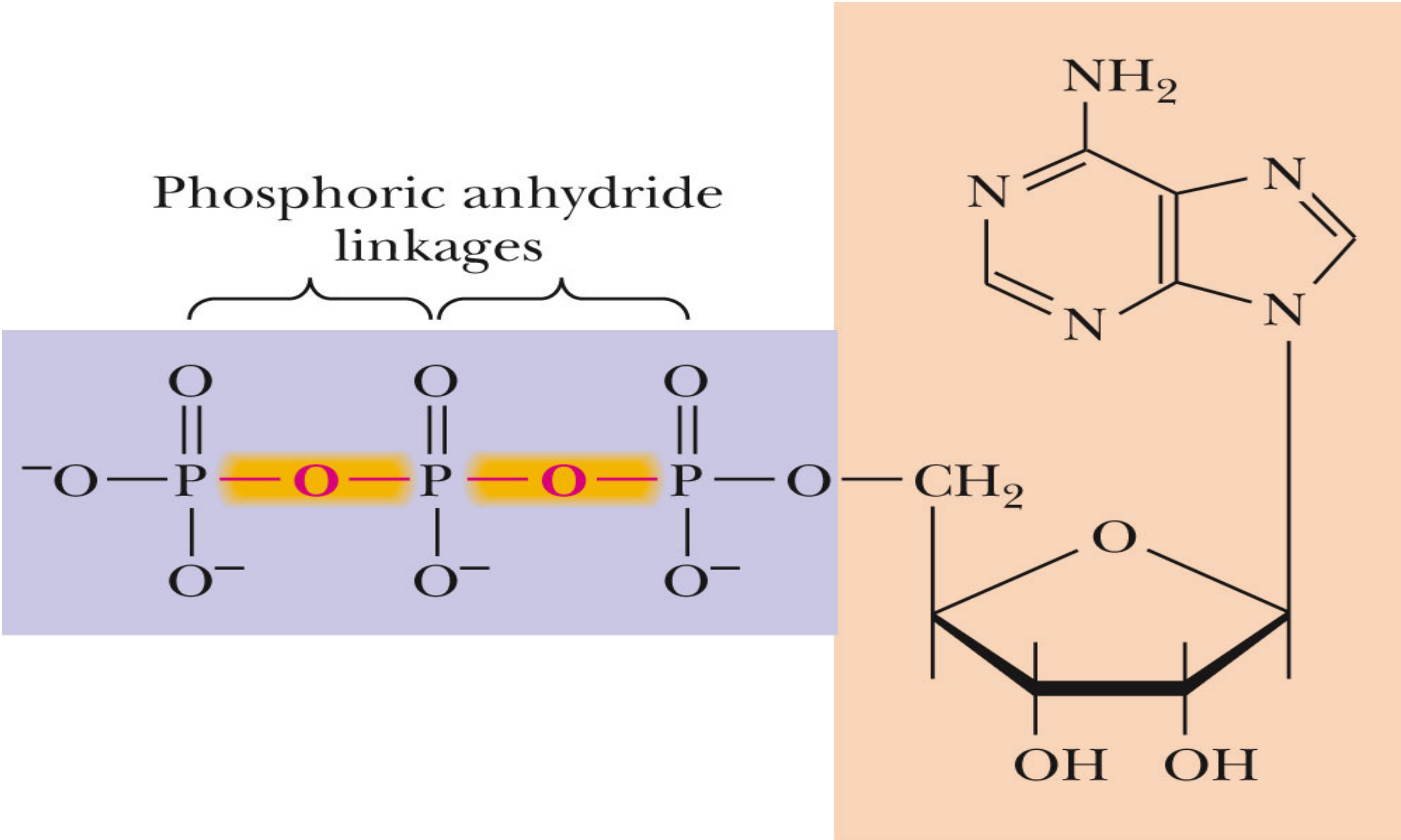
Know the structure of ATP



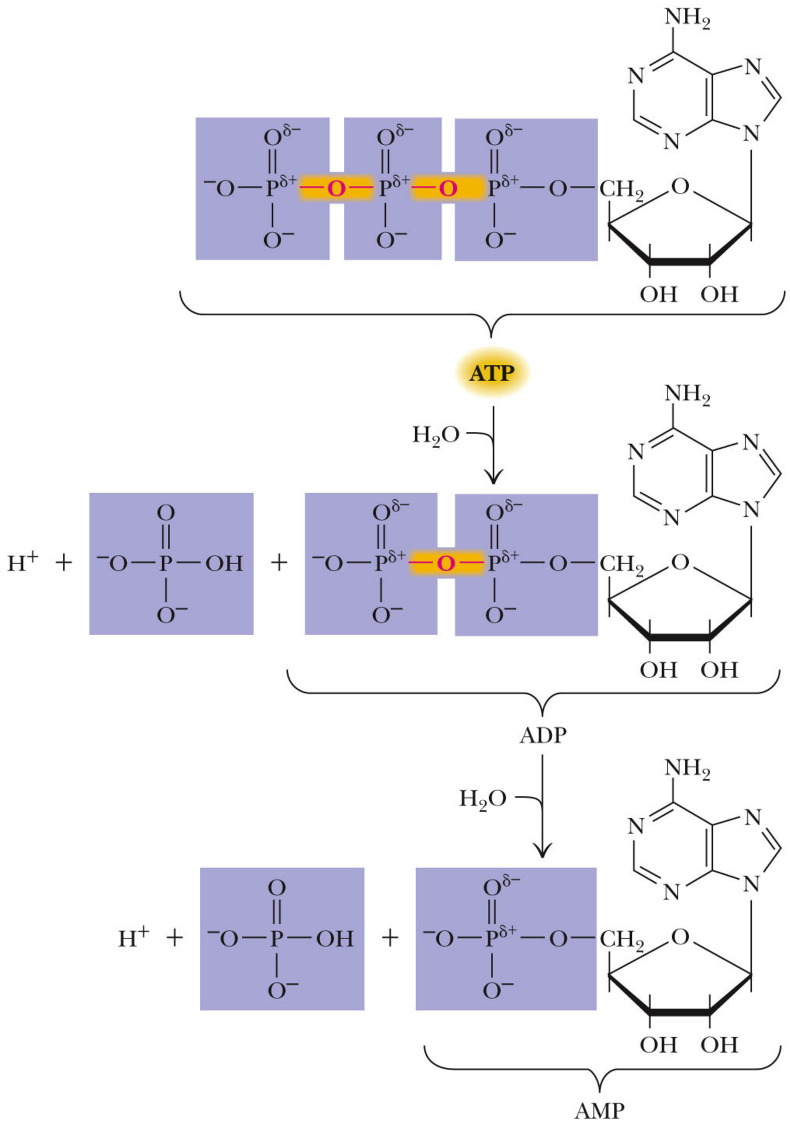
ATP
(adenosine-5'-triphosphate)

Hydrolysis of ATP is favourable

Bond strain in the anhydride due to electrostatic repulsion

Hydrolysis products resonance stabilised

Hydrolysis causes increased entropy

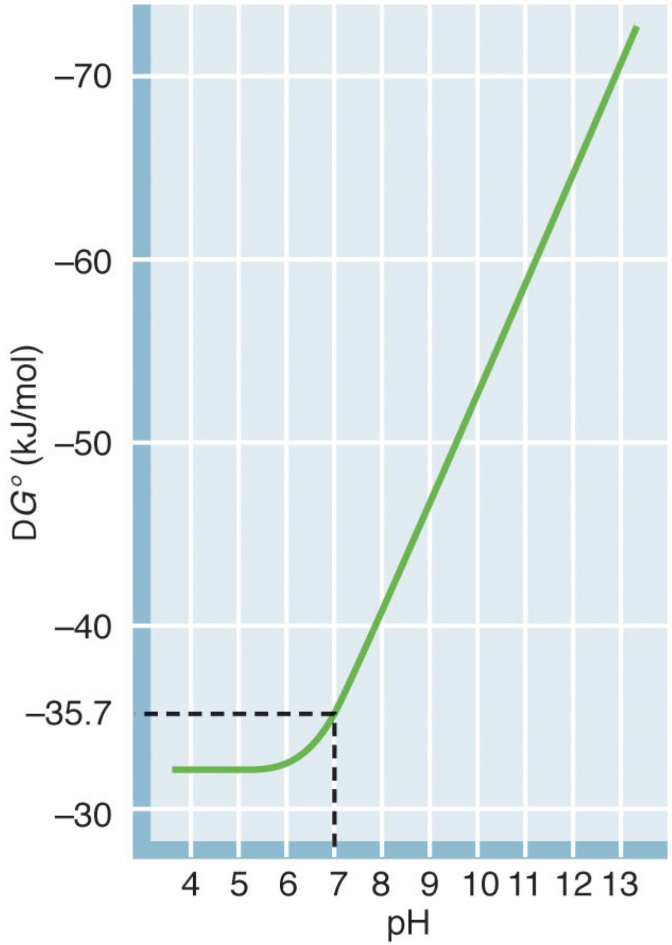


Complex equilibria involved in ATP hydrolysis

- pH dependent

Highest pKa of one of the protons is ~7

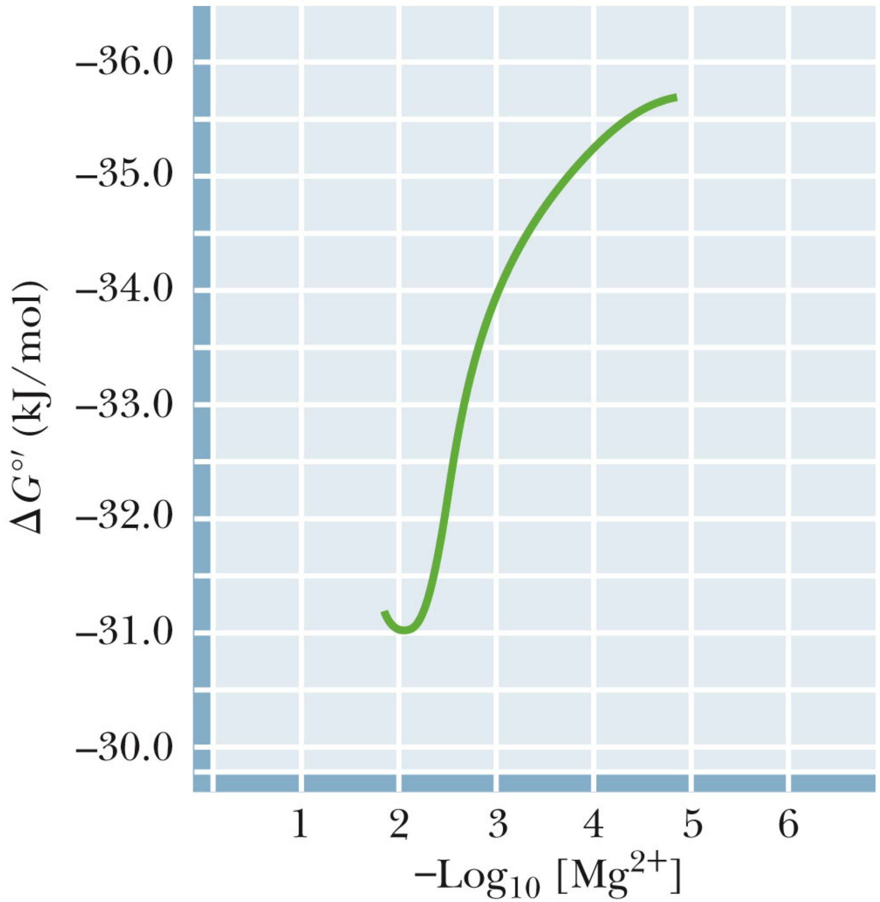
Multiple ionisations of ATP, ADP and phosphate affect the Keq and hence the ΔG^o of hydrolysis



Complex equilibria involved in ATP hydrolysis

- Binds metal cations

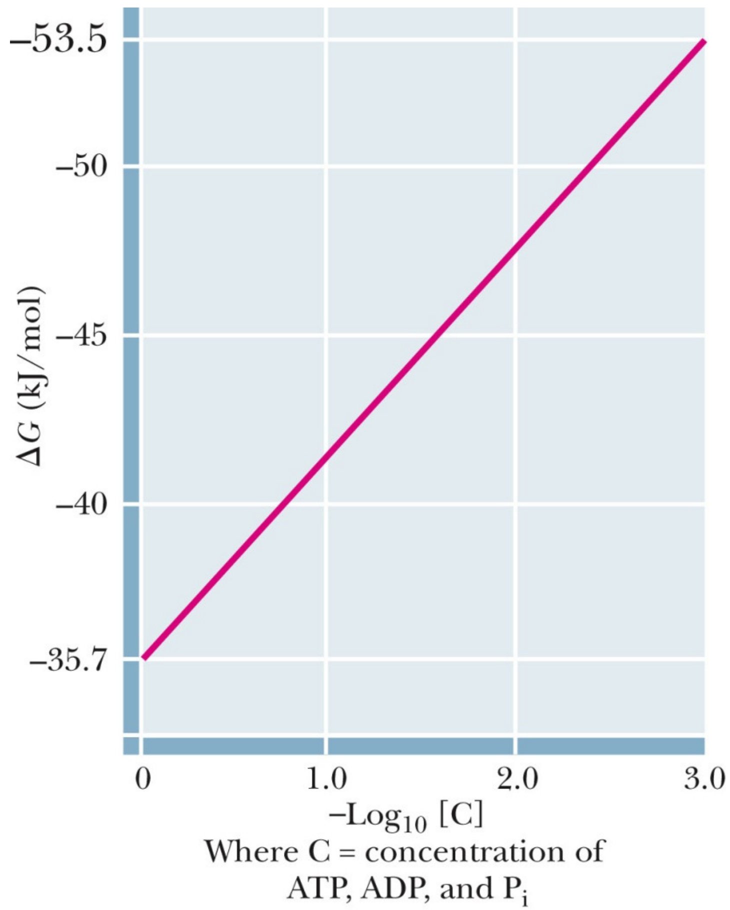
Less negative ΔGº of hydrolysis of ATP when in the presence of physiological concentrations of cations



Complex equilibria involved in ATP hydrolysis

- Far lower concentrations than standard conditions

At physiological concentrations, free energy of hydrolysis of ATP becomes more negative compared to under standard conditions



Daily human requirement for ATP

- Average human consumes:
- 50% efficiency
- Moles of ATP used each day:
- Mr ATP:
- Mass of ATP hydrolysed per day:

- Recycled:
- Commercial cost:

How ATP changes the Keq

Consider $A \leftrightarrow B$ with $\Delta G^{o'} = +\ 20$ kJ/mol

$\Delta G^{o'} = -RT\ \ln(Keq)$ (R=8.31 J/K.mol; T=298K)

Keq =__________= [B]/[A]

1 molecule of product formed for every ______ molecules of reactant

Suppose now, that $A \leftrightarrow B$ is coupled to ATP hydrolysis

$A \leftrightarrow B \qquad \Delta G^{o'} = 20$ kJ/mol

$\underline{ATP + H_2O \leftrightarrow ADP + P_i \qquad \Delta G^{o'} = -30 \text{kJ/mol}}$

$A + ATP + H_2O \leftrightarrow B + ADP + P \quad \Delta G^{o'} =$

Keq =

Given that in a typical cell, $[ADP] = 8 \times 10^{-3}$, $[P] = 10^{-3}$, $[ATP] = 8 \times 10^{-3}$

[B]/[A] =

Metabolism: An Overview

Chapter 17

Overview

- Metabolism:
- Sum of the chemical changes that convert **nutrients (substrate)** into **energy** into **products** via specific chemical **intermediates**
- Hundreds of enzymatic reactions organised into discrete pathways

Metabolic Diversity

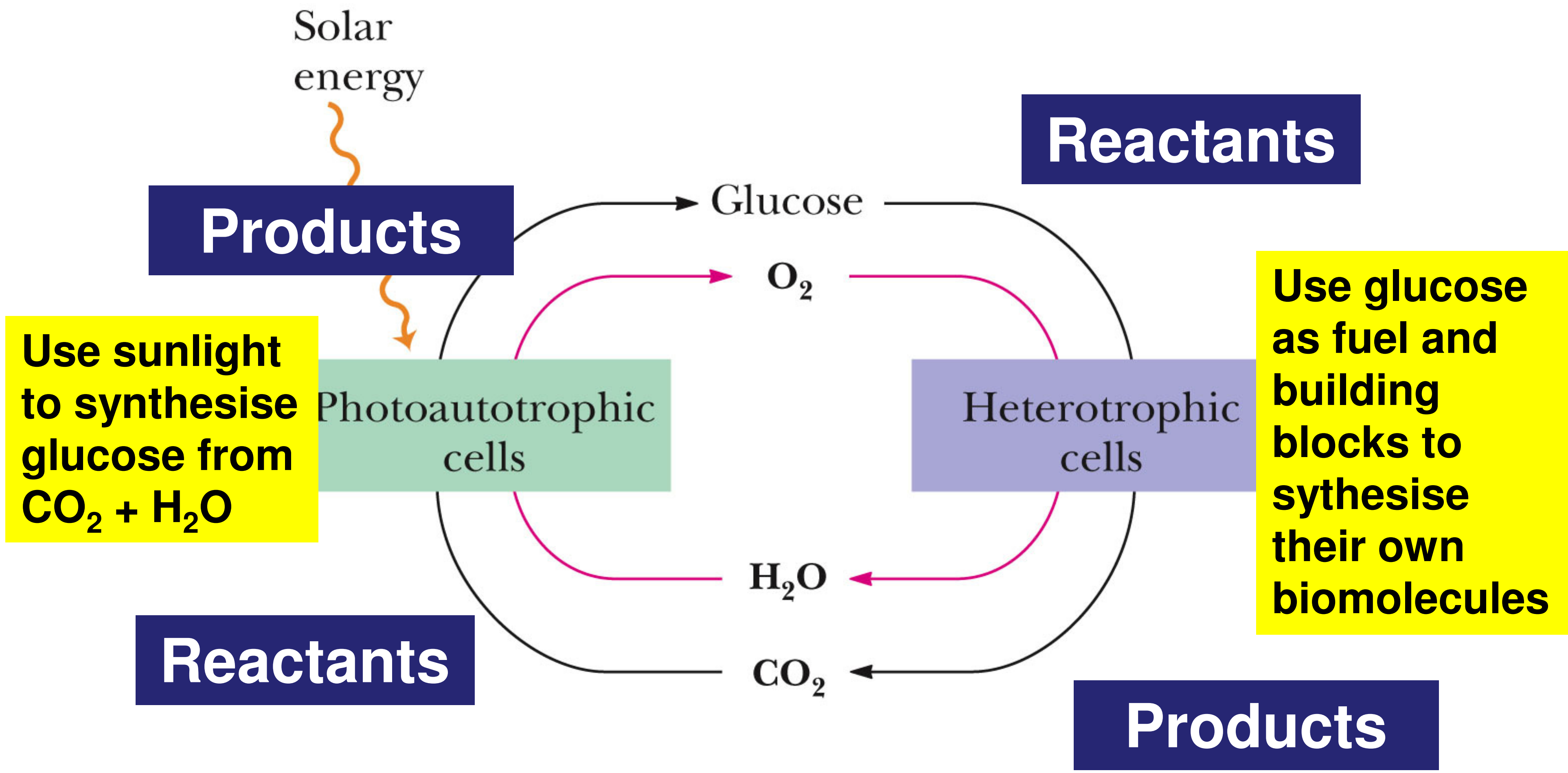
- Basic set of metabolic pathways

- Different cells and organisms may express alternate pathways

Diversity to metabolic processes

- Organisms are classified by how they obtain **carbon** and **energy**

Flow of energy in the Biosphere



Metabolic maps

- Indicate the **principal reactions** of metabolism of

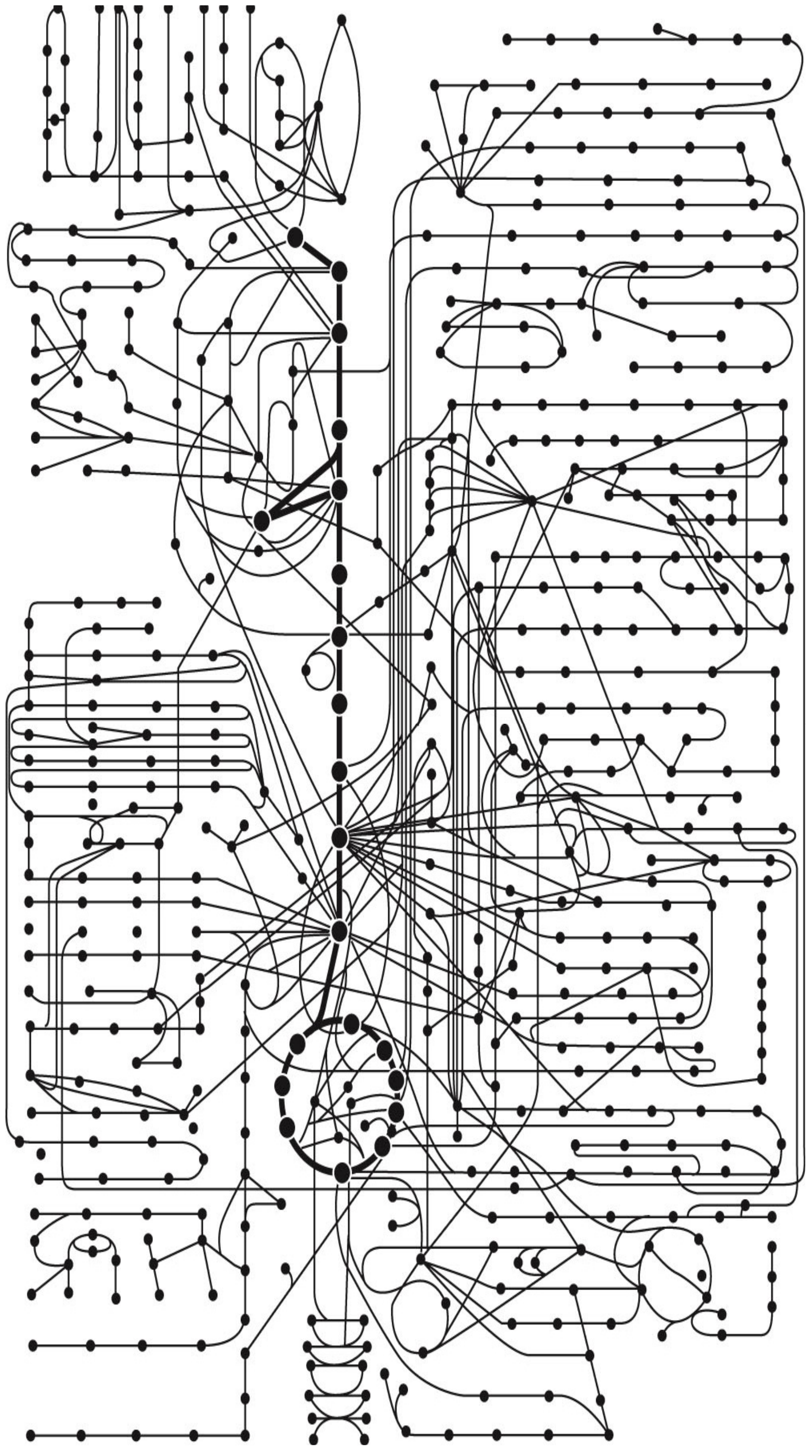
Carbohydrates
Lipids
Amino acids
Nucleotides

- Very complex

- Become easy to follow once the major metabolic routes are known and their functions understood

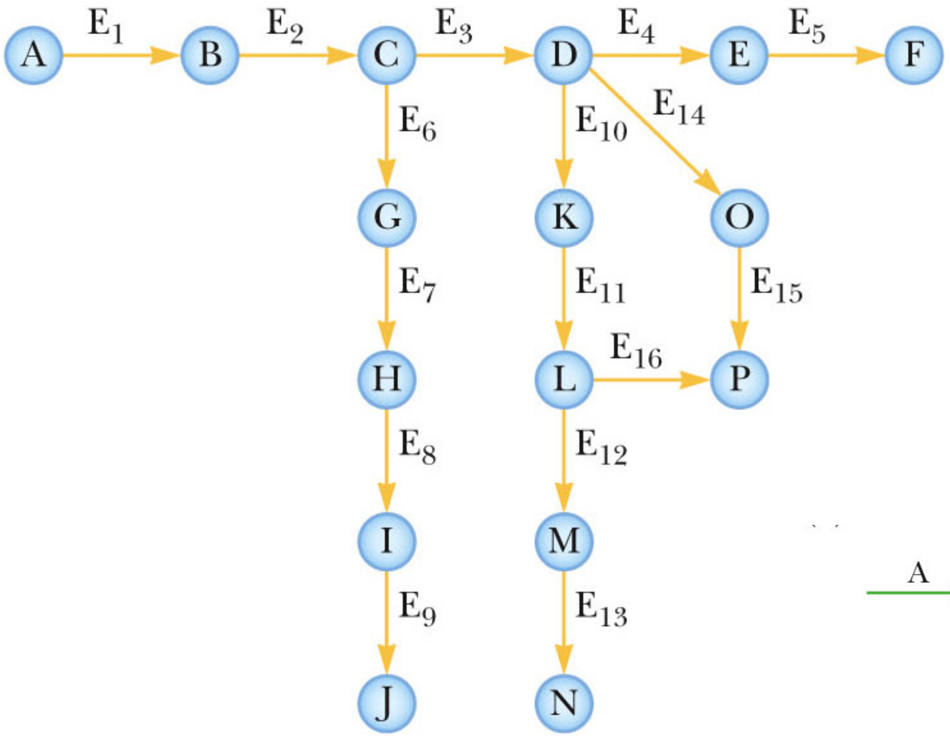
- Simplification: just 2 symbols
- **Dot** =
- **Line** =

TABLE 17.2	**Number of Dots (Intermediates) in the Metabolic Map of Figure 17.2, and the Number of Lines Associated with Them**
Lines	Dots
1 or 2	410
3	71
4	20
5	11
6 or more	8

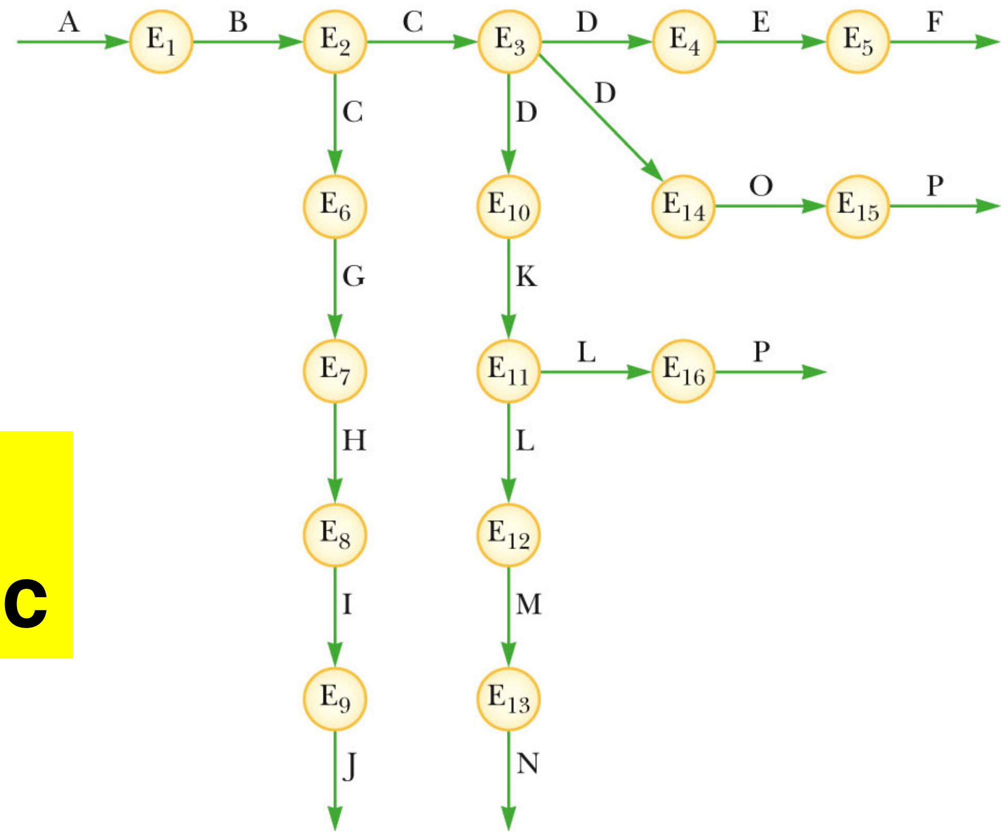


Alternative mapping of metabolic reactions

- Simpler portrayal of chemistry occurring in the organism
- **Spatial** and **temporal** portrayal of metabolites and enzymes
- Recast the metabolic maps in a **protein-centric** rather than metabolite-centric manner

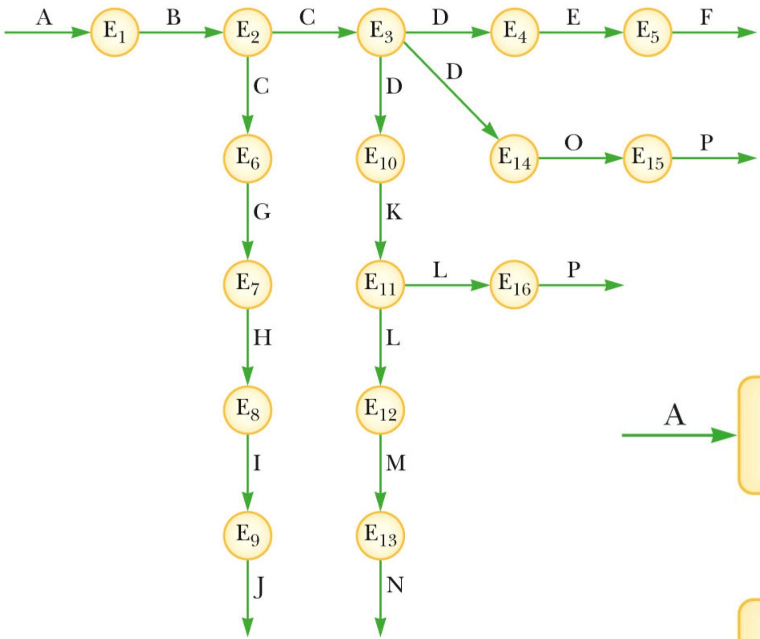


Traditional view:
metabolite-centric

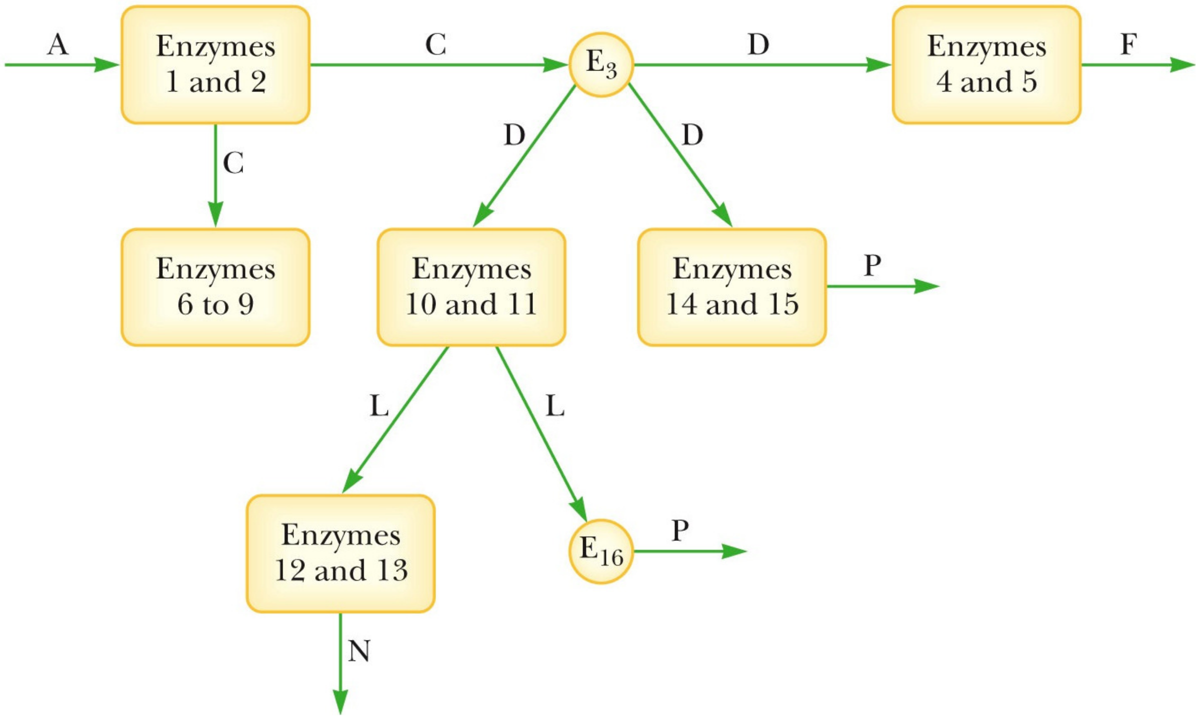


Recent view:
protein-centric

Further simplification of protein-centric maps

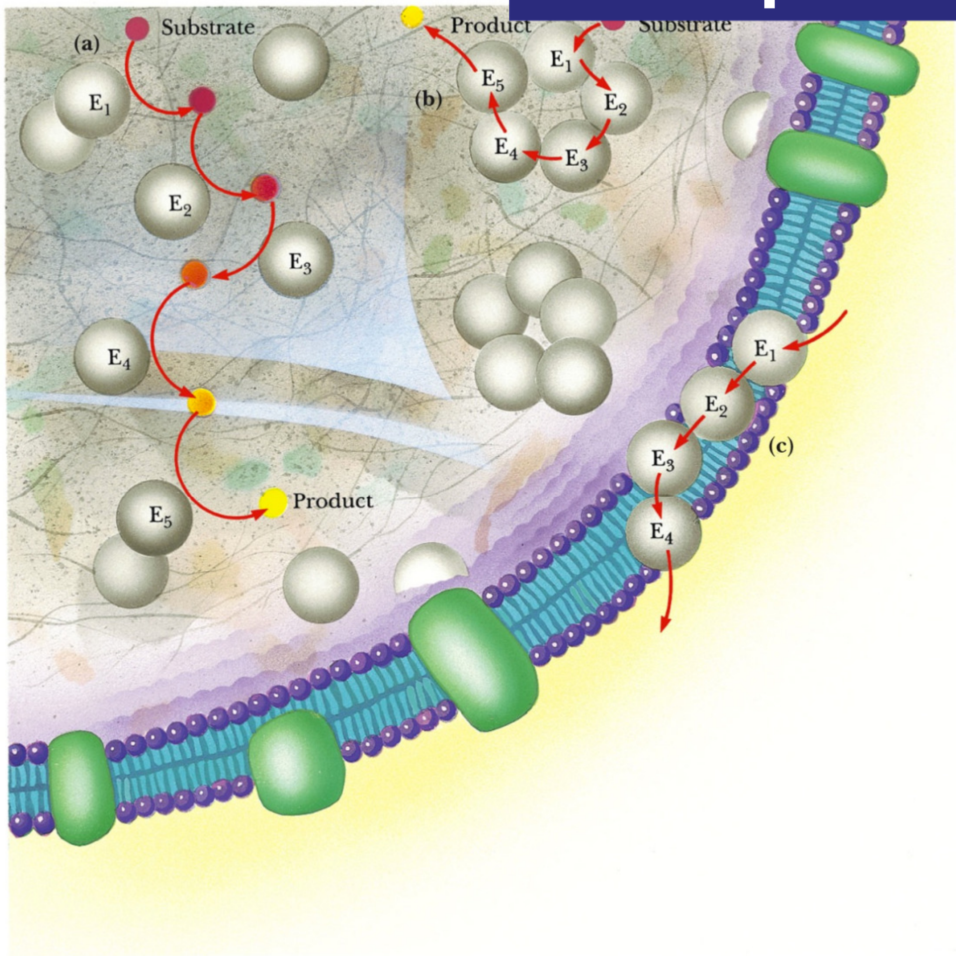


Multienzyme complexes

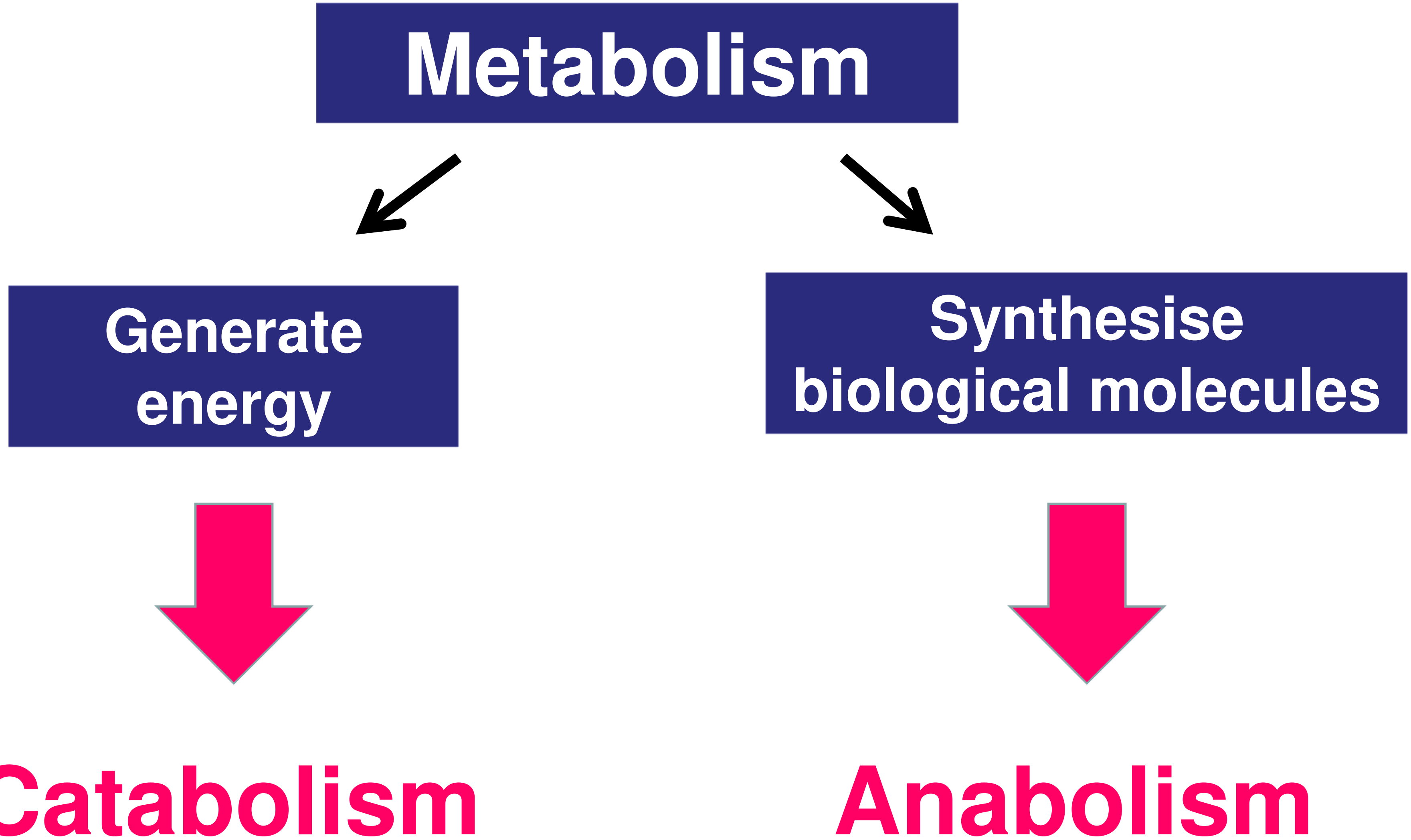


Multienzyme systems

Multienzyme complex



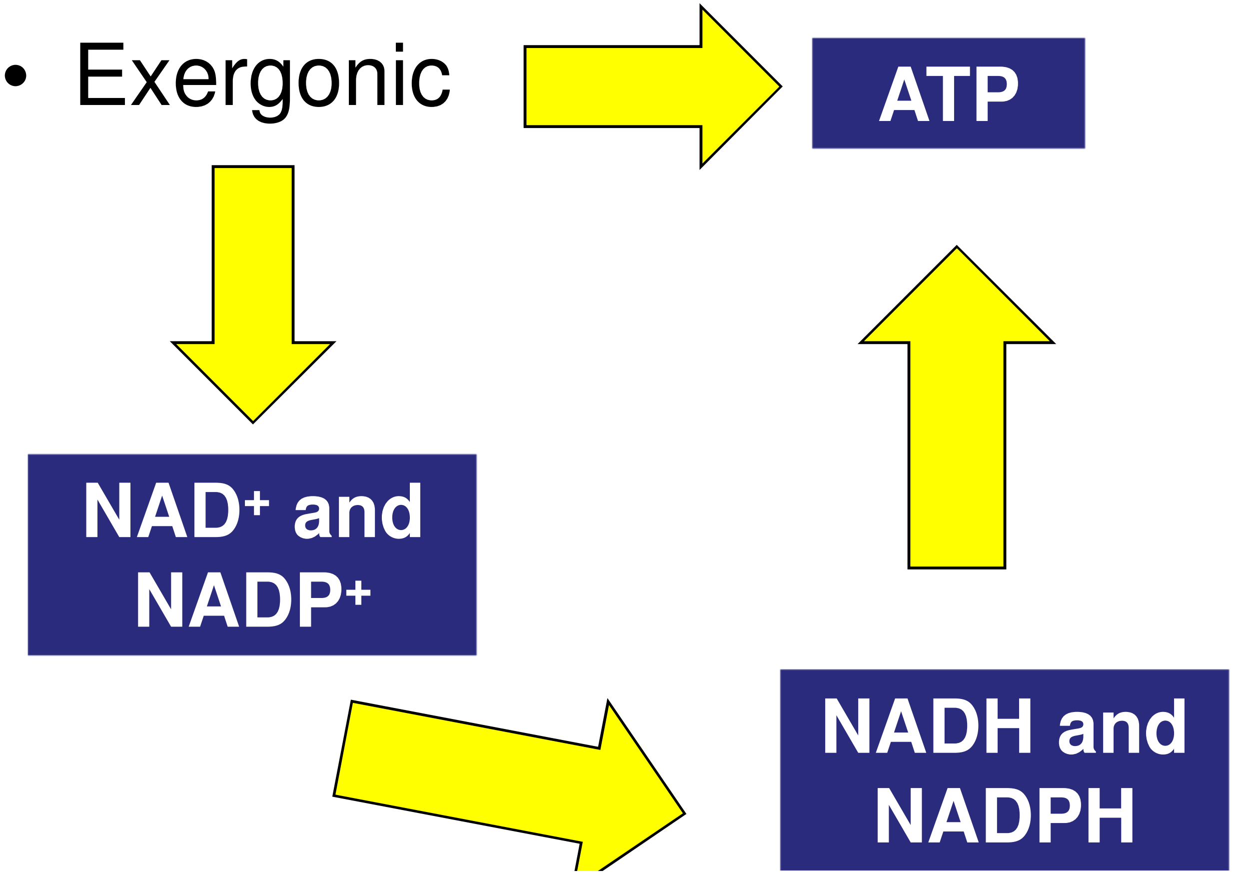
Anabolism and Catabolism



Catabolism

- Breakdown of complex nutrients

- Exergonic



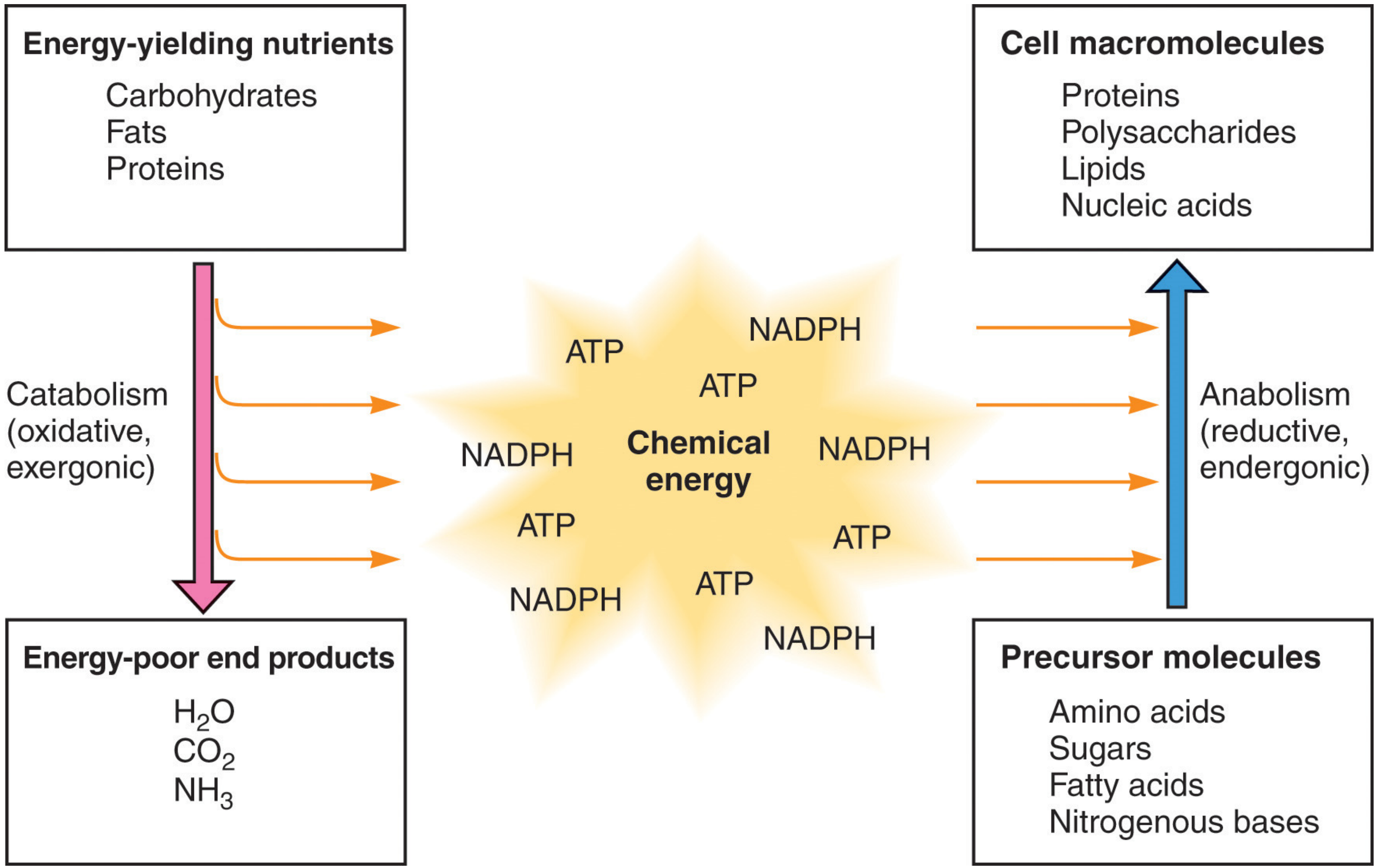
Anabolism

- Synthesis of complex biomolecules from simple precursors
- Endergonic

Energy required to form covalent bonds

ATP generated by catabolism

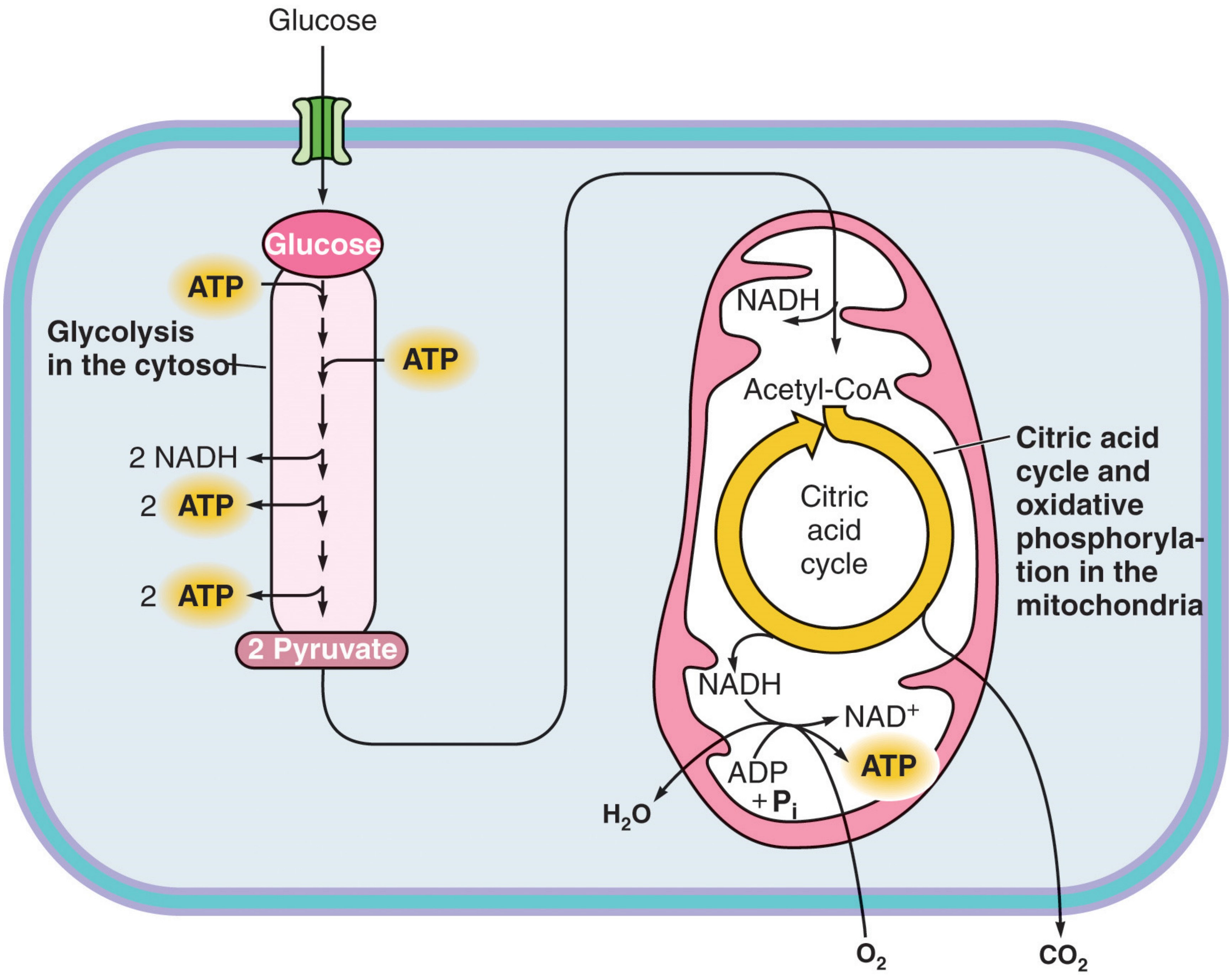
Electrons donated by NADPH


Energy-yielding nutrients
Carbohydrates
Fats
Proteins
Cell macromolecules
Proteins
Polysaccharides
Lipids
Nucleic acids
Catabolism
(oxidative,
exergonic)
ATP
NADPH
ATP
NADPH
Chemical energy
NADPH
ATP
ATP
NADPH
ATP
NADPH
Anabolism
(reductive,
endergonic)
Energy-poor end products
H_2O
CO_2
NH_3
Precursor molecules
Amino acids
Sugars
Fatty acids
Nitrogenous bases

- Tight control: metabolic needs served in an immediate and orderly fashion

- Competing metabolic pathways localised in **different cellular compartments** to avoid any interference

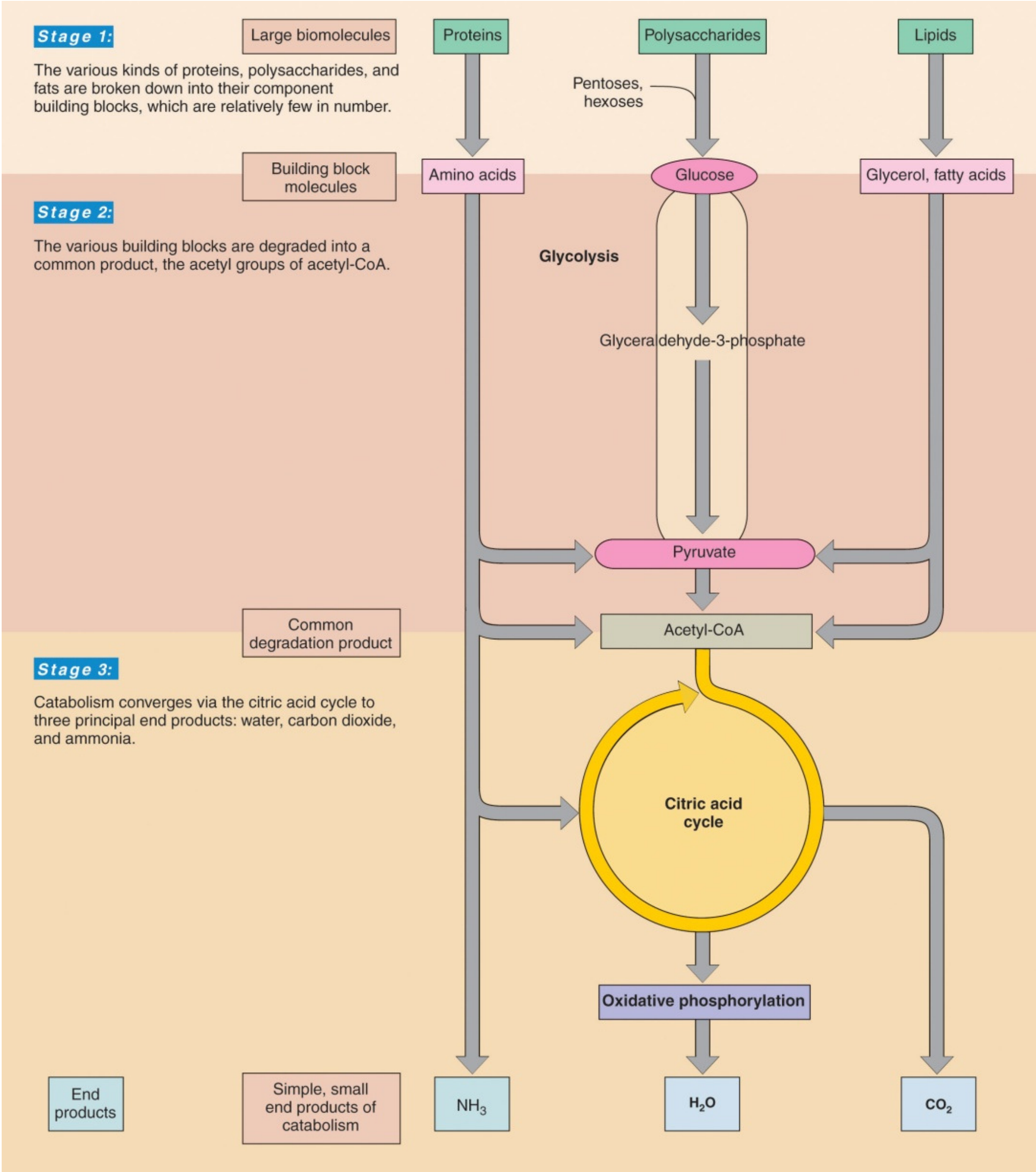
- E.g. enzymes involved in **catabolism of fatty acids** localised in **mitochondria** & enzymes for **fatty acid biosynthesis** located in **cytosol**



Glucose
Glucose
ATP
Glycolysis
in the cytosol
ATP
2 NADH
2 ATP
2 ATP
2 Pyruvate
NADH
Acetyl-CoA
Citric acid cycle
Citric acid cycle and oxidative phosphorylation in the mitochondria
NADH
NAD^+
ATP
ADP
$+ P_i$
H_2O
O_2
CO_2

3 Stages of Aerobic Catabolism

STAGE 1	Nutrients degraded into building blocks
STAGE 2	Building blocks degraded further into limited set of metabolic intermediates
STAGE 3	Acetyl-CoA converted to waste via citric acid cycle and oxidative phosphorylation


Stage 1:
The various kinds of proteins, polysaccharides, and fats are broken down into their component building blocks, which are relatively few in number.
Large biomolecules
Proteins
Polysaccharides
Lipids
Pentoses, hexoses
Building block molecules
Amino acids
Glucose
Glycerol, fatty acids
Stage 2:
The various building blocks are degraded into a common product, the acetyl groups of acetyl-CoA.
Glycolysis
Glyceraldehyde-3-phosphate
Pyruvate
Common degradation product
Acetyl-CoA
Stage 3:
Catabolism converges via the citric acid cycle to three principal end products: water, carbon dioxide, and ammonia.
Citric acid cycle
Oxidative phosphorylation
End products
Simple, small end products of catabolism
NH_3
H_2O
CO_2

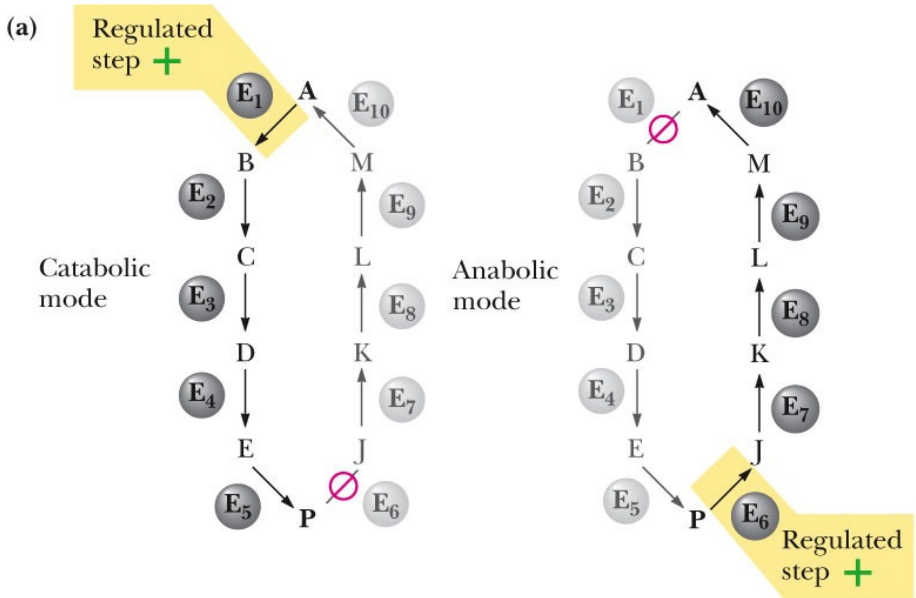
Catabolism, Anabolism and Amphibolism

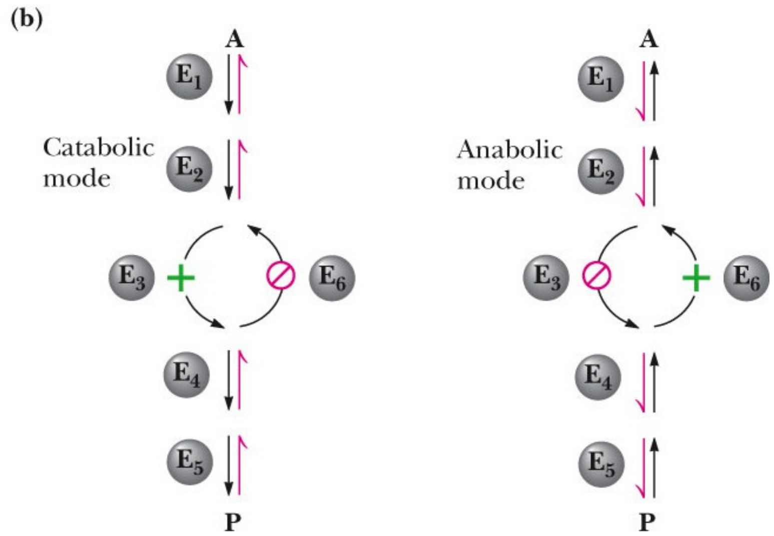
- Catabolism **converges** to a common intermediate
- Anabolism **diverges** from a small group of simple intermediates to a wide variety of biomolecules
- Some pathways have roles in both catabolism and anabolism and are said to be **amphibolic**

Catabolism and Anabolism

- Anabolic synthesis of a given end product does **not** correspond to the catabolic pathway of the same substance
- Eg catabolism of glucose to pyruvate vs. biosynthesis of glucose from pyruvate

Parallel pathways of catabolism and anabolism must differ by at least one step so that they can be <u>regulated independently</u>



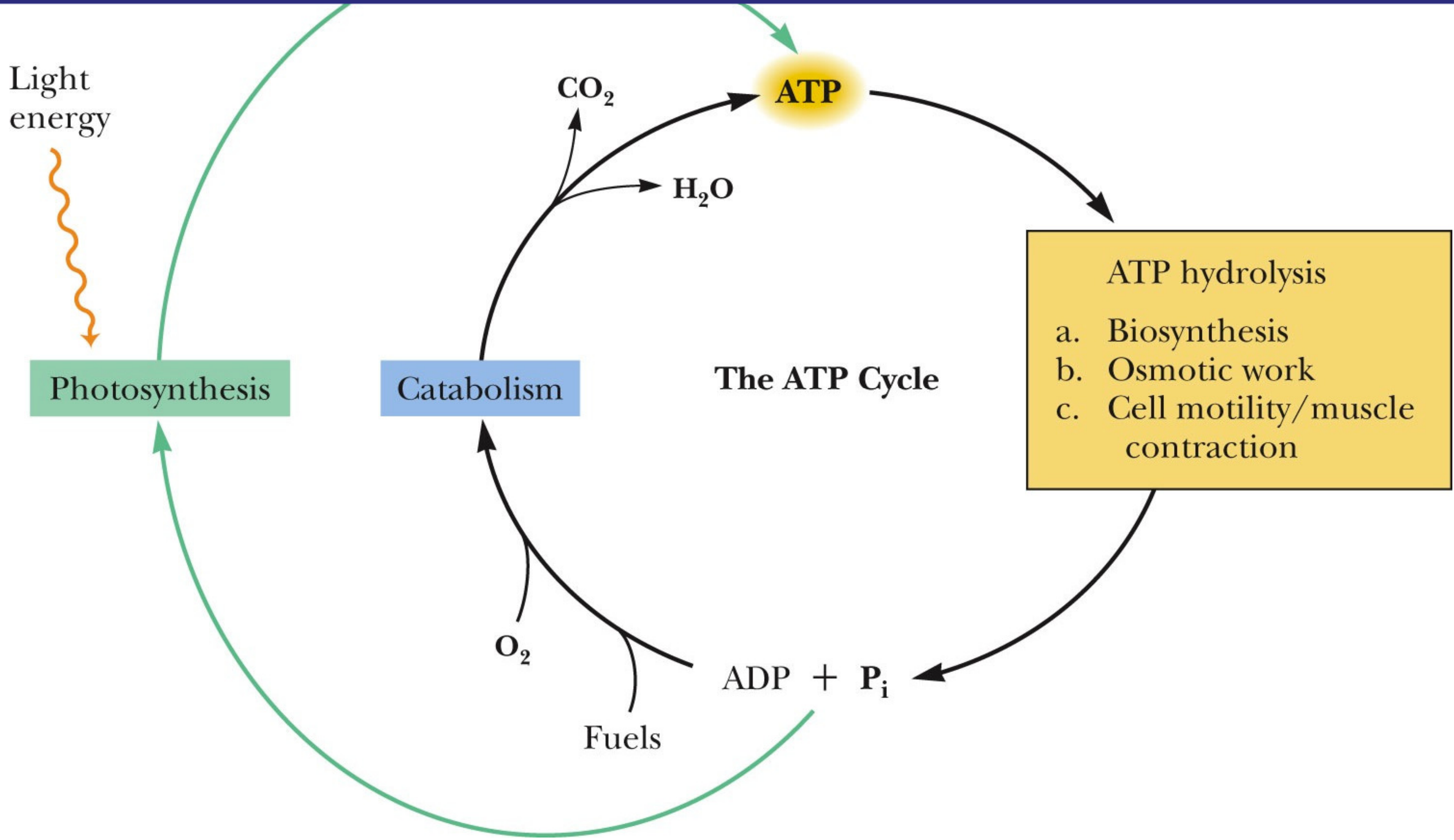


Independent routes between A and P

Only one reaction has 2 different enzymes

The ATP Cycle

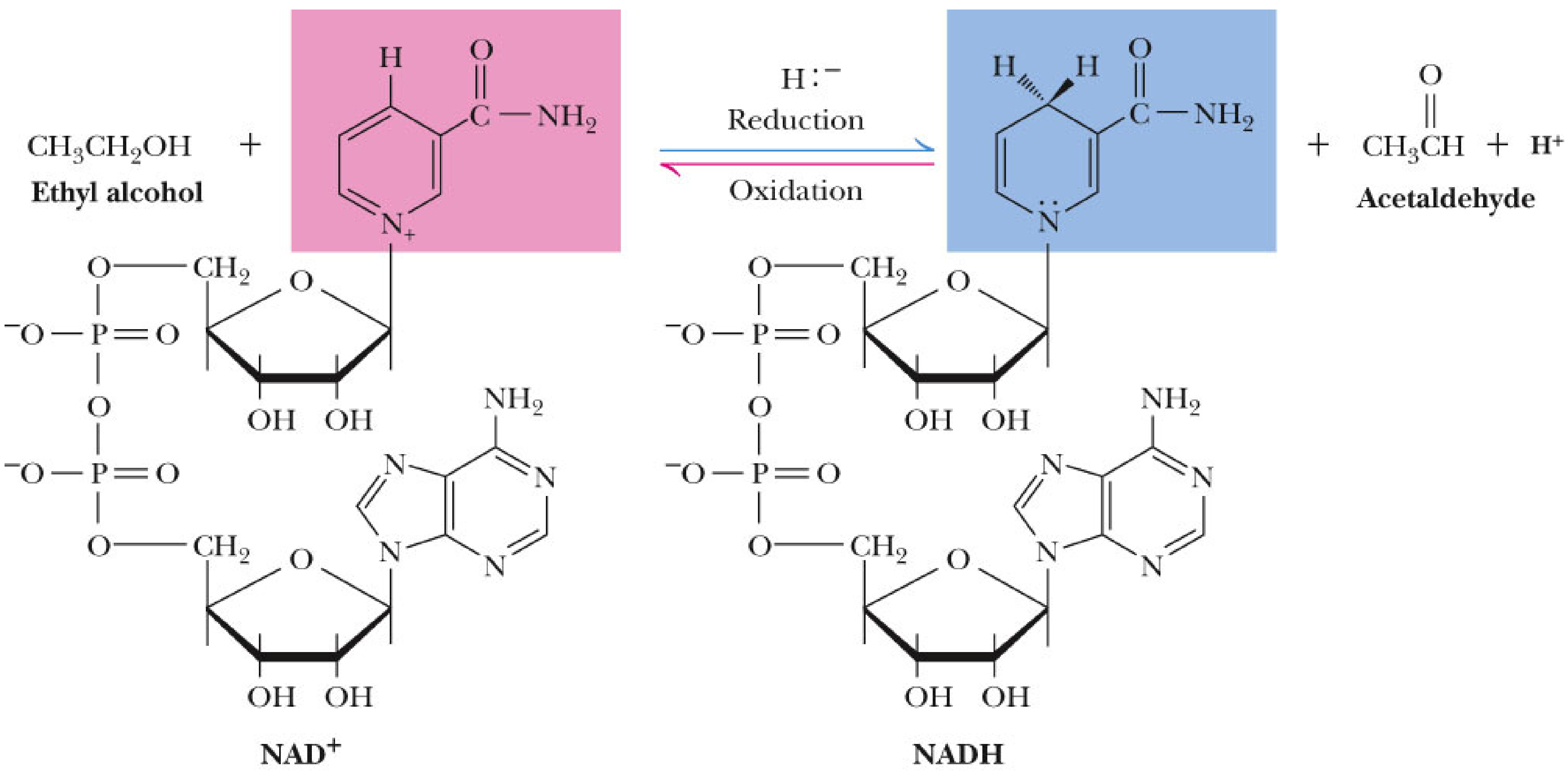
ATP produced by phototrophs and heterotrophs



The NAD^+/$NADP^+$ Cycle

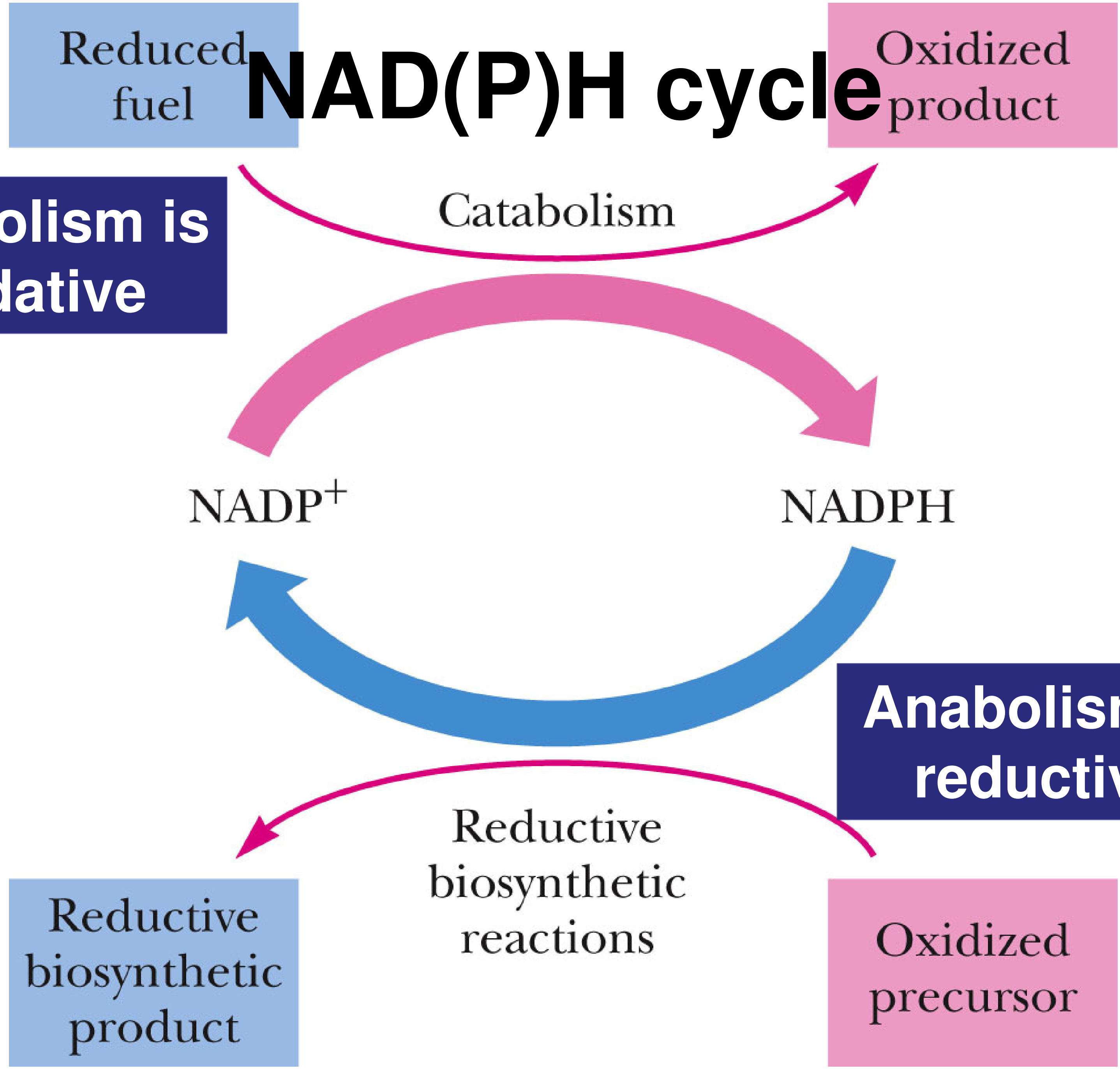
- Oxidative reactions of catabolism → **hydride ions** ($H :^-$) released
- Hydride ions transferred to NAD^+
- NAD^+ **reduced** to NADH
- NADH is **oxidised** to NAD^+ during anabolism
- Final electron acceptor is O_2 which becomes reduced to water

Hydride transferred to NAD^+ to form NADH + H^+



Nicotinamide Adenine Dinucleotide

NAD(P)H cycle



Catabolism is oxidative

Anabolism is reductive

Coenzymes and Vitamins

E.g. NAD^+ and $NADP^+$

“Vital amines”

- Vitamins cannot be synthesised by the organism
- Different organisms require different vitamins
- Low Mr substances that bring **unique chemical functionality** to enzymatic reactions