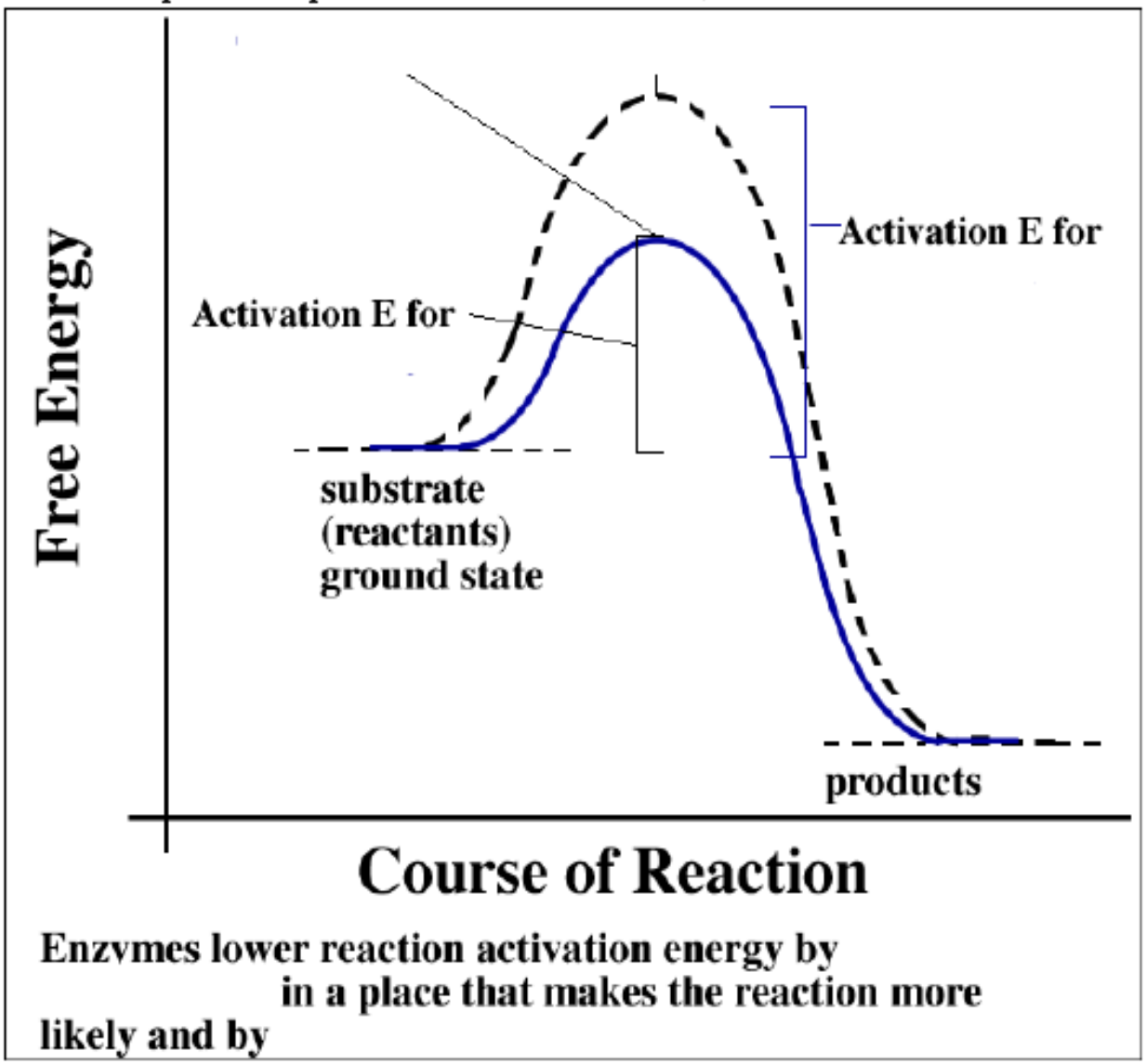
Lecture 7: Enzymes and an Introduction to Metabolism

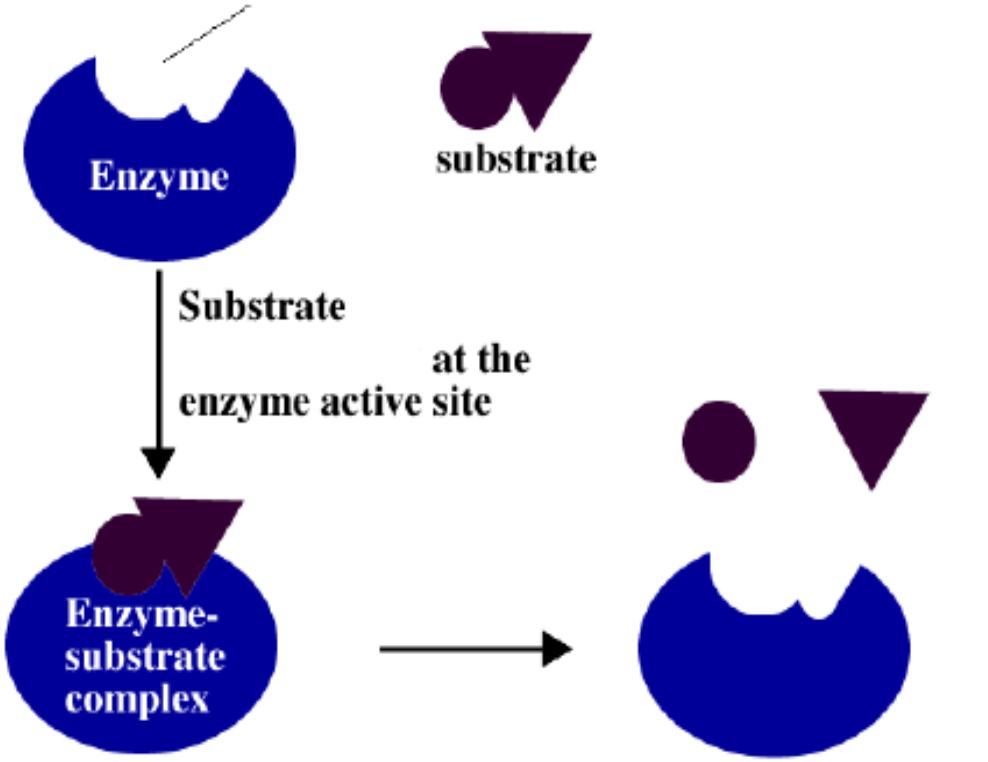
I. Enzymes

A. Mechanisms of Enzyme Action

1. Enzymes act as biological by to permit product formation ( ).



Enzymes lower reaction activation energy by in a place that makes the reaction more likely and by

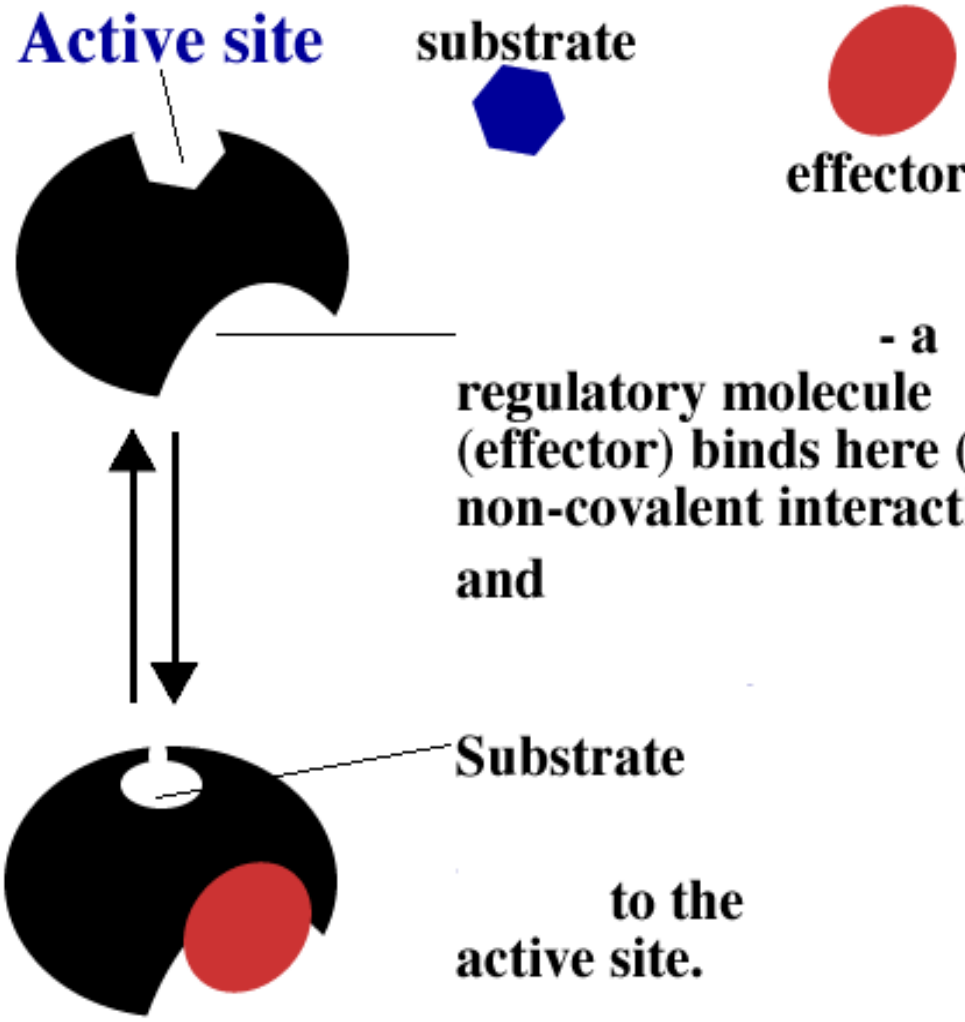


The enzyme either fits the substrate precisely ( ) or the enzyme undergoes a slight confromational change (shown here).

The substrate is held by the enzyme in a specific way so that the reaction and the products are formed.

The and the enzyme is

*Sometimes different enzymes recognize the (e.g. branching points in a pathway) but they and convert it to different products.

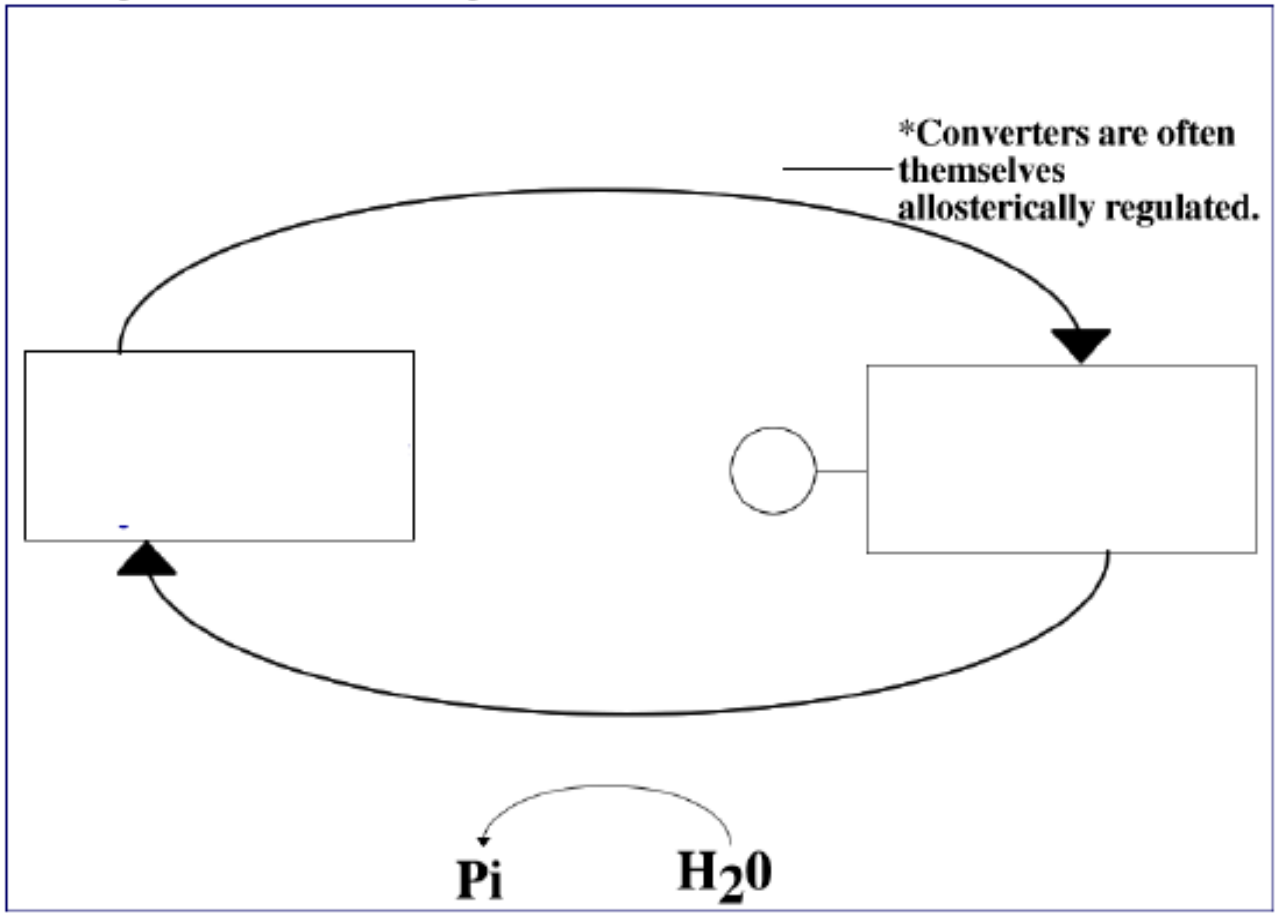


***In this case the allosteric regulator is an**

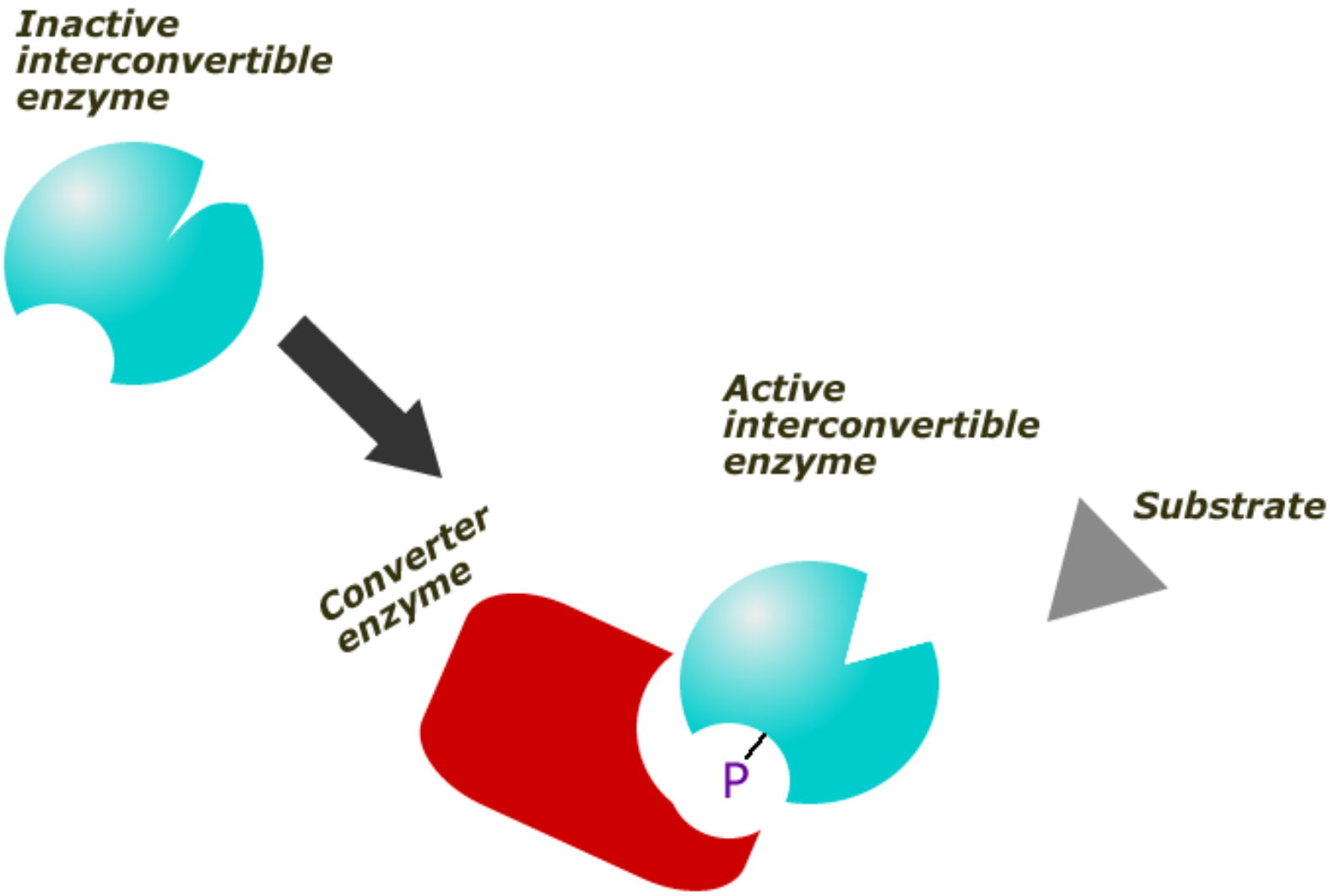
of many metabolic / biosynthetic pathways serve as allosteric regulators for enzymes in the pathways that produce them. This is called or end product inhibition.

2. Covalent modification -

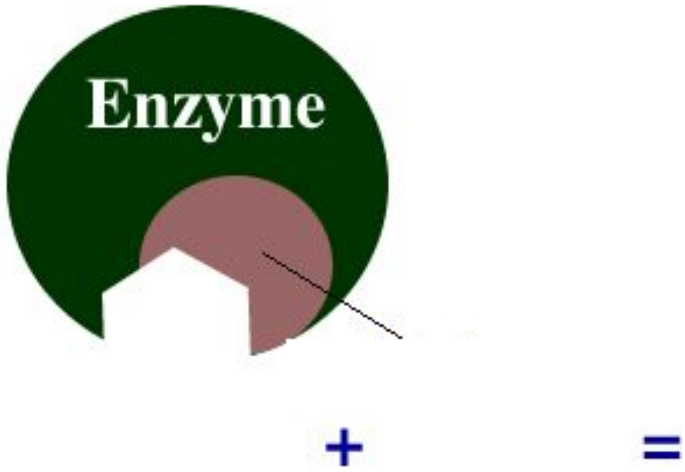
Enzymes regulated this way are called interconvertible enzymes and are modified by converter enzymes.

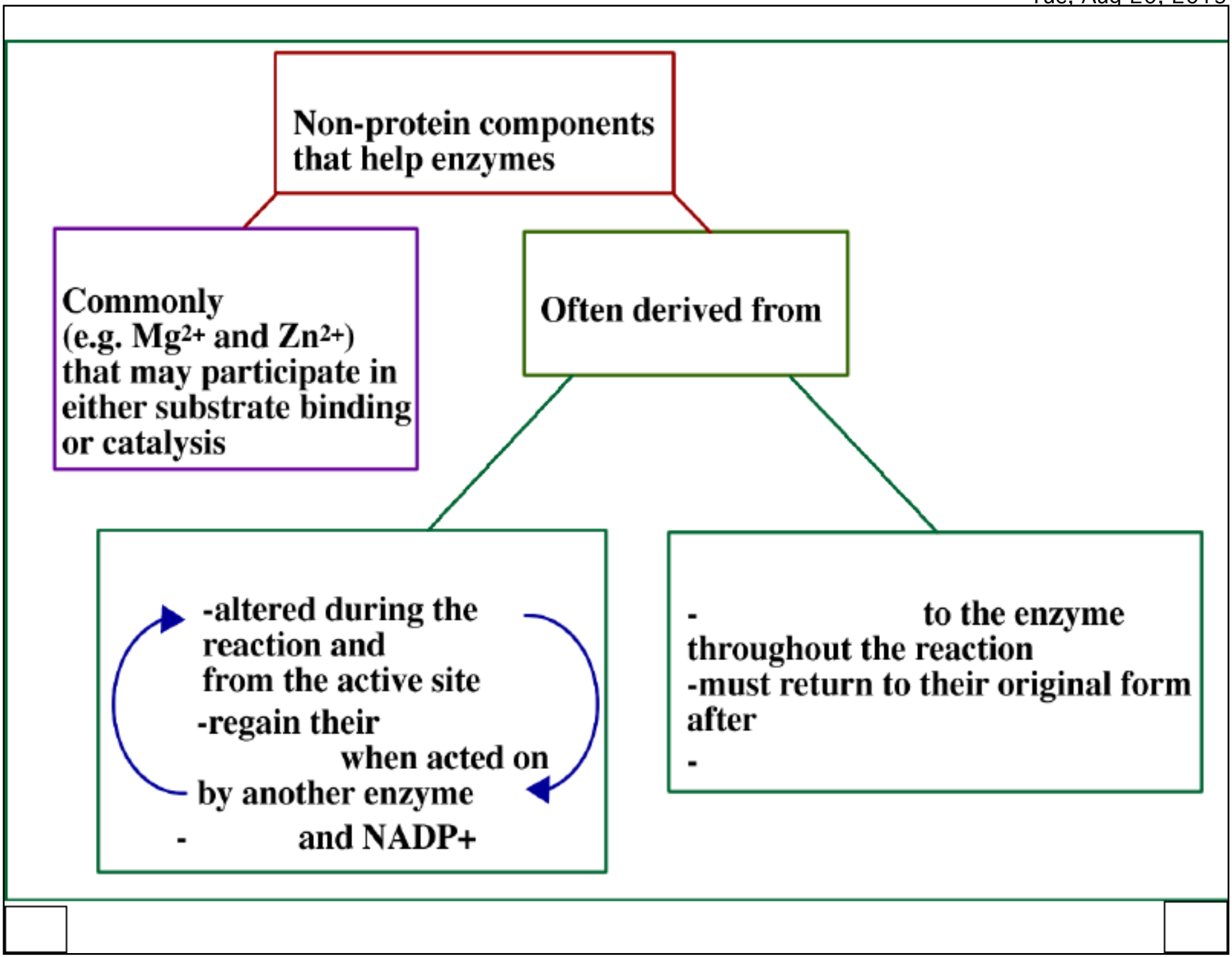


Regulated enzymes usually catalyze steps in a pathway or steps that These enzymes are often catalyzing the rate-limiting step of the pathway. Regulation of these enzymes reduces wasteful synthesis or degradation of metabolites are also often regulated to coordinate synthesis of multiple products.


Inactive interconvertible enzyme
Converter enzyme
Active interconvertible enzyme
Substrate
P

C. Cofactors

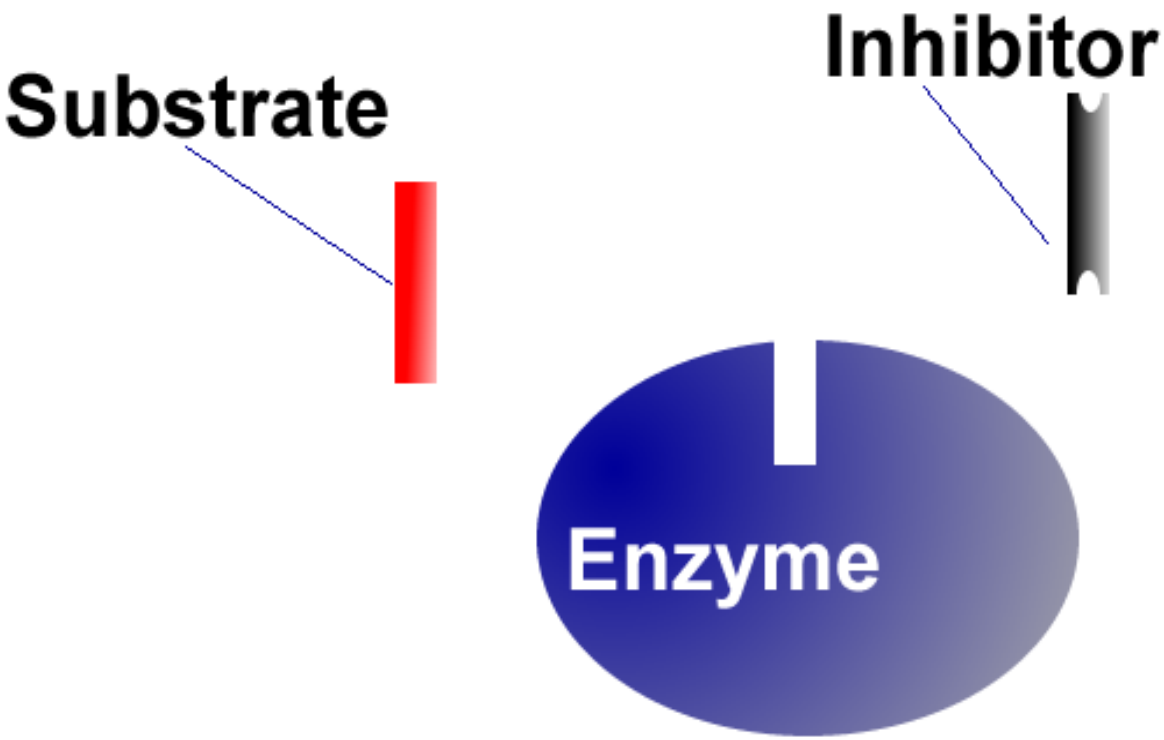



Non-protein components that help enzymes
Commonly (e.g. Mg^{2+} and Zn^{2+}) that may participate in either substrate binding or catalysis
Often derived from
-altered during the reaction and from the active site
-regain their when acted on by another enzyme
- and NADP+
- to the enzyme throughout the reaction
-must return to their original form after
-

D. Enzyme inhibition

1. Competitive inhibition

The inhibitor for binding to the active site.



Many drugs that are designed to kill or inhibit the growth of microorganisms are competitive enzyme inhibitors. The competitively inhibit an enzyme involved in the production of (a vitamin only synthesized by bacteria).

Analogues of what molecules make good competitive inhibitors? Why?

2. Noncompetitive inhibition

The inhibitor and substrate act at . Toxic heavy metals (e.g. mercury) are noncompetitive inhibitors.

3. Irreversible inhibition

a. The inhibitor binds to the enzyme causing irreversible damage.

b. is an irreversible inhibitor of some enzymes involved in cell wall synthesis.

4. Reversible inhibition

Inhibitor binds to the enzyme in a , leaving the enzyme .

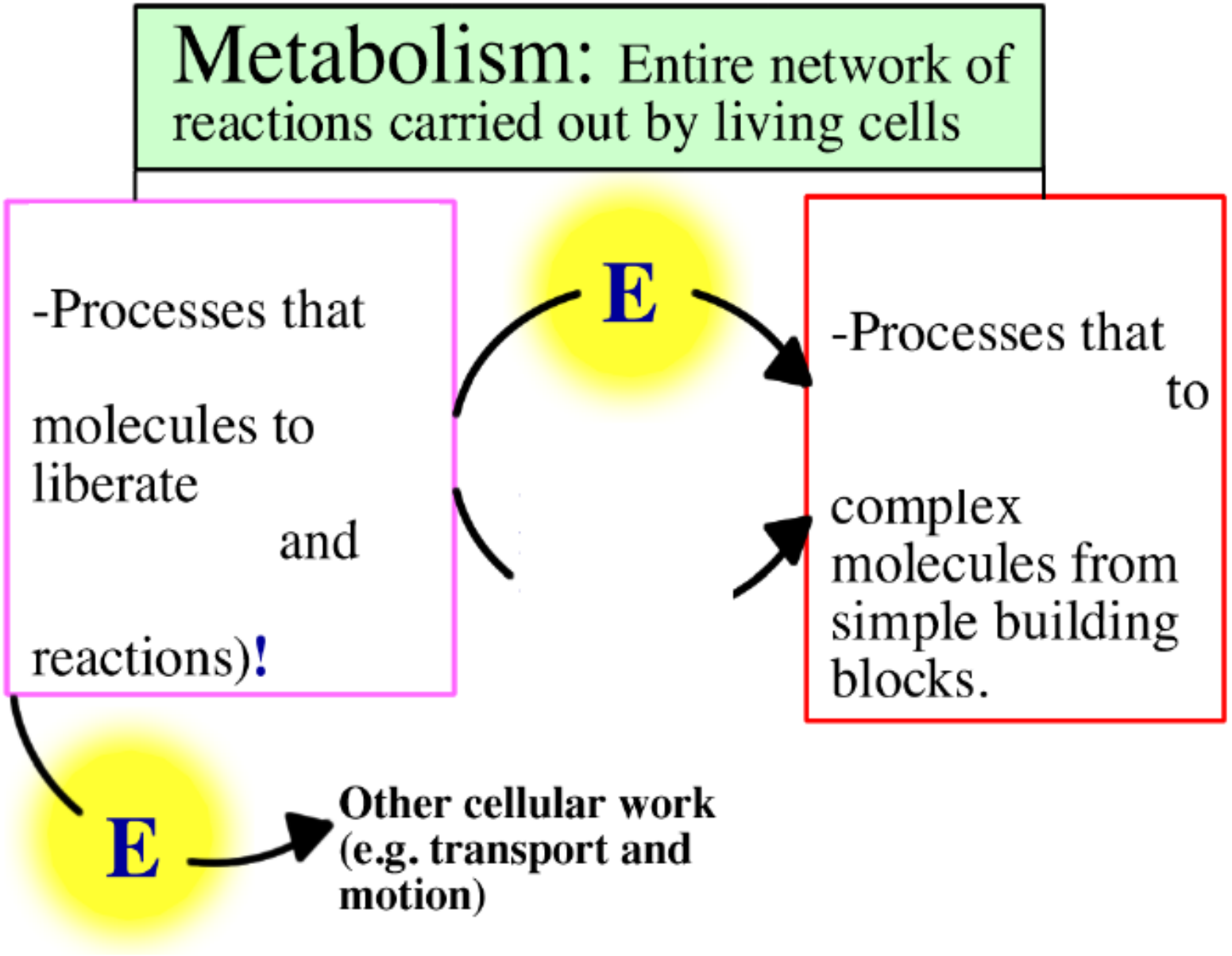
It wasn't until 1897, after much work by two talented chemists (Louis Pasteur and Eduard Buchner), that it was shown that it was yeast cells that convert sugar to CO_2 and alcohol in the production of wine.

Picture taken by Rachel in Cantebury, England (summer 2008)

How do the yeast cells benefit from the production of alcohol??

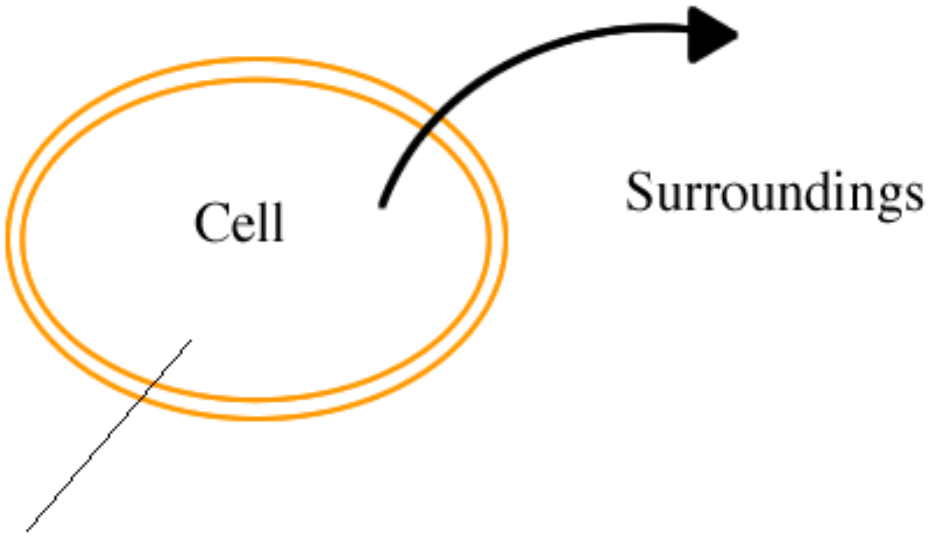
II. Metabolism: an overview

A. Two processes



B. Free-energy change

1. The of Thermodynamics - Energy can be converted from one form to another but it



The energy of the cell is called its . If the cell looses or gains energy, its total (ΔE). In biological systems the ΔE is due to that occur in which bonds are broken and new bonds reformed. A results from these reactions, this is called ΔH. Therefore, .

2. The of Thermodynamics - All natural processes proceed such that the disorder of the universe is . is a measure of the disorder of a system.

3. Gibb's Free Energy (ΔG) - an expression for the overall spontaneity of a reaction.

Enthalpy change

ΔG =

Entropy change

ΔG =

a. If , the reaction is and the cell looses energy = (energy yielding) process.

b. If , the reaction is The cell must gain energy in order for the reaction to proceed = (energy requiring) process.

4. ΔG depends on reaction conditions and therefore we have a set of reference conditions called the .

   T = 298 K (25°C)

   P = 1 atm

   [solute] = 1M

   ΔG under standard state is denoted

*A slight modification for biochemistry assumes that the [H+] = 1 X 10^{-7} M rather than 1 M.

ΔG under biological standard state is denoted

III. The big picture - Solar energy (kinetic energy) is trapped by photosynthetic microorganisms (photoautotrophs) and used to synthesize organic molecules (e.g. glucose). In this process, the

. Chemoheterotrophs degrade these organic molecules, allowing them .

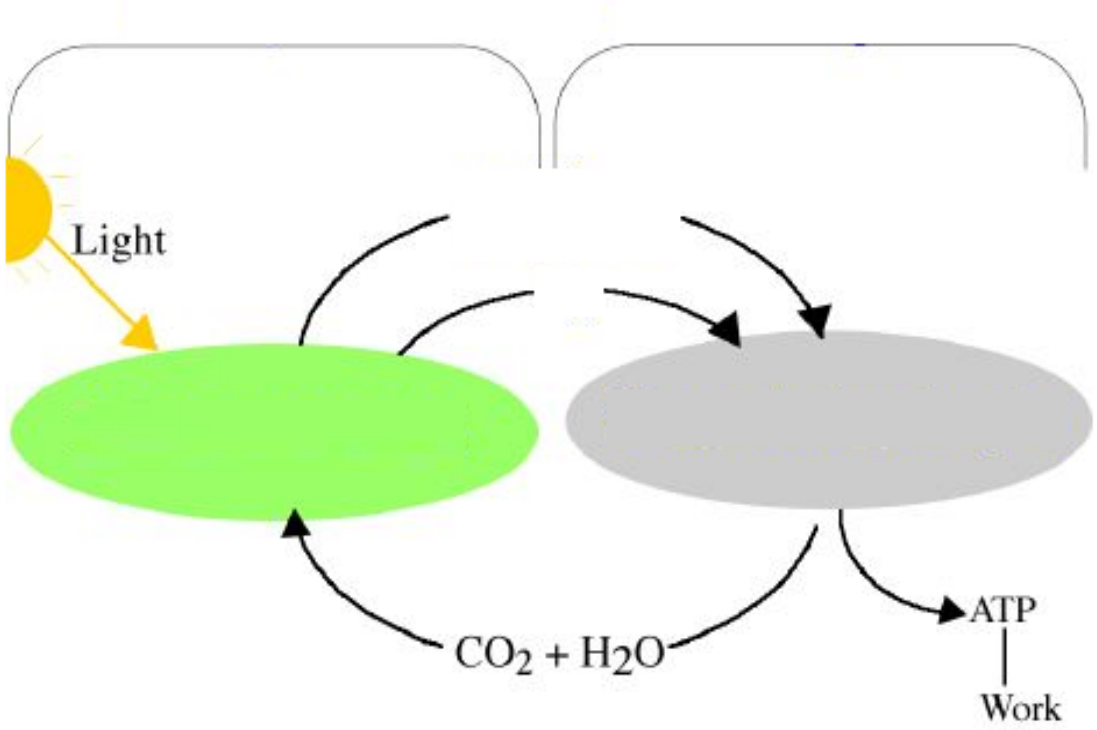
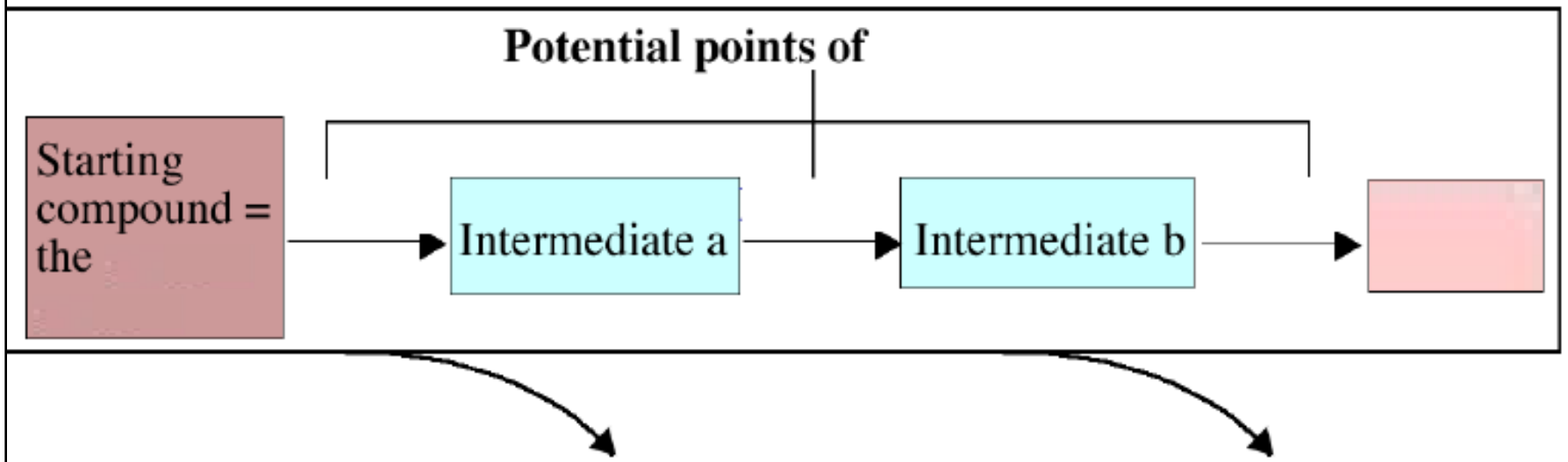


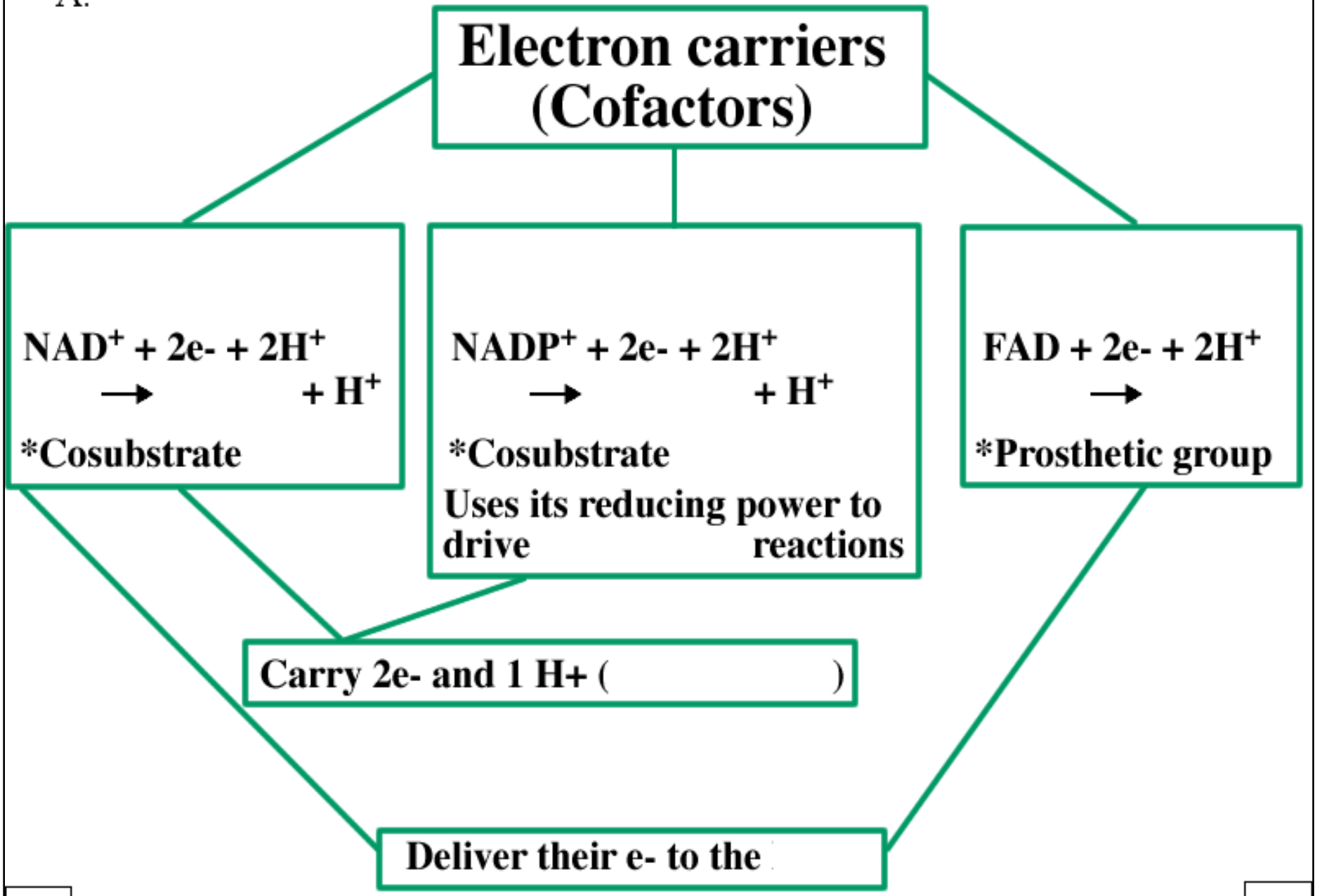
Figure adapted from Shelly Robertson's General Micro lecture notes

IV. = a series of sequential chemical reactions that are symphonically regulated to meet the ever-changing needs of a cell.



The source is broken down by and thus . These molecules can later be used to generate ATP.

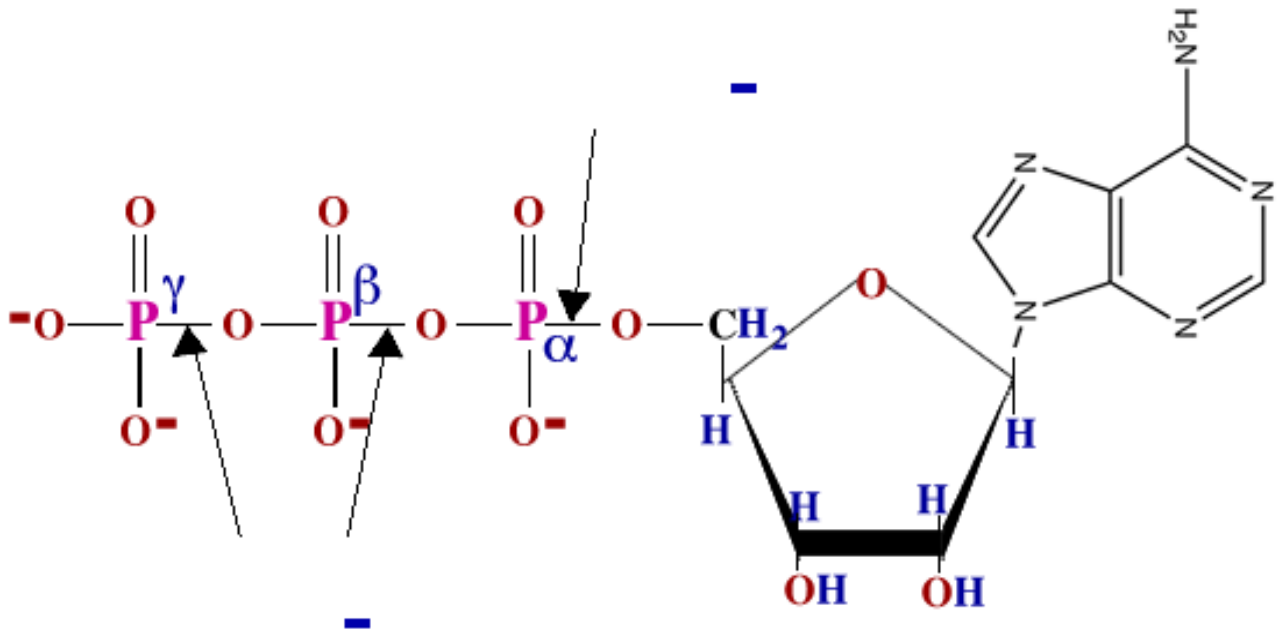
A.


Electron carriers (Cofactors)
NAD+ + 2e- + 2H+ → + H+
*Cosubstrate
NADP+ + 2e- + 2H+ → + H+
*Cosubstrate
Uses its reducing power to drive reactions
FAD + 2e- + 2H+ →
*Prosthetic group
Carry 2e- and 1 H+ ( )
Deliver their e- to the

*NADH and $FADH_2$ have less desire for their electrons (lower) than do the later components of the ETC (Table 9.1 (8th ed.) or 10.2 (9th ed.)). Thus electrons are transferred from these carriers to ETC carriers (like an electron relay team). This releases energy that can be used to pump protons and eventually make ATP! Because of this, we often say that NADH and $FADH_2$ have reducing power! They are one form of energy currency that can be exchanged for another form of energy currency (ATP) at the ETC 'bank'.

Standard reduction potentials of some important biological half-reactions	
Reduction Half Reaction	**$E^{o'}$ (V)**
Acetyl CoA + CO_2 + H^+ + $2e^-$ ---> pyruvate + CoA	-0.48
NADP+ + $2H^+$ + $2e^-$ ---> NADPH + H^+	-0.32
NAD+ + $2H^+$ + $2e^-$ ---> NADH + H^+	-0.32
FAD + $2H^+$ + $2e^-$ ---> $FADH_2$	-0.22
FMN + $2H^+$ + $2e^-$ ---> $FMNH_2$	-0.22
Acetaldehyde + $2H^+$ +$2e^-$ ---> Ethanol	-0.20
Pyruvate + $2H^+$ + $2e^-$ ---> Lactate	-0.18
Oxaloacetate + $2H^+$ + $2e^-$ ---> Malate	-0.17
Ubiquinone (Q) + $2H^+$ + $2e^-$ ---> QH_2	0.04
Cytochrome c, Fe^{3+} + e- ---> Fe^{2+}	0.23
1/2 O_2 + $2H^+$ + $2e^-$ ---> H_2O	0.82
*See table 9.1 in Prescott text	

B. The free-energy of ATP



1. Other nucleoside triphosphates (UTP, GTP and CTP) have $\Delta G^{o'}$ as ATP for analogous bonds.

*Why are the phosphoanhydride bonds so high in energy?

2. Hydrolysis of these bonds can be used to many endergonic reactions.

3. The phosphorylation of ADP to form ATP requires energy input!

Standard free energies of hydrolysis for common metabolites (adapted from Horton's Biochemistry)	
Metabolite	**$\Delta G^{o'}$hydrolysis (kJ mol^{-1})***
Phosphoenolpyruvate	-62
1,3-Bisphosphoglycerate	-49
phosphocreatine	-43
Succinyl-CoA	-32
ATP to ADP + Pi	-30
Glucose 1-phosphate	-21
Glucose 6-phosphate	-14

These groups have have high phosphoryl-group transfer potentials. They can

**Note that the tabulated values are for break-down (hydrolysis) of each metabolite. If the reaction indicates a synthesis of the metabolite, an equivalent amount of free energy must be input. For example, consider the following reaction: ATP + Glucose ---> Glucose 6-phosphate + ADP. Since ATP is broken down (hydrolyzed), 30 kJ/mol are liberated (-30 kJ/mol). Glucose 6-phosphate, however is synthesized. Thus, 14 kJ/mol are consumed (+14 kJ/mol). Thus, to calculate the overall free energy change: -30 kJ/mol + 14 kJ/mol = -16 kJ/mol*

Use the table of phosphoryl group transfer potentials to answer the following question:

In the following reaction, 1,3-Bisphosphoglycerate is transferring a phosphoryl group to ADP to make ATP:

1, 3-Bisphosphoglycerate + ADP ----> 3-Phosphoglycerate + ATP

Which statement/s is / are TRUE?

a. The overall deltaG°' for this reaction is -19 kJ/mol.
b. ATP is generated in this reaction via substrate-level phosphorylation.
c. This reaction is endergonic.
d. a and b
e. b and c

V. Major pathways in cells