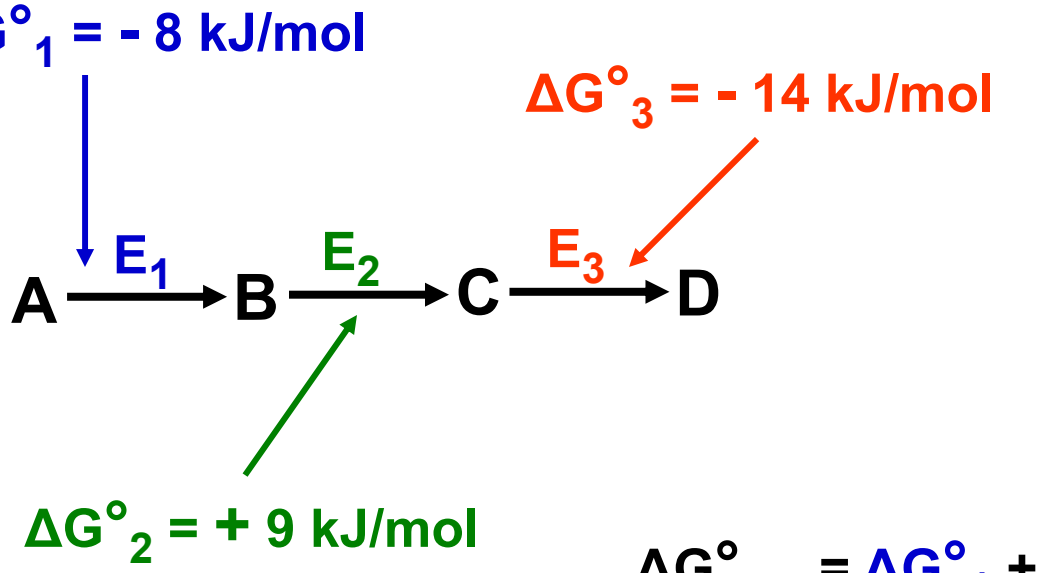
BIO 311C
Spring 2010

Lecture 25 – Wednesday 31 Mar.

A metabolic pathway must have a net negative ΔG value in order to progress in the forward direction. However, it is not necessary for every reaction in the pathway to have a negative ΔG° value in order for the pathway to proceed in the forward direction.



$\Delta G^\circ_{net} = \Delta G^\circ_1 + \Delta G^\circ_2 + \Delta G^\circ_3$

$= (-8 + 9 - 14)$ kJ/mol $= -13$ kJ/mol

Reaction 1 "pushes" reaction 2 in the forward direction.
Reaction 3 "pulls" reaction 2 in the forward direction.

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Most metabolic pathways fall into two broad categories:

- **Catabolic pathways**
- **Anabolic pathways**

Catabolic pathways may be described as "breakdown" pathways.

Anabolic pathways may be described as "build-up" pathways.

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General Characteristics of Catabolic Pathways

- Catabolic pathways result in the conversion of relatively large and/or complex initial reactant into smaller and/or simpler final products.

- Individual reactions of catabolic pathways often result in a substrate becoming more oxidized as hydrogen atoms are removed.

- Individual reactions of catabolic pathways pathway often release enough energy that a portion of the energy can be captured by the synthesis of ATP or can be stored in another form.

- The final products of catabolic pathways are generally of less potential value to the cell than was the starting reactant.

Not all catabolic pathways display all four of these listed features.

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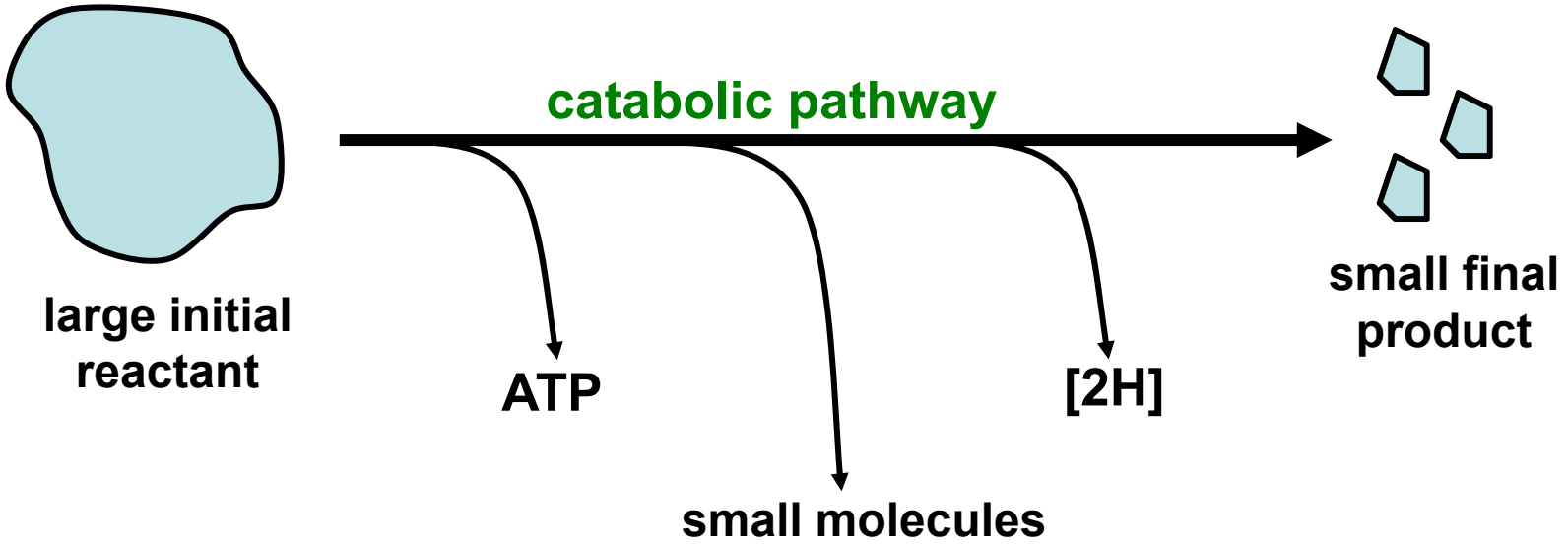
Representation of a Catabolic Pathway



The main value to cells of most catabolic pathways is the capture of energy and reducing units. The small and oxidized final products are often discarded as waste.

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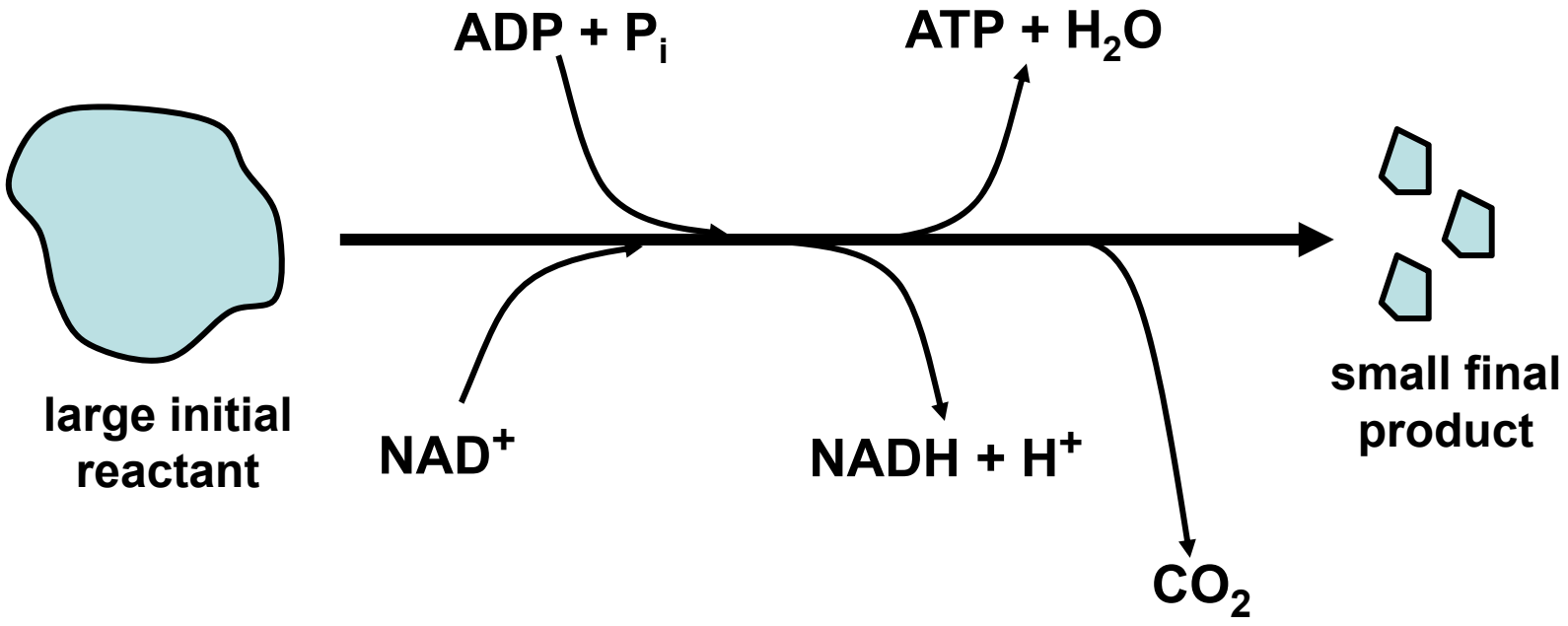
Example of a Catabolic Pathway (shown in more detail)



Written as an equation:

$$\text{(large rct.)} + (ADP + P_i) + NAD^+ \xrightarrow[\textit{pathway}]{\textit{catabolic}} \text{(small prod.)} + (ATP + H_2O) + (NADH + H^+) + CO_2$$

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General Characteristics of Anabolic Pathways*

- Anabolic pathways result in the conversion of relatively small and/or simple reactant(s) into a larger and/or more complex final product.

- Individual reactions of anabolic pathways often result in a substrate incorporating hydrogen atoms to become more reduced.

- Individual reactions of anabolic pathways often require energy that is supplied by the hydrolysis of ATP, or by another source of metabolic energy.

- The final products of anabolic pathways are of more value to the cell than were the starting reactants.

*Not all anabolic pathways display all four of these listed features.

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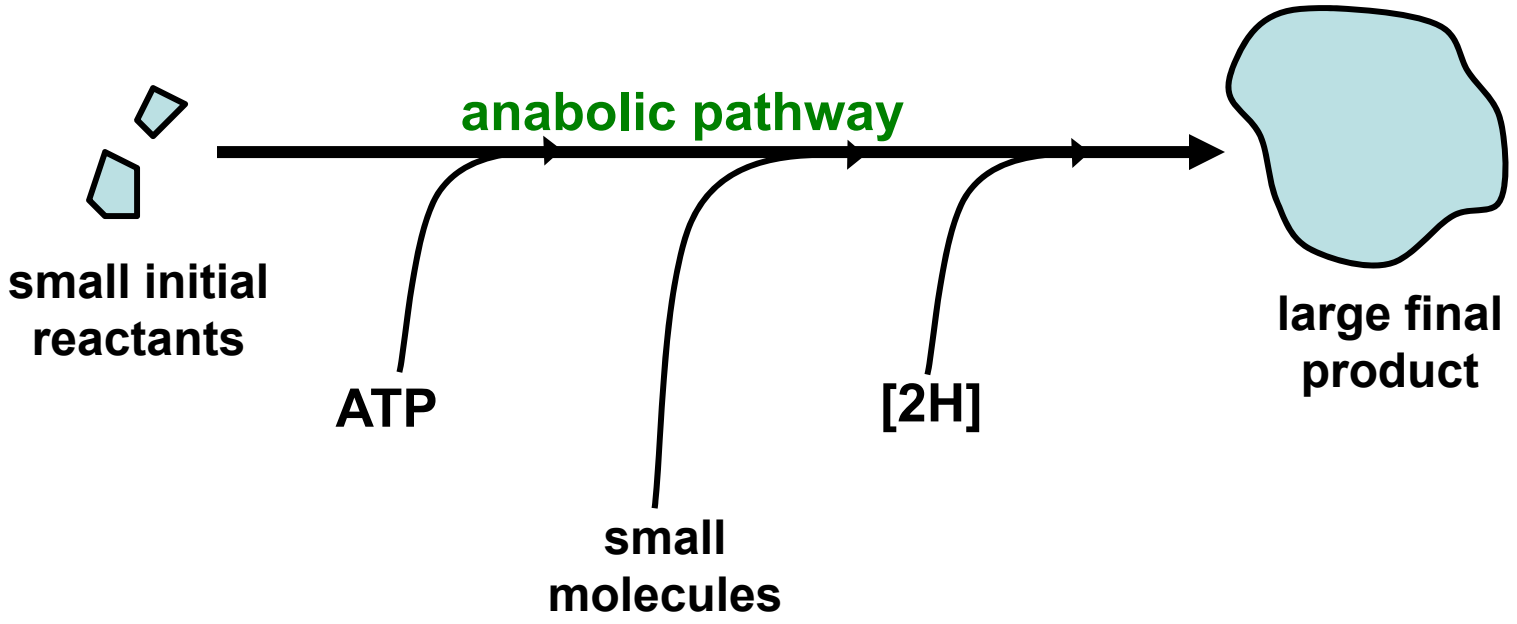
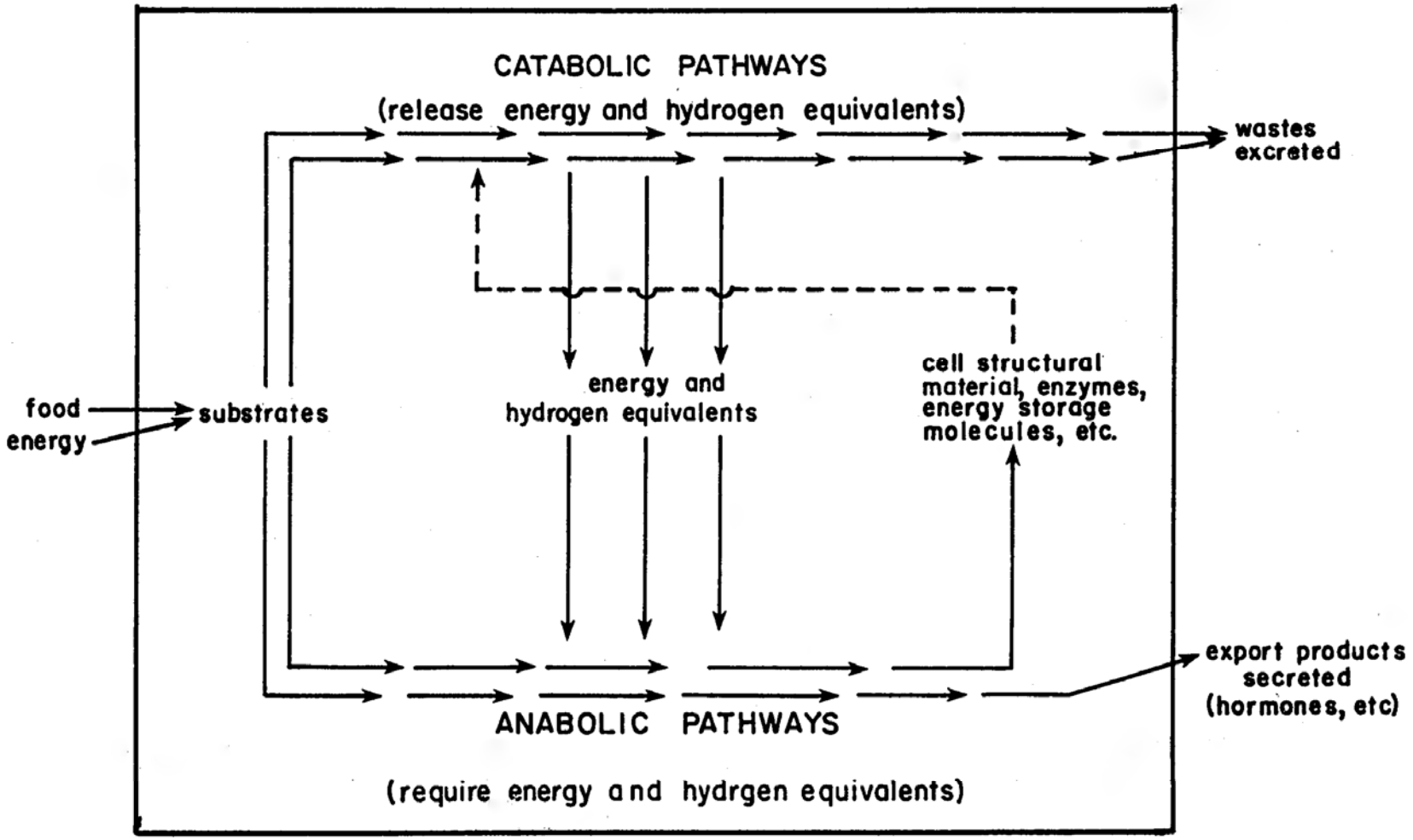
Representation of an Idealized Anabolic Pathway



The main value to cells of most anabolic pathways is the resulting final product, which is often used as a building material or to perform some function in the cell.

You should be able to show in more detail an example of an anabolic pathway, as was shown for a catabolic pathway. *

Summary of Metabolism in a Living Cell



GENERALIZED CELL

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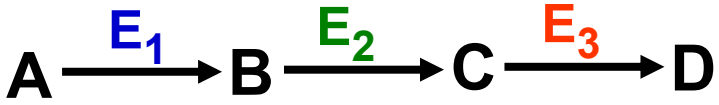
The basic unit of regulation of cellular metabolism is the metabolic pathway.



Two Mechanisms of Regulation of Metabolic Pathways

- Control of Enzyme Expression
  (Induction or Repression)

- Control of Enzyme Function
  (Allosteric Activation or Inhibition)

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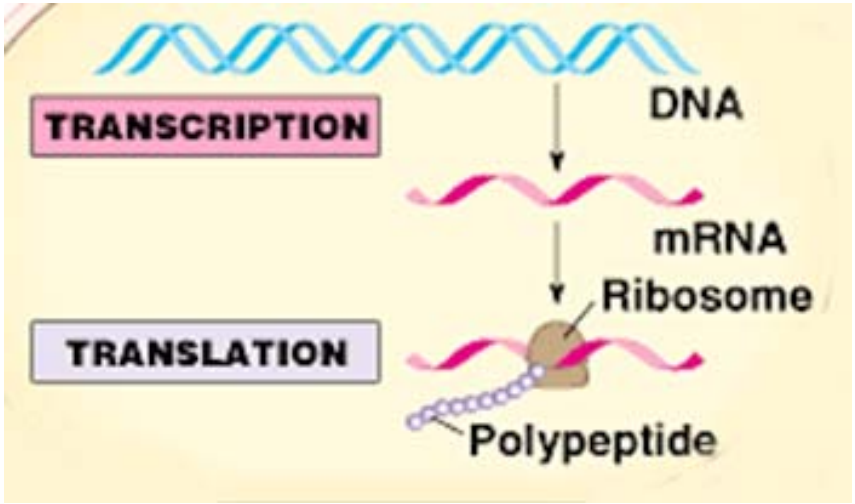
All proteins in all cells are synthesized by the same general mechanism, sometimes called the Central Dogma of Molecular biology.

From textbook Fig. 17.3, p. 329

Transcription is the process whereby information content of DNA is converted into corresponding information of mRNA.



Translation is the process whereby information content of mRNA is converted into corresponding information of polypeptide chains.

(not shown) The molecules of mRNA that are produced from coded information of DNA are often modified prior to translation in a process called post-transcriptional processing. The polypeptides that are produced from coded information of mRNA and folded into proteins are often modified in order to become functional proteins in a process called post-translational processing.

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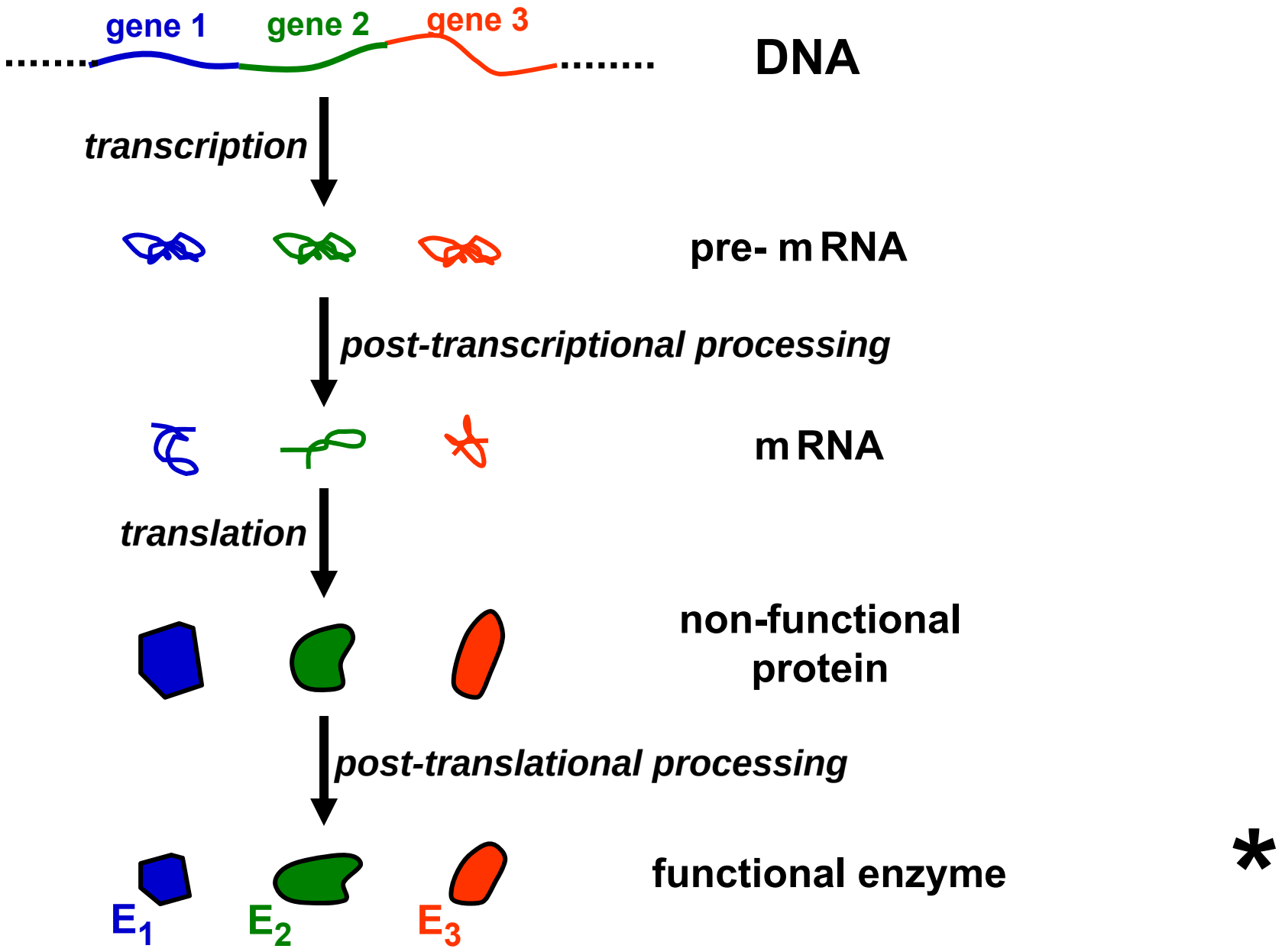
Steps in the Synthesis of Enzymes of a Metabolic Pathway



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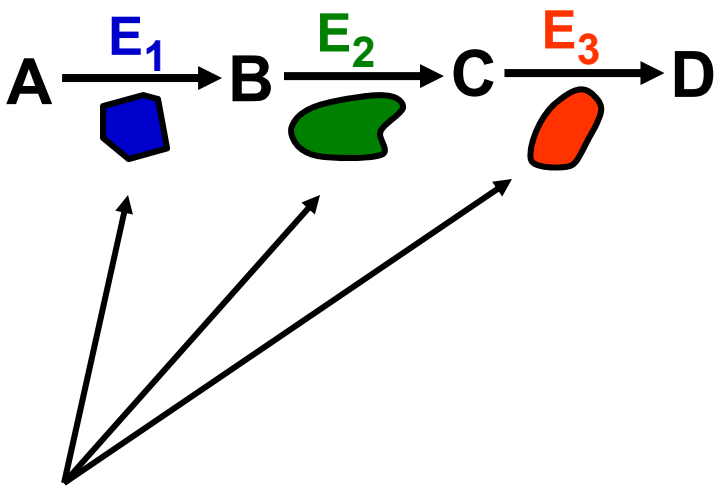
Induction or Repression



Repression is a decrease in the concentration of enzymes E_1, E_2 and E_3.
Induction is an increase in the concentration of enzymes E_1, E_2 and E_3.

Repression or induction can result from cellular regulation of transcription, post-transcriptional processing, translation or post-translational processing, any of which may affect the concentration of functional enzymes.

Typically the concentrations of all enzymes of a metabolic pathway are controlled together as a unit.

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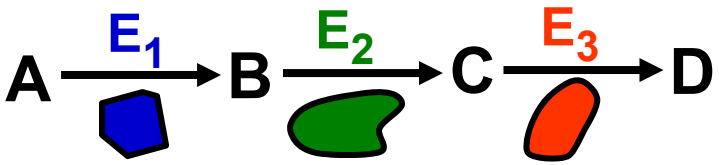
For the metabolic pathway shown, the higher the concentrations of Enzymes E_1, E_2 and E_3, the faster initial reactant A can be converted to final product D (providing that ample initial reactant "A" is available).



In a separate set of processes (not considered here), the rate of destruction of functional enzymes is also regulated in cells.

The steady-state concentration of an enzyme is the result of a balance between the rate of synthesis and the rate of degradation of the enzyme.

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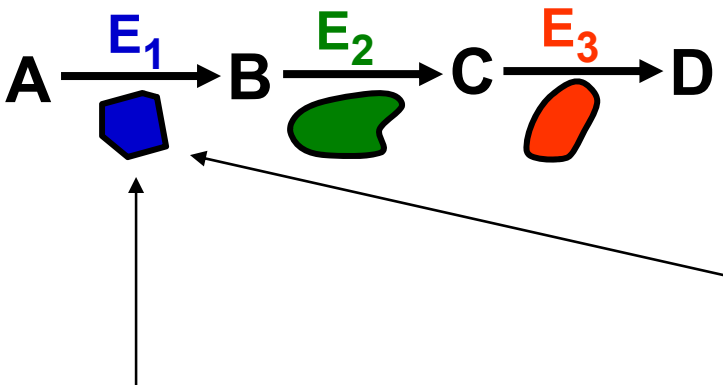
Activation and Inhibition describe a process that controls how rapidly the enzyme catalyzing the <u>first</u> reaction of a metabolic pathway can function.



Enzyme that catalyzes the first reaction.

In addition to its active site for binding substrate A, Enzyme E_1 has one or more allosteric (regulatory) sites to which an allosteric affector can bind.

When the allosteric affector binds to E_1, then the rate of catalysis of the reaction A ⟶ B is altered, so the rate of production of substrate B is altered. That, in turn, causes an altered rate of production of substrate C and final product D.

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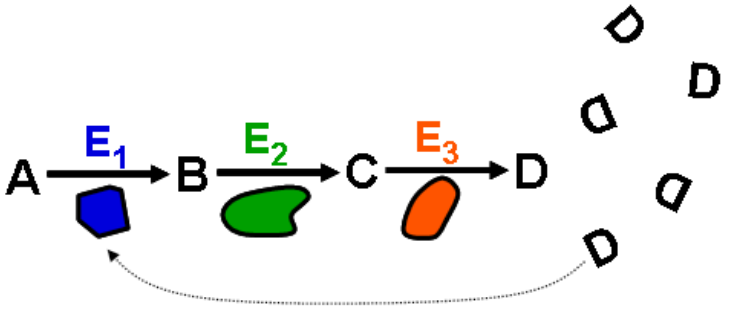
Feedback Inhibition
An Example of Allosteric Regulation



In this metabolic pathway, final product D is an allosteric inhibitor of Enzyme E_1. Final product D, at low concentrations, does not bind to E_1. But when D accumulates to high concentrations, it then effectively binds to an allosteric site on E_1, inhibiting E_1 function. That causes a slowdown or stoppage of production of B and all "downstream" substrates leading to final product D.

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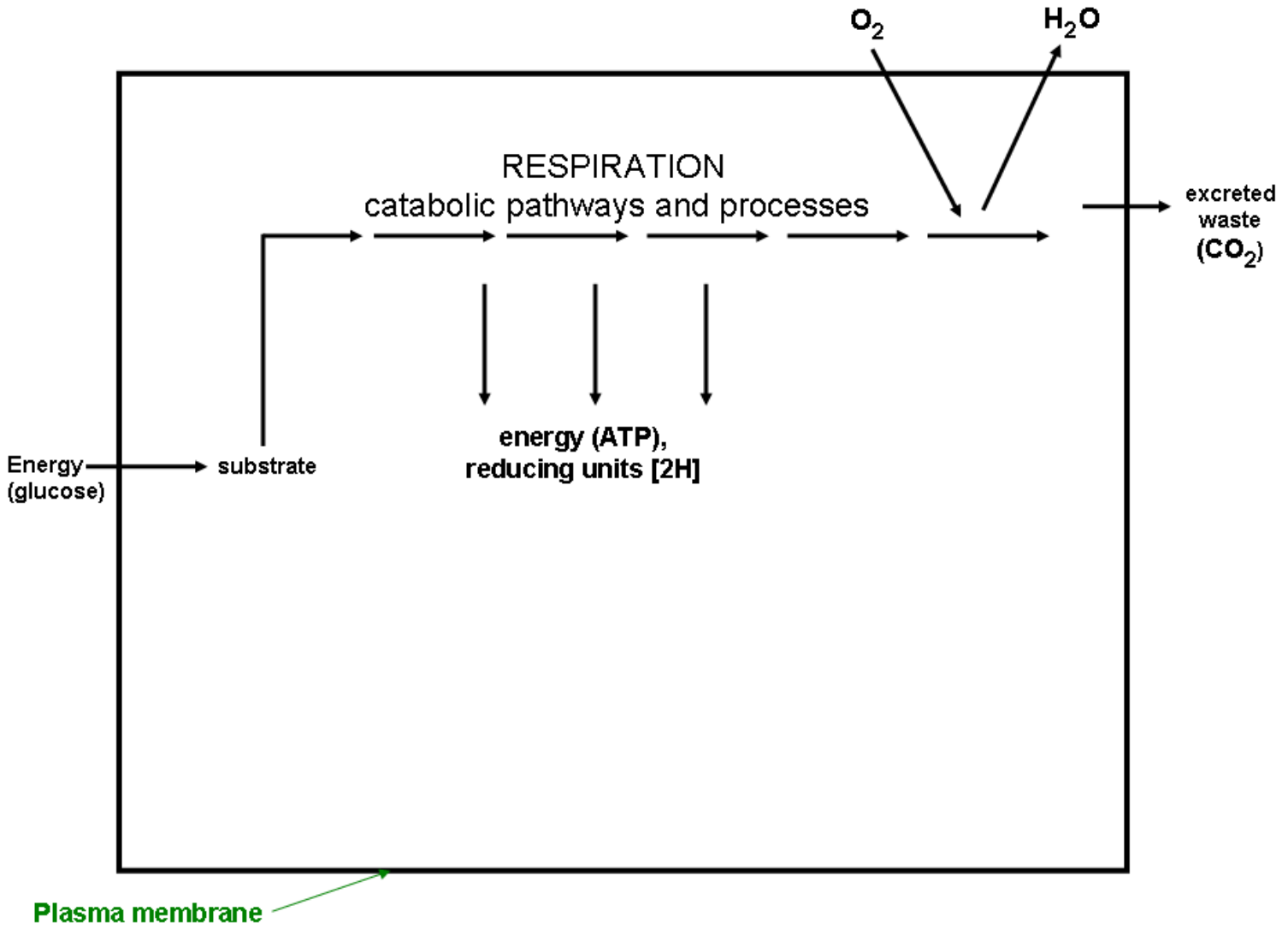
Respiratory Metabolism



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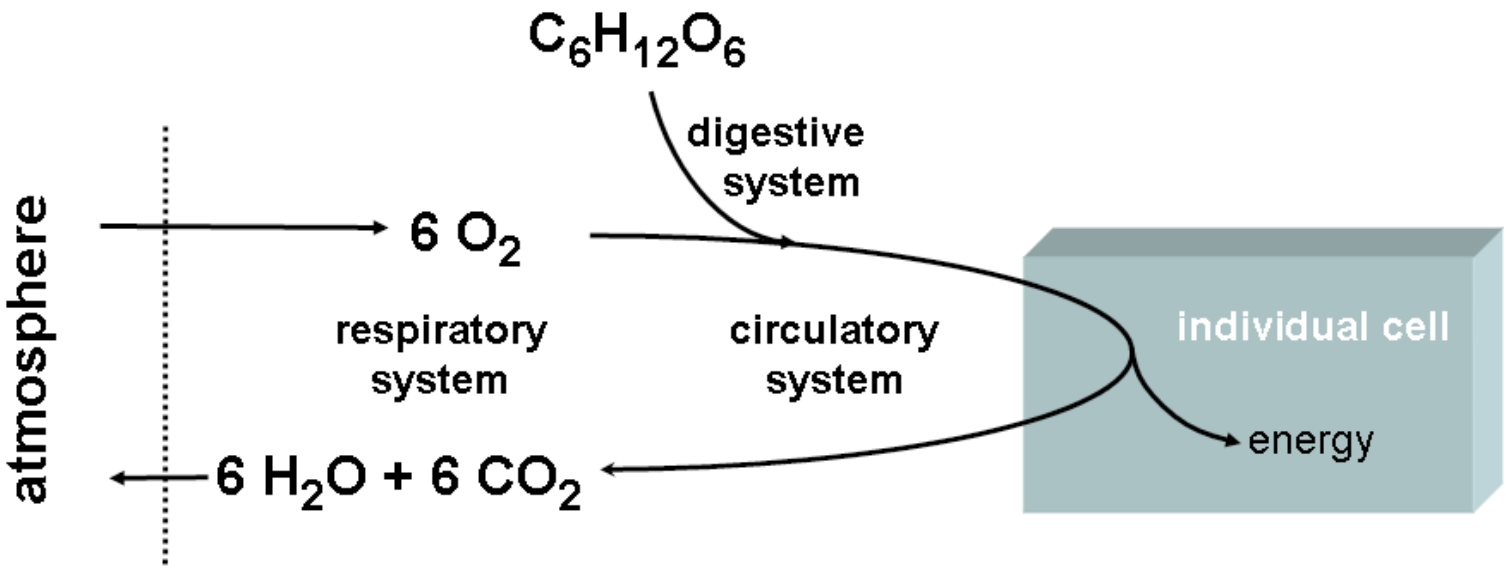
Respiration in higher animals such as humans, from a physiological perspective



net reaction

$$C_6H_{12}O_6 + 6\ O_2 \xrightarrow{\text{respiration}} 6\ CO_2 + 6\ H_2O + \text{energy}$$

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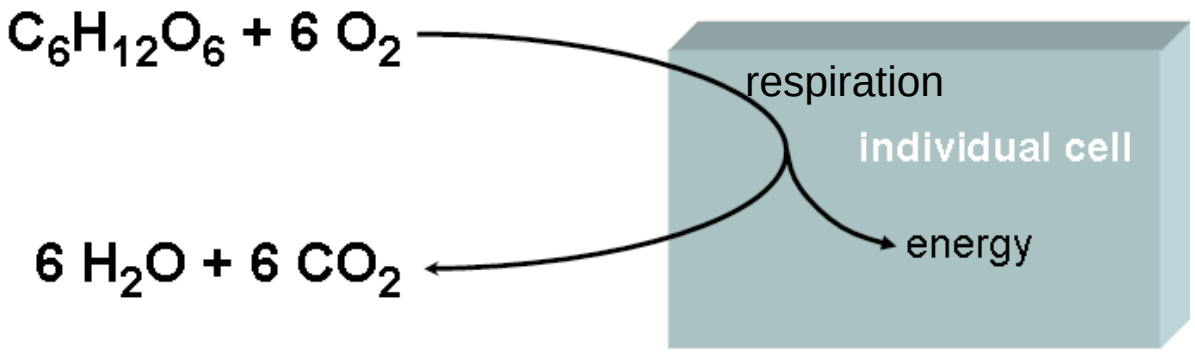
Respiration at the cellular level can be shown superficially with the same chemical reaction as at the whole organism level.



Respiration is a metabolic system that occurs entirely within living cells. It includes several metabolic pathways and processes.

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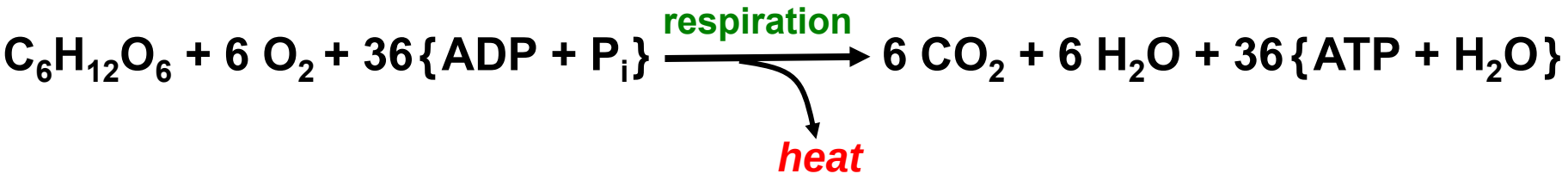
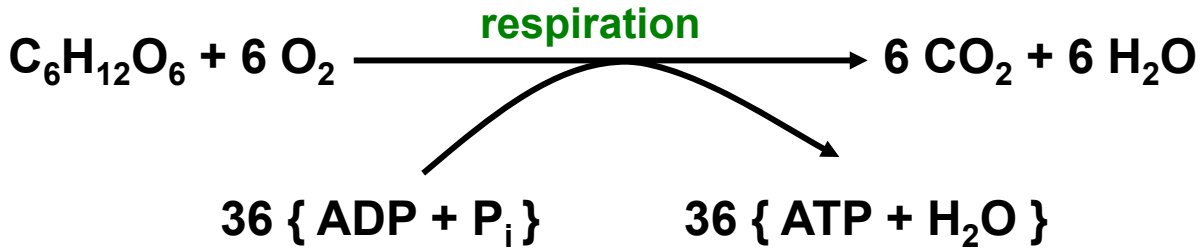
A more complete illustration of respiration as a metabolic system is shown here as a single chemical reaction.



This system may be shown as two connected processes:



This equation illustrates that much of the energy released during oxidation of an organic molecule in respiration is captured in the form of ATP. Energy released as heat is generally not shown in metabolic pathways.

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This equation also illustrates that respiration is a catabolic process.