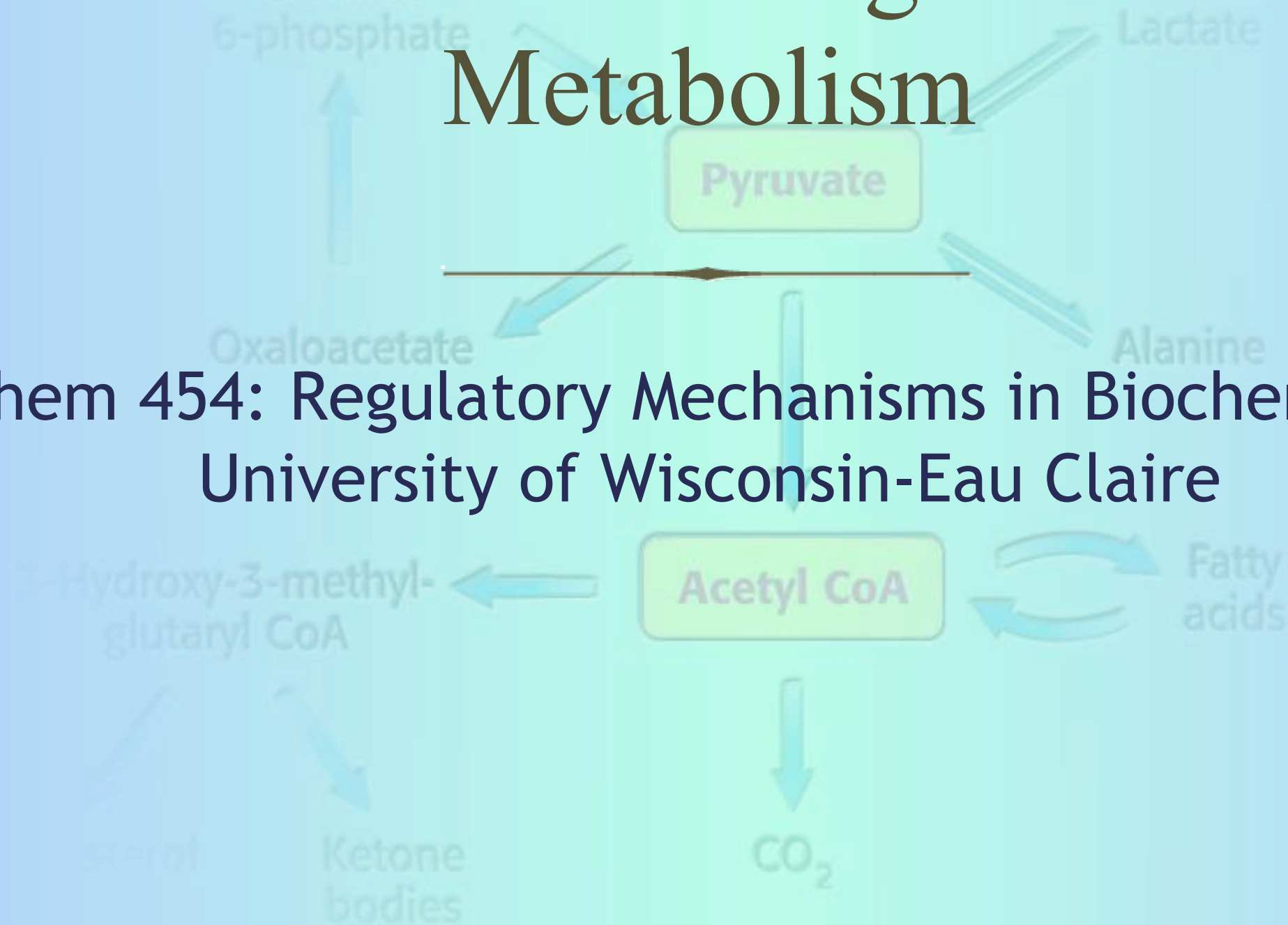


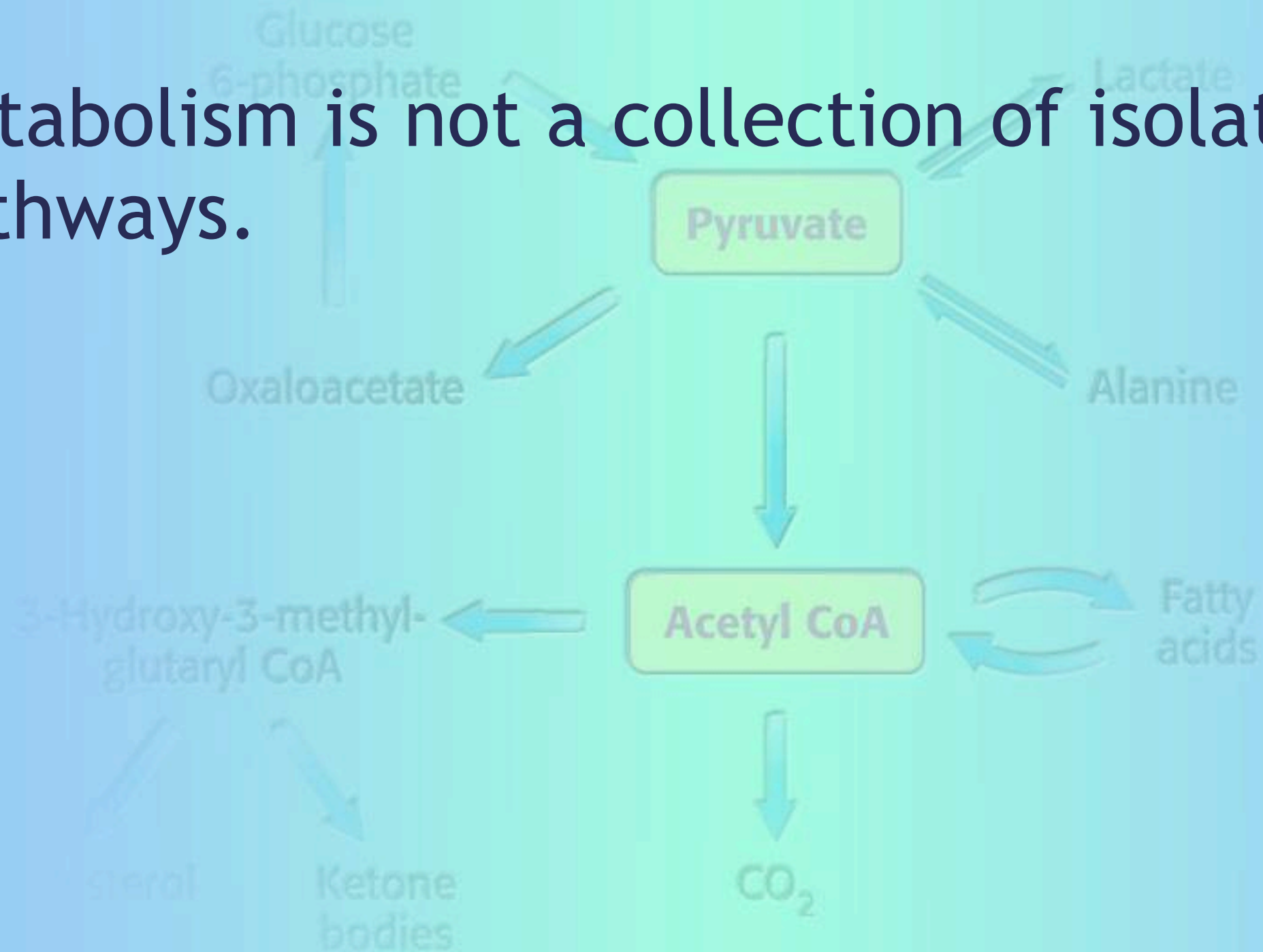
Lecture 13 - Integration of Metabolism

Chem 454: Regulatory Mechanisms in Biochemistry
University of Wisconsin-Eau Claire



Introduction

Metabolism is not a collection of isolated pathways.



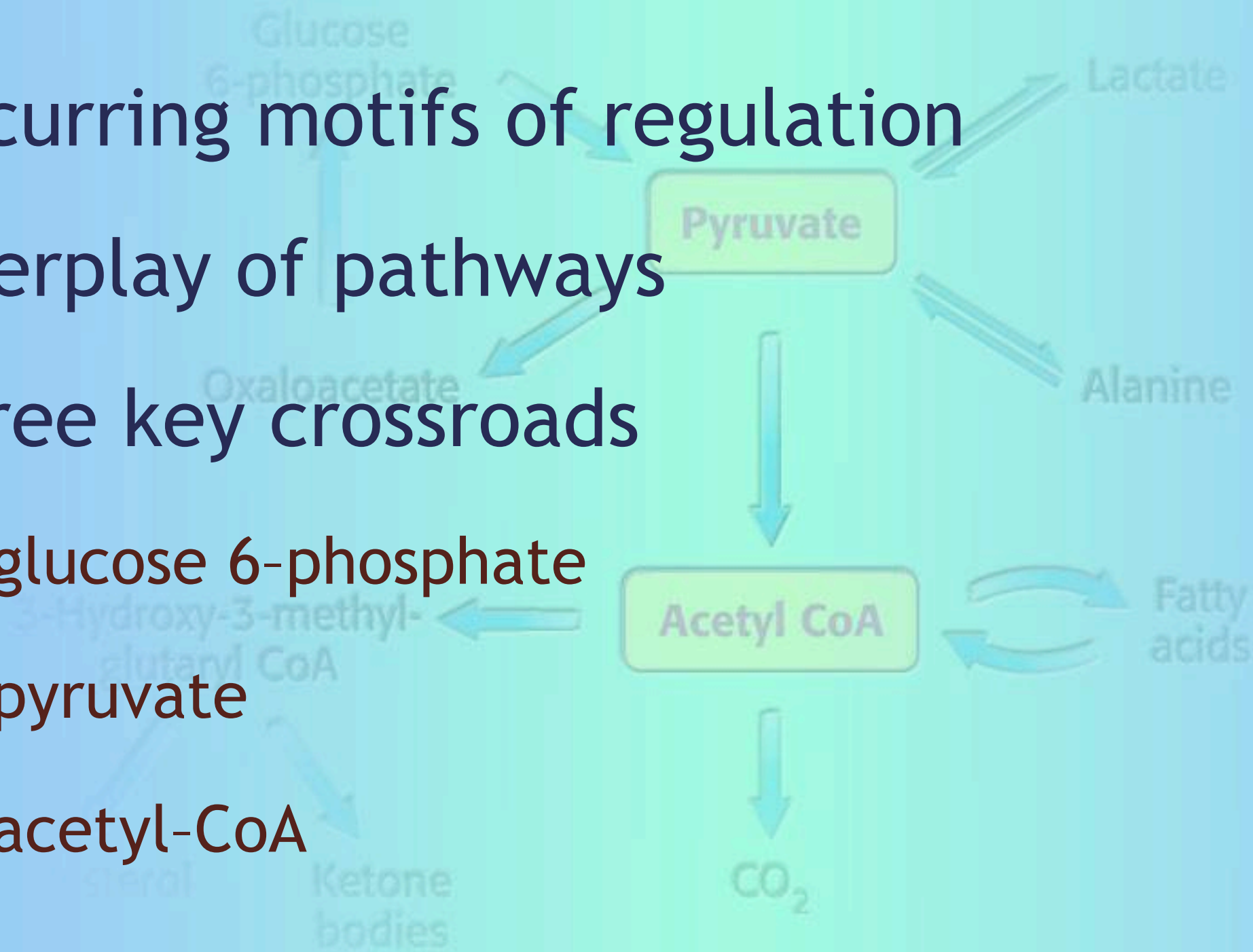
Introduction

Recurring motifs of regulation

Interplay of pathways

Three key crossroads

- glucose 6-phosphate
- pyruvate
- acetyl-CoA



Introduction

Tissue and organ differences

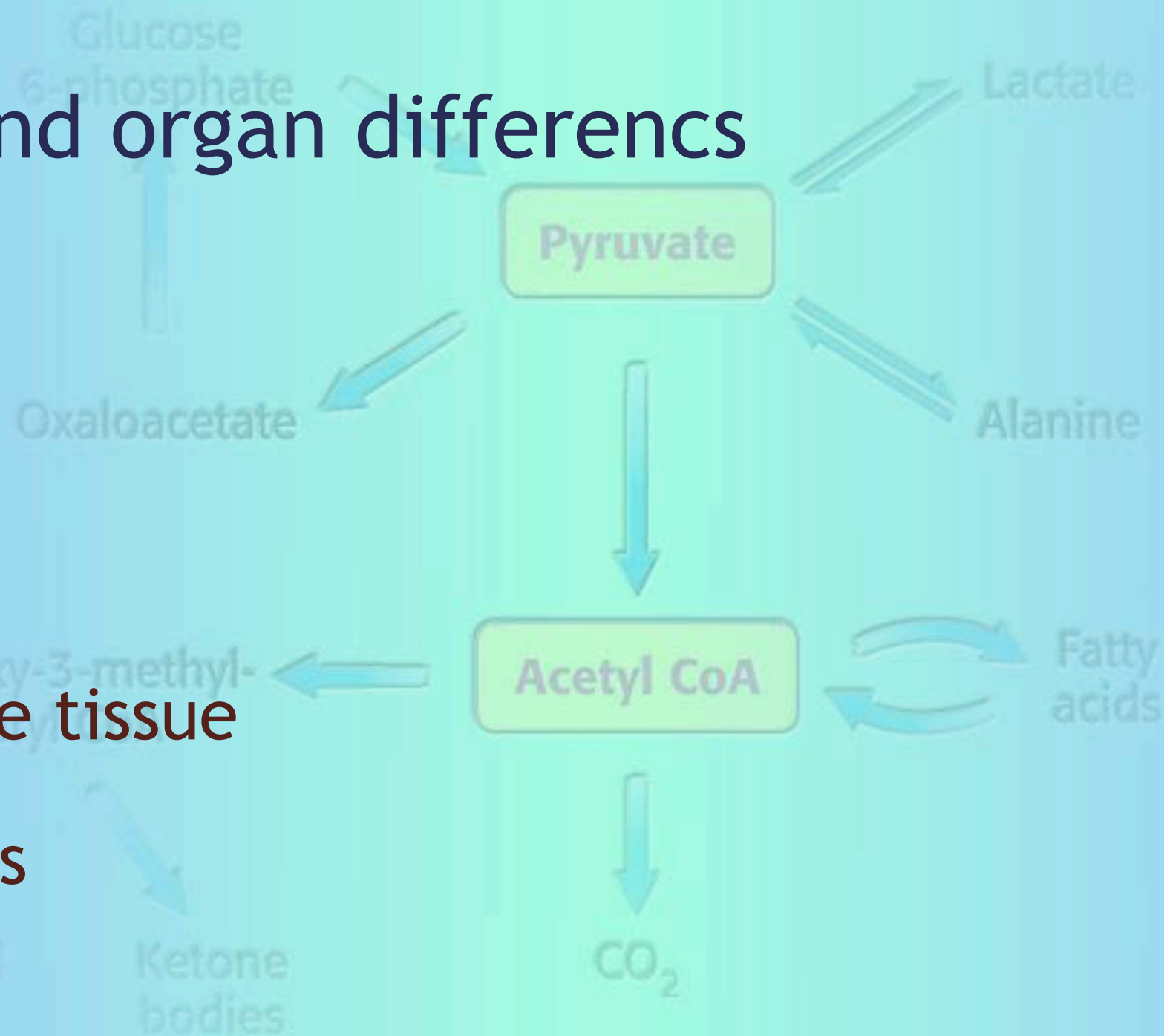
- Muscle

- Liver

- Brain

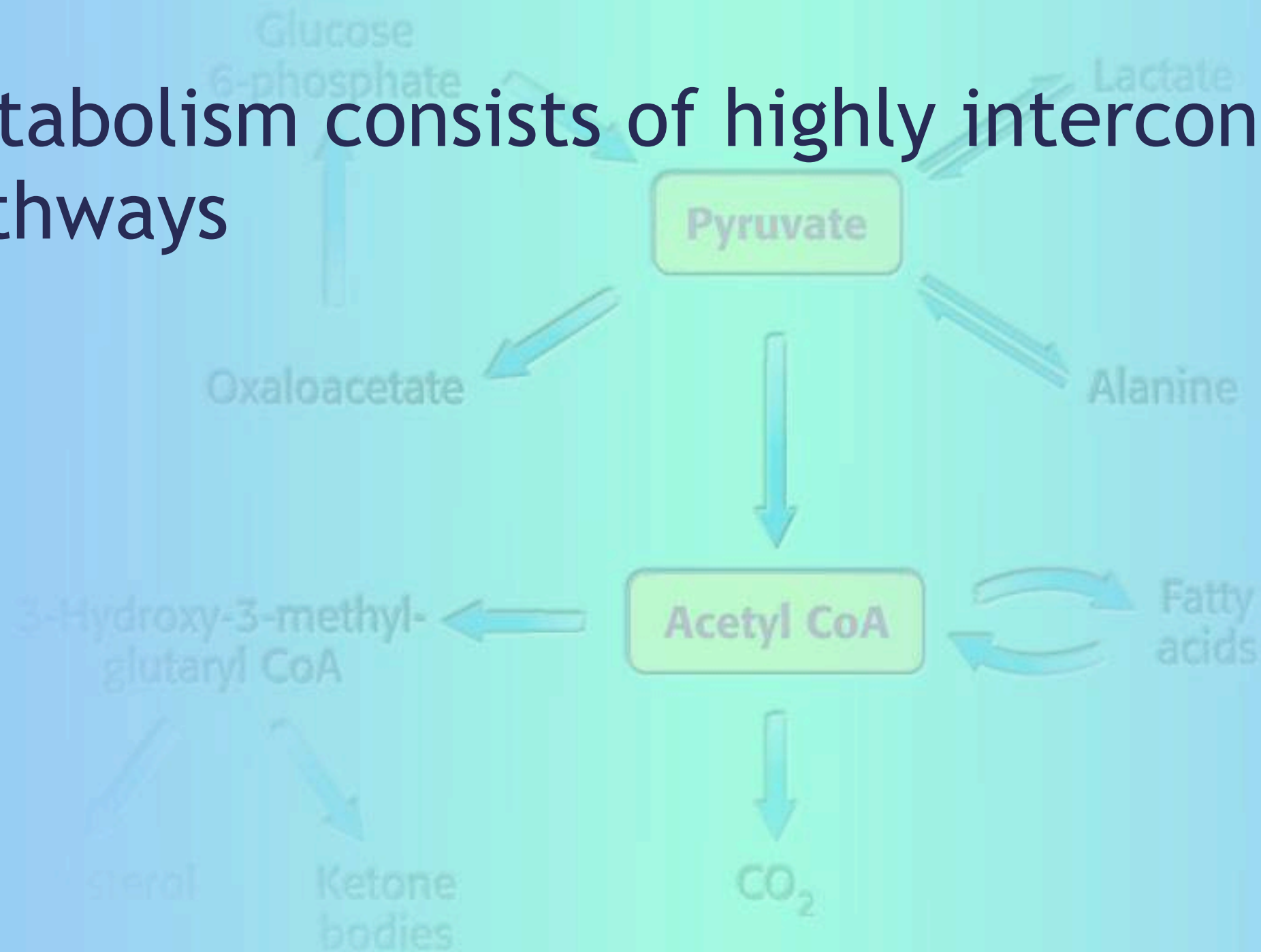
- Adipose tissue

- Kidneys



1. Interconnected Pathways

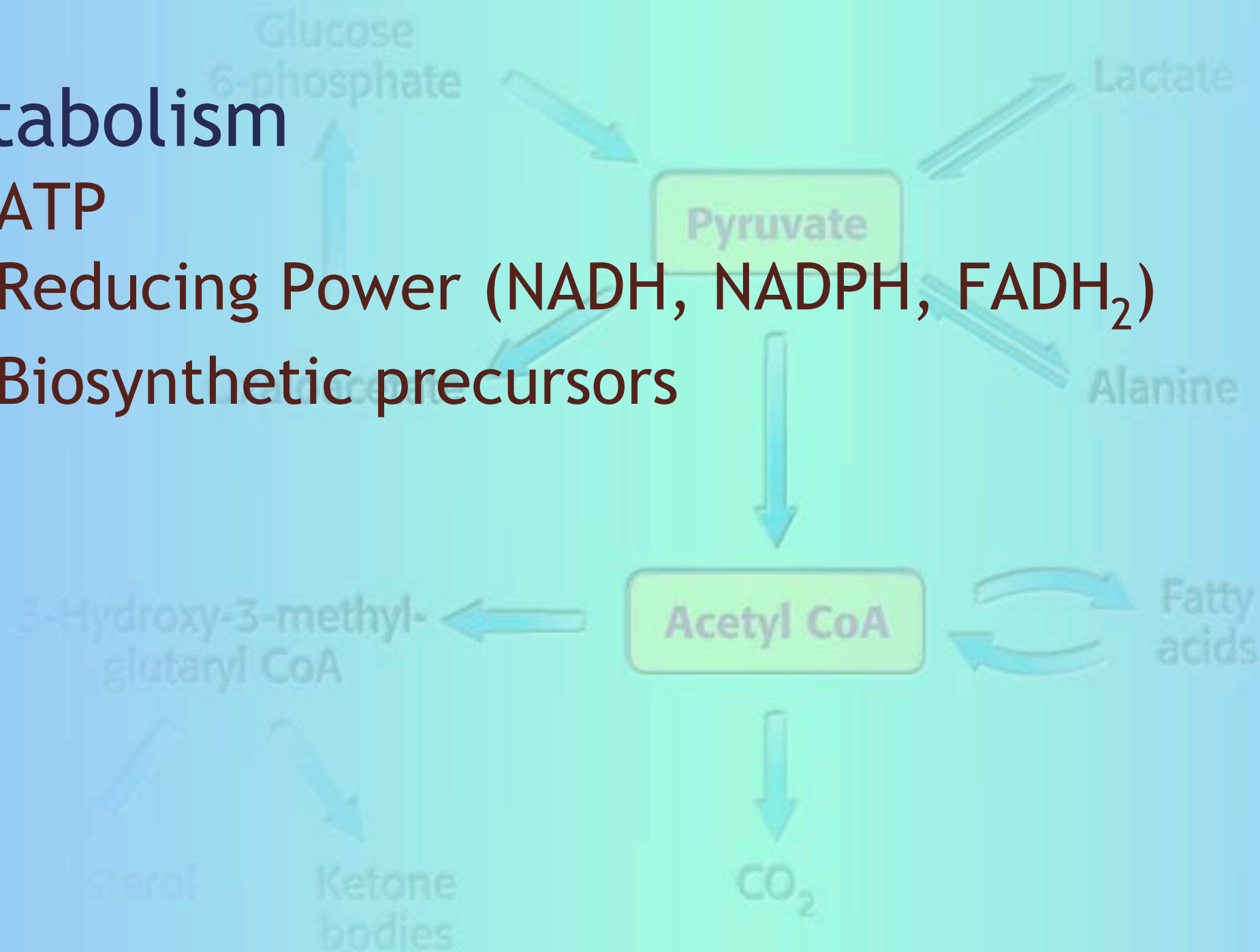
Metabolism consists of highly interconnected pathways



1. Interconnected Pathways

Catabolism

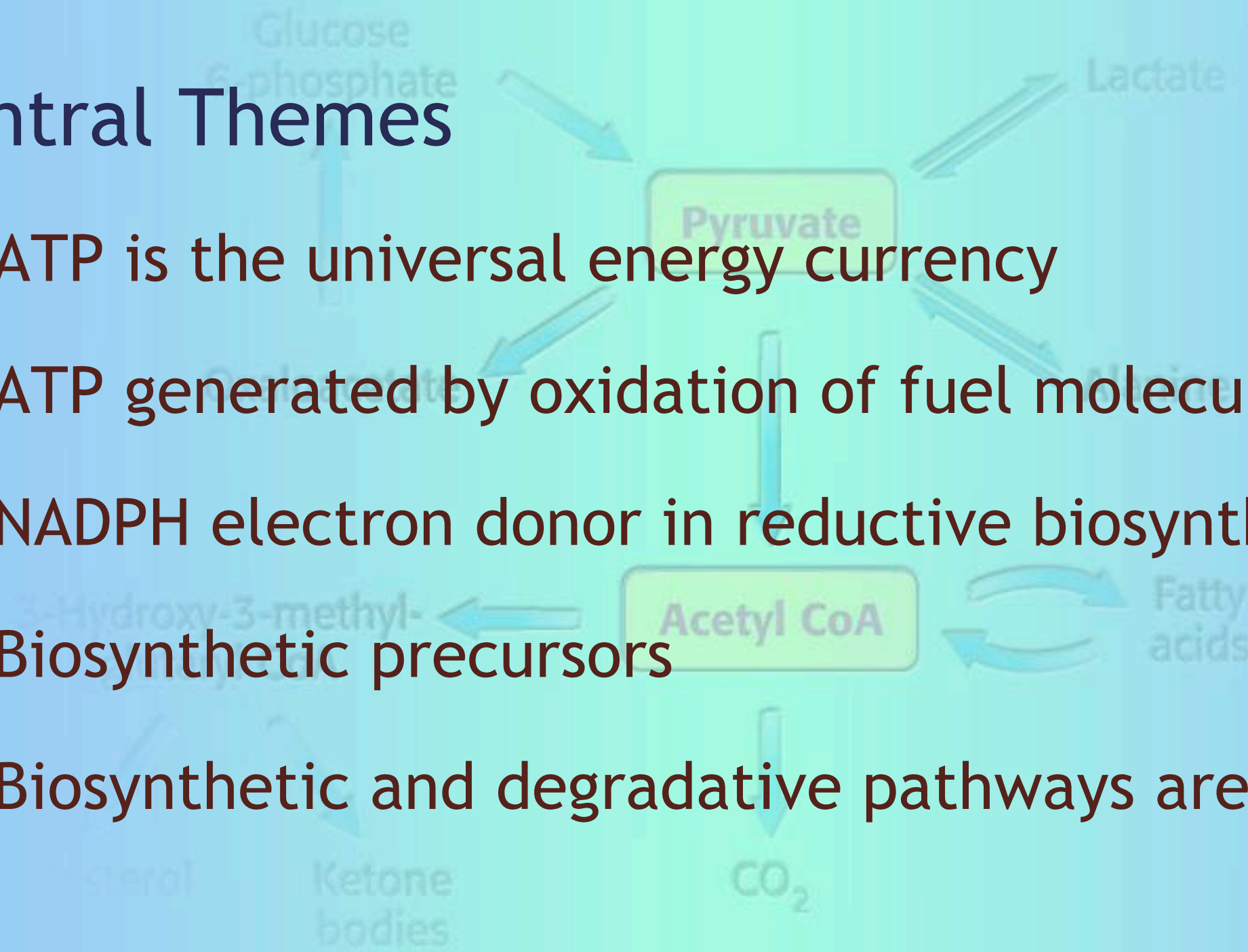
- ATP
- Reducing Power (NADH, NADPH, FADH₂)
- Biosynthetic precursors



1. Interconnected Pathways

Central Themes

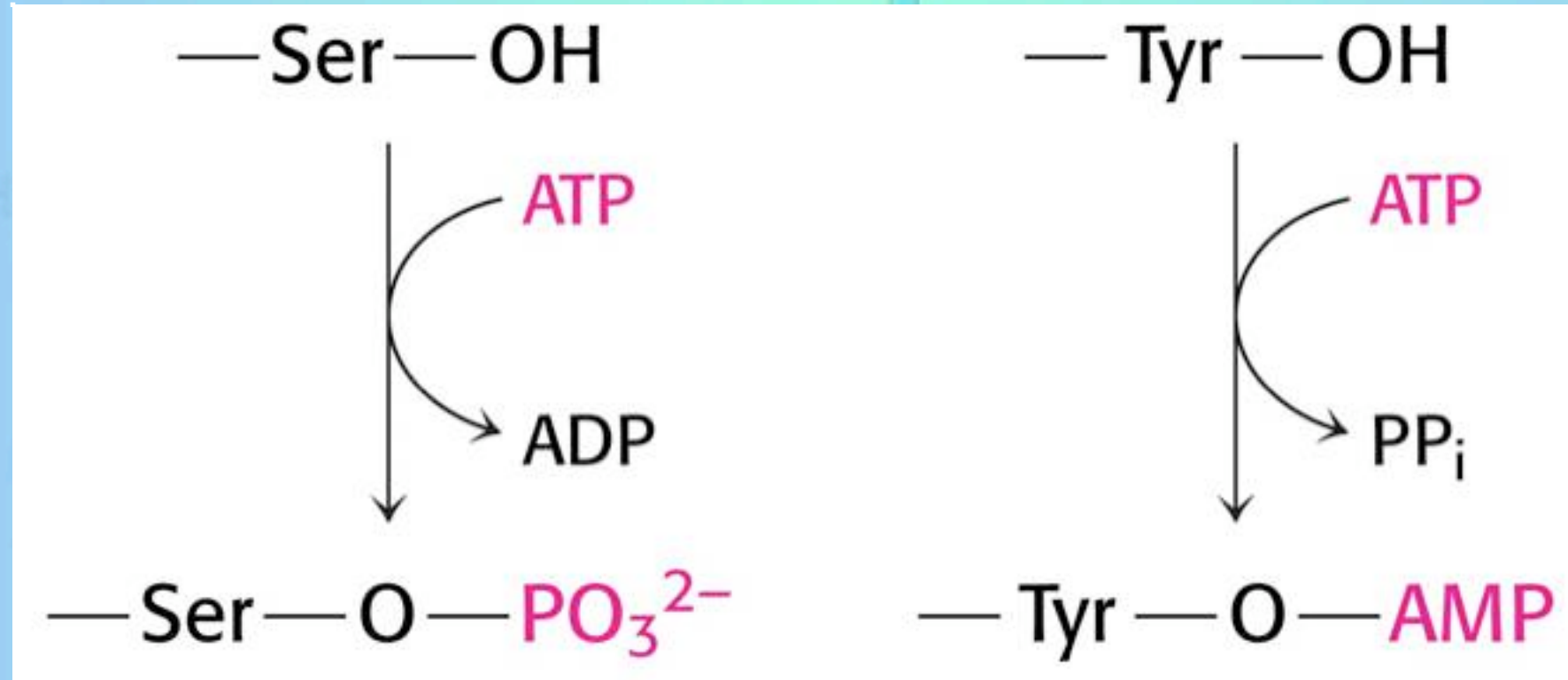
- ATP is the universal energy currency
- ATP generated by oxidation of fuel molecules
- NADPH electron donor in reductive biosynthesis
- Biosynthetic precursors
- Biosynthetic and degradative pathways are distinct



1.1 Recurring Motifs in Metabolic Regulation

Anabolism and catabolism must be precisely regulated:

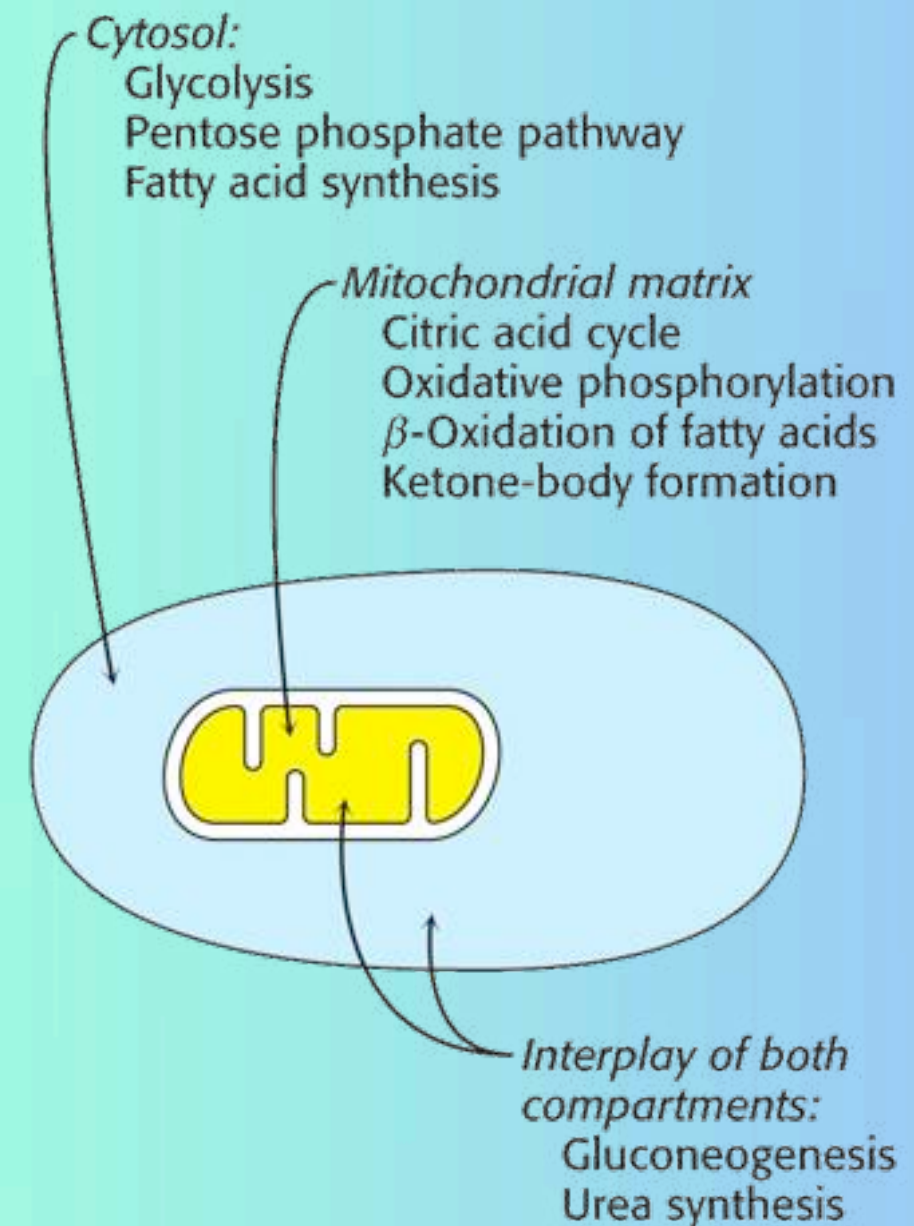
- Allosteric interactions
- Covalent modification



1.1 Recurring Motifs in Metabolic Regulation

Anabolism and catabolism must be precisely regulated:

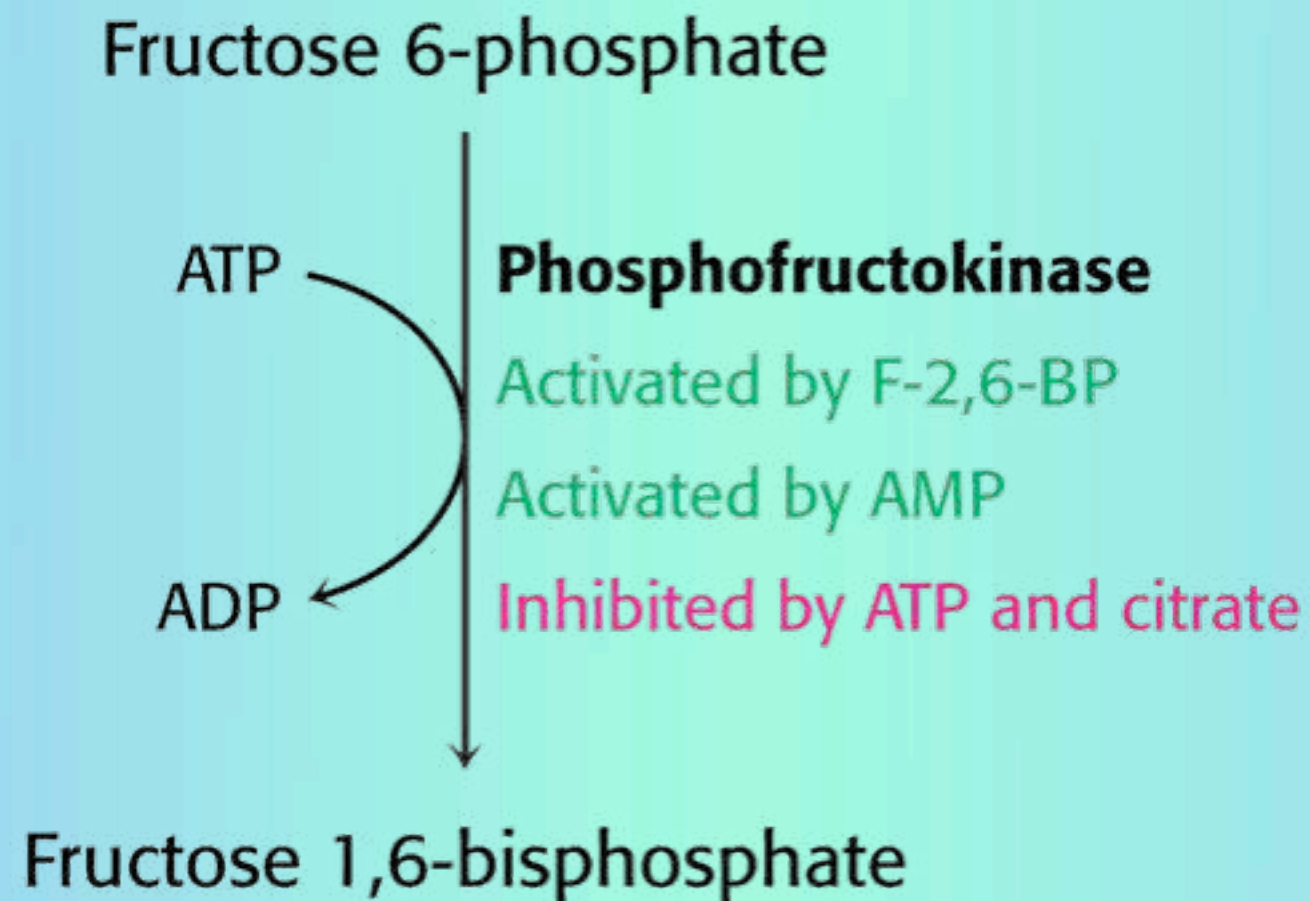
- Enzyme levels
- Compartmentalization
- Specialization of organs



1.2 Major Control Sites

Major metabolic pathways and control sites

- **Glycolysis**
 - Phosphofructokinase



1.2 Major Control Sites

Major metabolic pathways and control sites

- Citric acid cycle and oxidative phosphorylation
 - Electron donors are oxidized and recycled back to the citric acid cycle only if ADP is simultaneously phosphorylated to ATP.
 - ATP inhibits activity of
 - Isocitrate dehydrogenase
 - α -Ketoglutarate
 - Citric acid cycle also has anabolic role
 - pyruvate carboxylase

1.2 Major Control Sites

Major metabolic pathways and control sites

- Pentose phosphate pathway
 - oxidative phase
 - produces NADPH and ribose 5-phosphate
 - non-oxidative phase
 - regenerates glycolytic intermediates

1.2 Major Control Sites

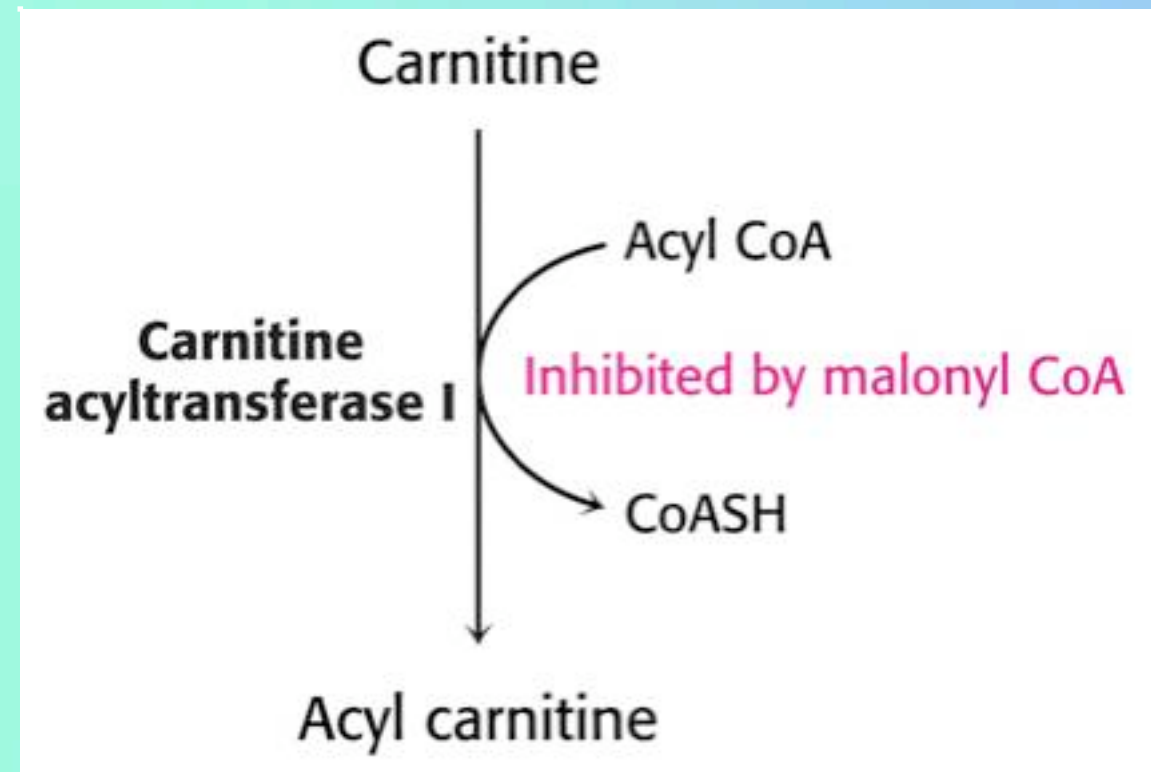
Major metabolic pathways and control sites

- **Gluconeogenesis**
 - Glycolysis and gluconeogenesis are reciprocally regulated
- **Glycogen synthesis and degradation**
 - Hormonally controlled
 - Phosphorylation and allosteric control

1.2 Major Control Sites

Major metabolic pathways and control sites

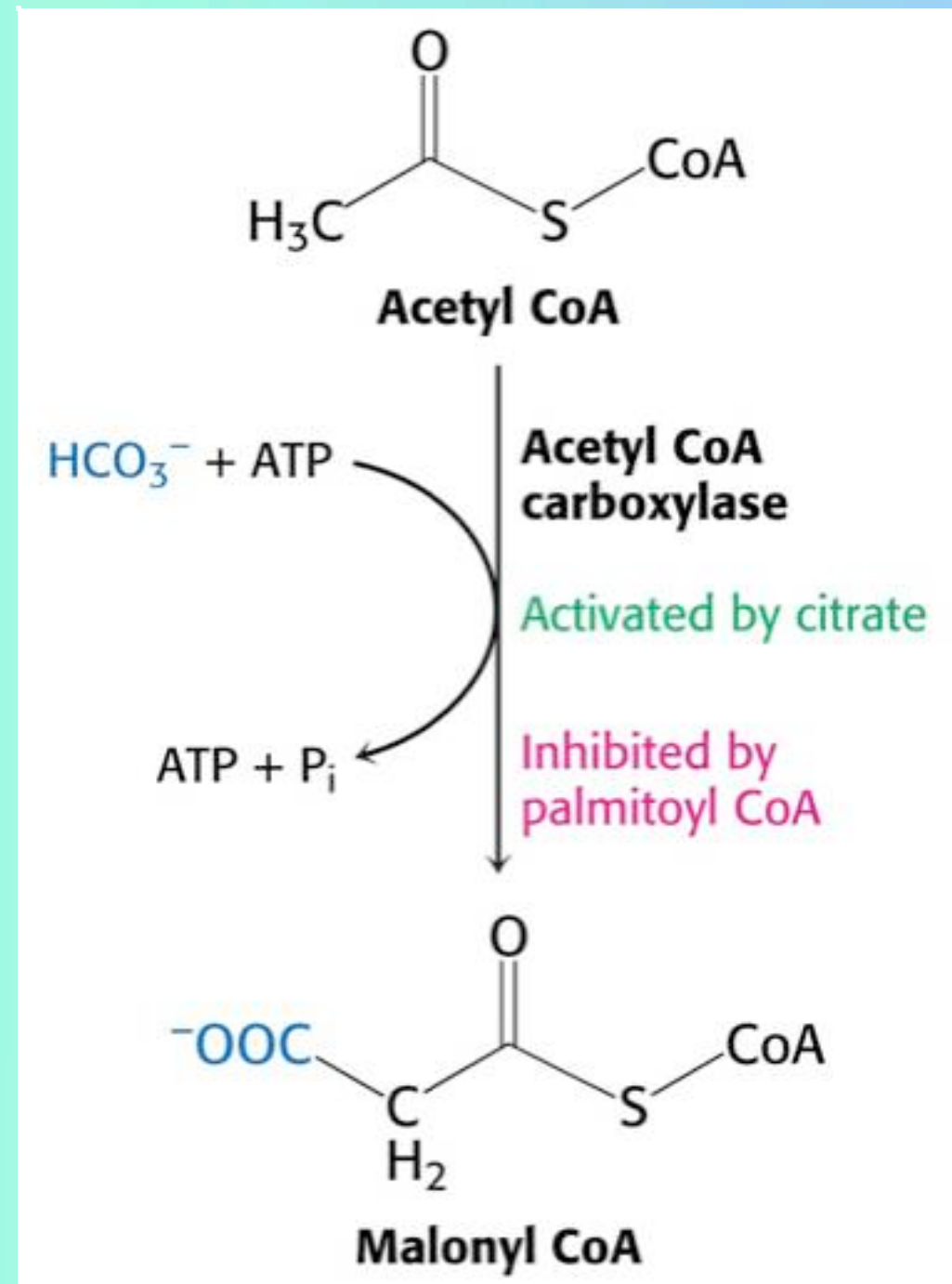
- Fatty acid synthesis and degradation
Matrix vs. cytosol



1.2 Major Control Sites

Major metabolic pathways and control sites

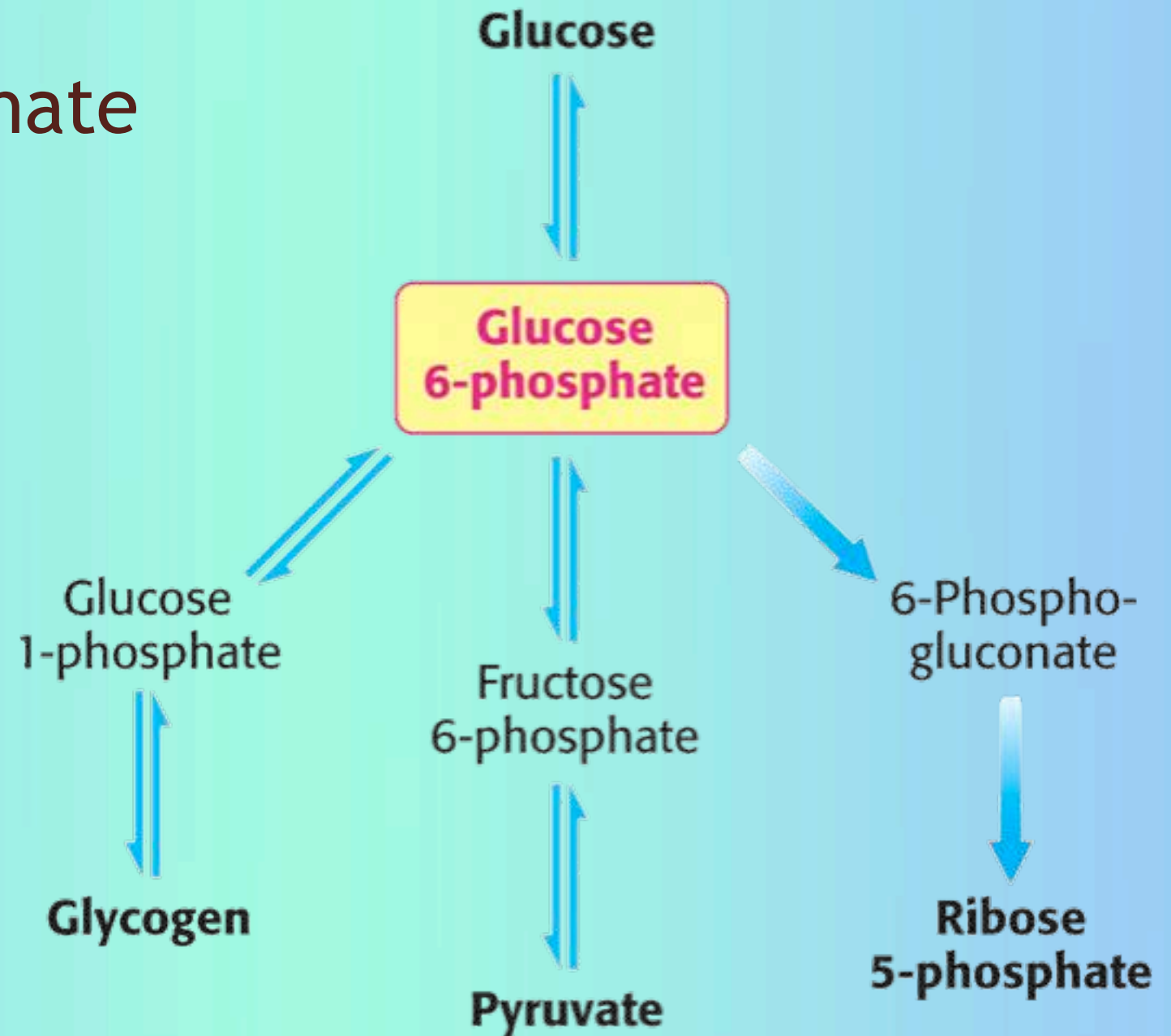
- Fatty acid synthesis and degradation
Matrix vs. cytosol



1.3 Key Junctions

Key junctions:

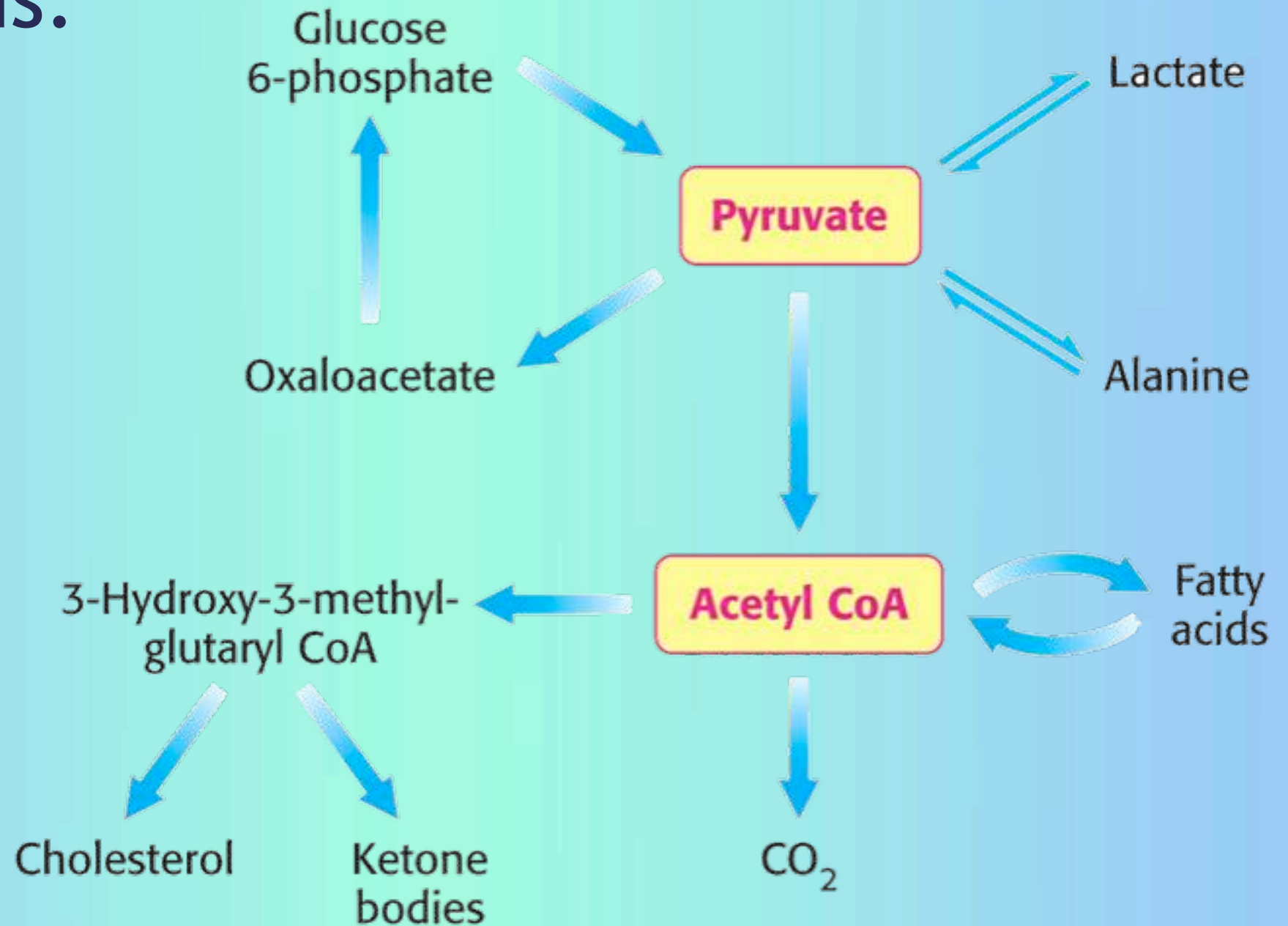
- Glucose 6-phosphate



1.3 Key Junctions

Key junctions:

- Pyruvate
- Acetyl-CoA



2. Organ Differences

Each organ has a unique metabolic profile

- **Brain**

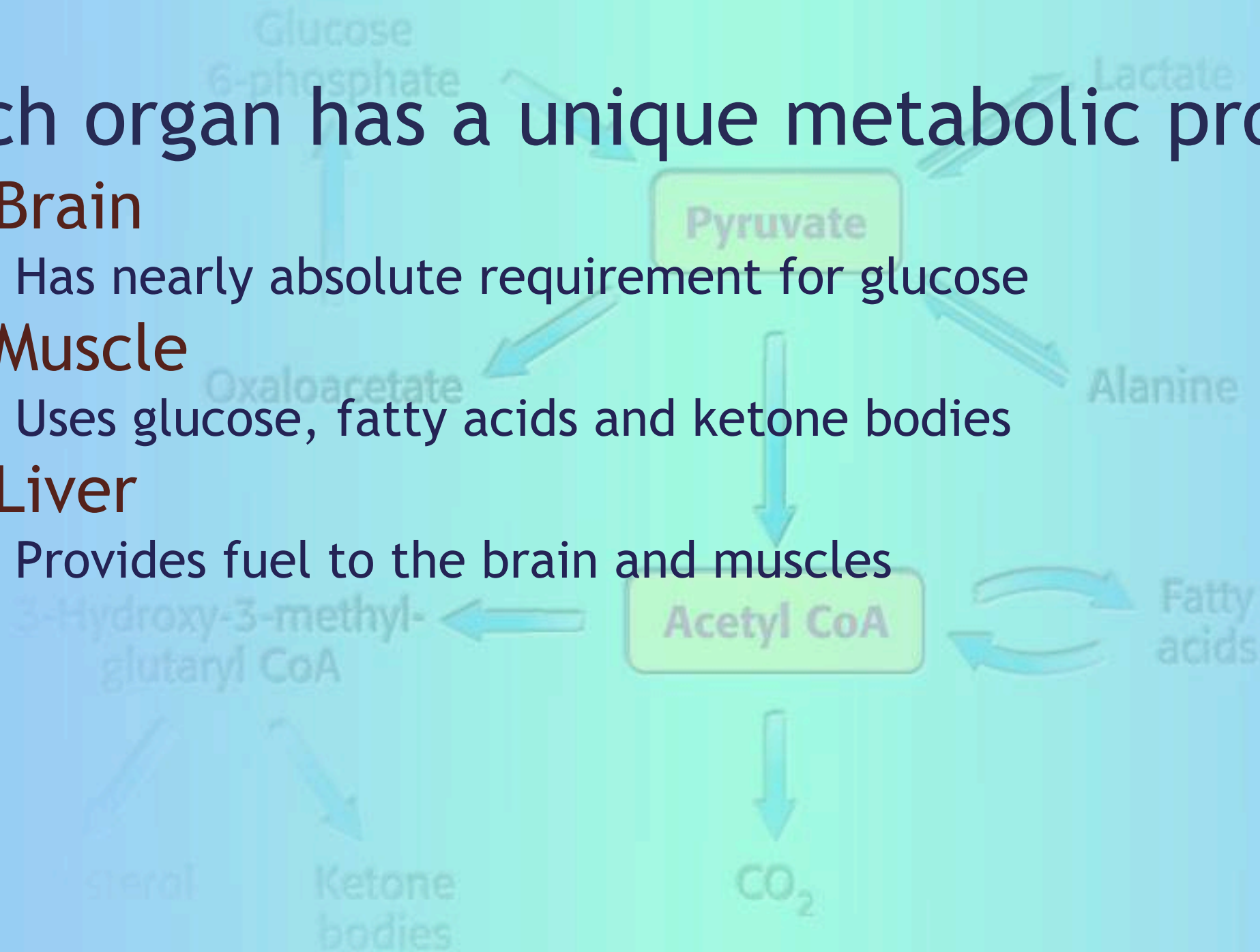
Has nearly absolute requirement for glucose

- **Muscle**

Uses glucose, fatty acids and ketone bodies

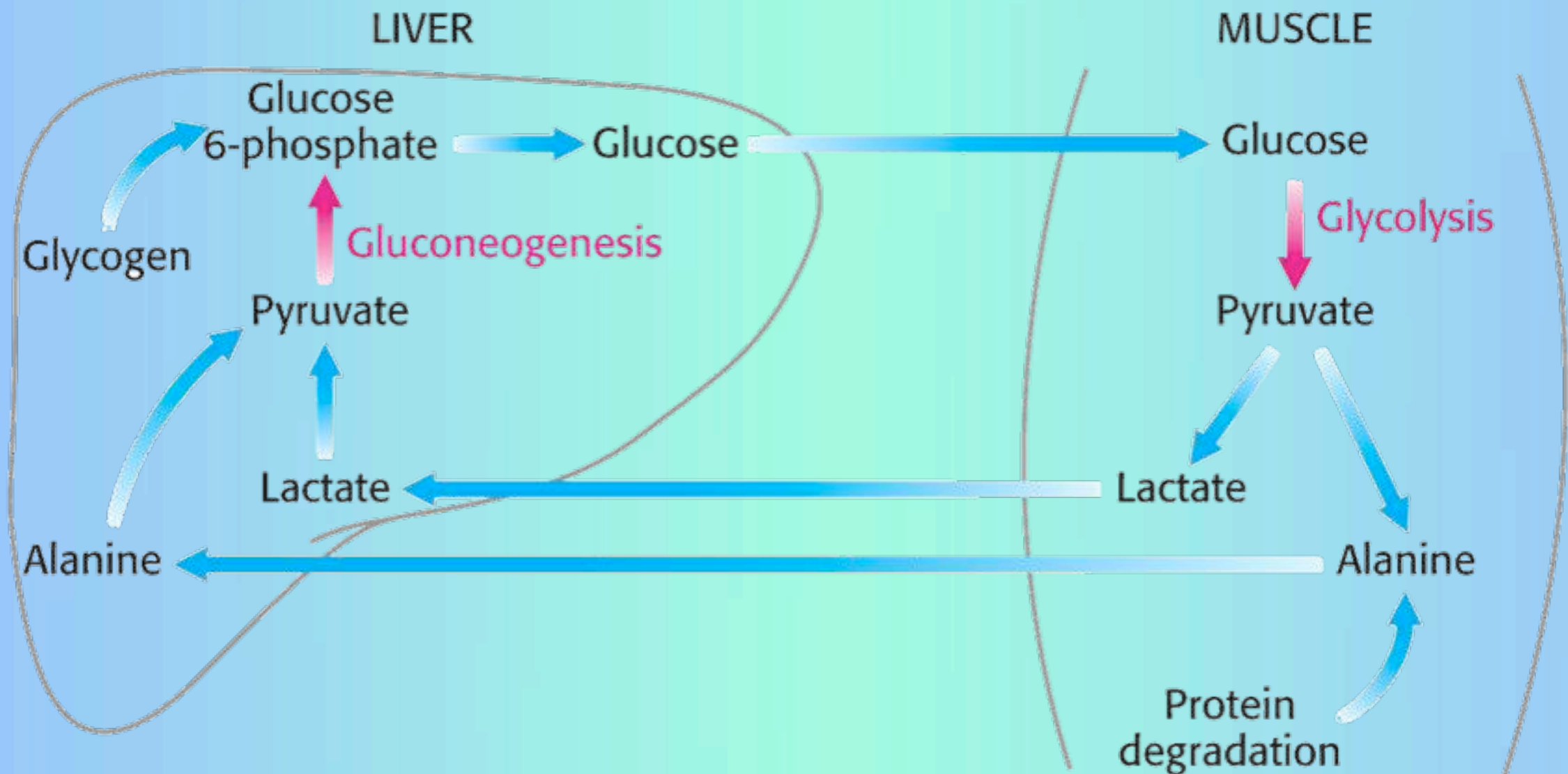
- **Liver**

Provides fuel to the brain and muscles



2. Organ Differences

Each organ has a unique metabolic profile



2. Organ Differences

Each organ has a unique metabolic profile

- Adipose tissue

