Chem 352 - Lecture 10
Lipid, Amino Acid, and Nucleotide Metabolism
Part II: Amino Acid Metabolism

Introduction

Amino acid metabolism is complex

We will focus on a couple of important themes:

- 17.1 Nitrogen fixation and the nitrogen cycle
- 17.2 Assimilation of ammonia
- 17.3 Synthesis of amino acids (Ala, Asp, Asn, Glu, Gln, Arg, Pro, Ser, Gly)
- 17.4 Amino acids as precursors
- 17.7 The urea cycle

Nitrogen Fixation

Inorganic sources of nitrogen include

- N_2 from the atmosphere
- NO_2^- (nitrite) and NO_3^- (nitrate) ions

Both are reduced to NH_3 for assimilation into living systems.

Most animals get their nitrogen from amino acids.

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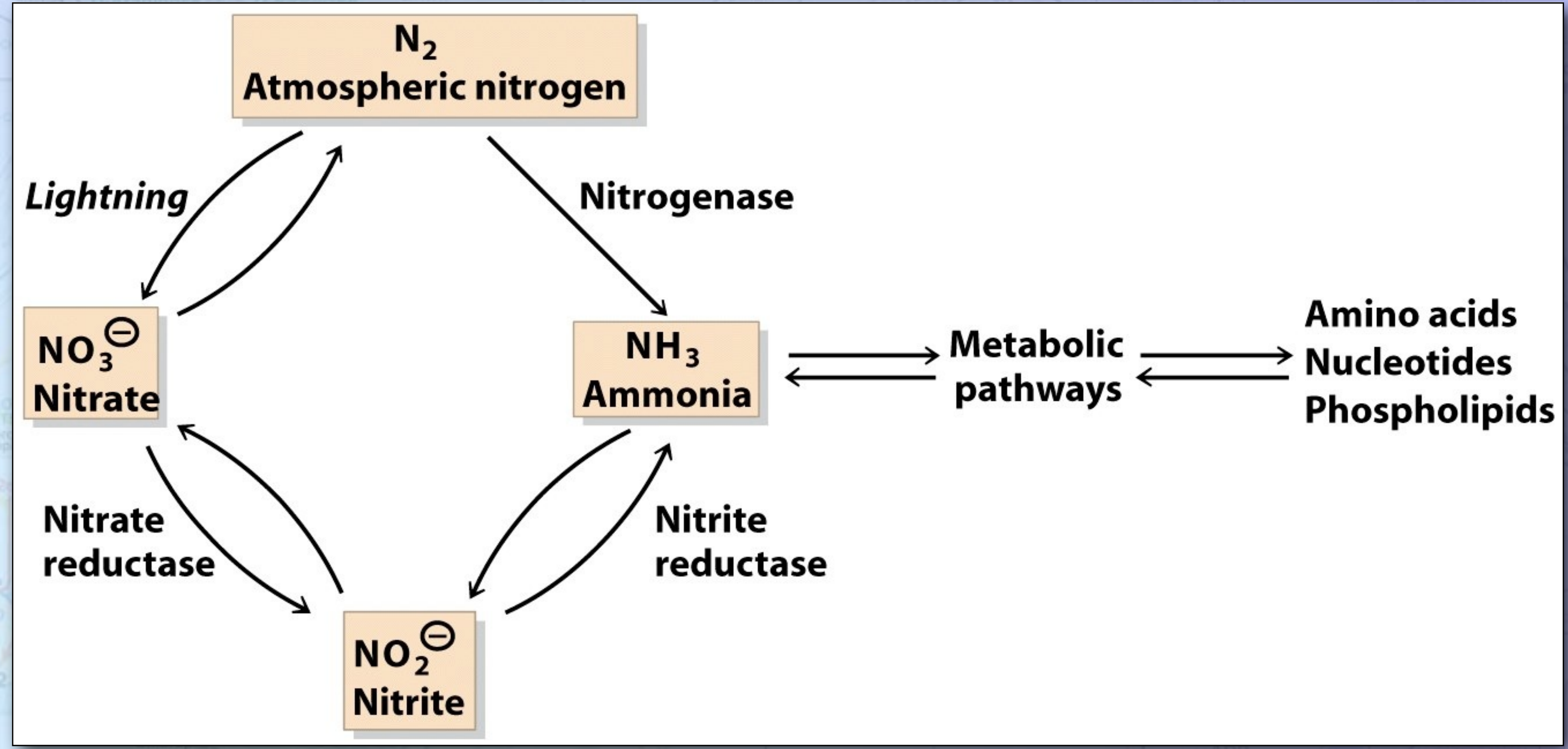


Nitrogen Fixation

Nitrogen fixation.

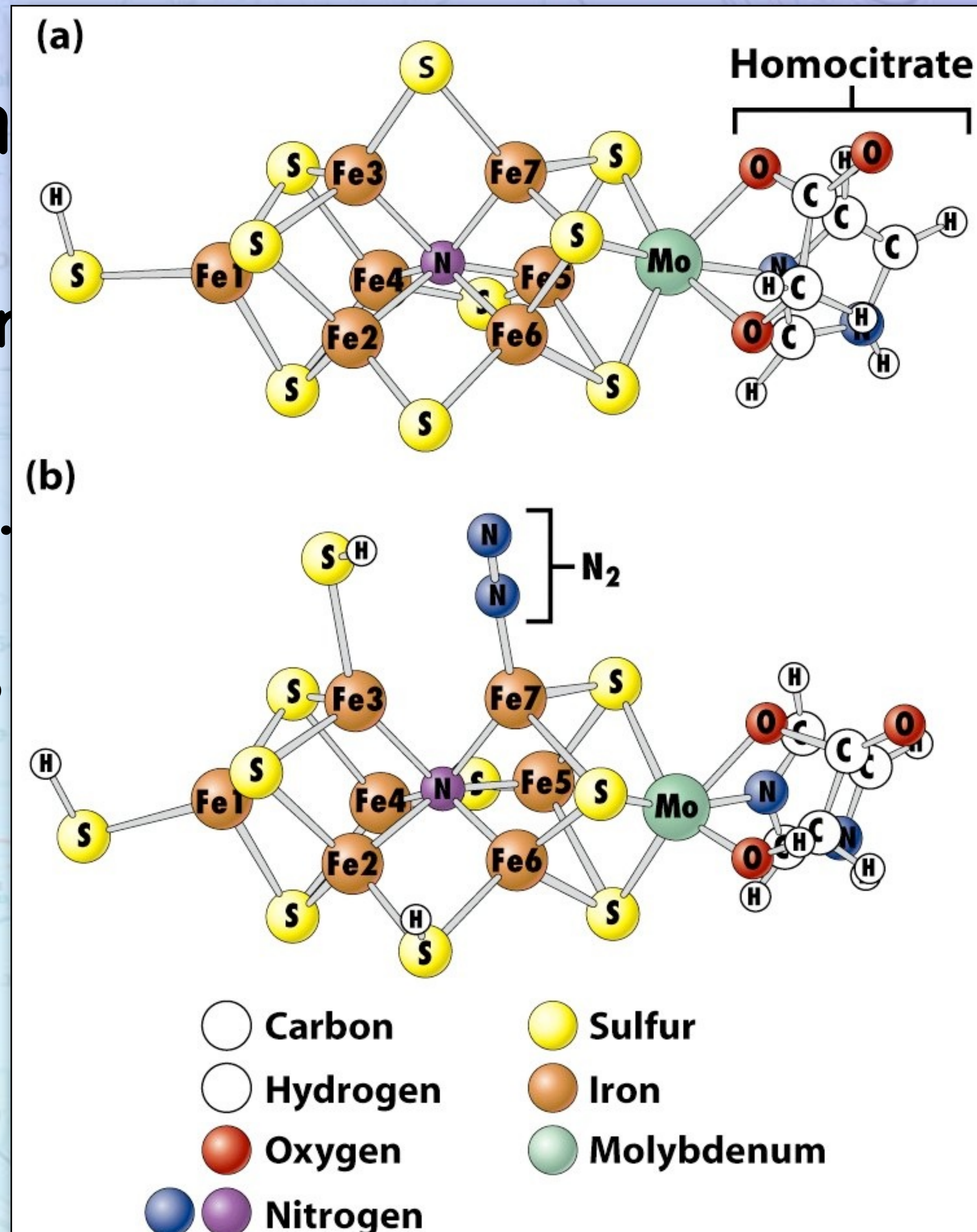
- Carried out by a limited number of bacteria
  - Most notably, the symbiotic Rhizobacteria found in the root nodules of leguminous plants.

$$N_2 + 8\,H^+ + 8\,e^- + 16\,ATP \longrightarrow 2\,NH_3 + H_2 + 16\,ADP + 16\,P_i$$

Nitrogen Fixation

Nitrogen

- Carried ... bacteria
  - Most n... bacteria found ... inous plants.



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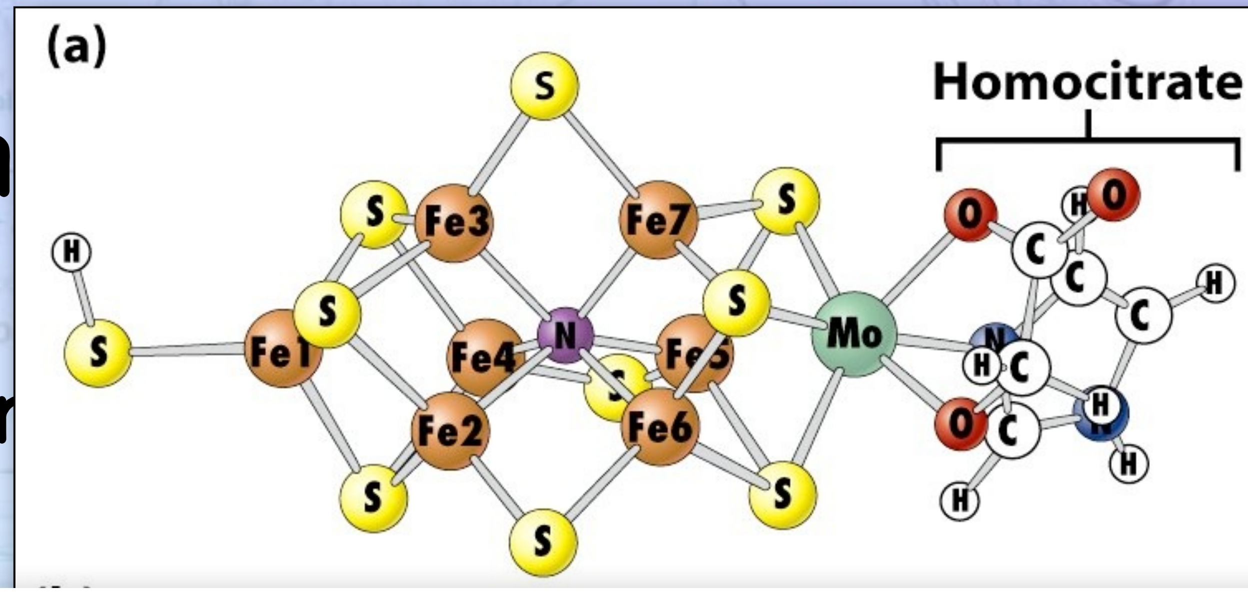

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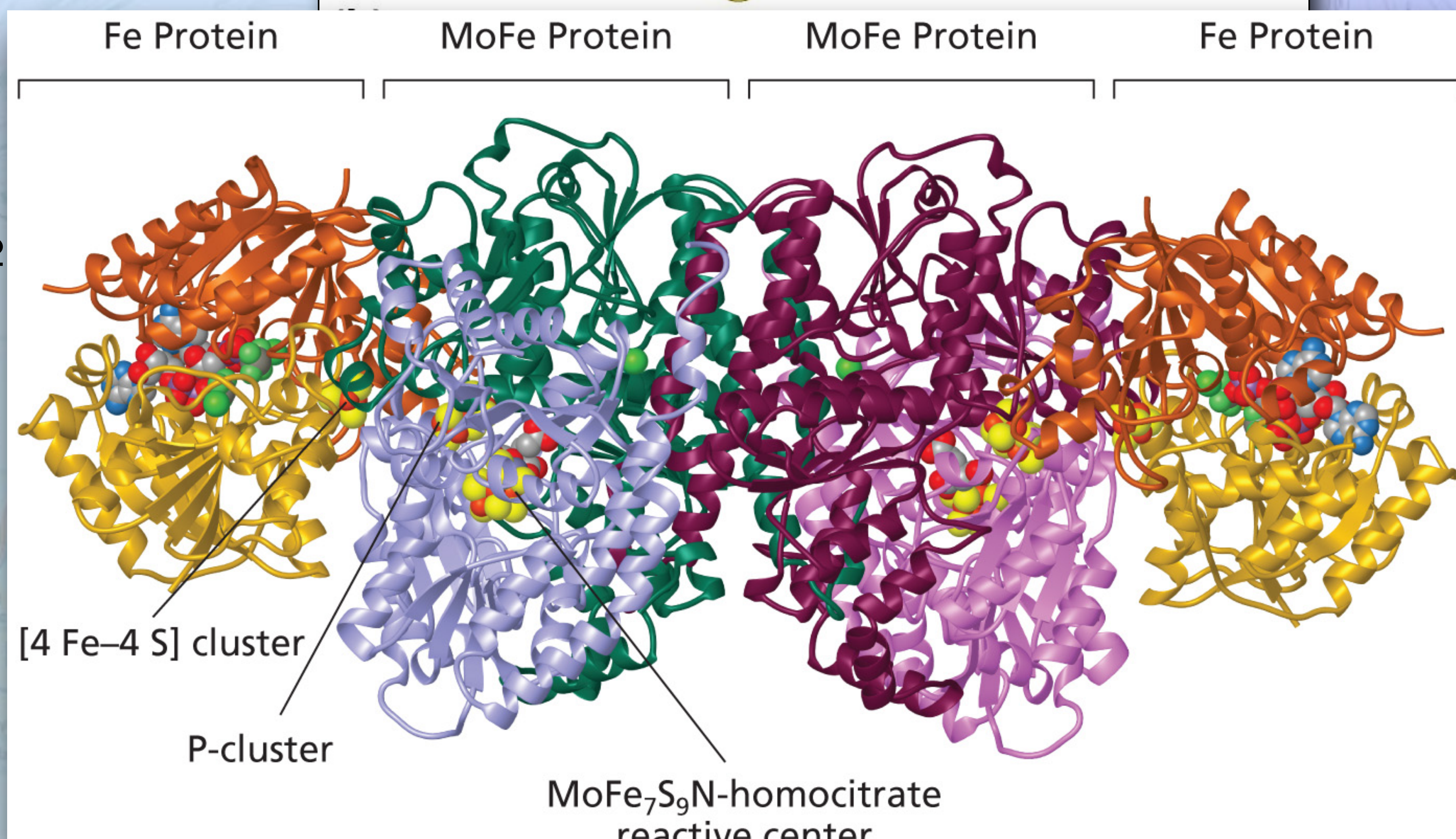

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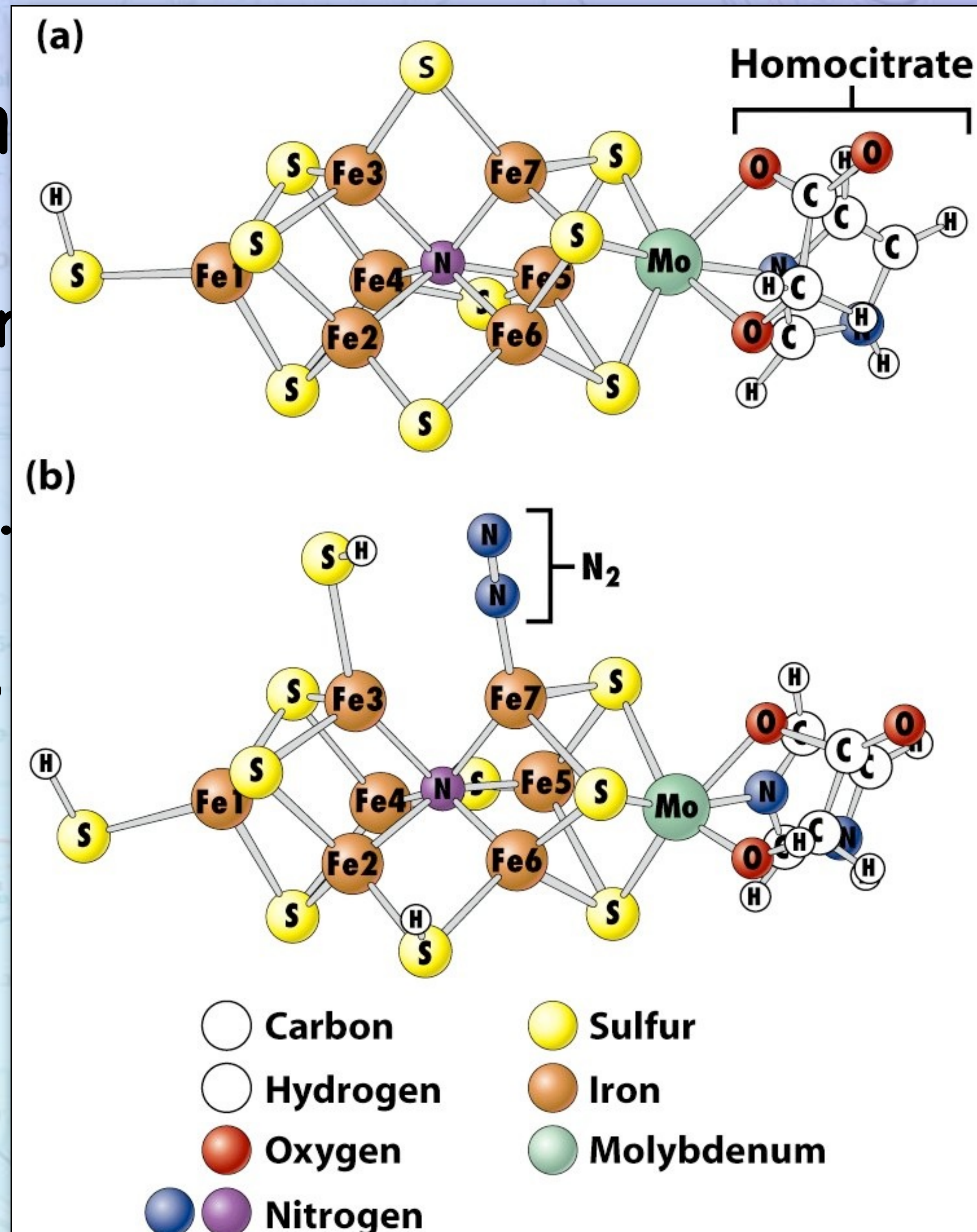

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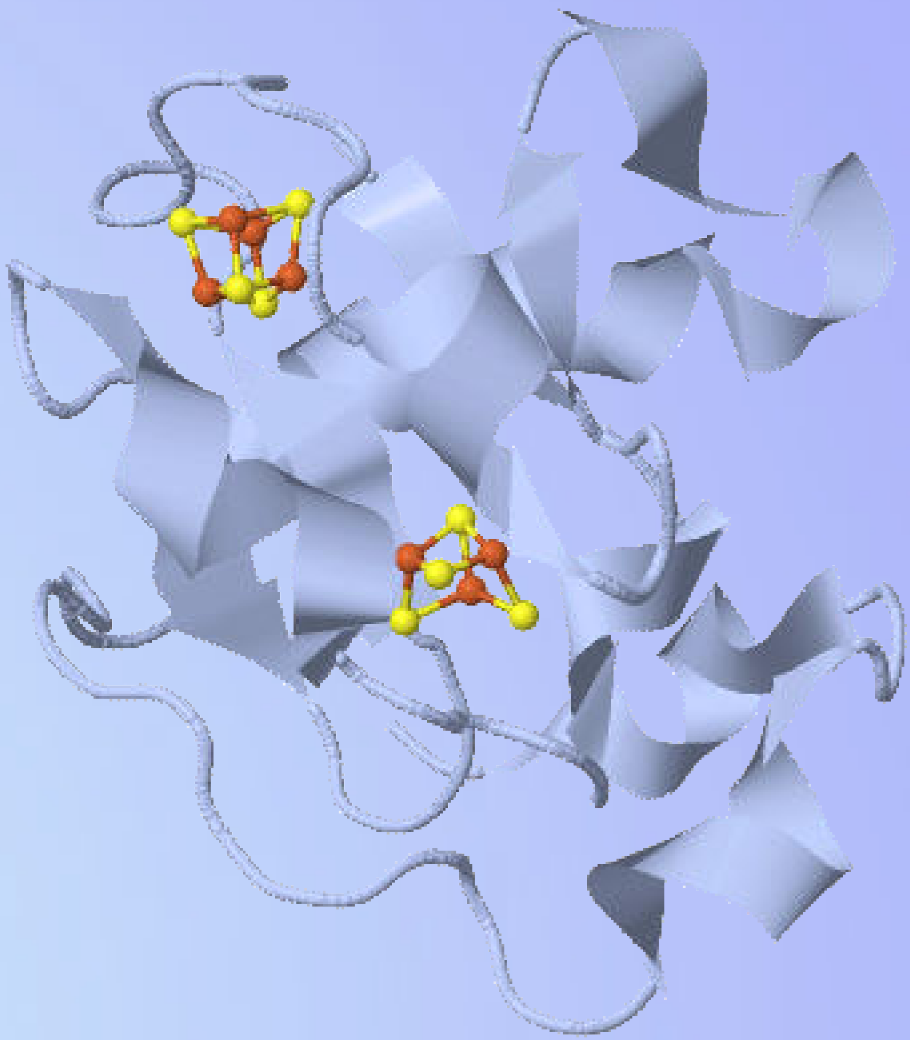
Nitrogen Fixation

Nitrogen fixation.

- The source of electrons are the electron tranport proteins **ferredoxin** and **flavodoxin**
- We saw ferredoxin in in the light reactions of photosynthesis

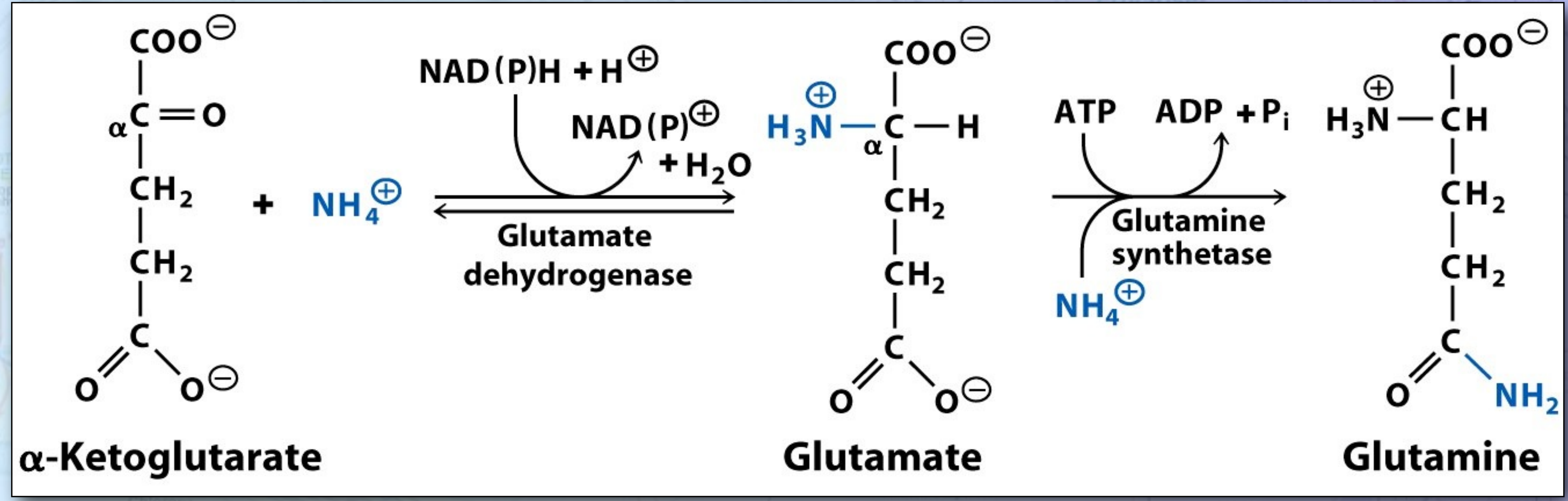


Ferredoxin

Assimilation of Ammonia

Ammonia is assimilated primarily through the amino acids glutamate and glutamine.

- Mammals do not assimilate much NH_3 directly.



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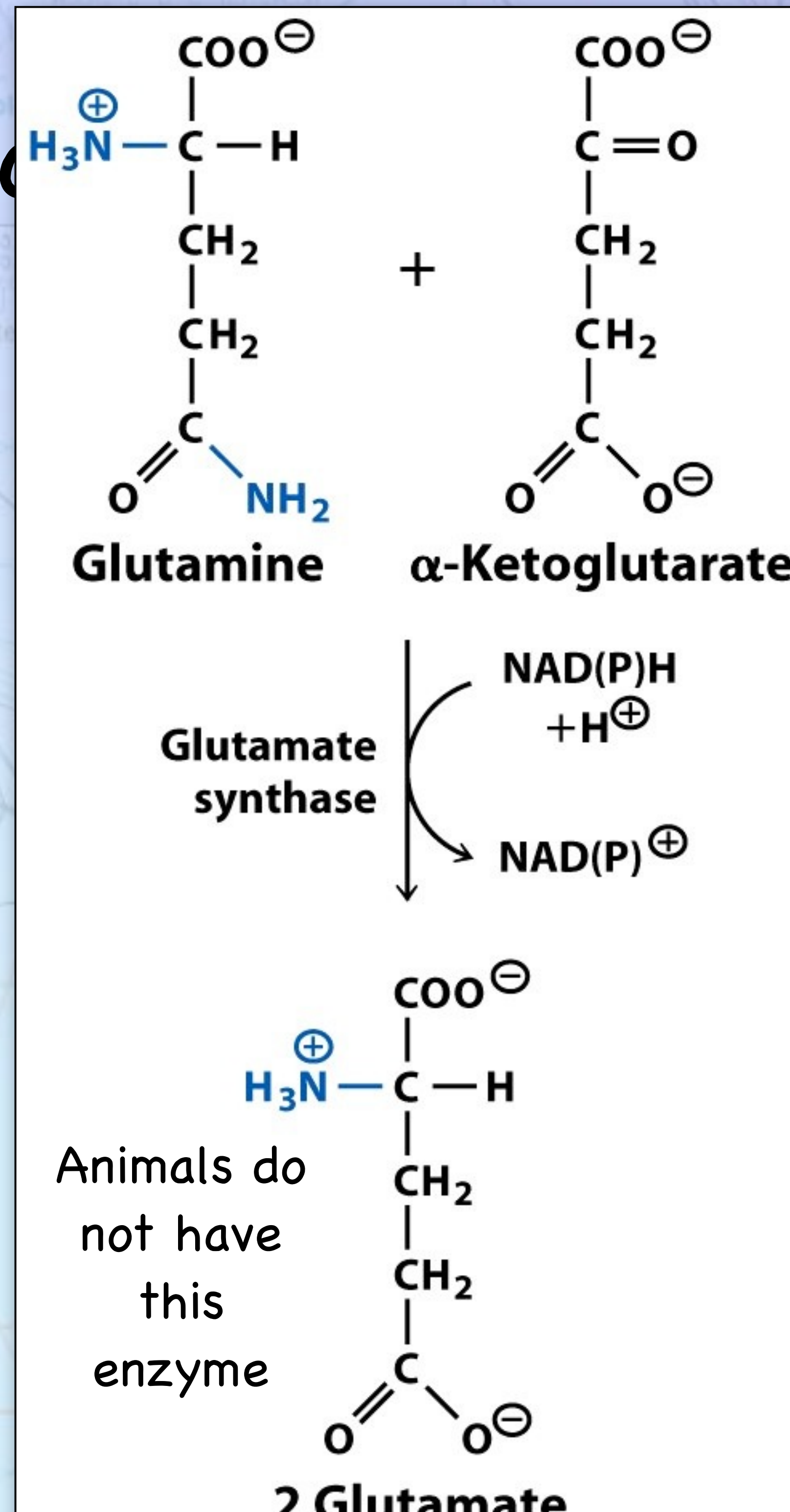

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Nitrogen can then transferred to other amino acids using the transamination reaction.

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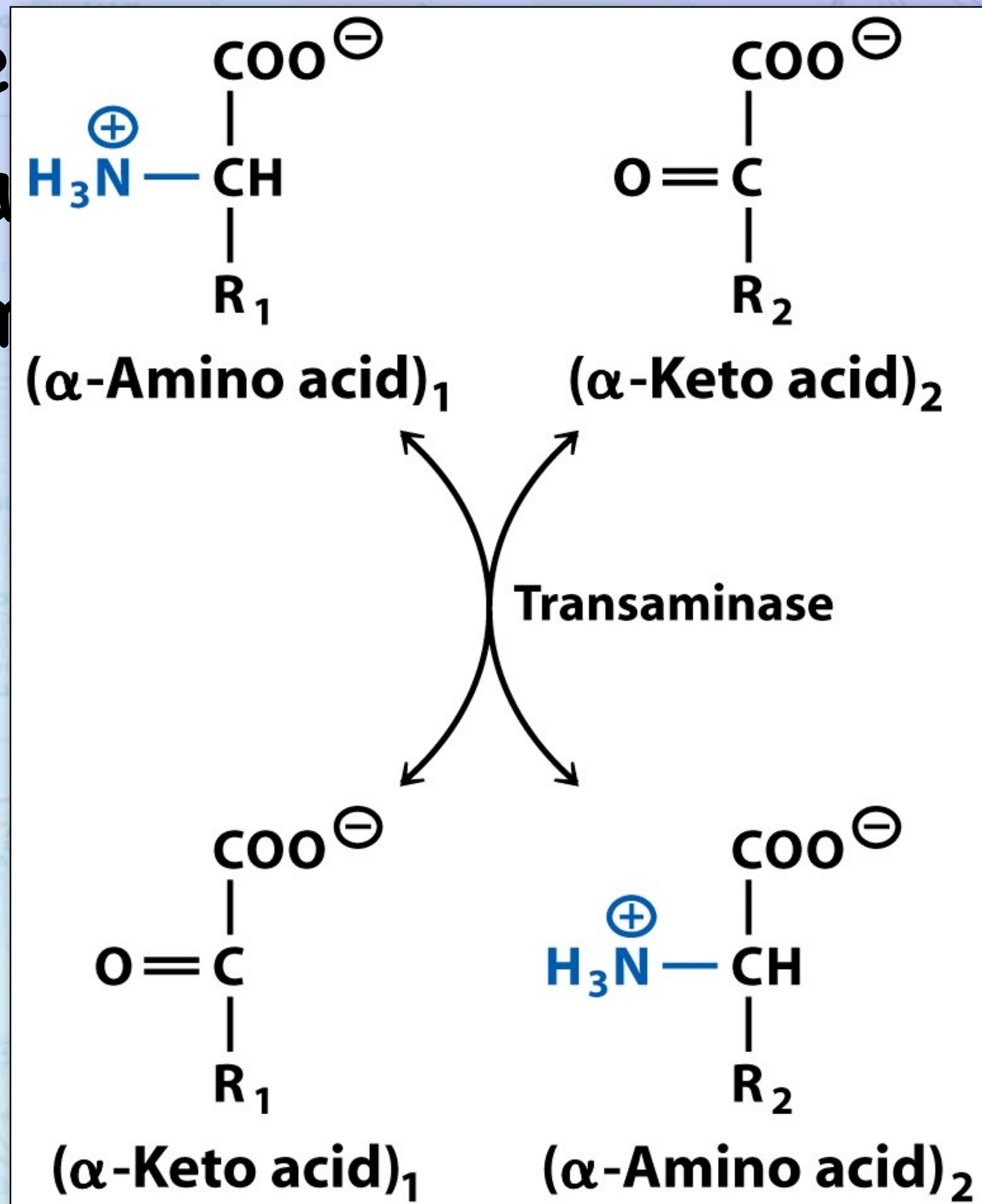

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- The transamination reactions uses the coenzyme **pyridoxal phosphate (PLP, Chapter 7.8)**

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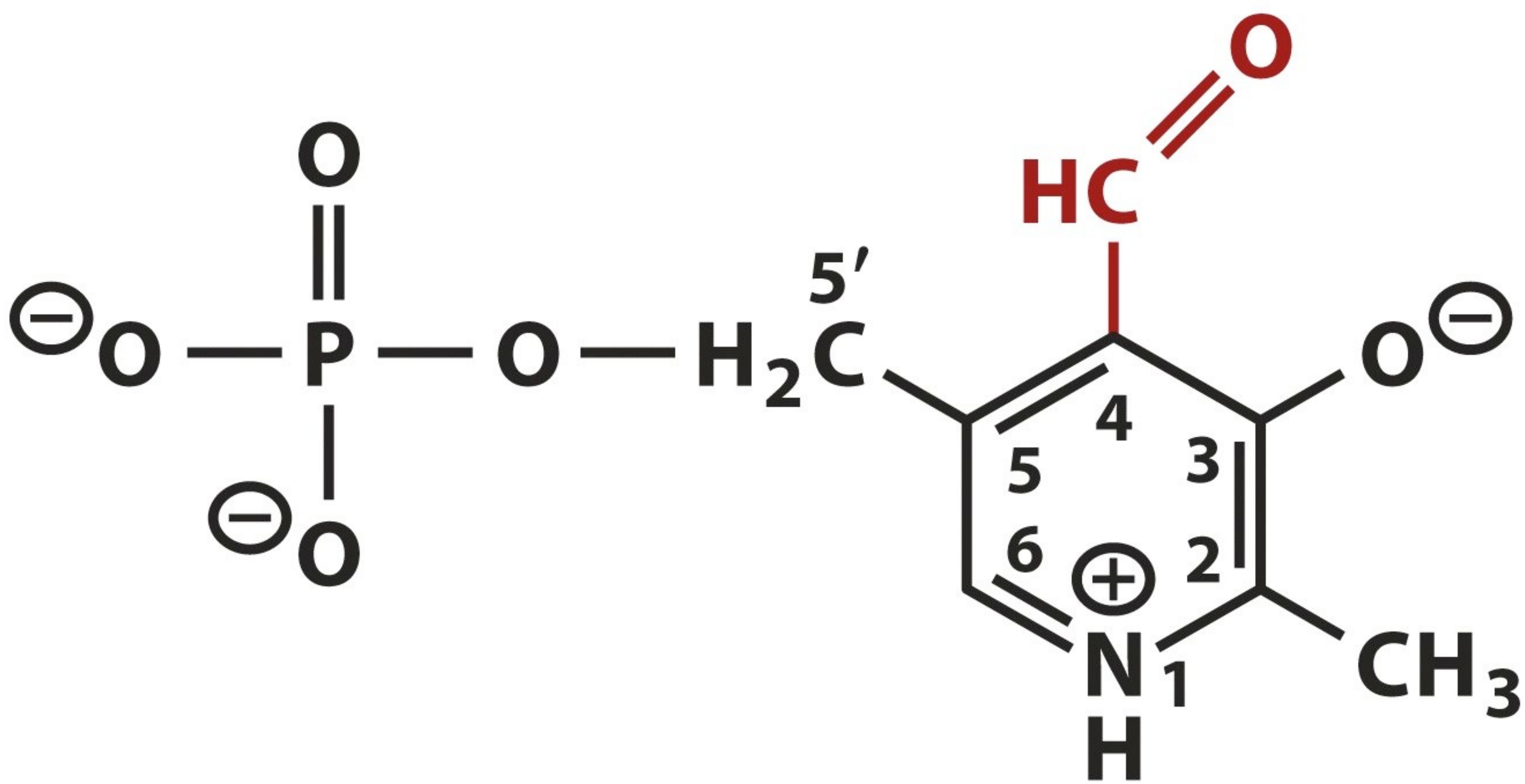

Pyridoxal 5′-phosphate (PLP)

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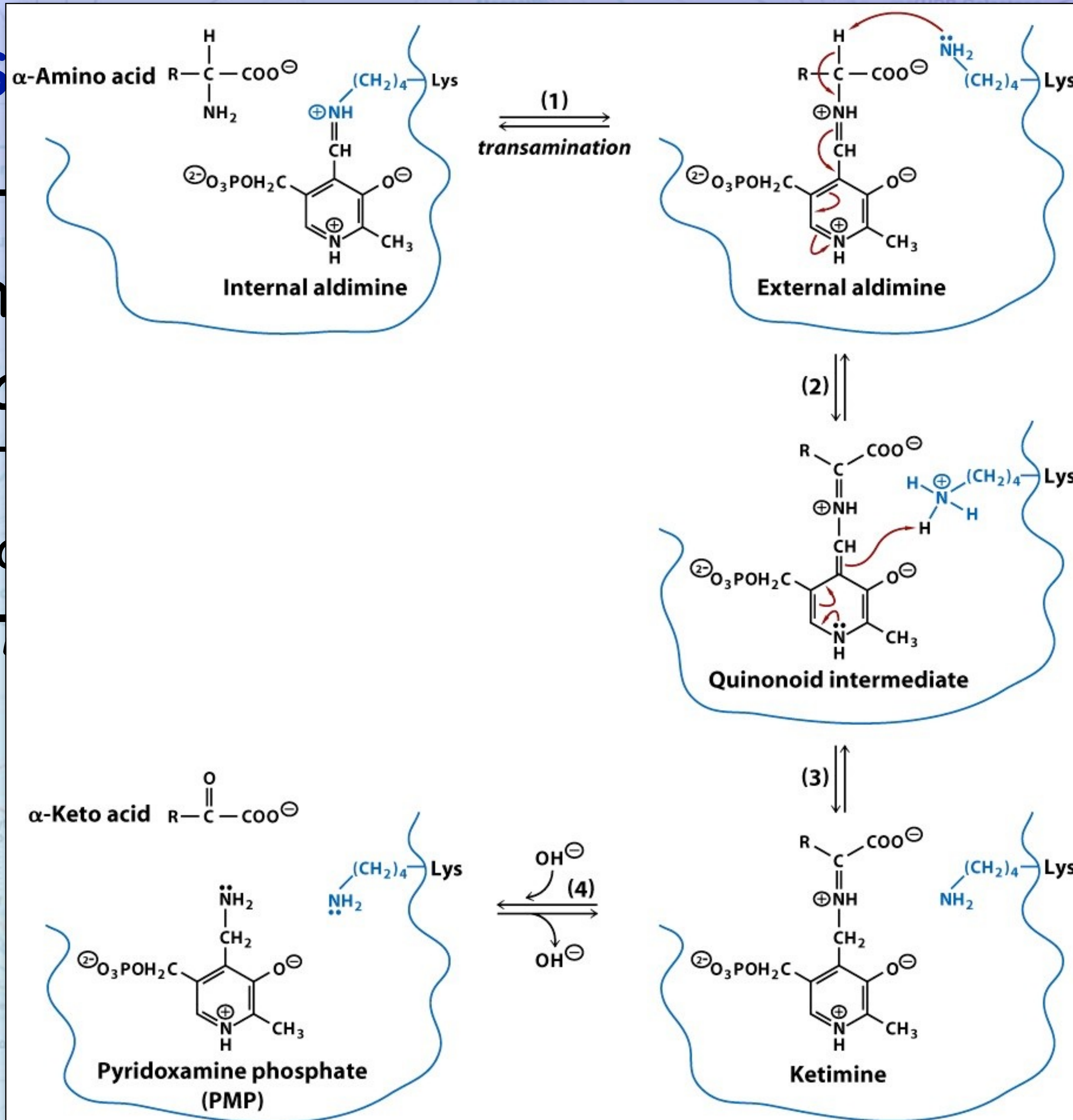

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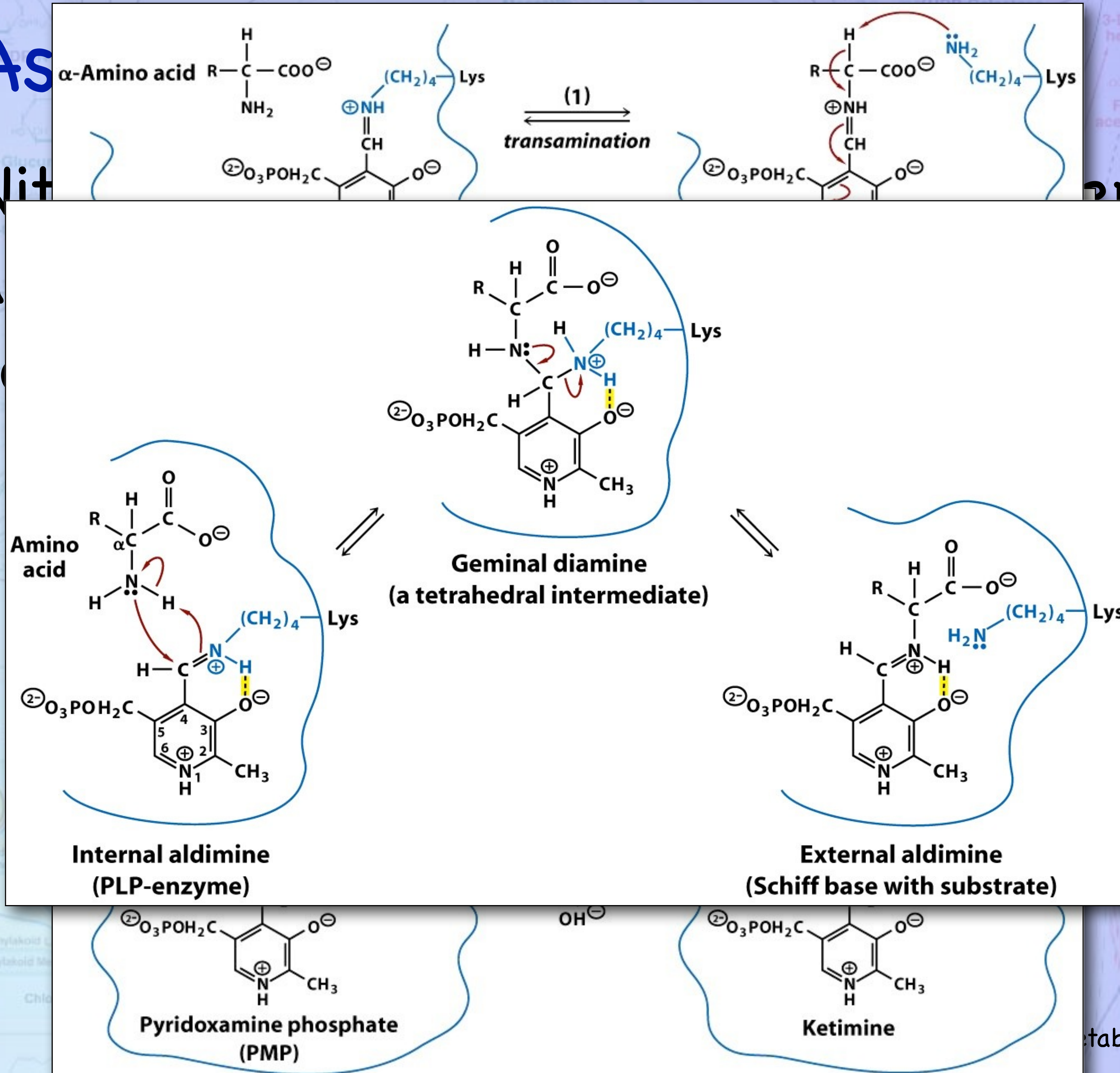

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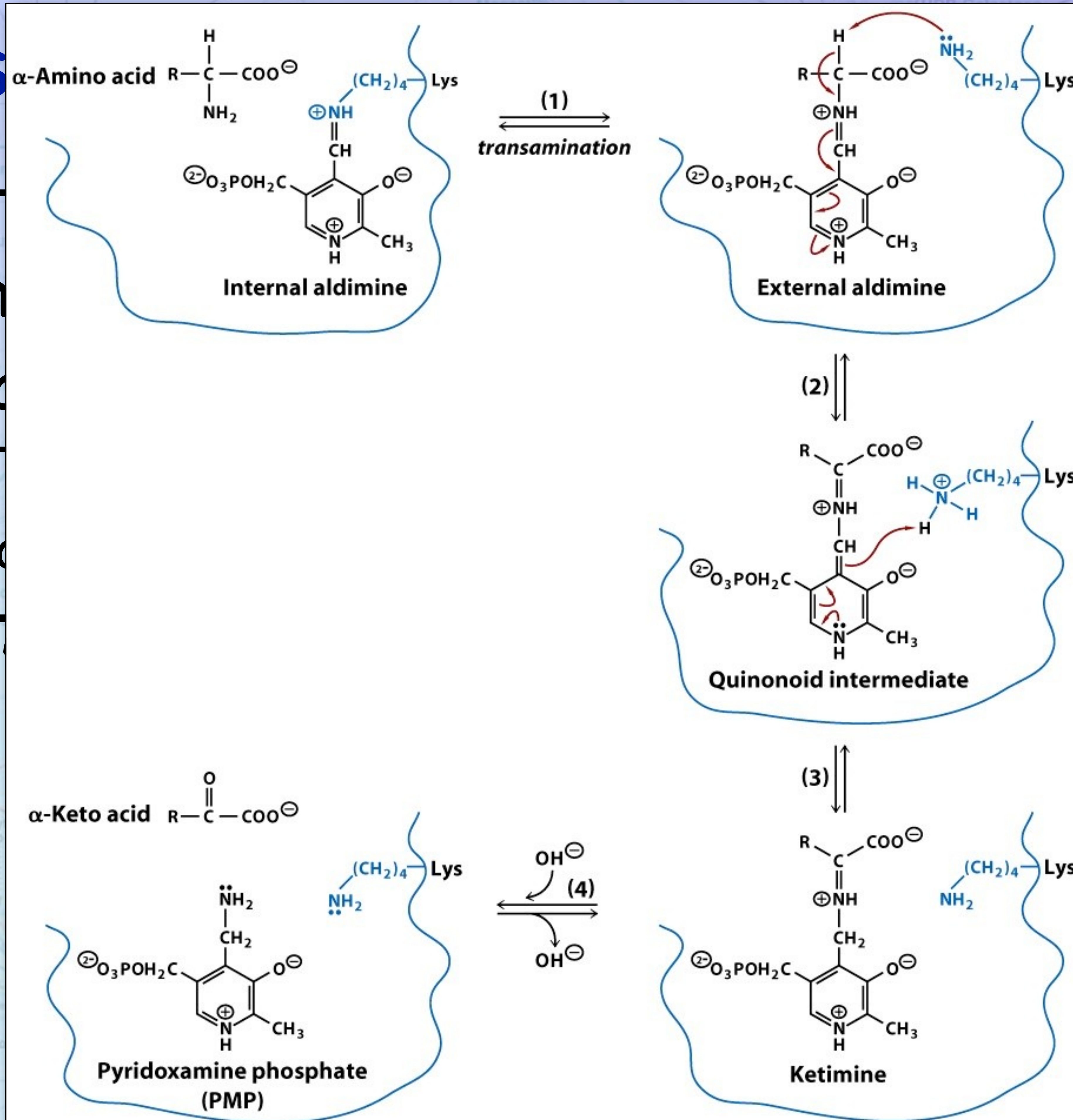

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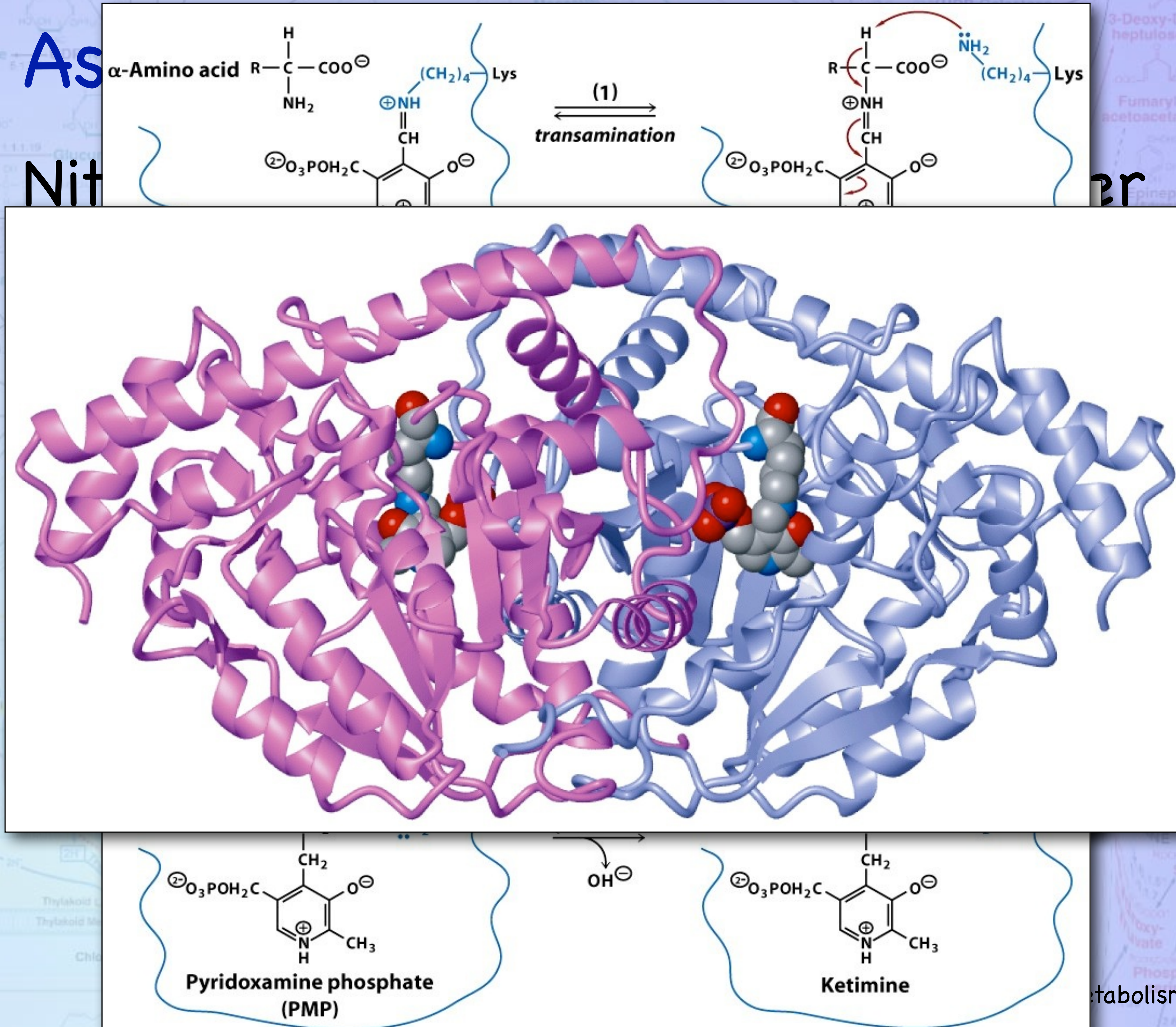
α-Amino acid
H
R
COO⊖
NH2
(CH2)4
Lys
⊕NH
CH
⊖O3POH2C
O⊖
(1)
transamination
NH2
Pyridoxamine phosphate
(PMP)
CH2
CH3
OH⊖
Ketimine

Assimilation of Ammonia

Nitrogen is then transferred to other amino acids by the transamination reaction.

- The transamination reactions uses the coenzyme **pyridoxal phosphate (PLP, Chapter 7.8)**

Assimilation of Ammonia

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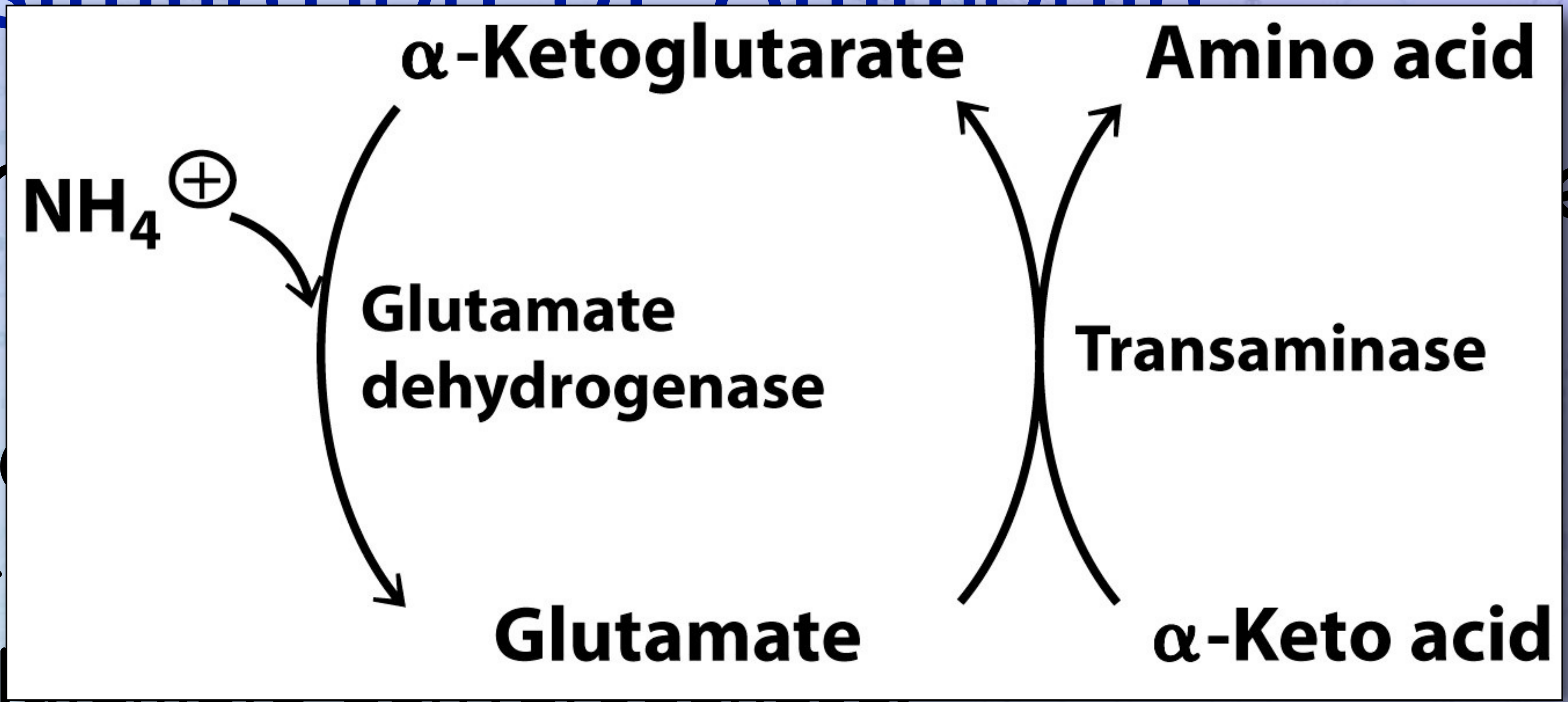

Assimilation of Ammonia

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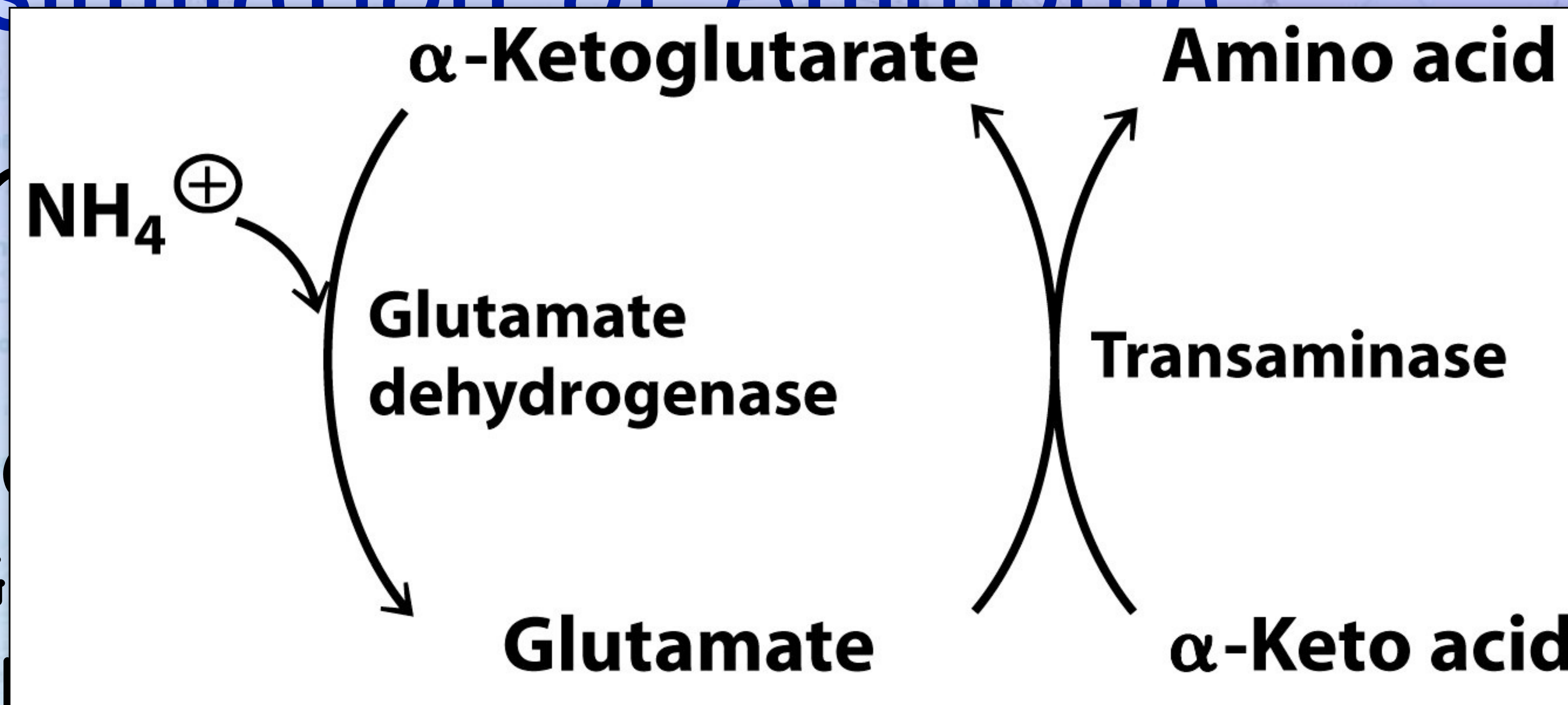
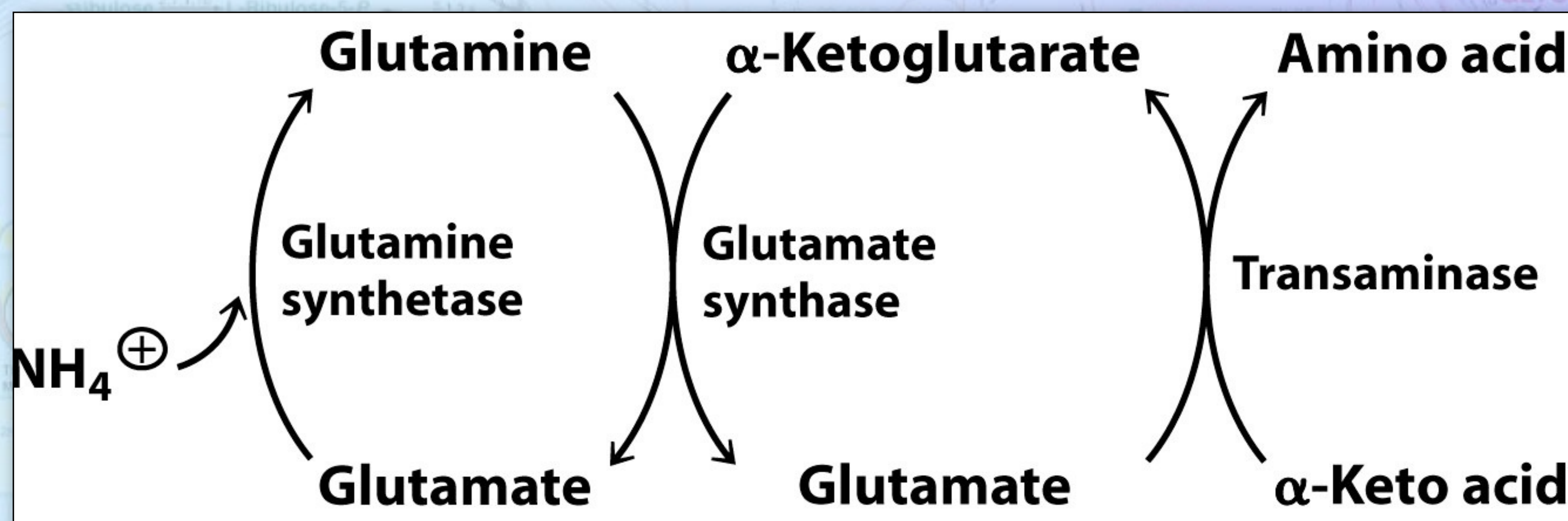




Assimilation of Ammonia

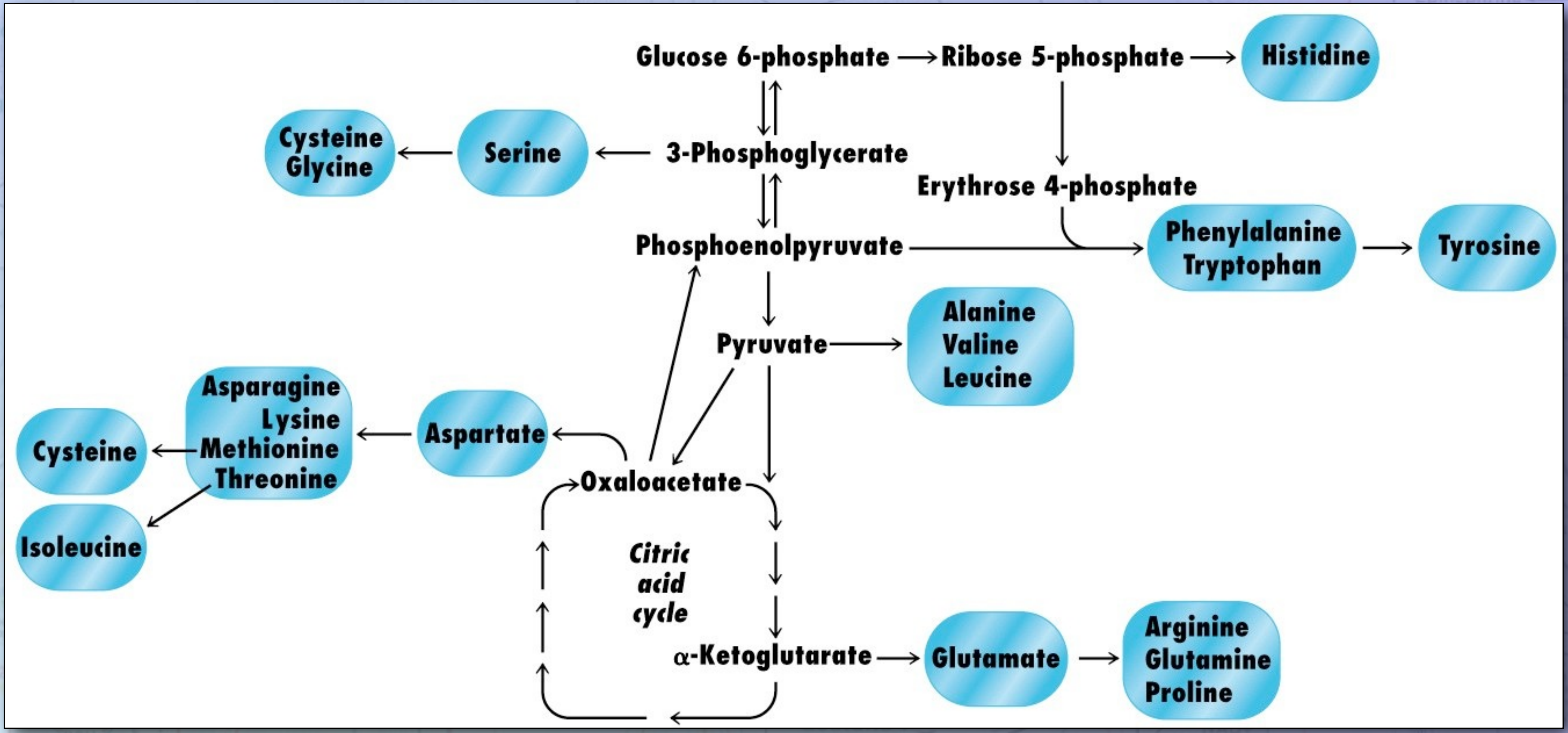
Nitrogen is then transferred to other amino acids by the transamination reaction.

- Glutamine synthetase has a lower K_m than glutamate dehydrogenase.

Assimilation of Ammonia

Nitrogen is then transferred to other amino acids by by additional transamination reactions.

Synthesis of Amino Acids



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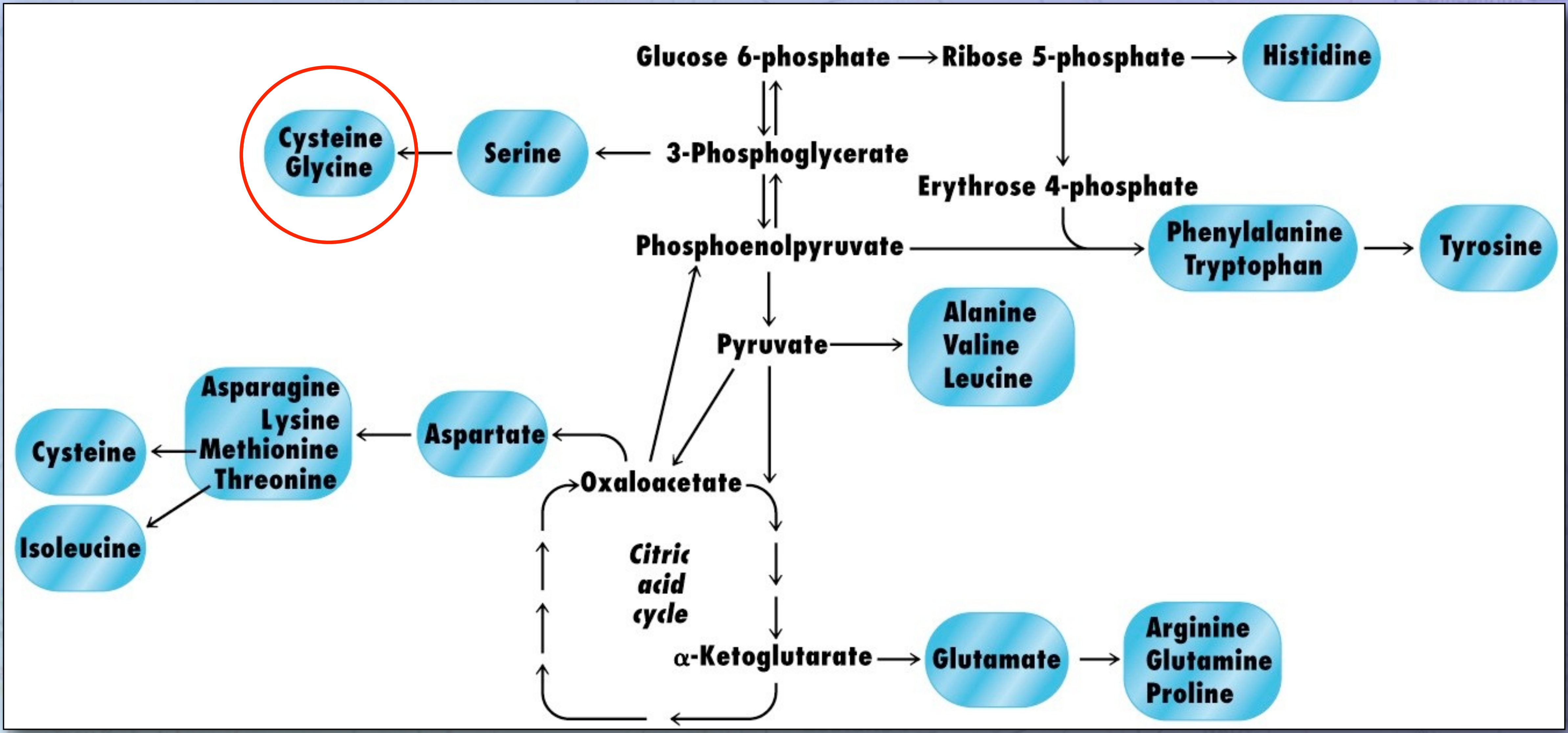

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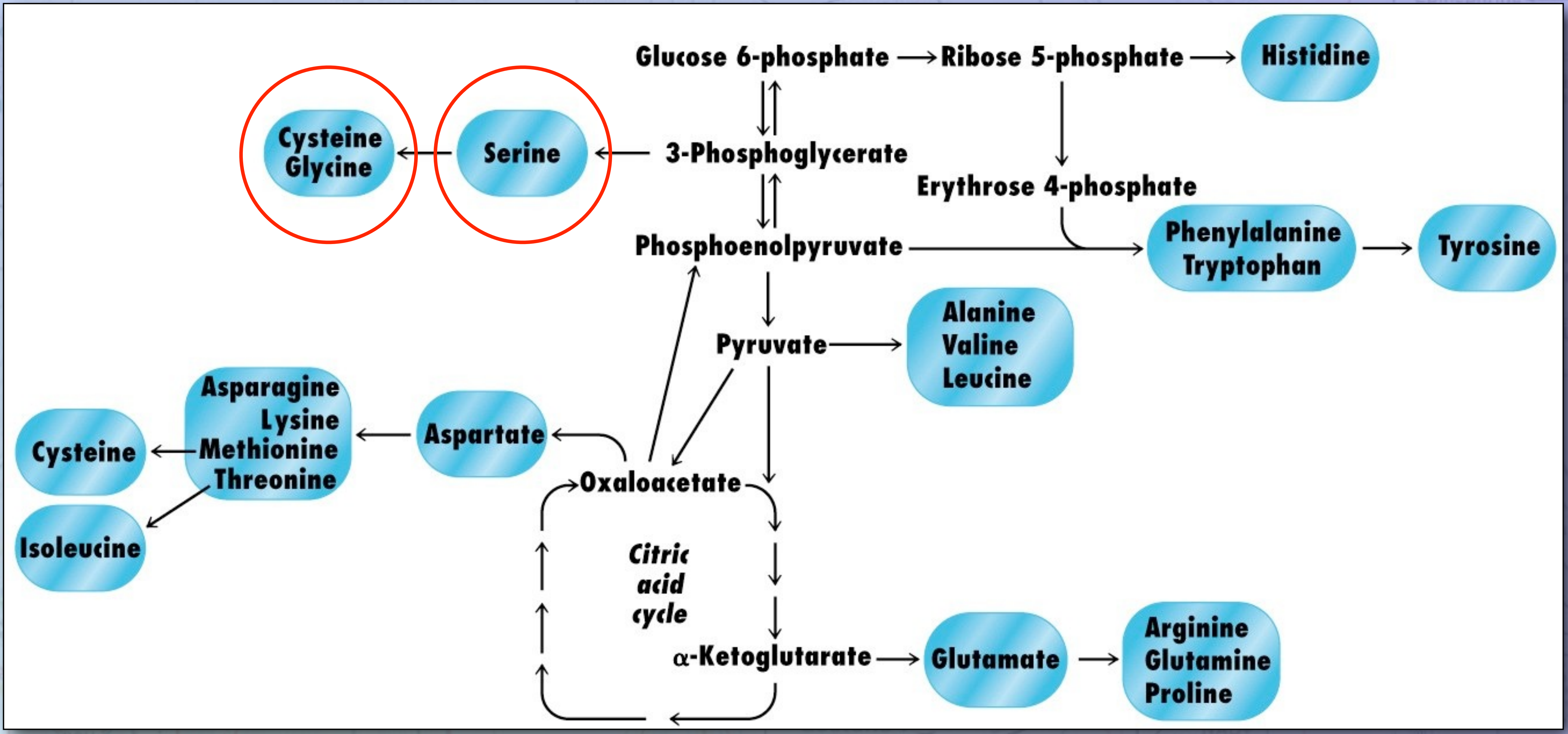

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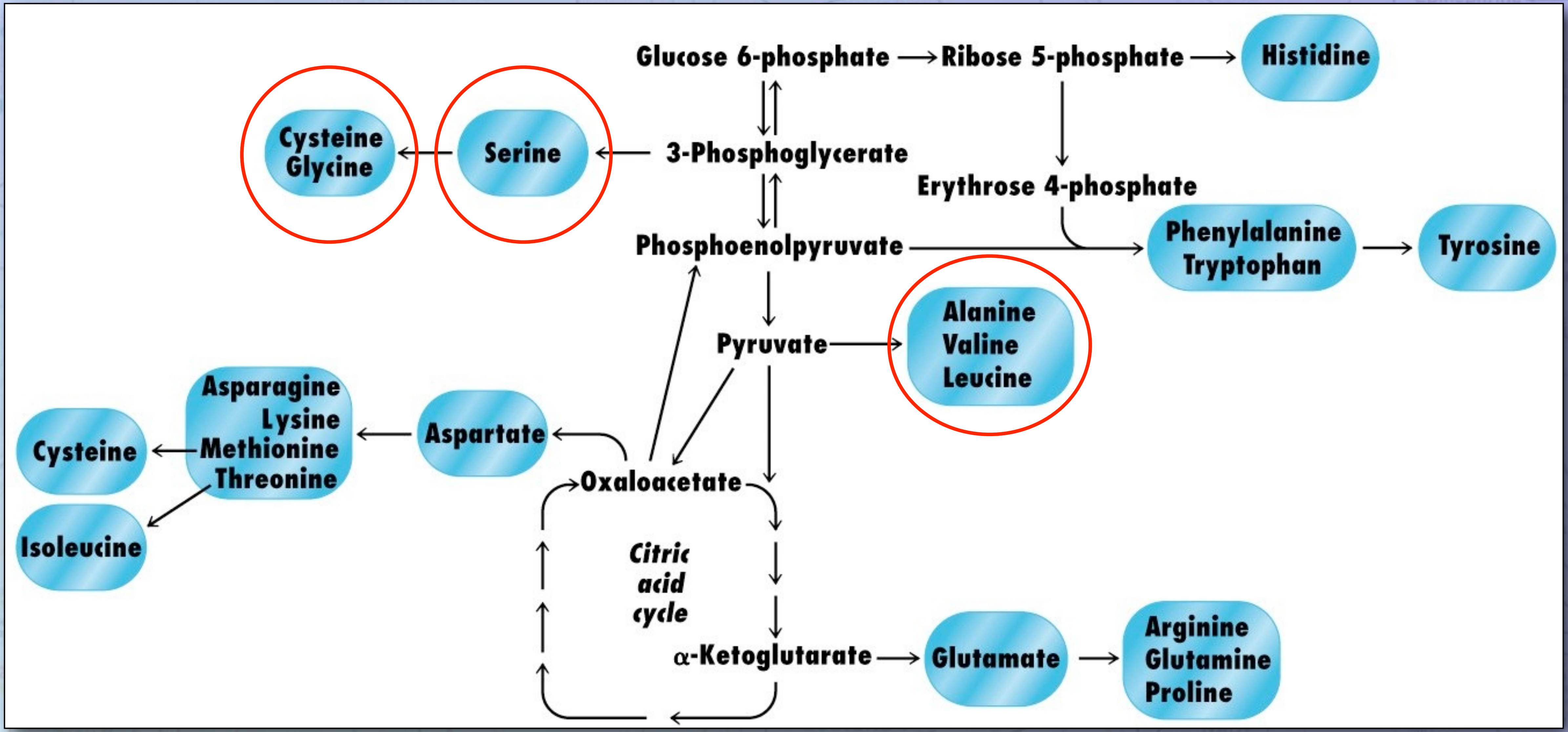

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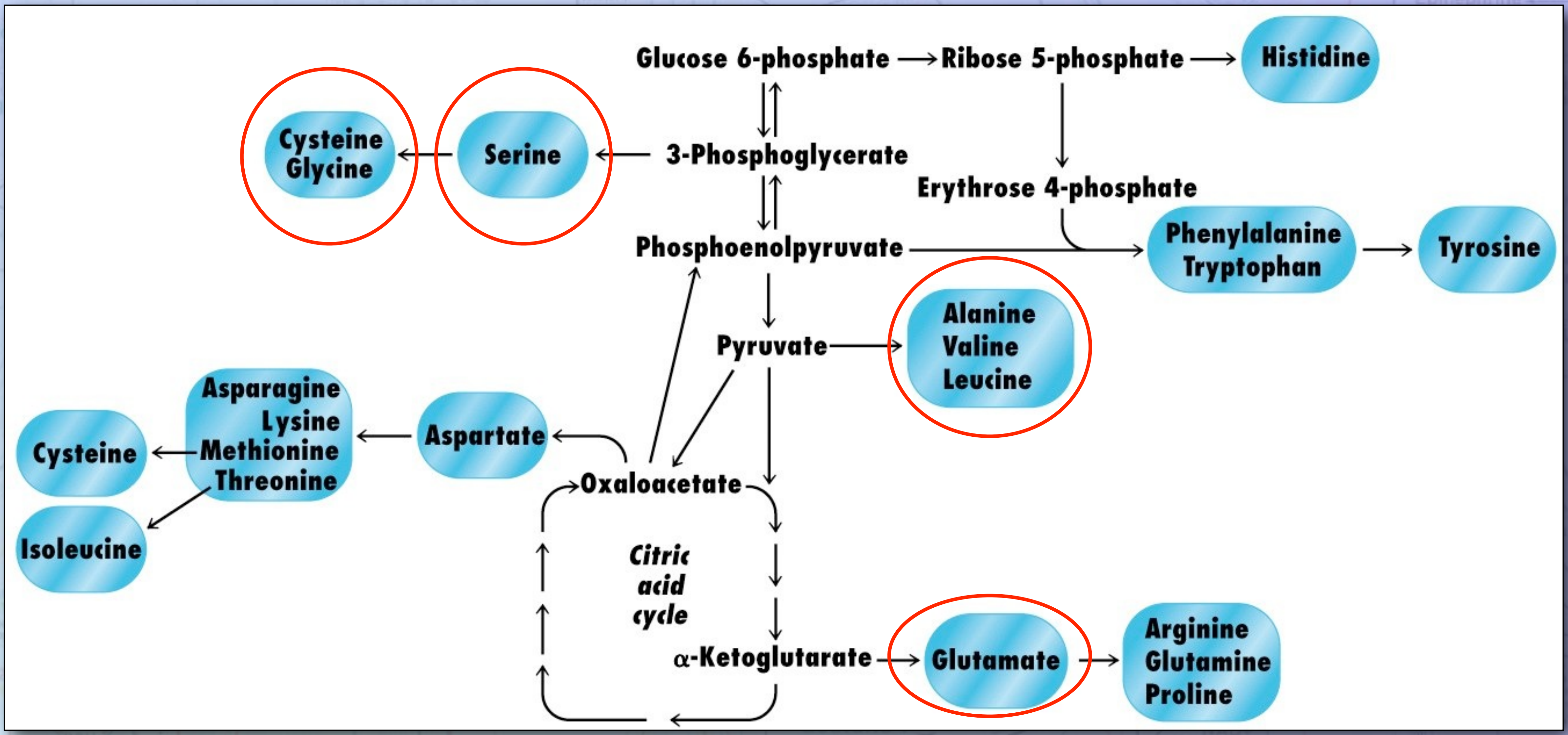

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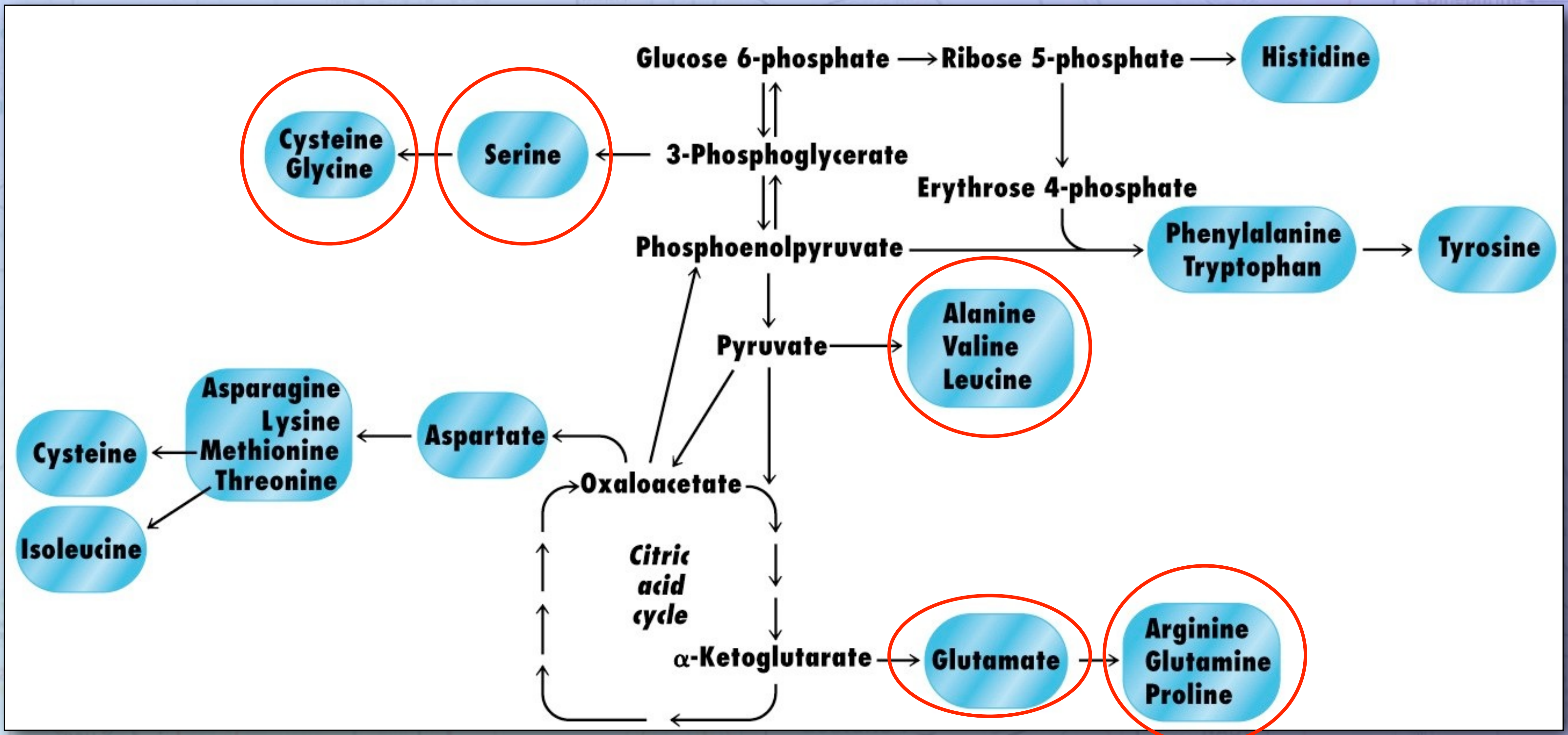

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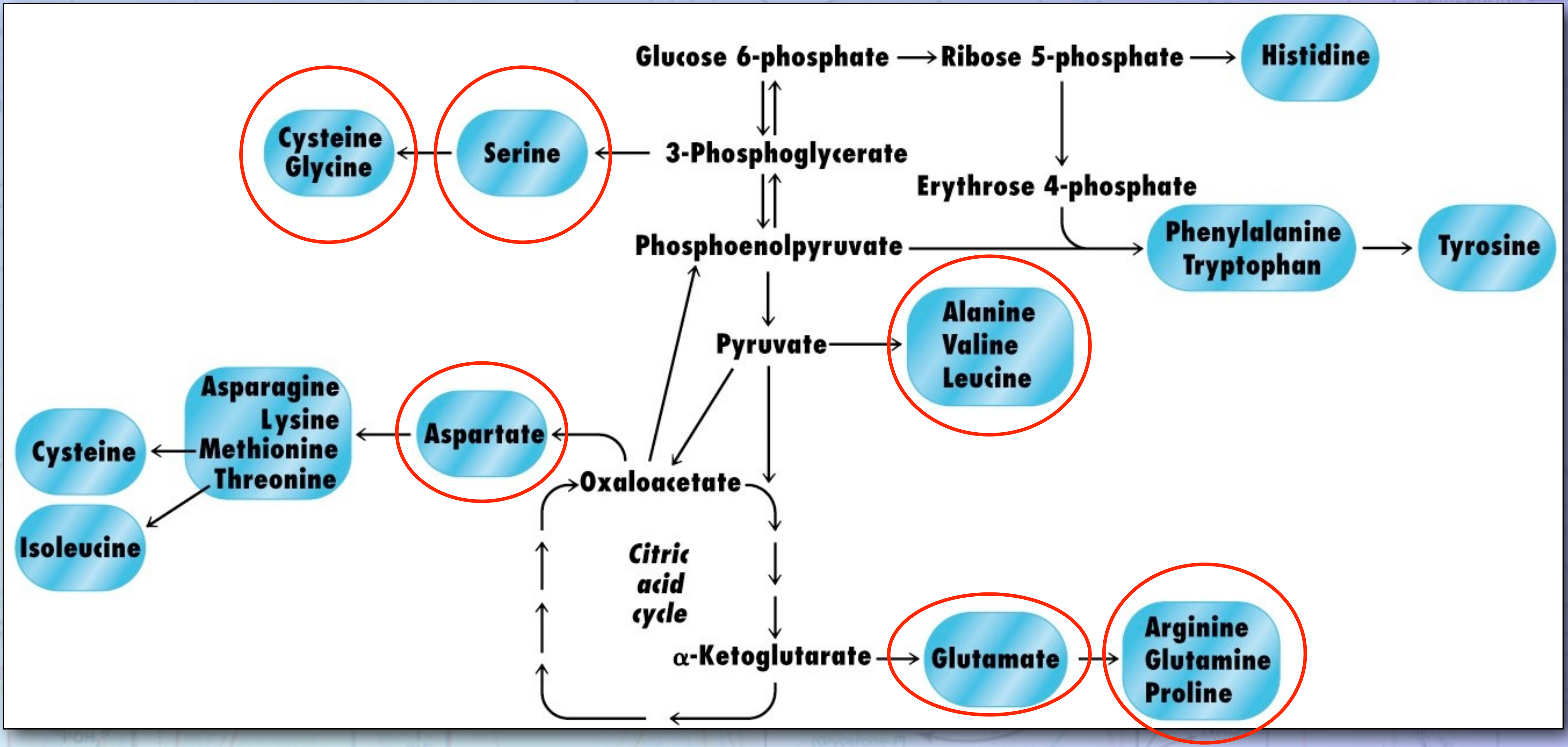
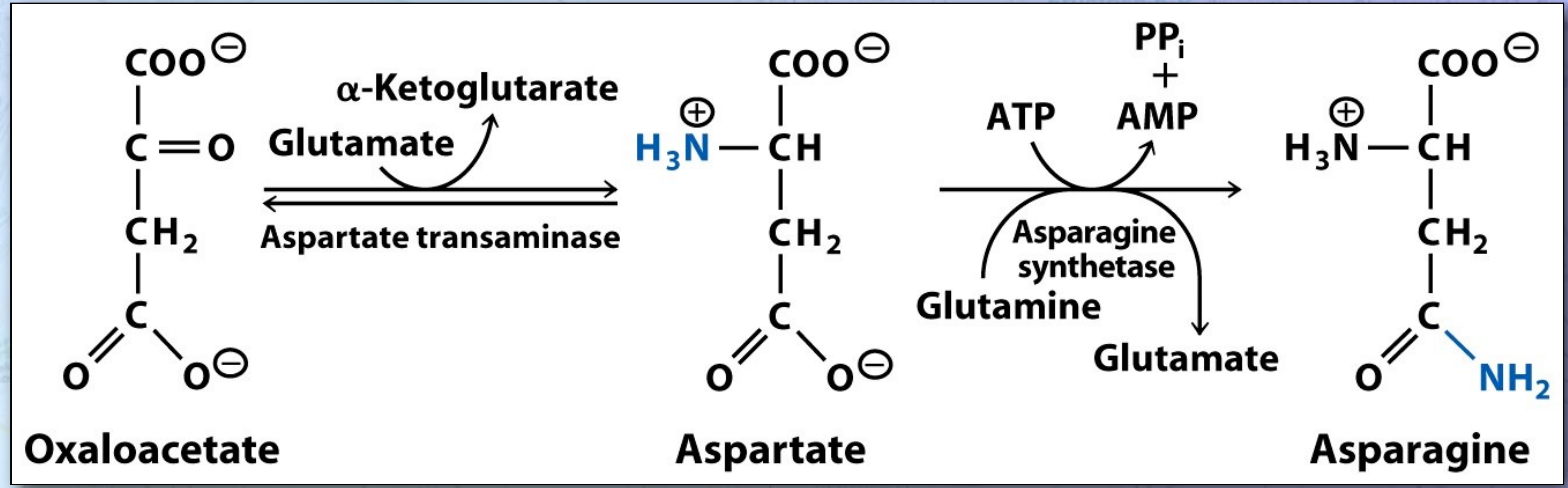


Synthesis of Amino Acids

Aspartate (Asp) & Asparagine (Asn)

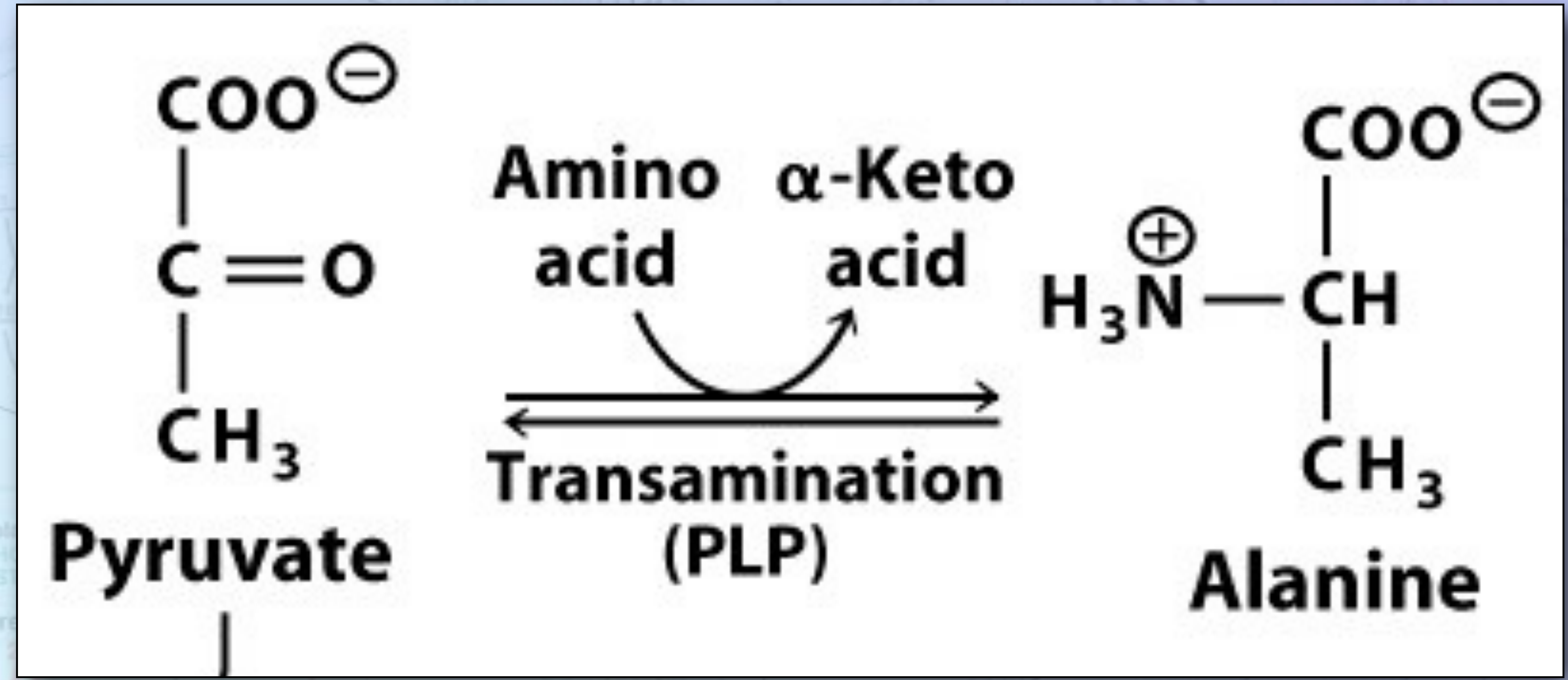
- Start at oxaloacetate



Synthesis of Amino Acids

Alanine (Ala)

- Start at pyruvate



Synthesis of Amino Acids

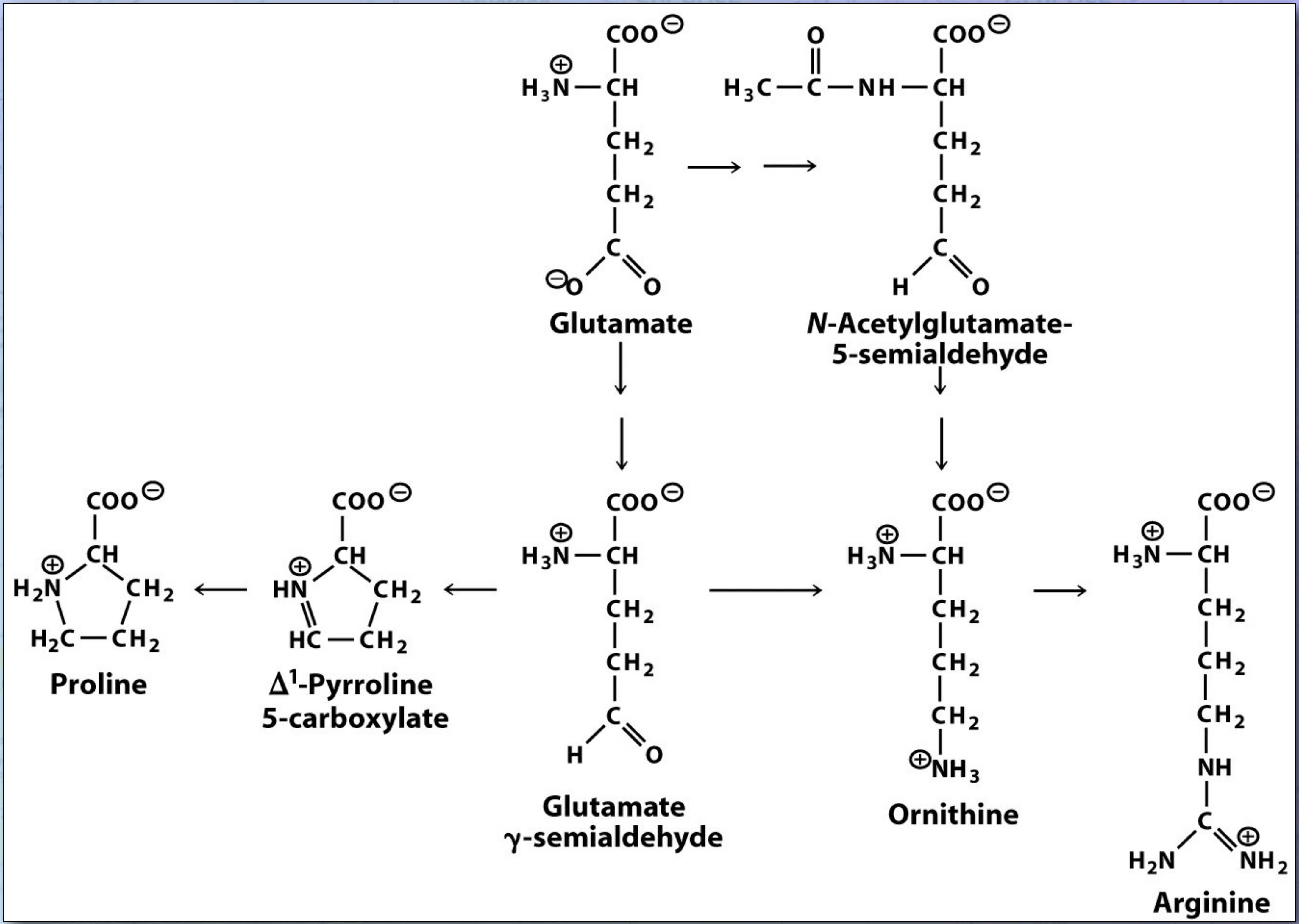
Glutamate (Glu) & Glutamine (Gln)

- Start at α-ketoglutarate and transminate

Proline (Pro) & Arginine (Arg)

- Start at Glutamate

Synthesis of Amino Acids



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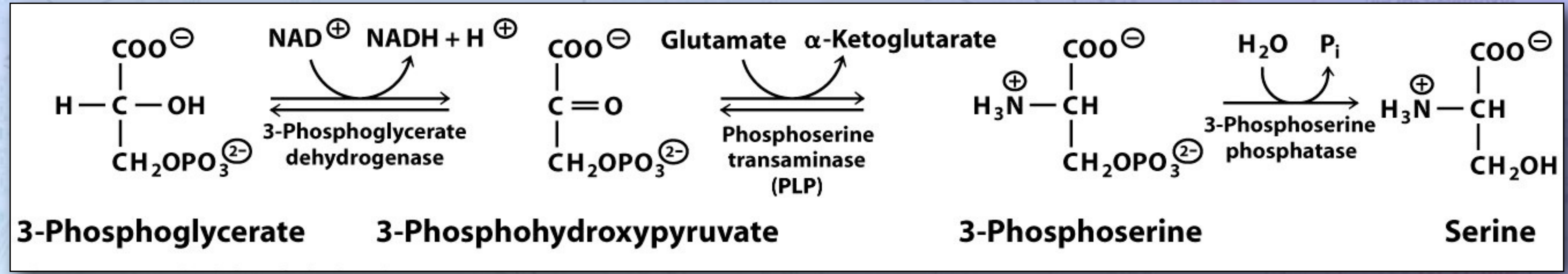
Synthesis of Amino Acids

Serine (Ser)

- Start at 3-phosphoglycerate



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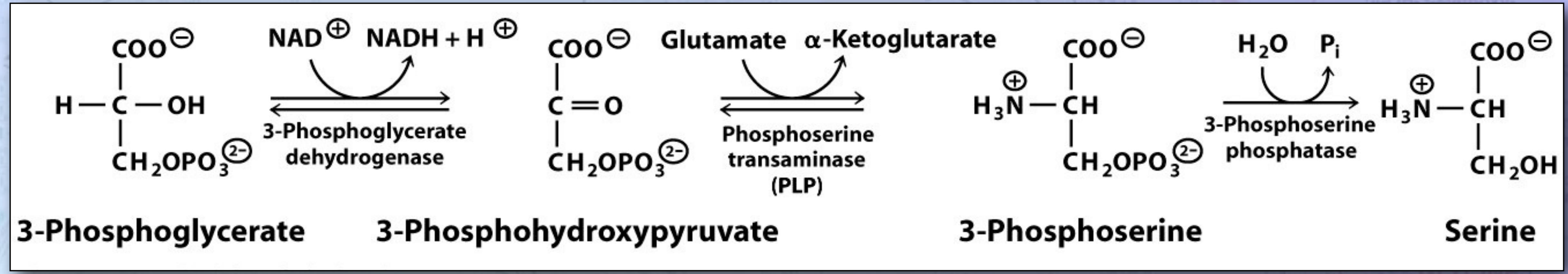
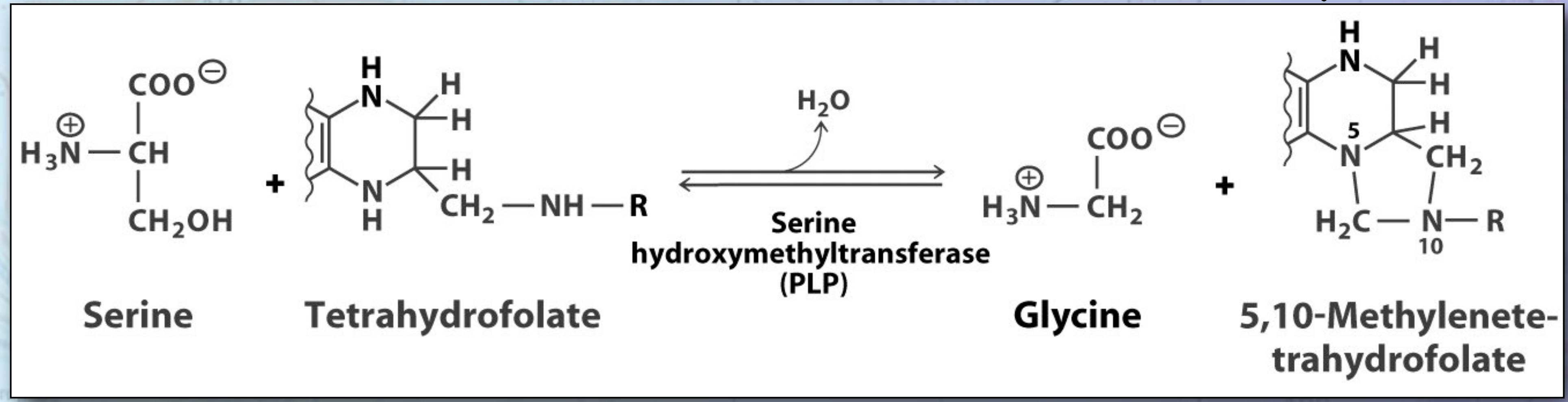


Glycine (Gly)

- Start at serine (Tetrahydrofolate, Chapter 7.11)



Synthesis of Amino Acids

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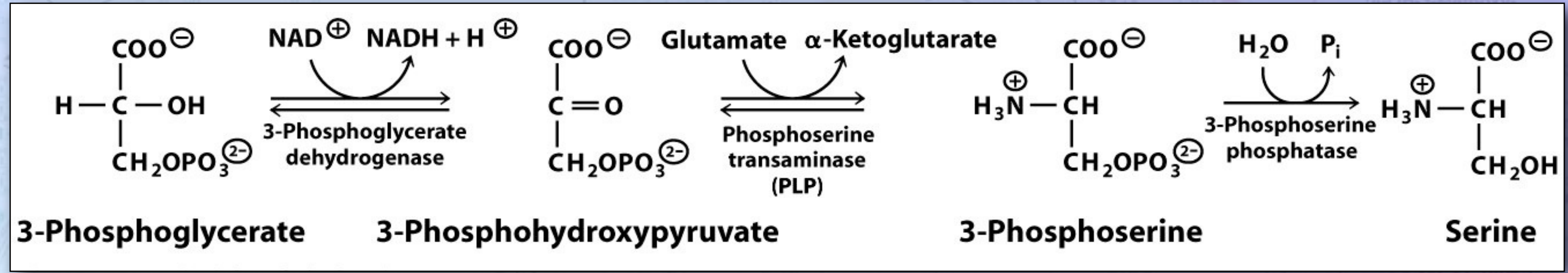

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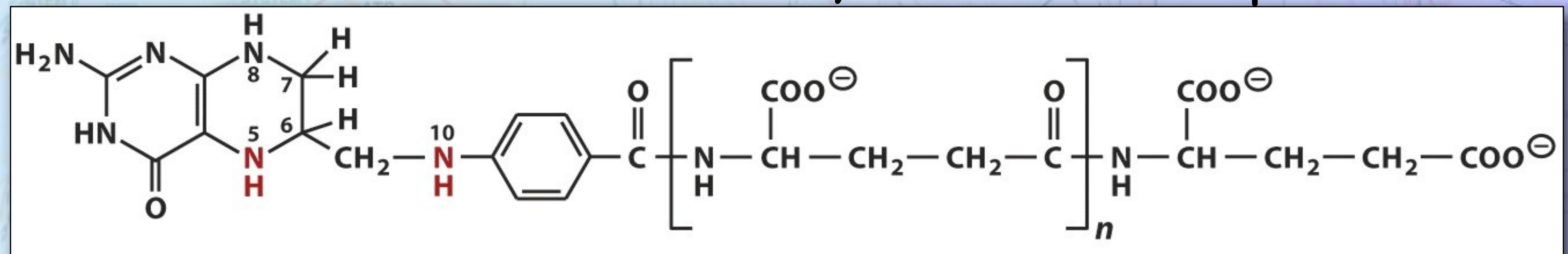
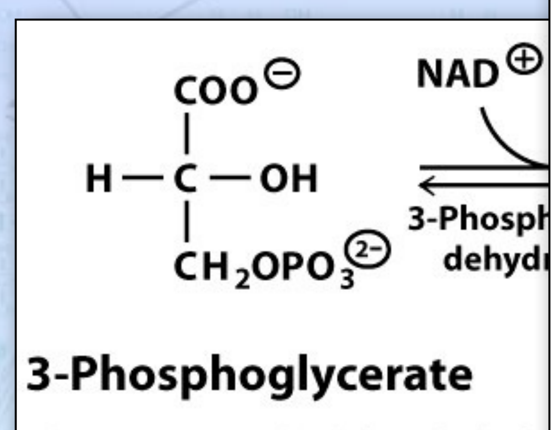


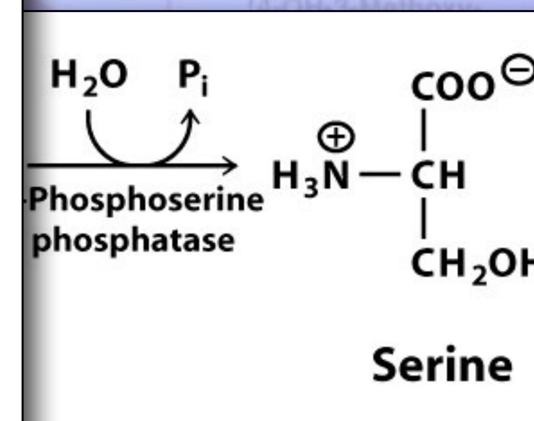
Tetrahydrofolate (Tetrahydrofolyl polyglutamate)

Synthe…

Serine (

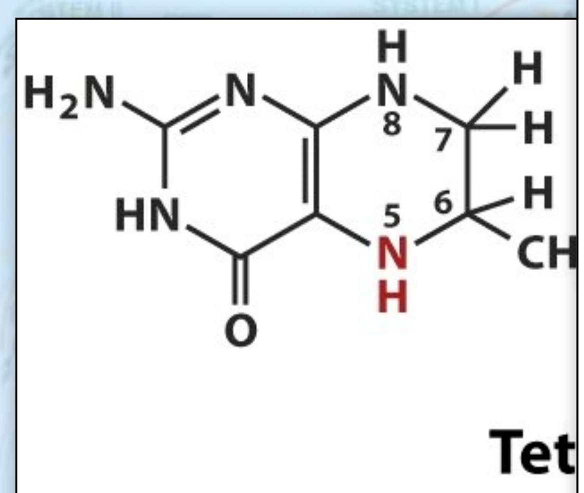
- Start a…

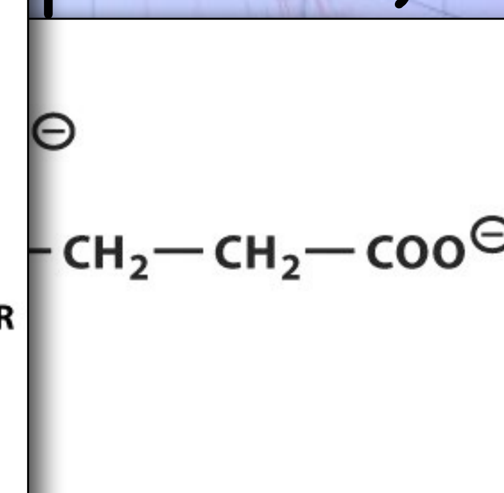


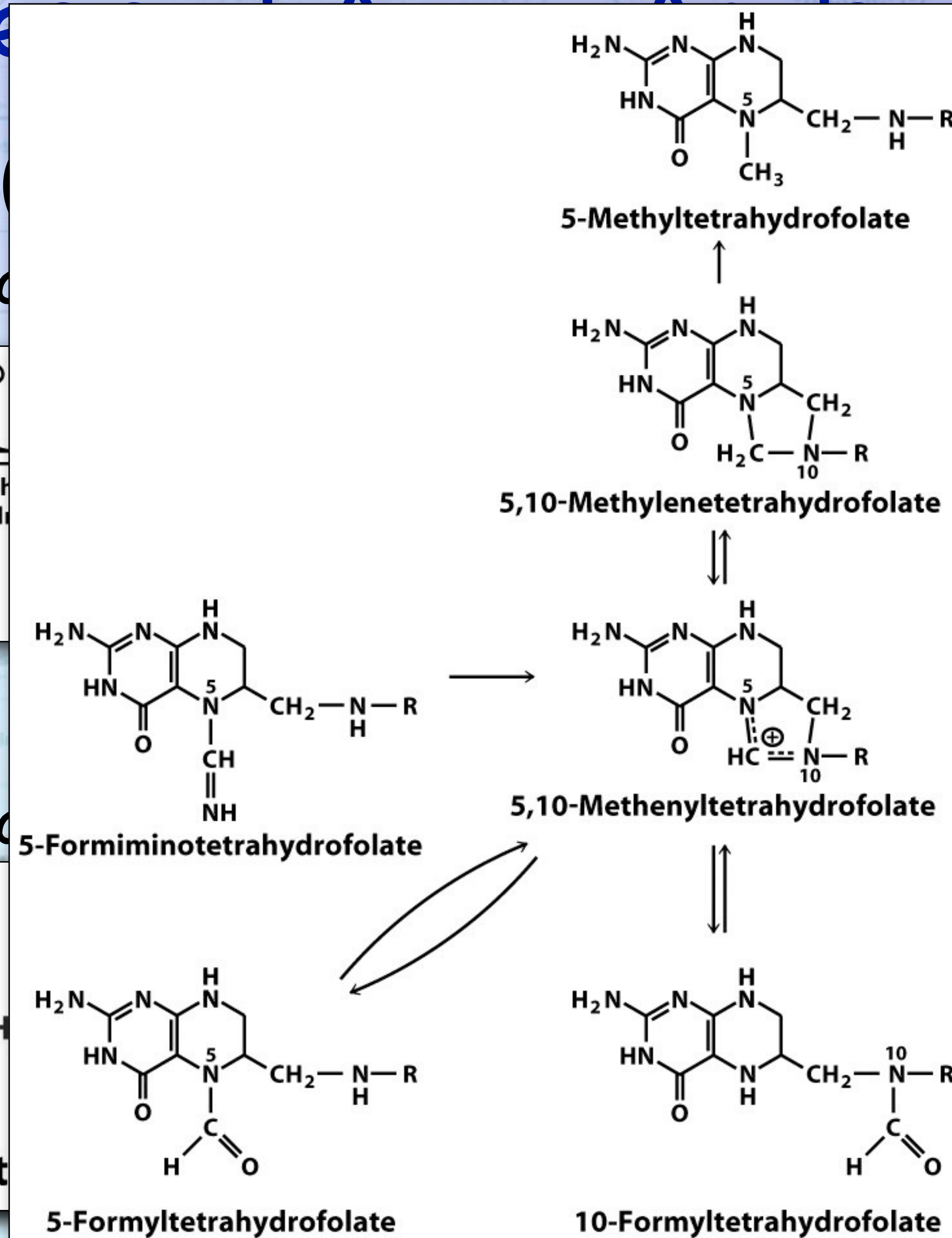


Glycine

- Start a… …pter 7.11)







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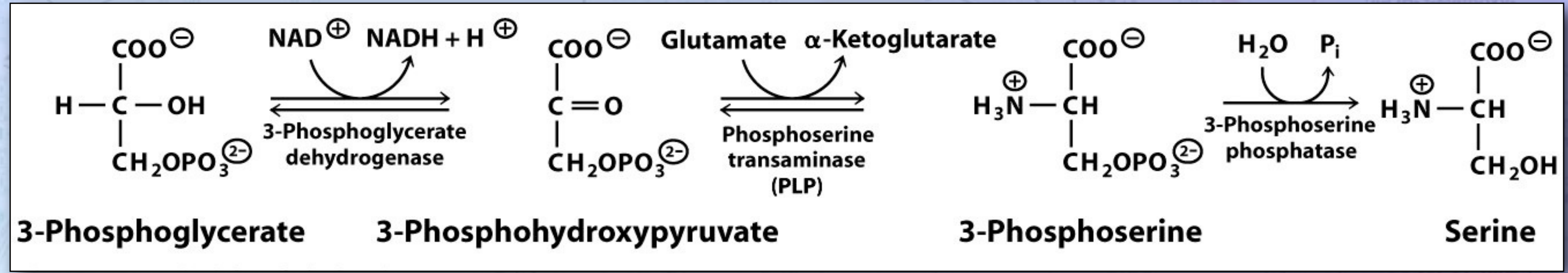

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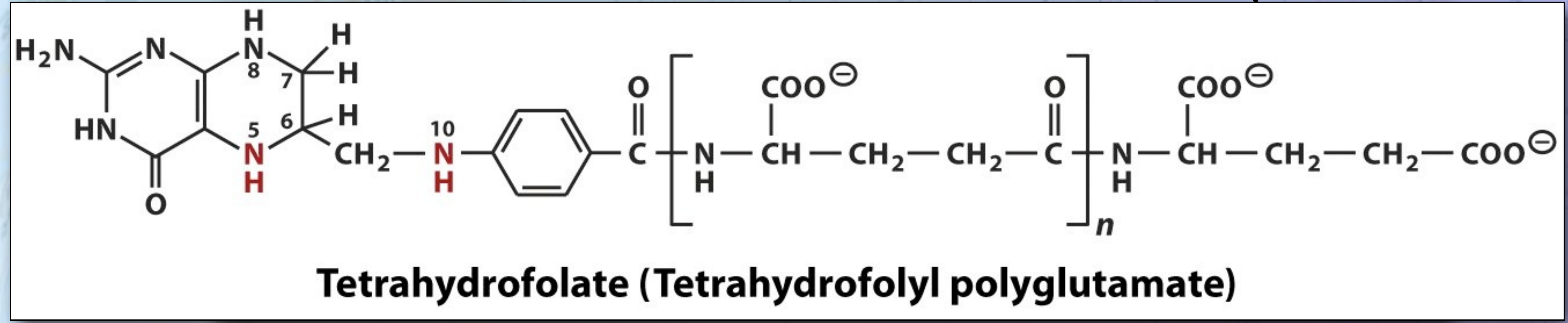

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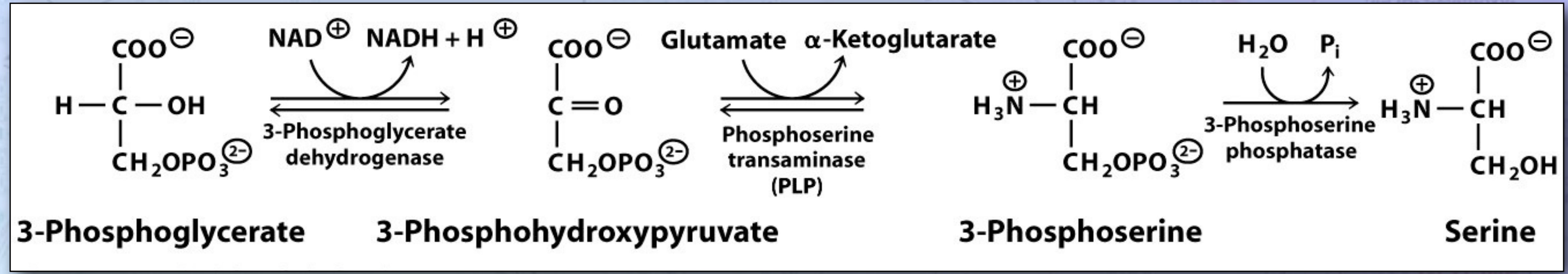

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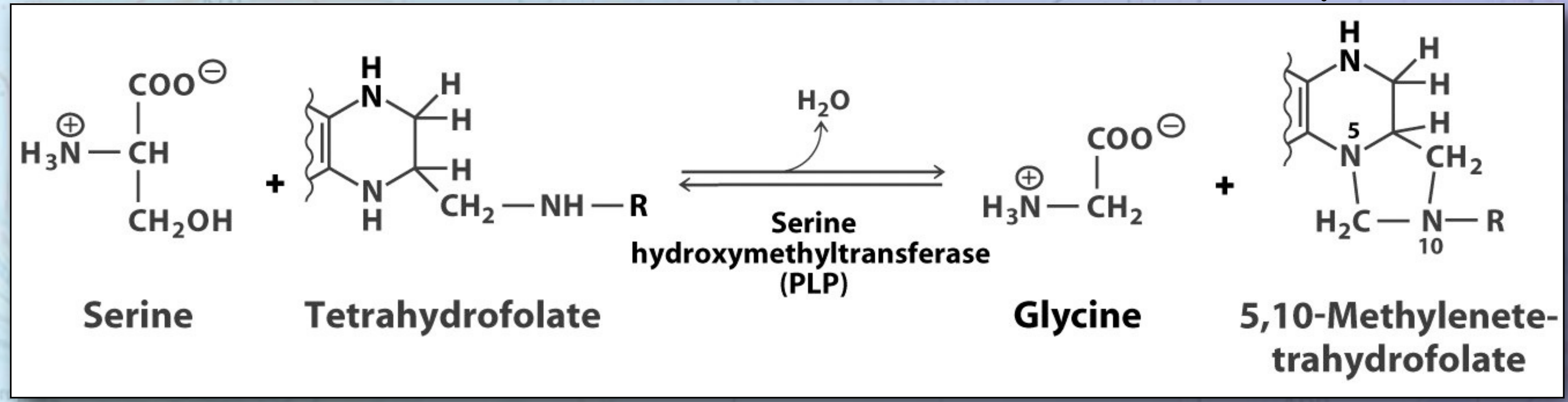
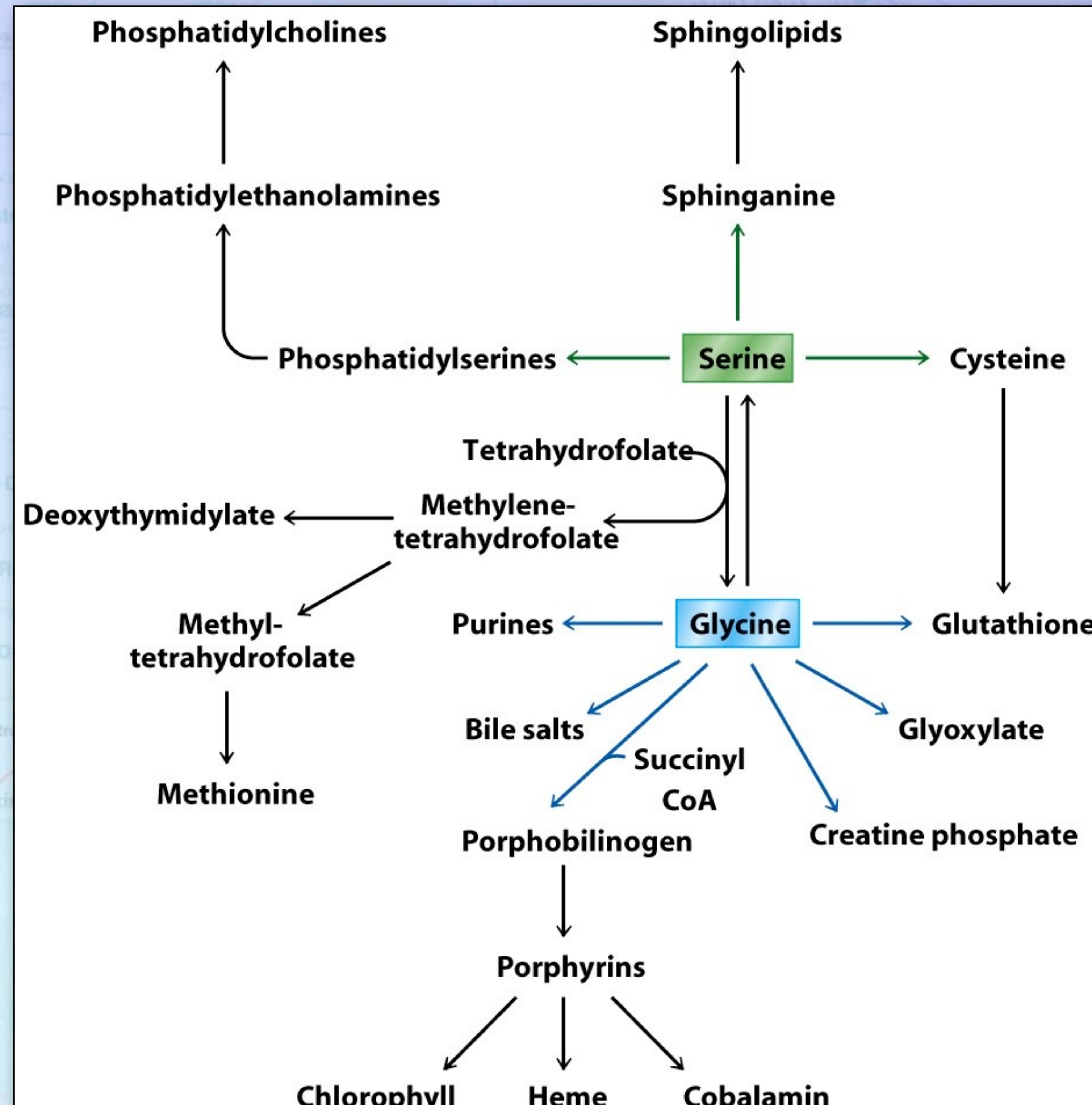


Amino Acids as Precursors



Amino Acids as Precursors

Nitric oxide (NO)

- Science Magazines 1992 “Molecule of the Year)
- Messenger molecule that stimulates the formation of cGMP
- Used by macrophages to kill bacteria
- Smooth muscle relaxant, which lowers blood pressure.

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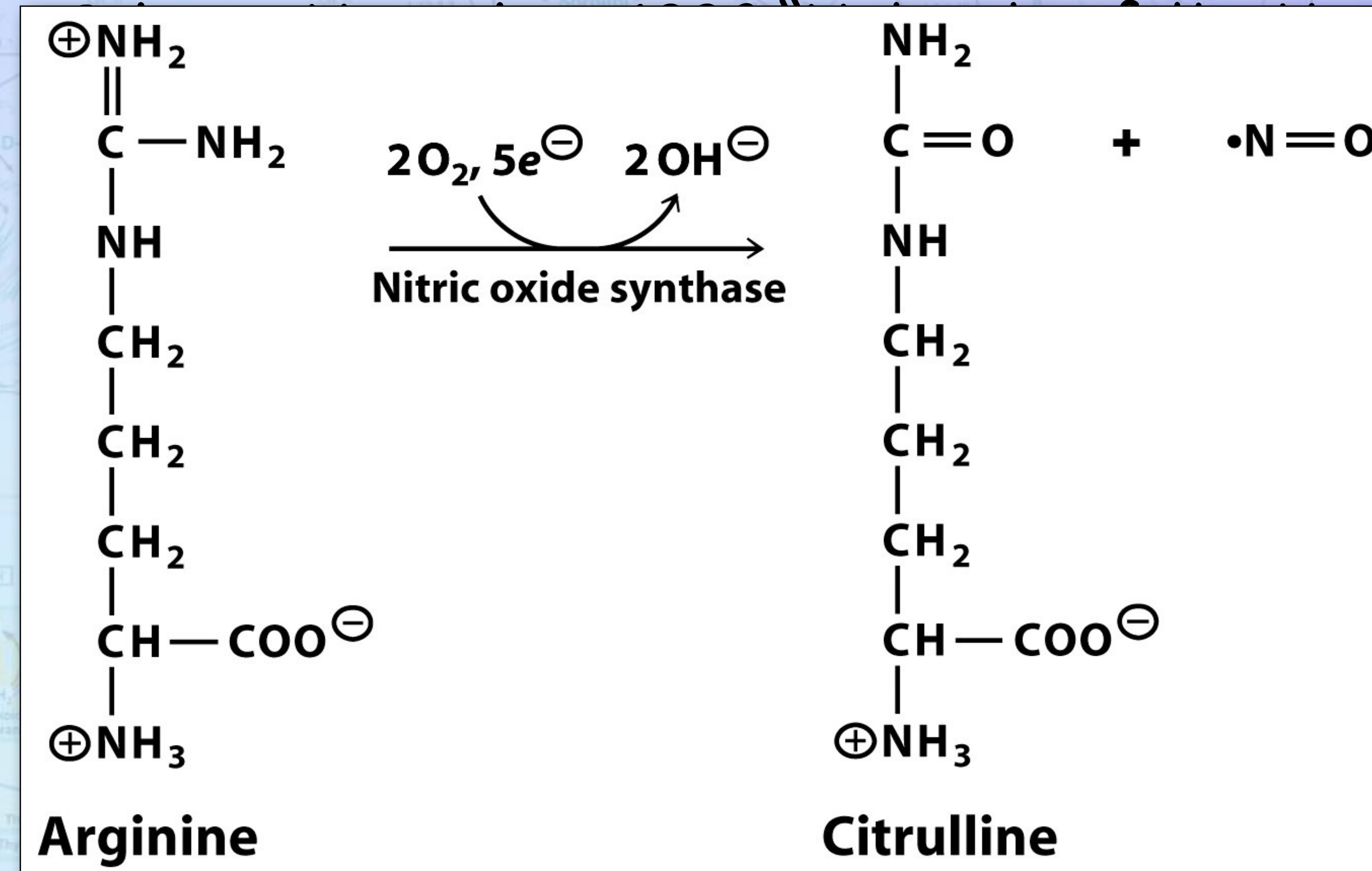

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Amino Acids Degradation

Will focus on the strategies that have evolved for the removal of excess nitrogen.

- NH_3 - aquatic organisms allow ammonia to diffuse into the surroundings.
- Urea - terrestrial animals excrete urea along with other liquid wastes
- Uric acid - avian animals excrete uric acid along with other solid wastes

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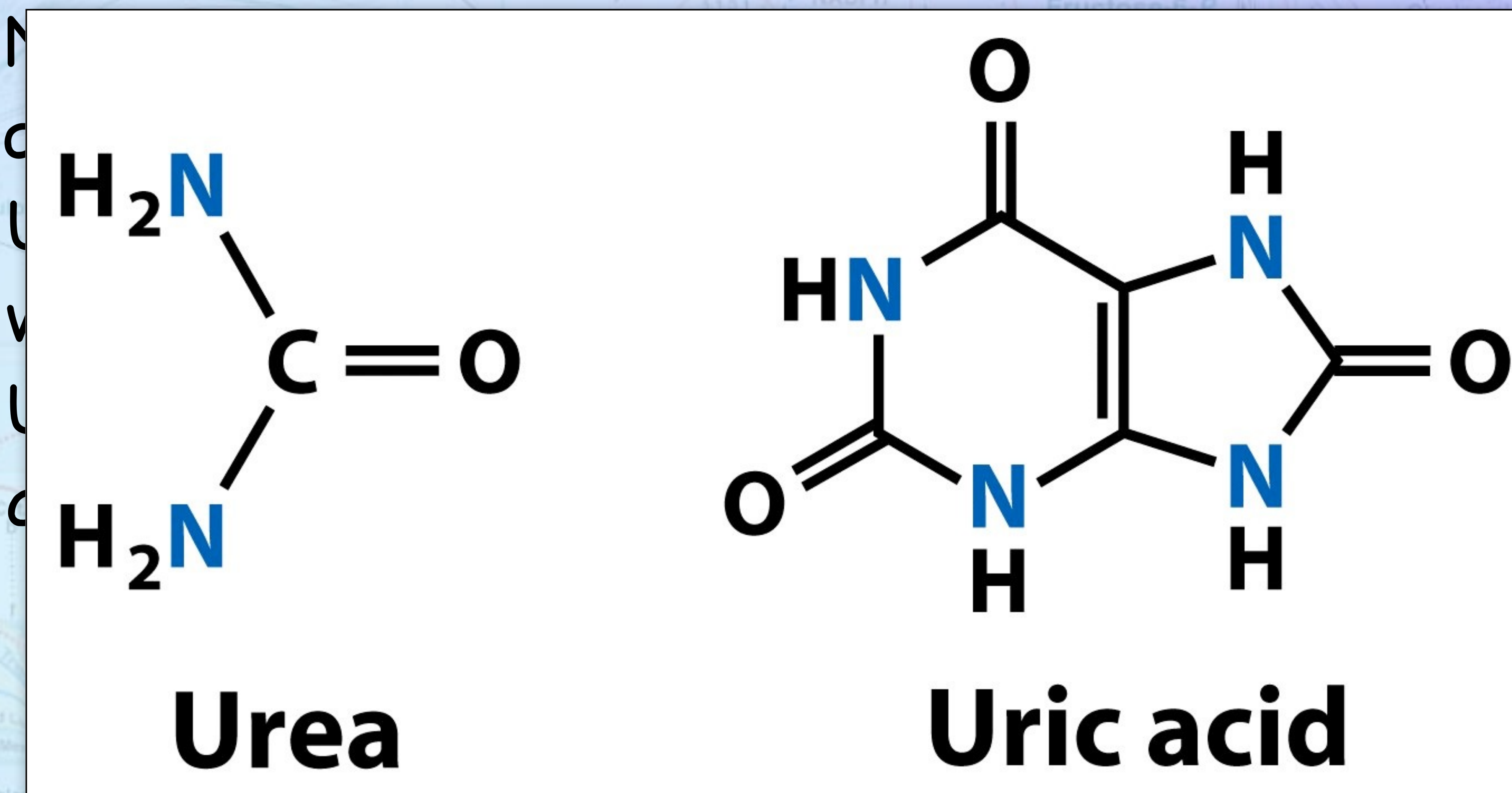

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The Urea Cycle

Discovered by Hans Krebs in the 1930's shortly before he discovered the citric acid cycle.

- The first step is the synthesis of carbamoyl phosphate I.
  - In the mitochondria of liver cells
- The NH_3 comes from the oxidative deamination of glutamate.

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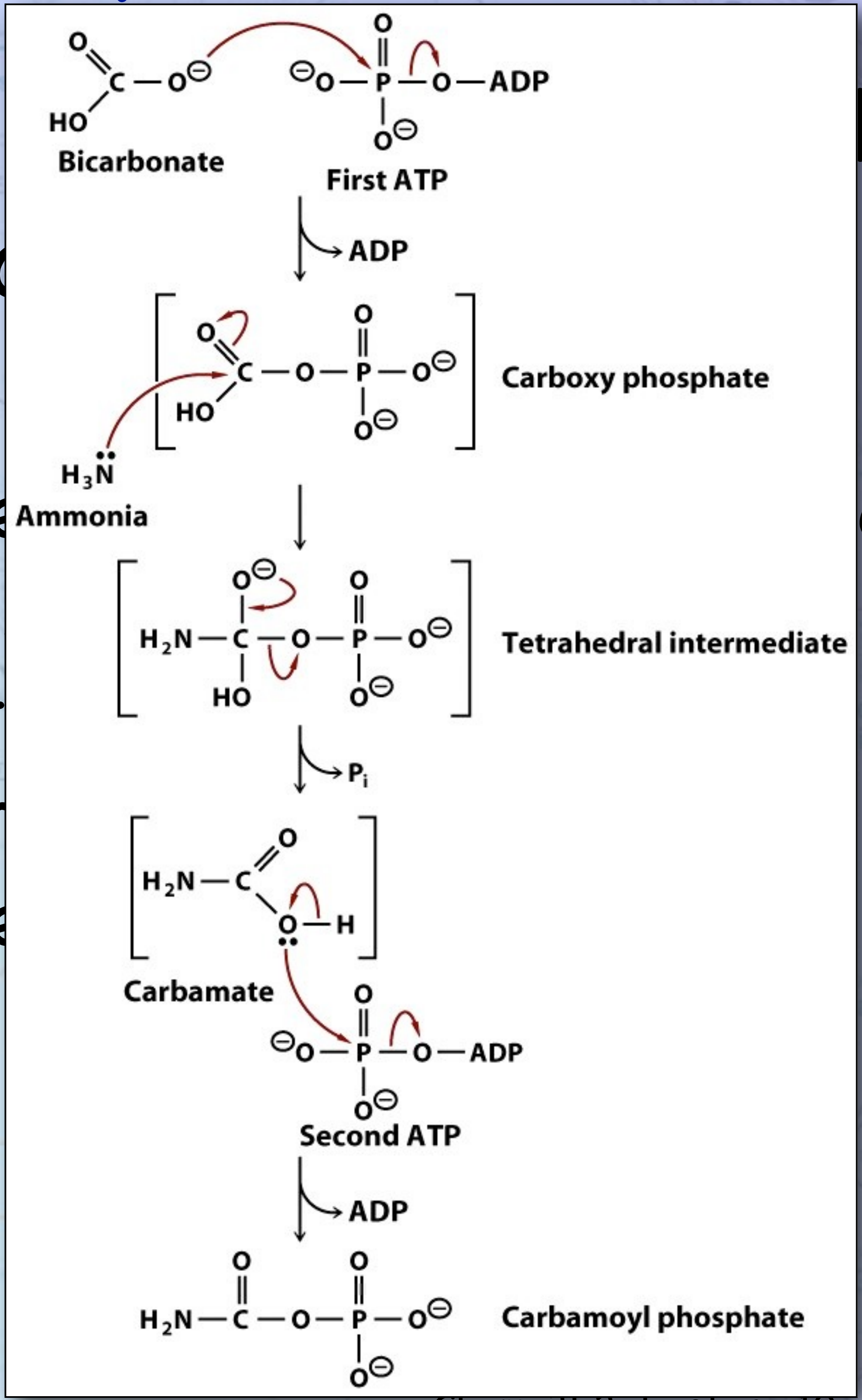

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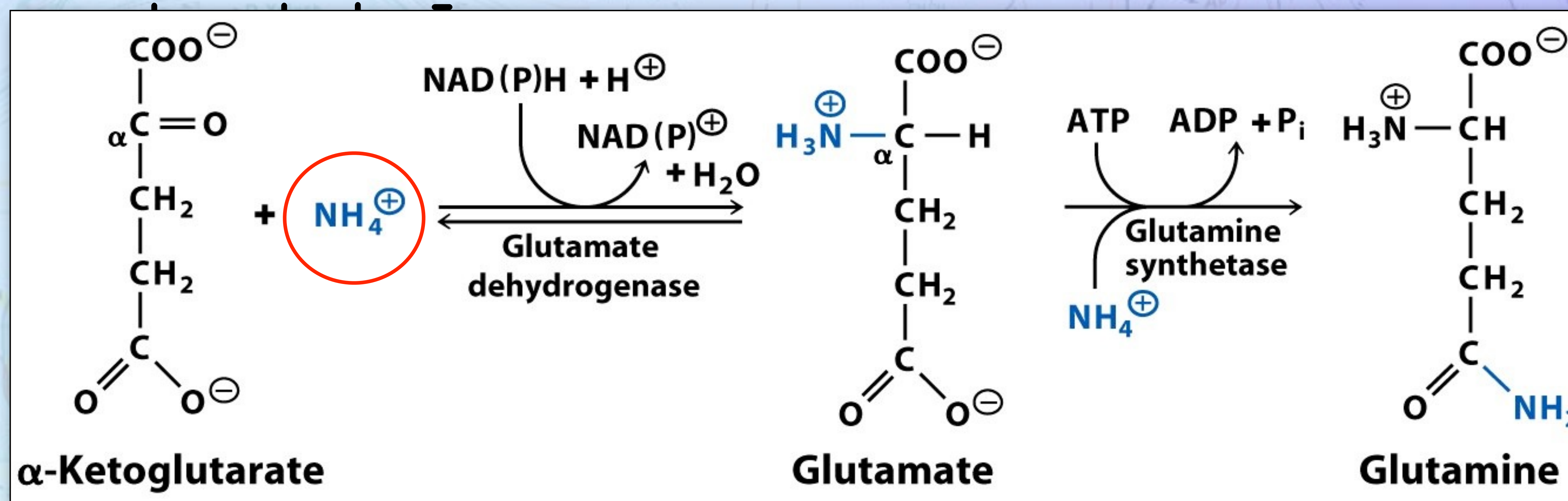

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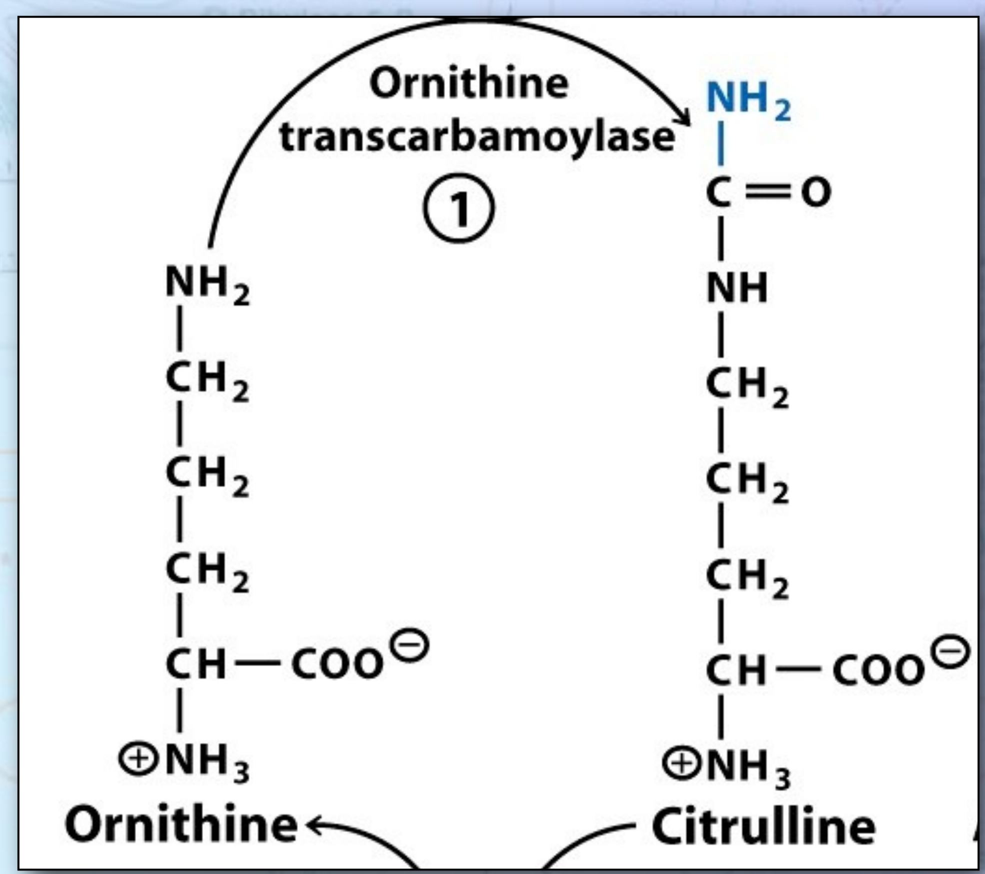
The Urea Cycle

- The urea cycle involves two new α-amino acids.
  - Ornithine - which is similar to lysine.
  - Citrulline - which is similar to arginine



The Urea Cycle

Question:

What feature distinguishes **ornithine** from **lysine**?

The Urea Cycle

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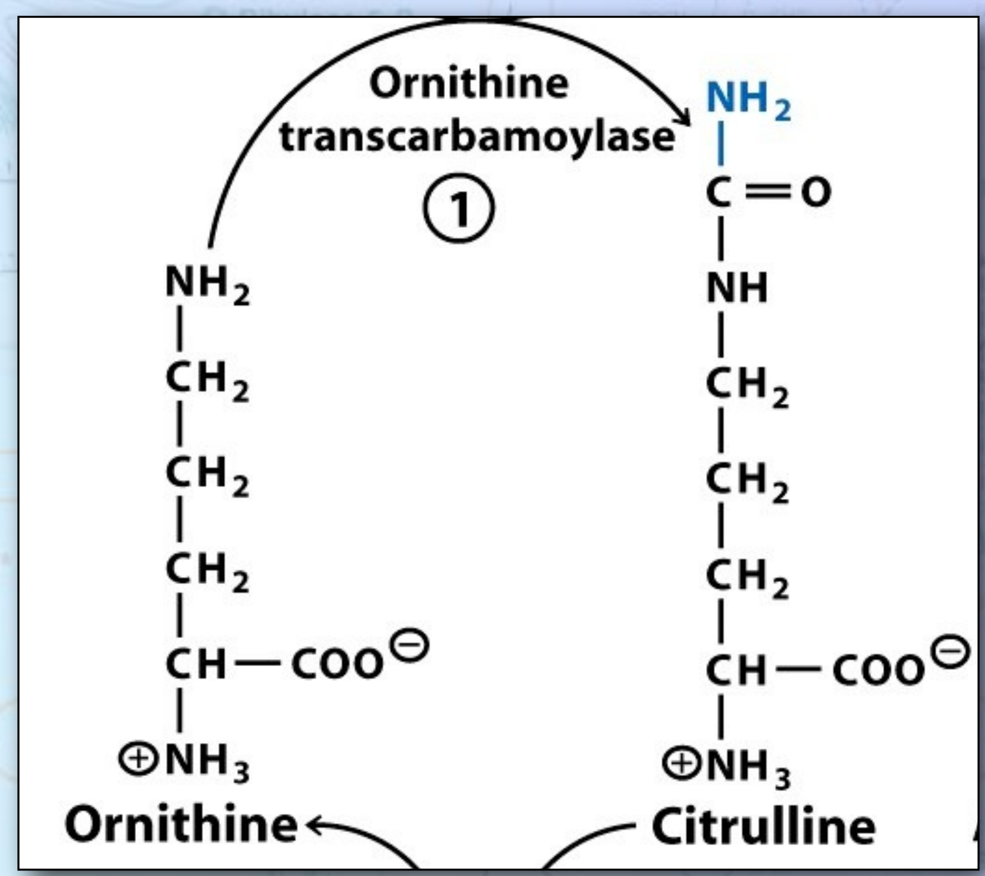

The Urea Cycle

Question:

What feature distinguishes **citrulline** from **arginine?**

The Urea Cycle

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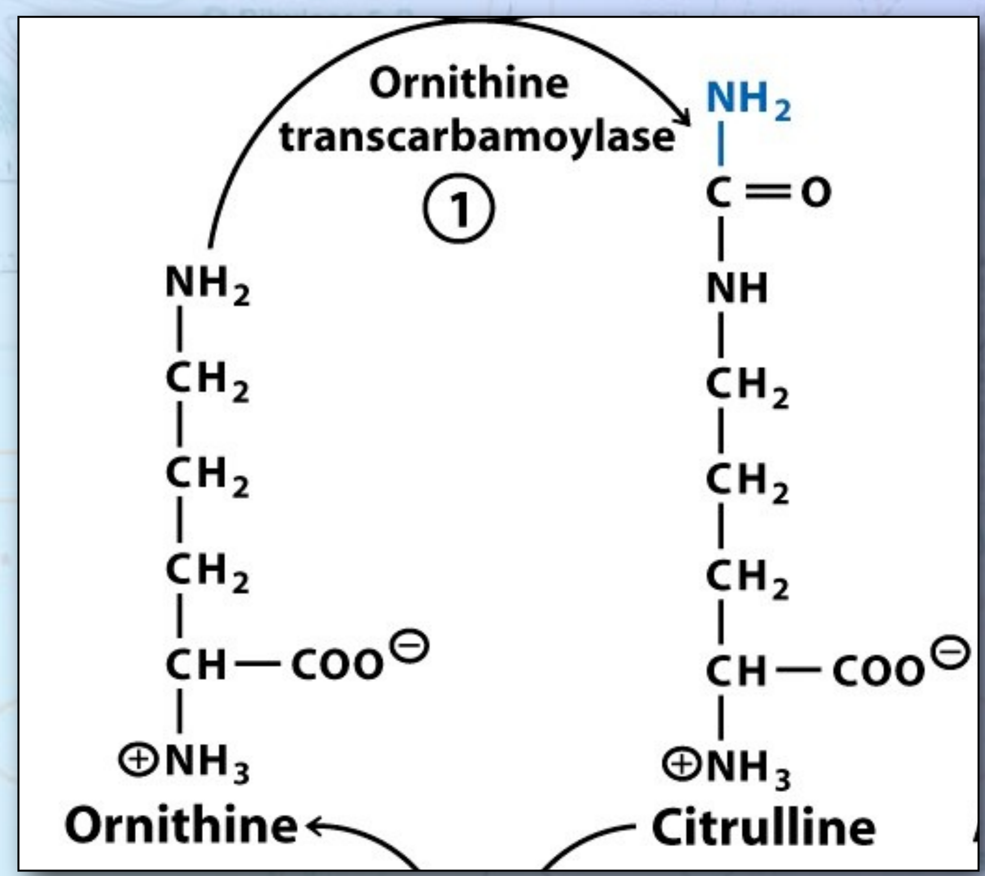
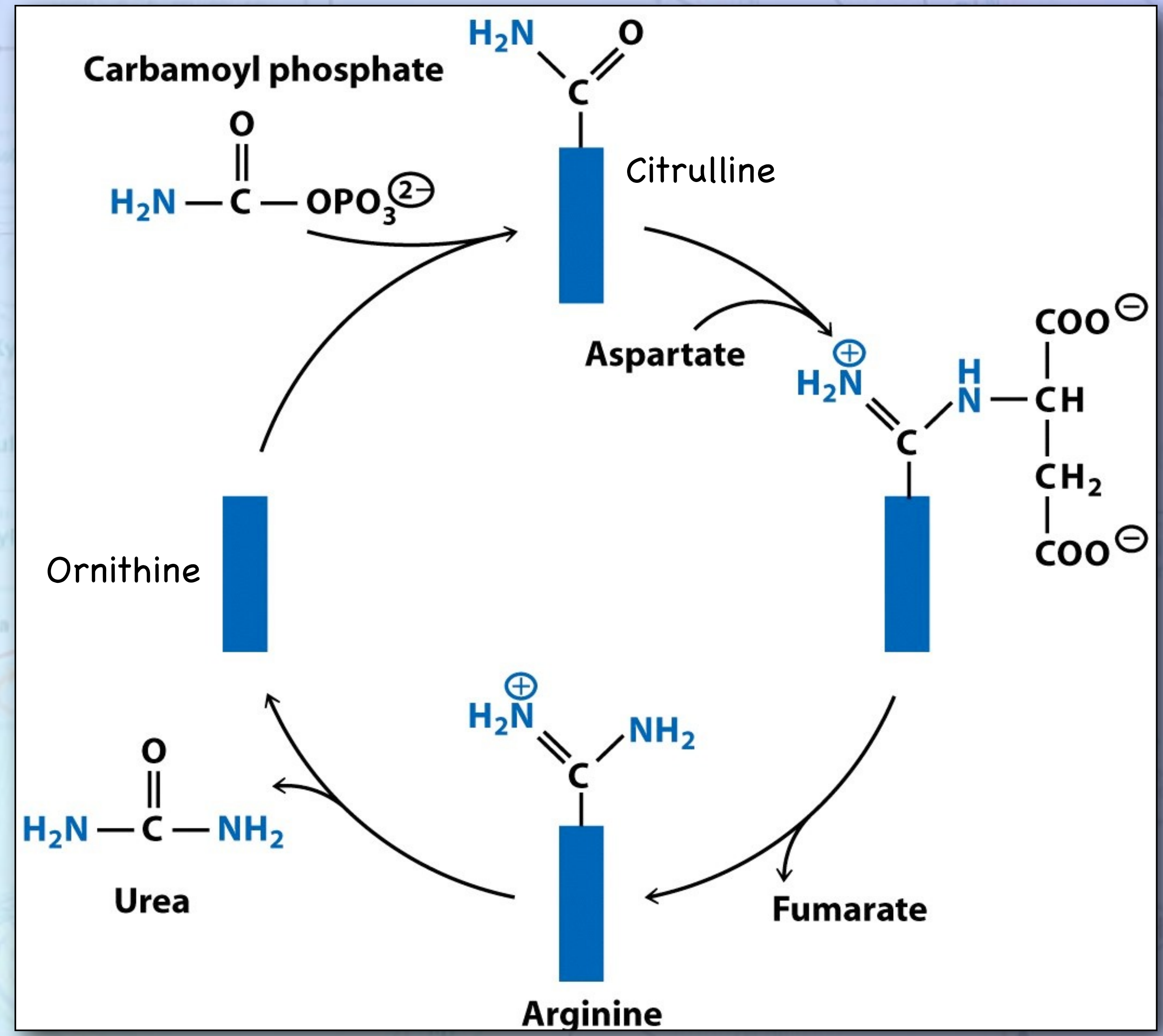


The Urea Cycle

- The reactions of the urea cycle.



The Urea Cycle

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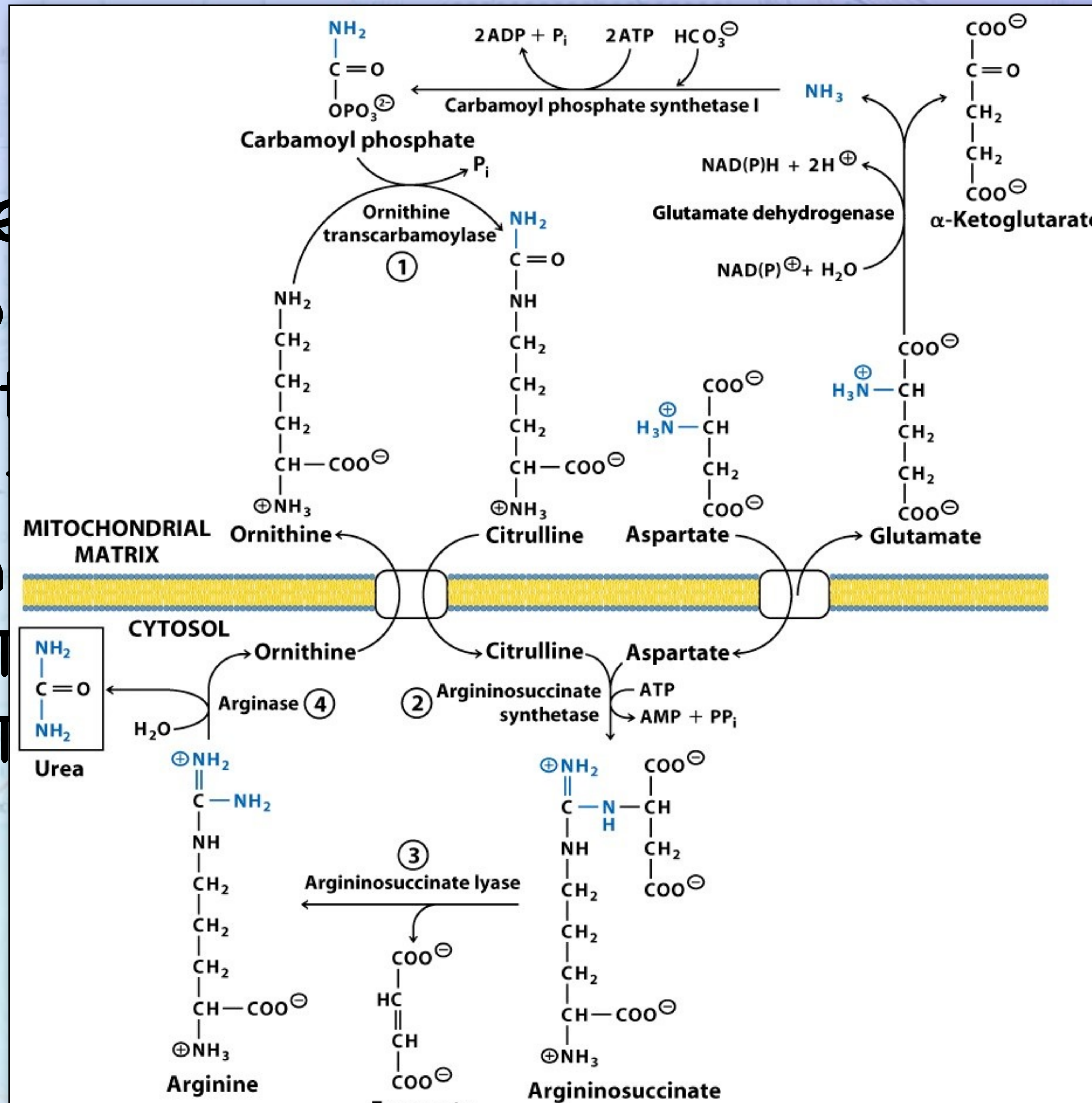


The Urea Cycle

- The net reaction:

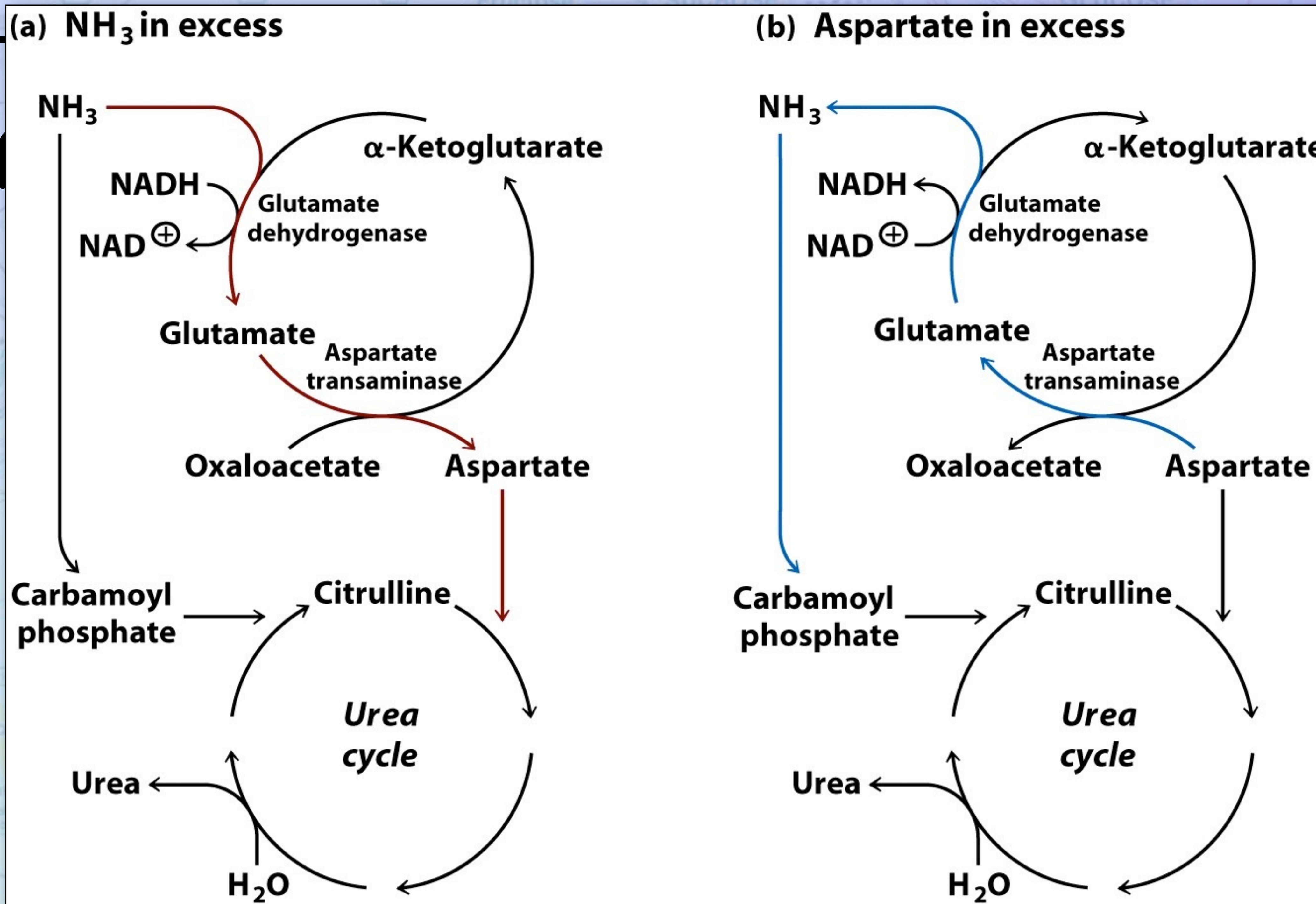
$$NH_3 + HCO_3^- + \text{Aspartate} + 3\,\text{ATP} \longrightarrow \text{Urea} + \text{Fumarate} + 2\,\text{ADP} + 2\,P_i + \text{AMP} + PP_i$$

The Urea Cycle

The nitrogen atoms in urea comes from NH_3 and aspartate.

- The needs for these two sources can be balanced by altering the flow material.

The Urea Cycle



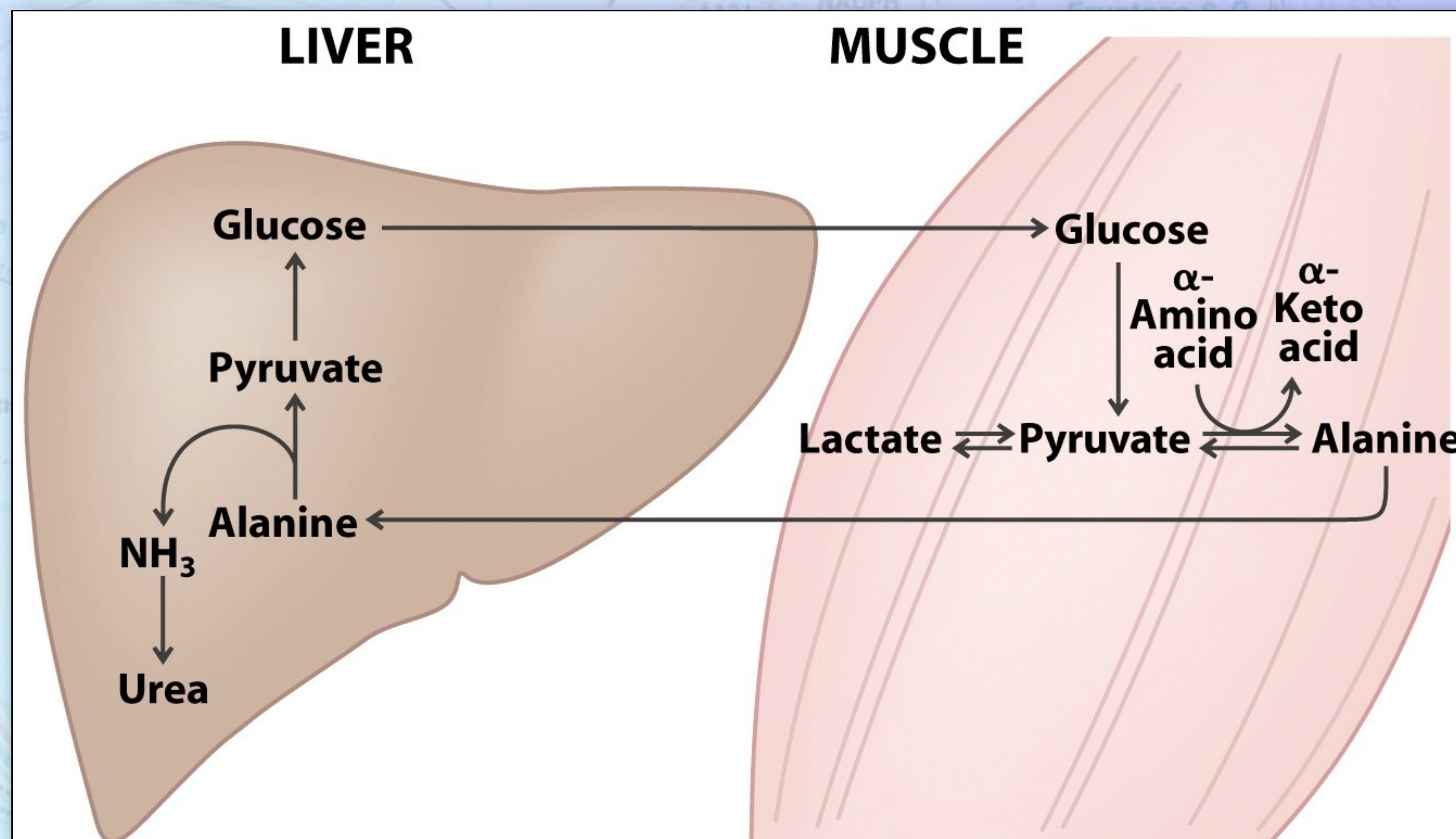
The Urea Cycle

The nitrogen atoms in urea comes from NH_3 and aspartate.

- The needs for these two sources can be balanced by altering the flow material.

The Urea Cycle

The pyruvate/aspartate shuttles is used to remove excess NH_3 from the muscles.



Next Up

Lecture 10 - Part III, Nucleotide metabolism (Moran et al, Chapter 18)

Lecture 11 - Nucleic acids