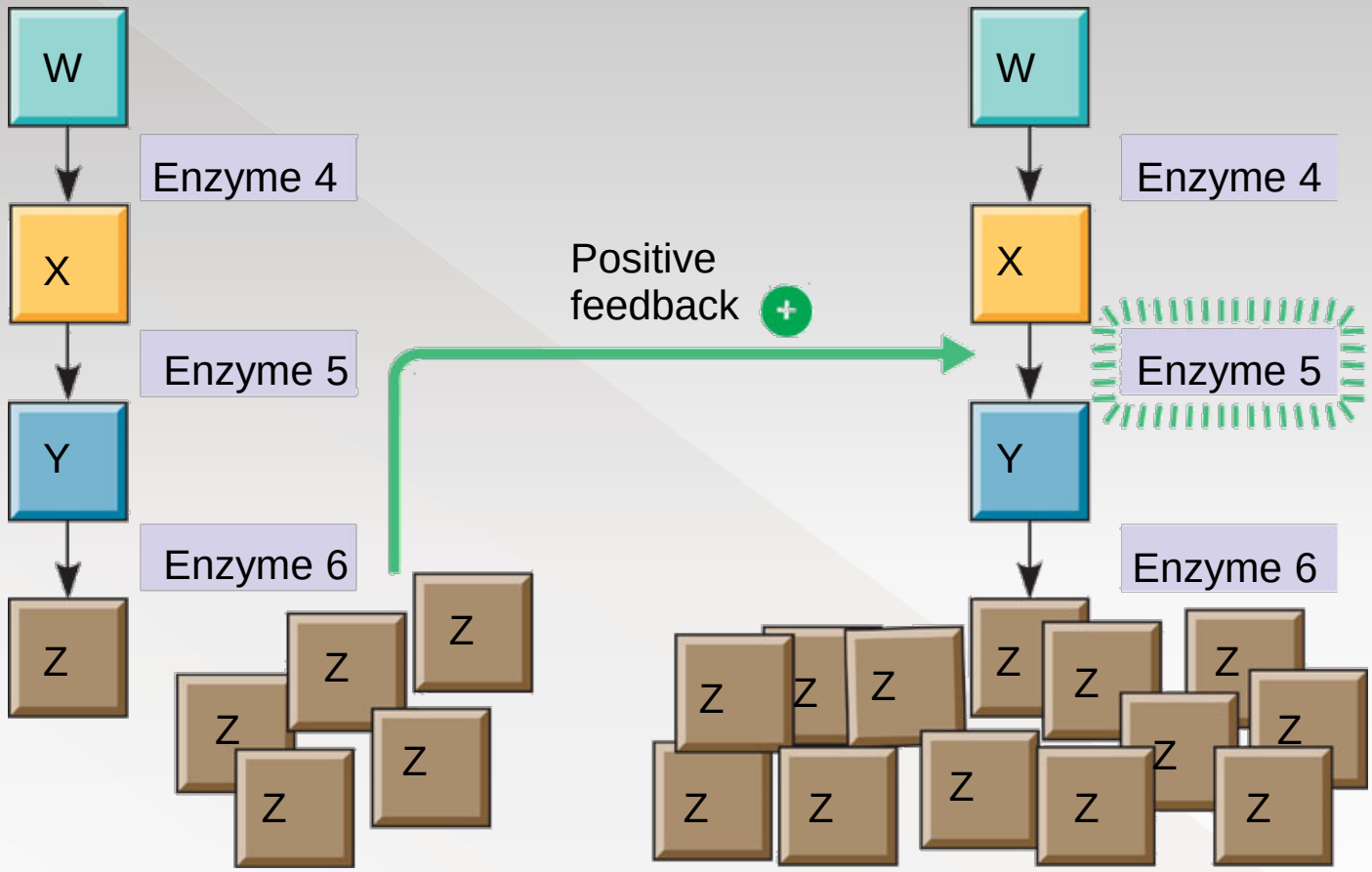
Example: sugar breakdown generates ATP; excess ATP inhibits an enzyme near the beginning of the pathway

Figure 8.21



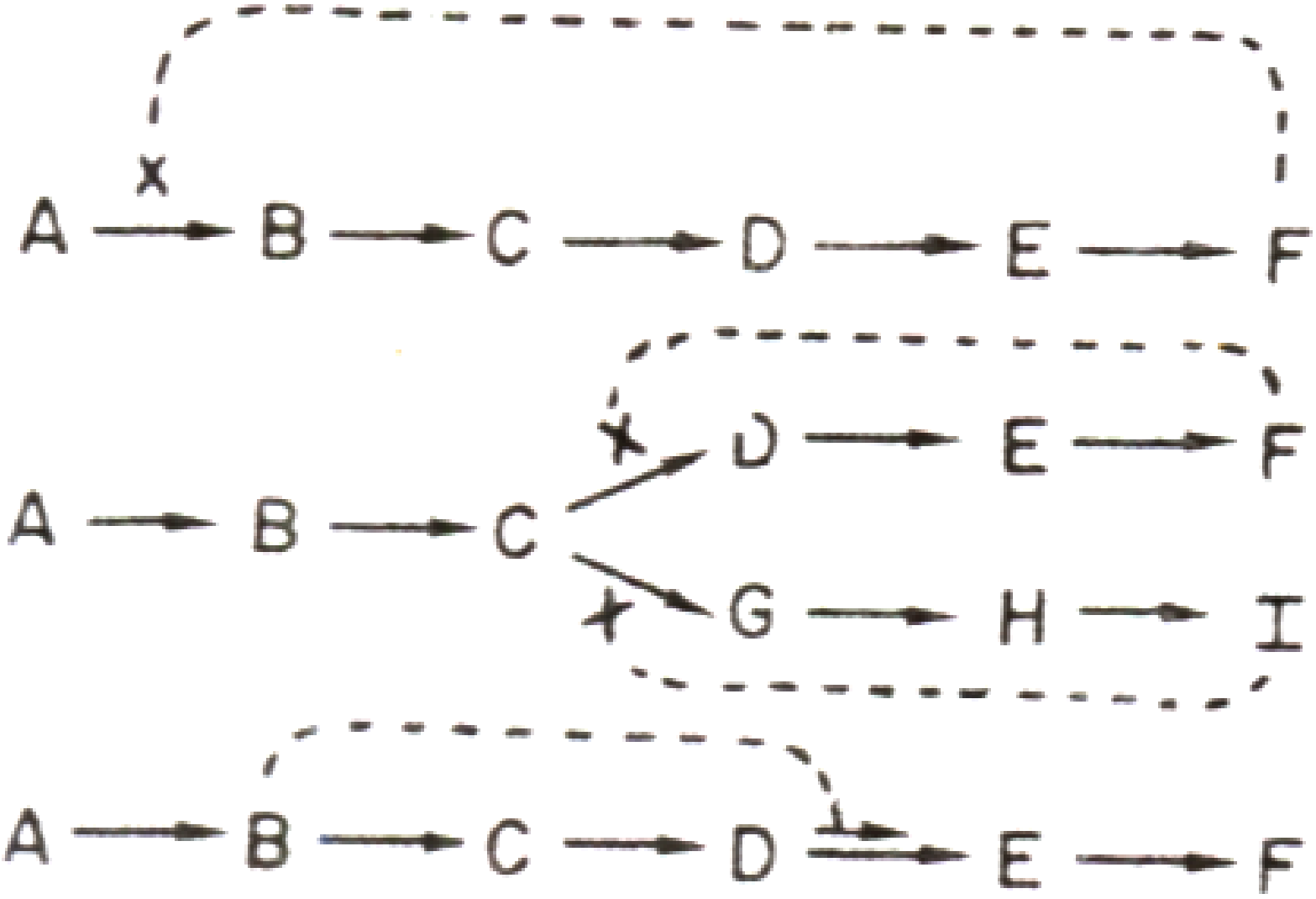
POSITIVE FEEDBACK (less common)

- The end product speeds up production



EXAMPLE: Chemicals released by platelets that accumulate at injury site, attract MORE platelets to the site.

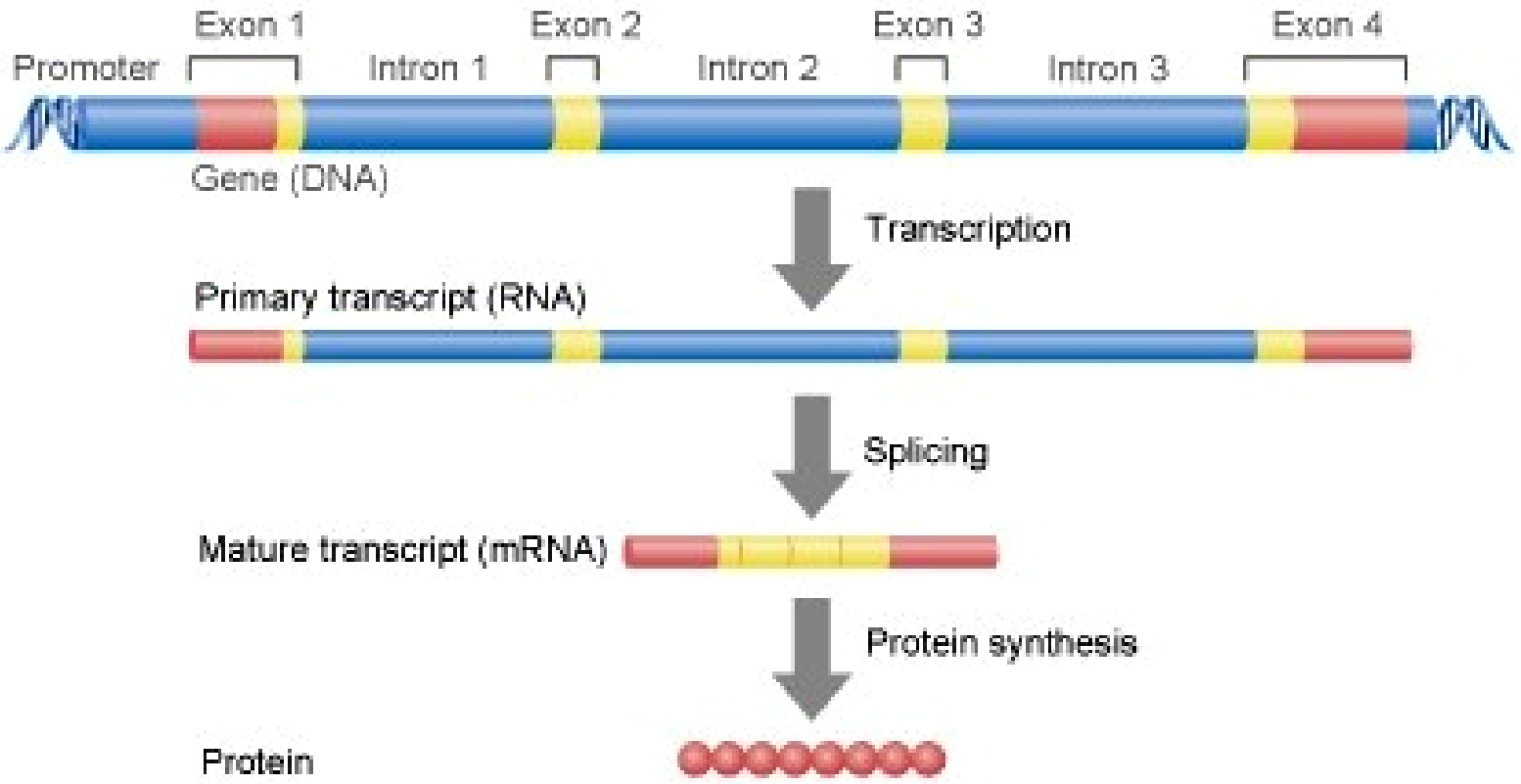
Modulation at enzyme



Model 2. Modulation at enzyme

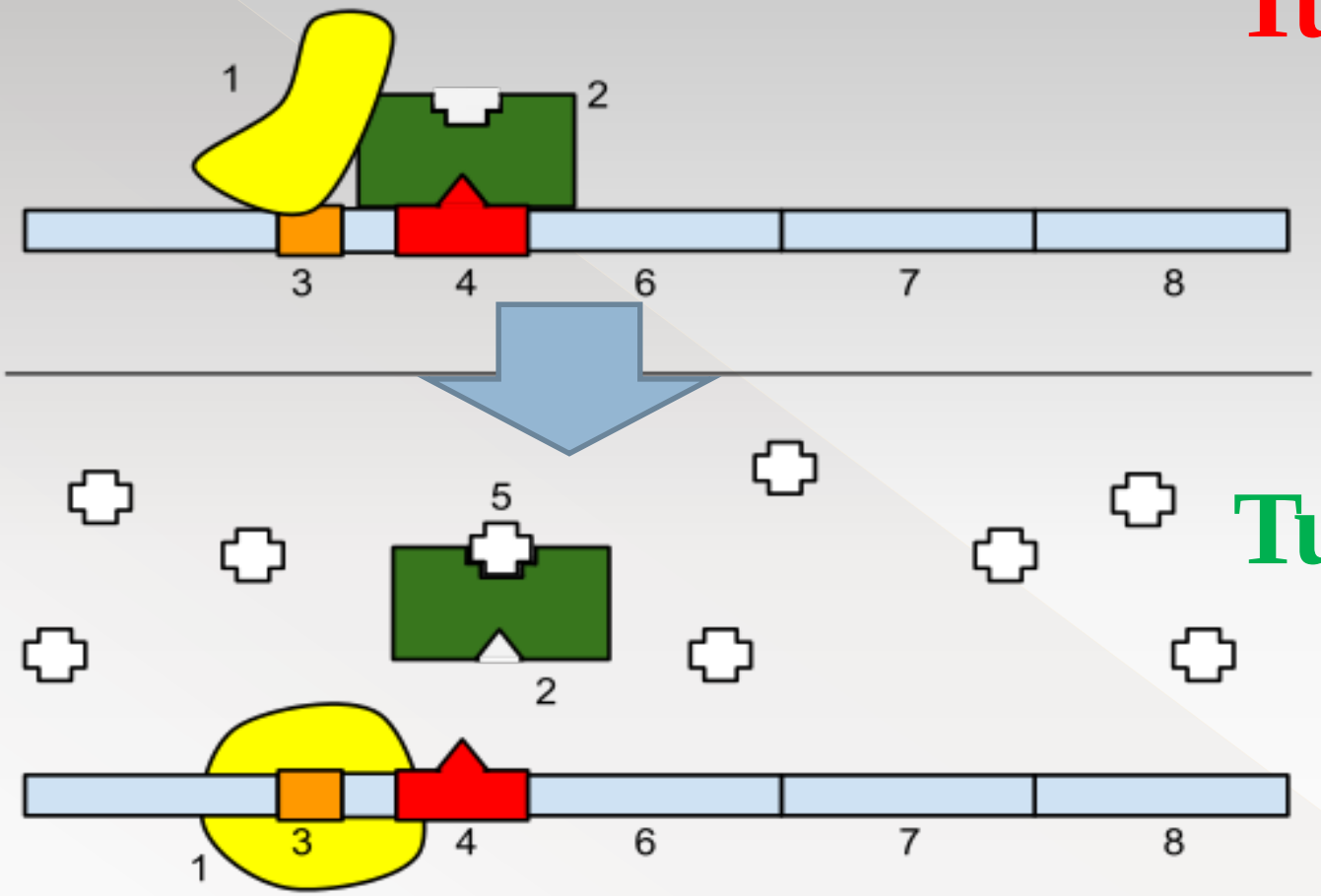
Model 2.2. Modulation at enzyme numbers

Type 1. Gene expression



ตย. Type 1. Gene expression

Turned off



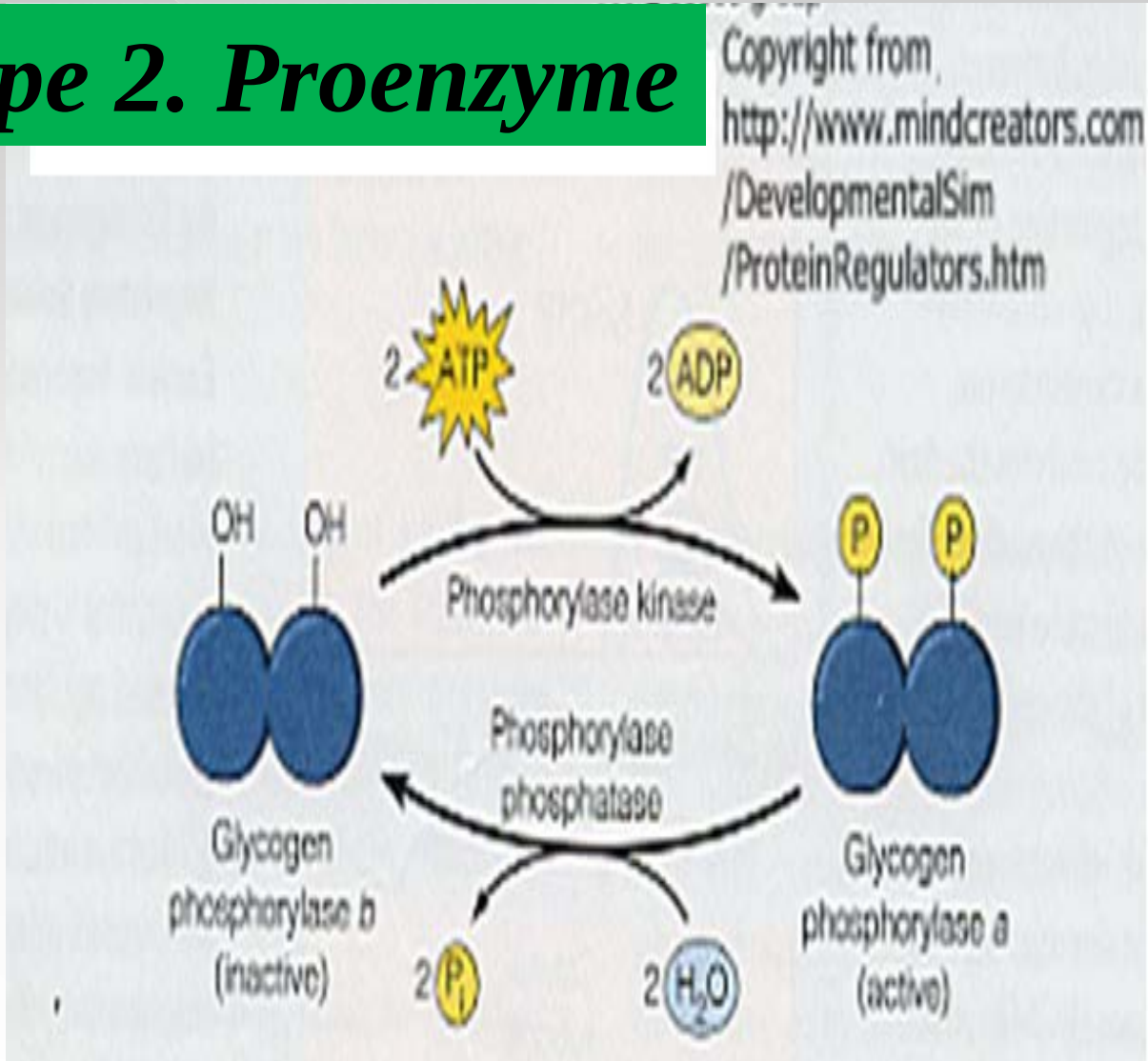
Turned on

***1*: RNA Polymerase, *2*: Repressor, *3*: Promoter,**
***4*: Operator, *5*: Lactose, *6*: lacZ, *7*: lacY, *8*: lacA.**

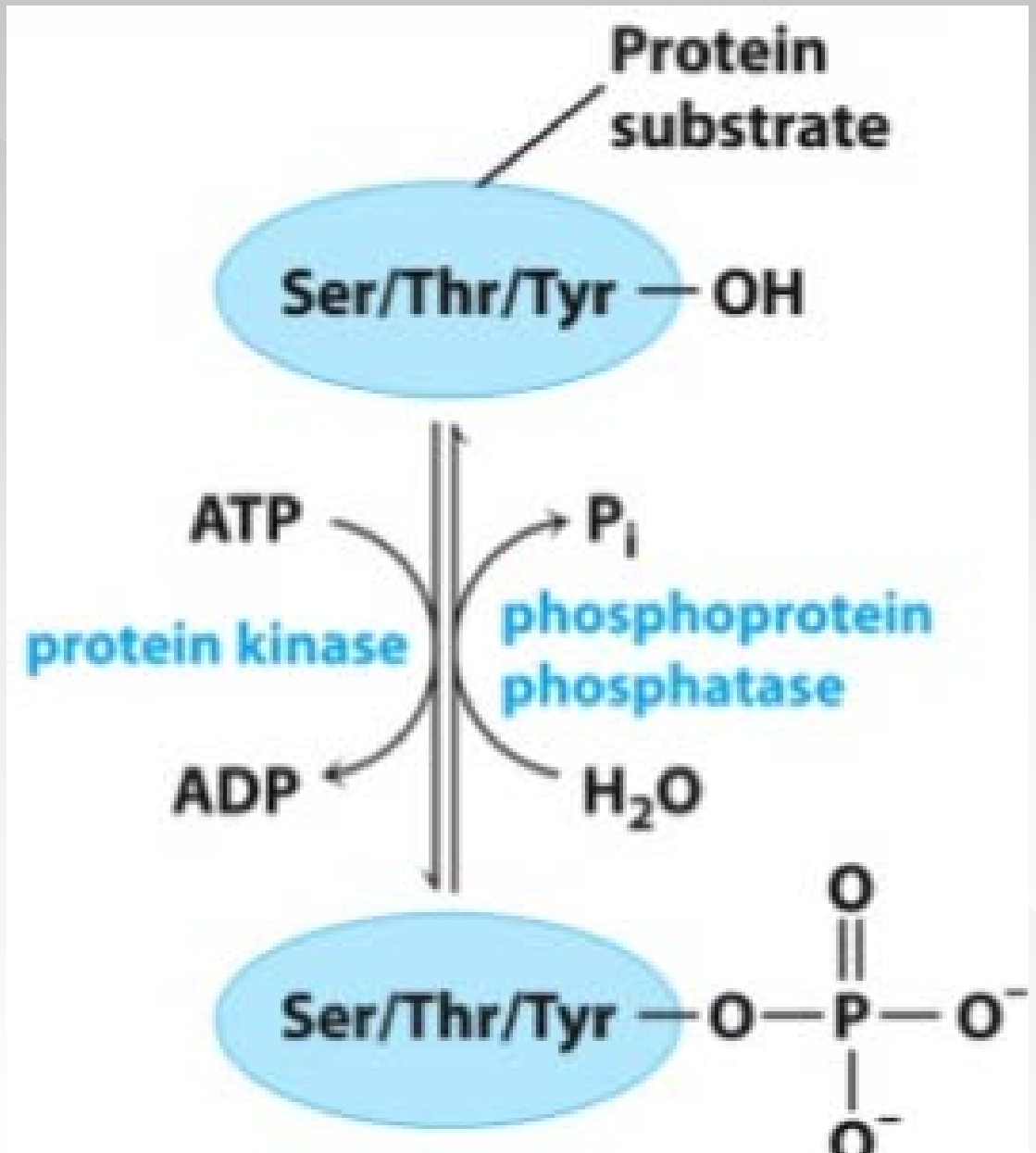
Model 2. Modulation at enzyme

Model 2.2. Modulation at enzyme numbers

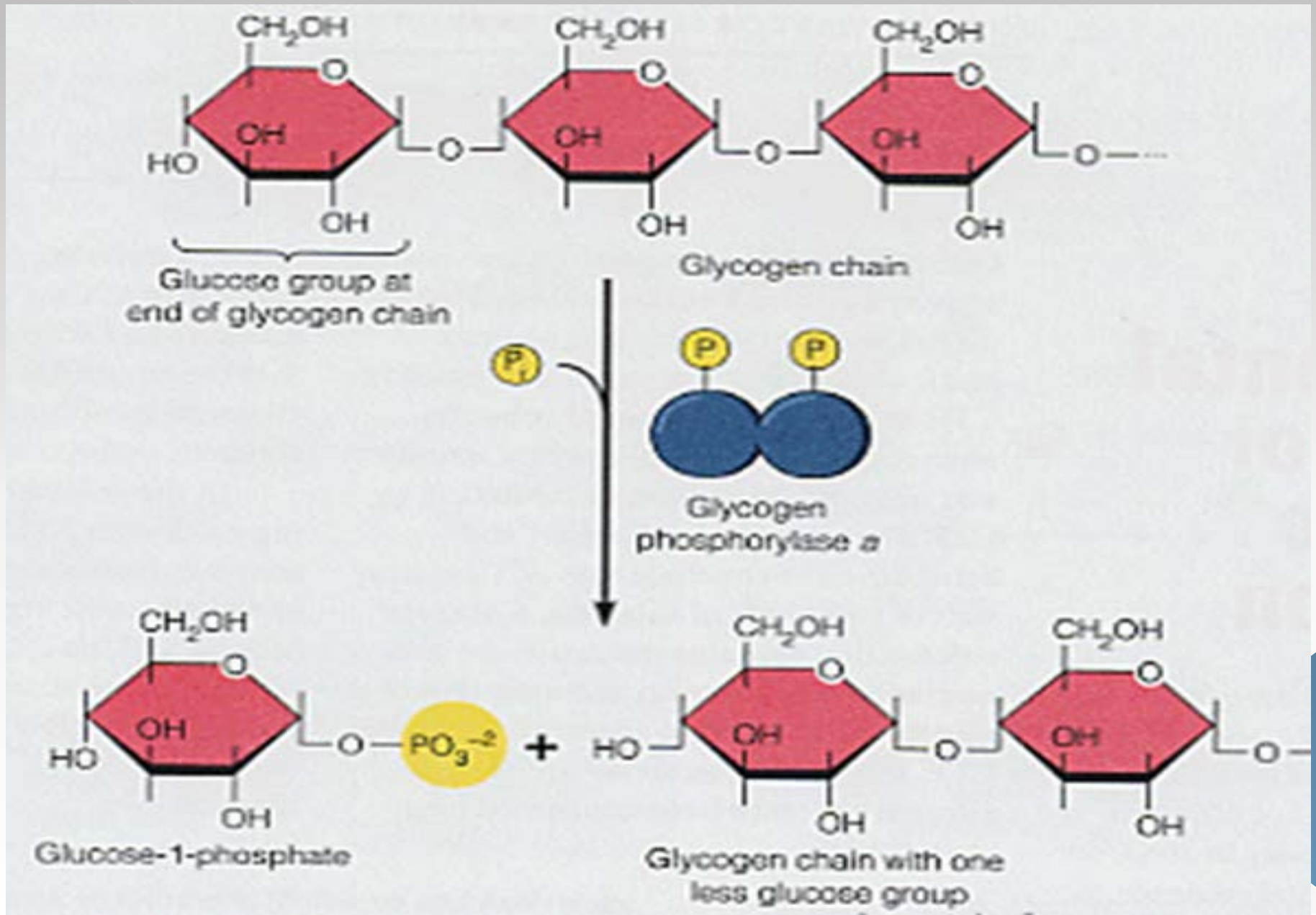
Type 2. Proenzyme



Phosphorylation of Enzyme affects their activity



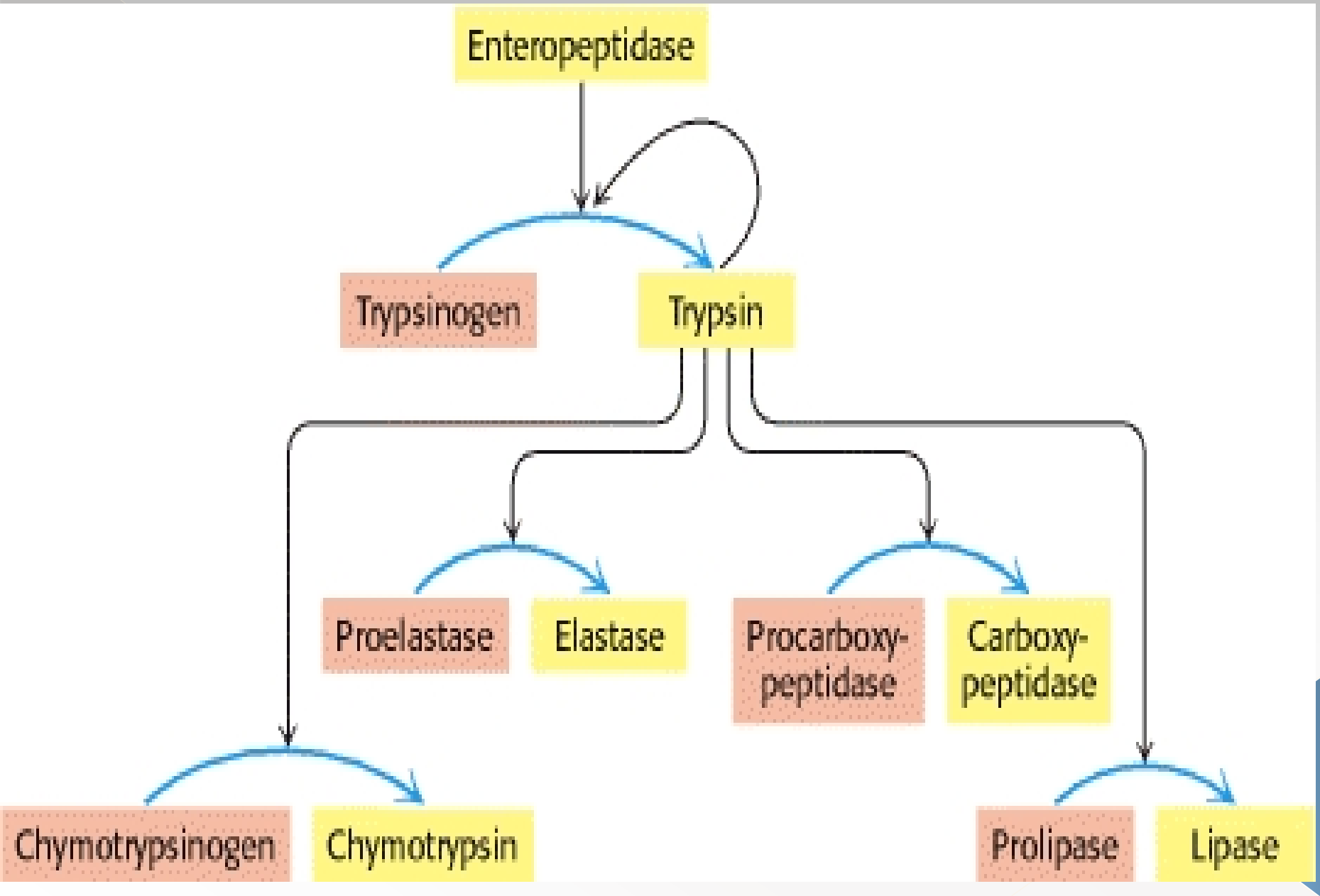
Proenzyme with phospholytic activation



Proenzyme with proteolytic activation

Site of synthesis	Zymogen	Active enzyme
Stomach	Pepsinogen	Pepsin
Pancreas	Chymotrypsinogen	Chymotrypsin
Pancreas	Trypsinogen	Trypsin
Pancreas	Procarboxypeptidase	Carboxypeptidase
Pancreas	Proelastase	Elastase

Proteolytic Activation of Digestic Enzyme




Thank You
For Your Atten