Proteins
Nitrogen balance

Seminar No. 4

- Chapter 10 -

Overall metabolism of proteins

- Schemes on p. 53 and 54
- all proteins in the body are continuously degraded (metabolized) and newly synthesized
- free AA from food, tissue proteins and non-essential AA from synthesis make AA pool
- AA pool is used for:

  new body proteins

  specialized products (amines, NO, porphyrines, NA bases ...)

  catabolic proceses (energy gain)

AA pool

~ 80 % in muscles

~ 10 % in liver

~ 5 % in kidney

~ 5 % in blood

AA pool is not reserve !!

There is not a specific protein reserve in human body in contrast to saccharides (liver glycogen) and lipids (adip. tissue) !!

AA in blood

Resorption phase

- predominate Val, Leu, Ile
- liver does not take them up from circulation (no specific aminotransferases in liver for Val, Leu, Ile)

Postresorption phase and fasting

- predominate Gln and Ala
- released from muscles (Gln + Ala) and liver (Gln)

There are eight essential aminoacids

- valine
- leucine
- isoleucine
- threonine
- phenylalanine
- tryptophan
- lysine
- methionine

Conditionally essential aminoacids

histidine, arginine (in childhood and youth)

alanine, glutamine (in metabolic stress)

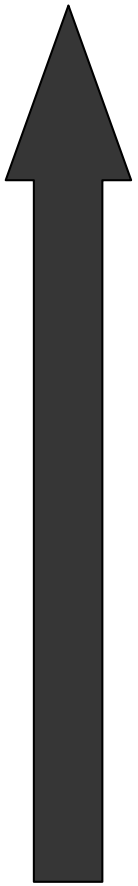
Biological value of proteins (BV) the amount of endogenous proteins made in body from 100 g of dietary proteins

about 30 % of methionine requirement can be made up by cysteine

about 50 % of phenylalanine requirement can be made up by tyrosine

Biological value of some proteins

Protein	BV (%)
Egg white	100
Whey	100
Whole egg	96
Casein	80
Beef	77
Pork	70
Oats	60
Wheat flour	53
Beans	46
Gelatine	25



Whey

- a by-product at (cottage) cheese production
- yellowish liquid (the colour comes from riboflavin)
- cca 12 % of high quality proteins (lactoalbumin, lactoglobulins)
- rich in other B-complex vitamins and lactose
- dried whey is available in shops (esp. fitness centres)

Catabolic pathways of AA

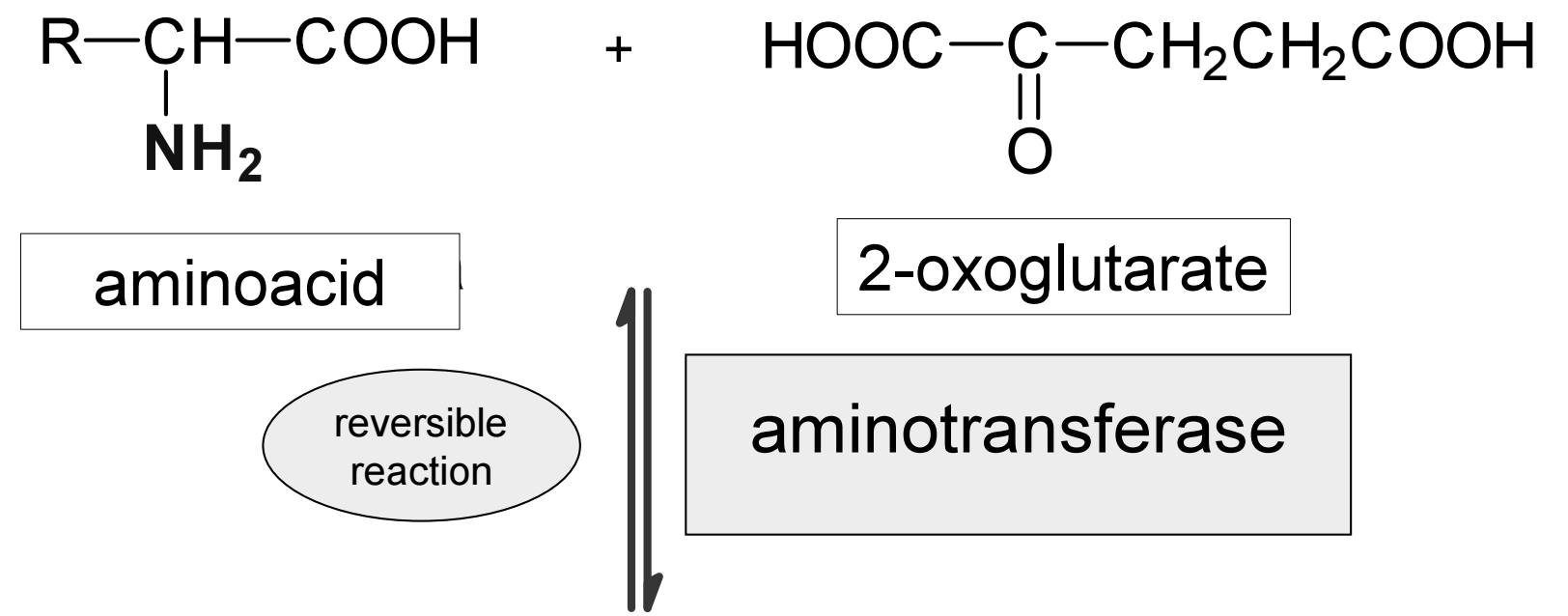
- dietary **proteins** → **AA** (GIT, pepsin, trypsin etc.)
- transamination of AA in cells → **glutamate**
- dehydrogenation deamination of glutamate → **NH_3**
- detoxication of ammonia → **urea, glutamine**

blue colour indicates the pathway of nitrogen

Q. (p. 54)

Write a general equation of a reaction catalyzed by aminotransferases.

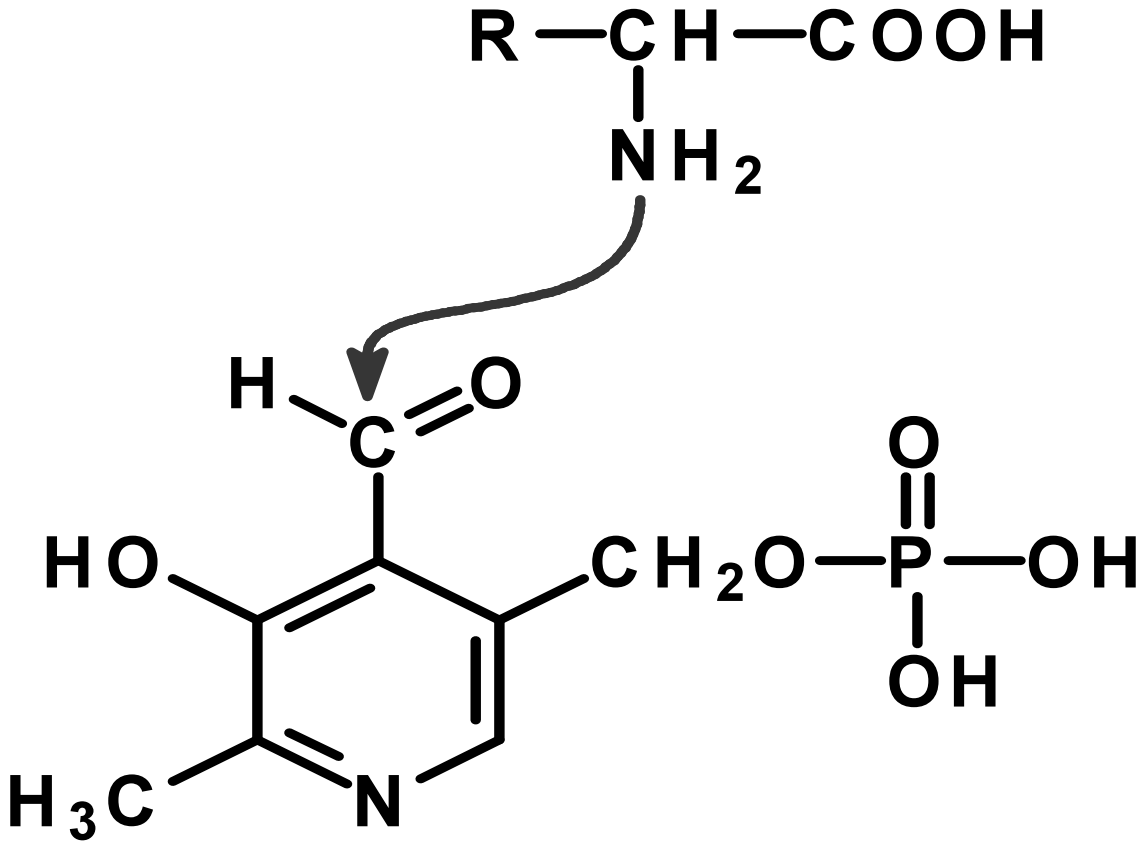
General scheme of transamination



Q. (p. 54)

Which cofactor is used by aminotransferases?

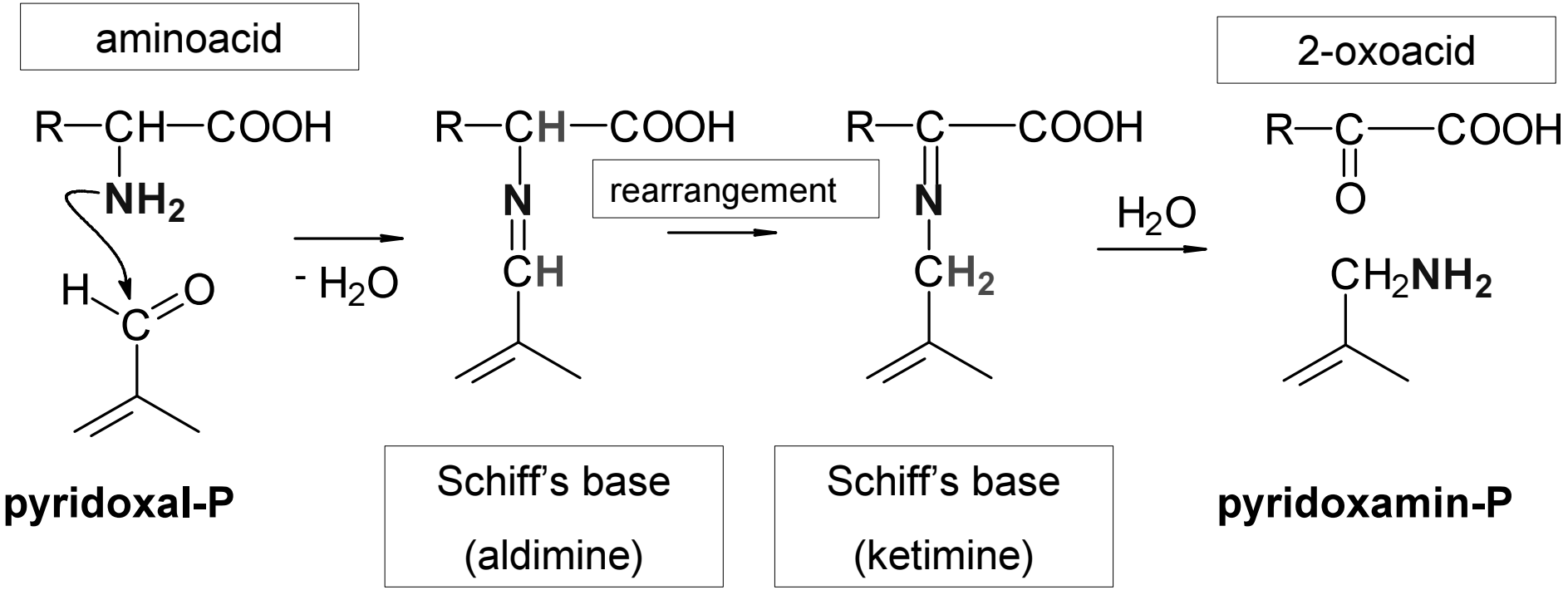
Pyridoxal phosphate



1. Phase of transamination

aminoacid → oxoacid

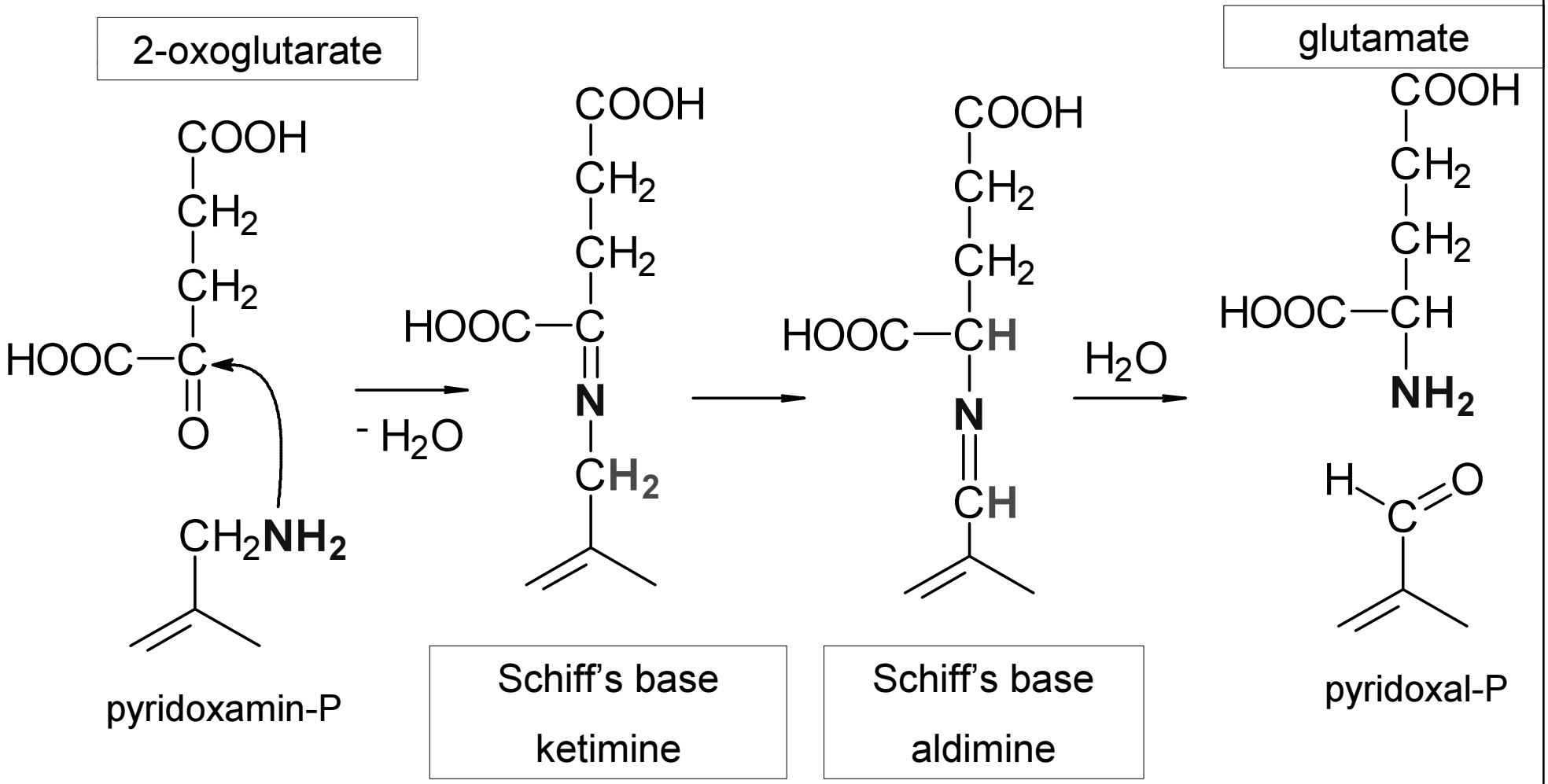
pyridoxal-P → pyridoxamine-P



2. Phase of transamination

2-oxoglutarate → glutamate

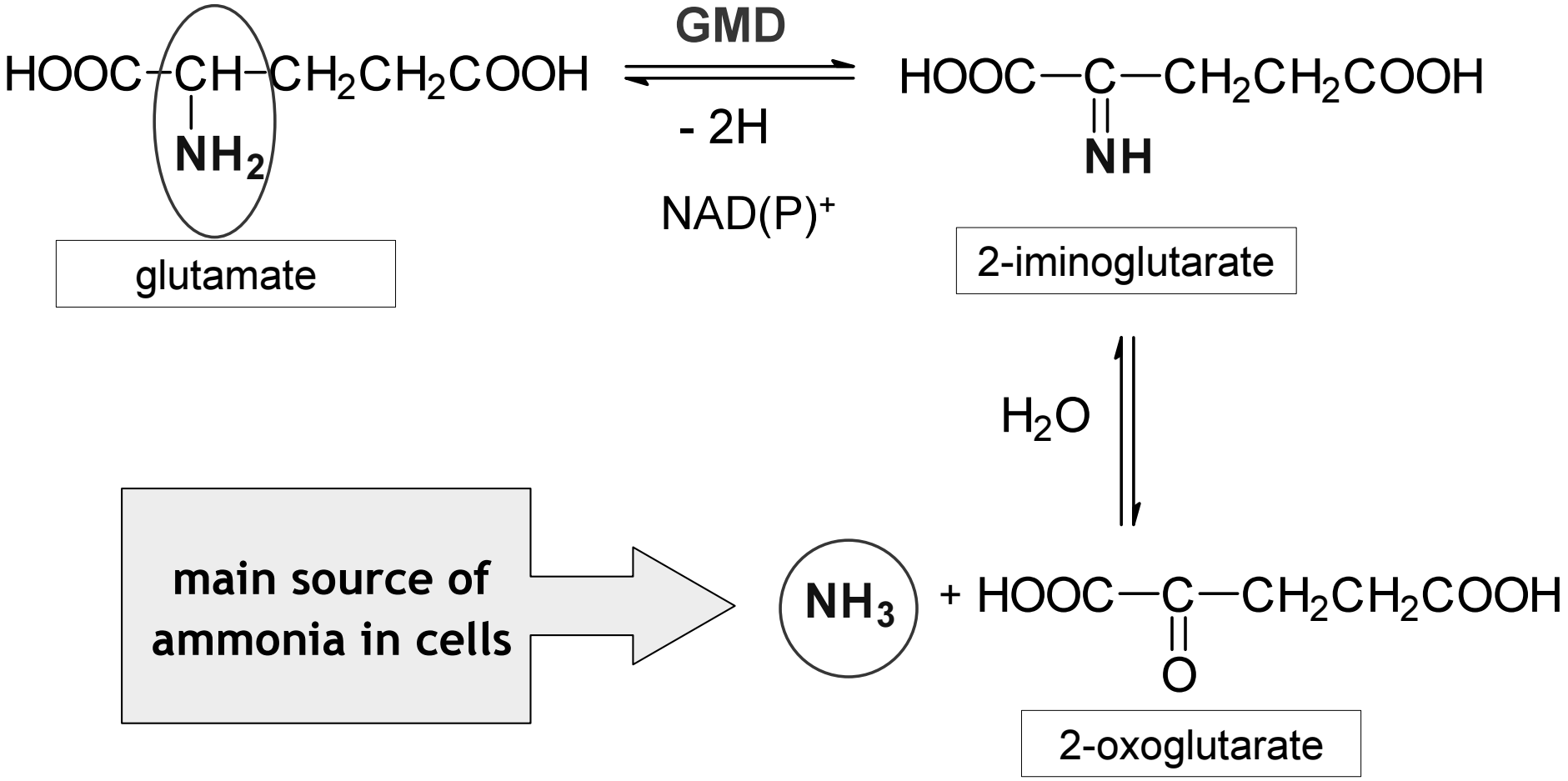
pyridoxamine-P → pyridoxal-P



In transaminations, nitrogen of most AA is concentrated in glutamate

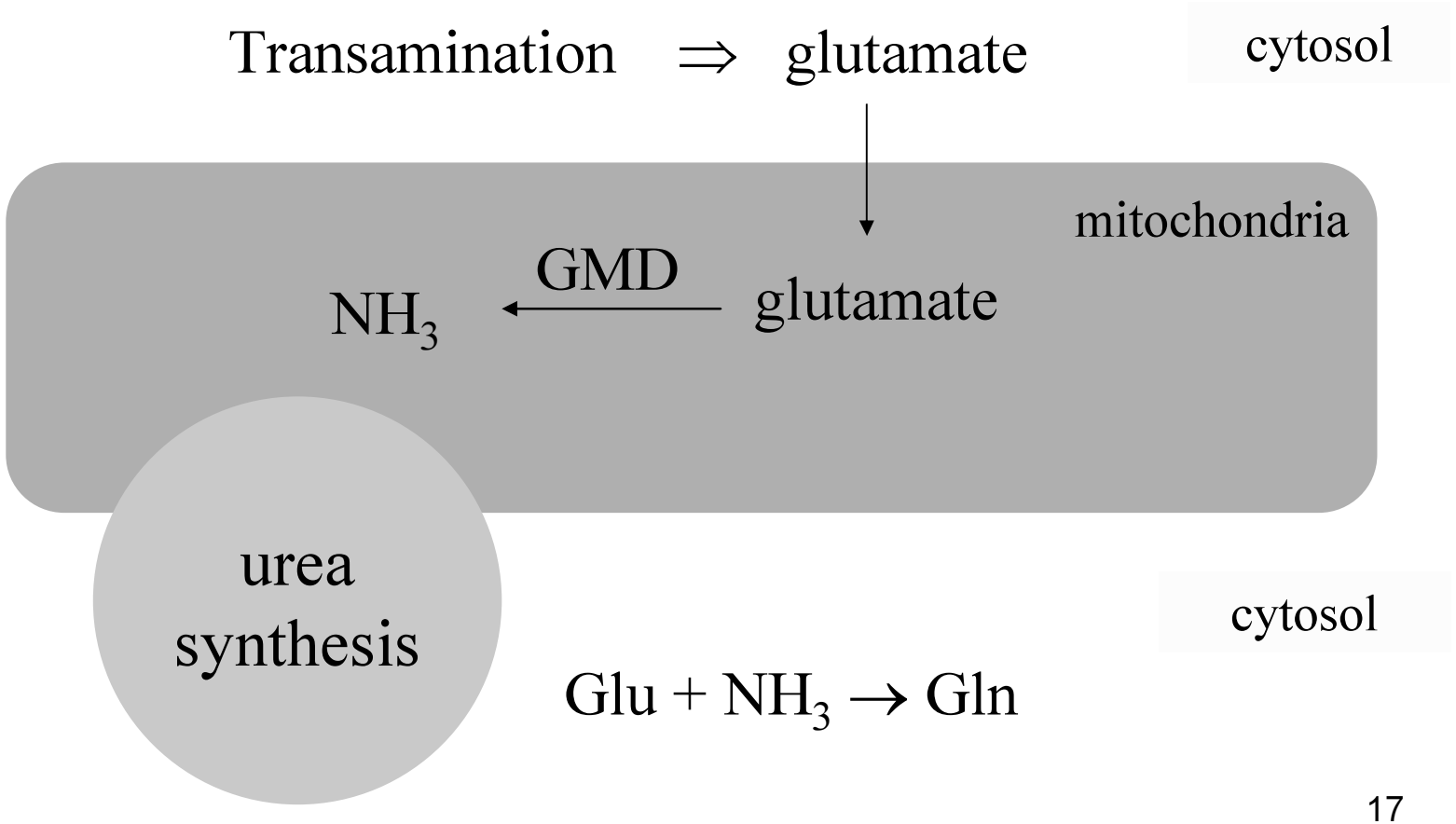
Glutamate then undergoes dehydrogenation deamination and releases **free ammonia NH_3**

Dehydrogenation deamination of glutamate is a reversible reaction



GMD = glutamate dehydrogenase

Intracellular localization



Q.

What are **two** main sources of ammonia

in human body?

Two main sources of ammonia in body

- **<u>Dehydrogenation deamination of glutamate</u>**

  in cells of most tissues

- **<u>Bacterial fermentation of proteins in large intestine</u>**

  ammonia diffuses freely into portal blood $\Rightarrow$

  portal blood has high concentration of NH_3 $\Rightarrow$

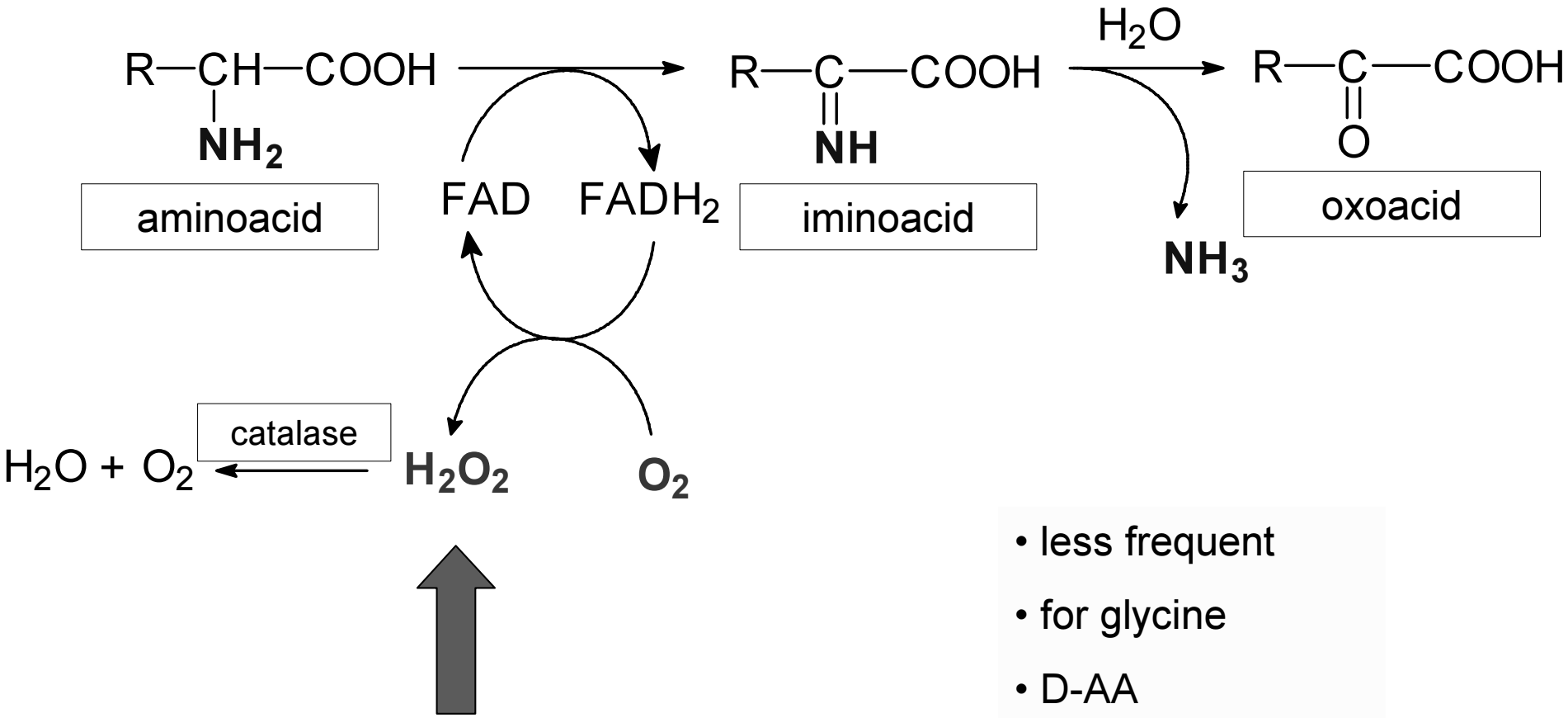
  NH_3 is eliminated by liver (under normal cond.)

Other ways of deaminations

- deamination of glutamate in purine nucleotide cycle (p. 55)
- oxidative deamination of some AA ($\rightarrow H_2O_2$)
- oxidative deamination of biogenous amines ($\rightarrow H_2O_2$)
- desaturation deamination of His $\rightarrow$ urocanic acid + $\mathbf{NH_3}$
- oxidative deamination of lysinu

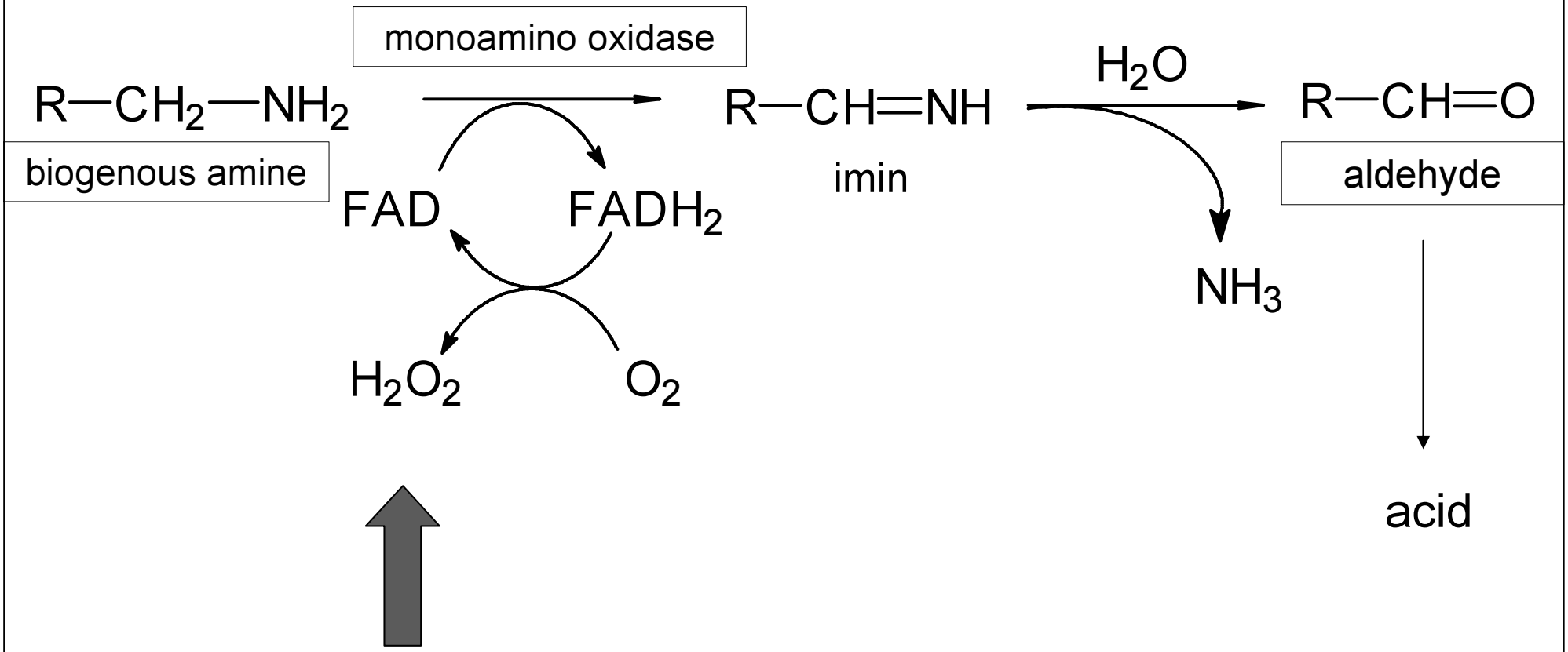
  lysyloxidase (Cu^{2+}): Lys + O_2 $\rightarrow$ $\mathbf{NH_3}$ + allysine + H_2O (p. 114)

Oxidative deamination of some AA

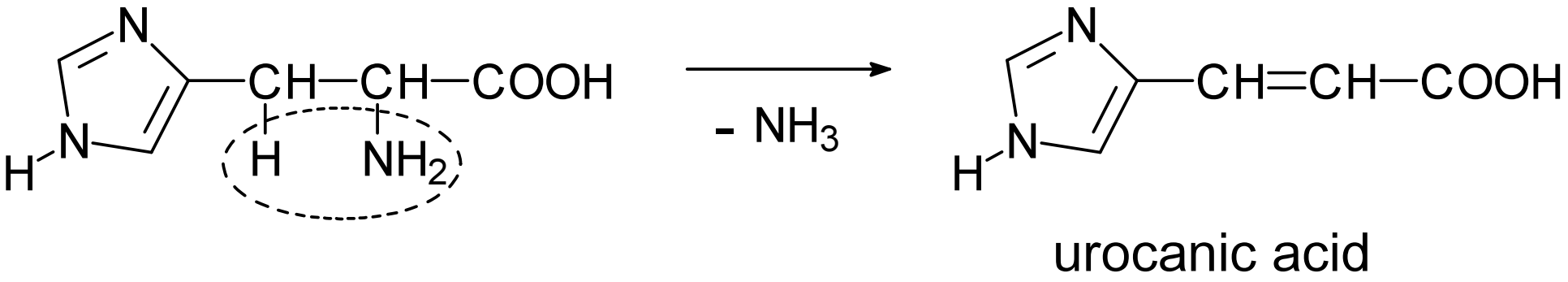


- less frequent
- for glycine
- D-AA

Oxidative deamination of amines



Desaturation deamination of histidine



urocanic acid

Other sources of ammonia in tissues

- **non-enzymatic carbamylation of proteins**

  Prot-NH_2 + NH_2-CO-NH_2 $\rightarrow$ **NH_3** + Prot-NH-CO-NH_2

- **catabolism of pyrimidine bases**

  cytosine/uracil $\rightarrow$ **NH_3** + CO_2 + β-alanine

  thymine $\rightarrow$ **NH_3** + CO_2 + β-aminoisobutyrate

- **hem synthesis**

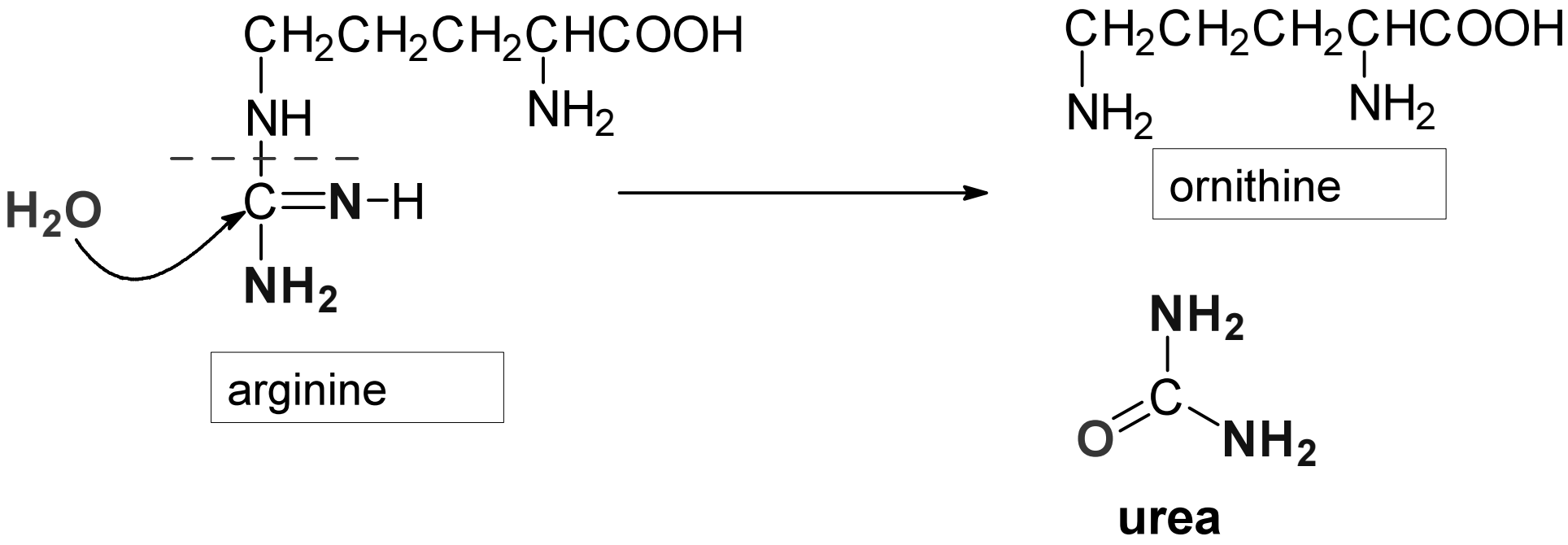
  4 porfobilinogen $\rightarrow$ **4 NH_3** + uroporfyrinogen

Three ways of ammonia detoxication

Feature	Urea	Glutamine (Gln)	Glutamate (Glu)
Relevance	★ ★ ★ ★ ★ ★	★ ★ ★ ★	★
Compound type	H_2CO_3 diamide	γ-amide of Glu	α-aminoacid
Reaction	urea cycle	Glu + NH_3	hydrog. amin. 2-OG
Enzyme	5 enzymes	Gln-synthase	GMD
Energy needs	3 ATP	1 ATP	1 NADH[a]
Intracell localiz.	mitoch. + cytosol	cytosol	mitochondria
Organ localiz.	only liver	liver + other	mainly brain

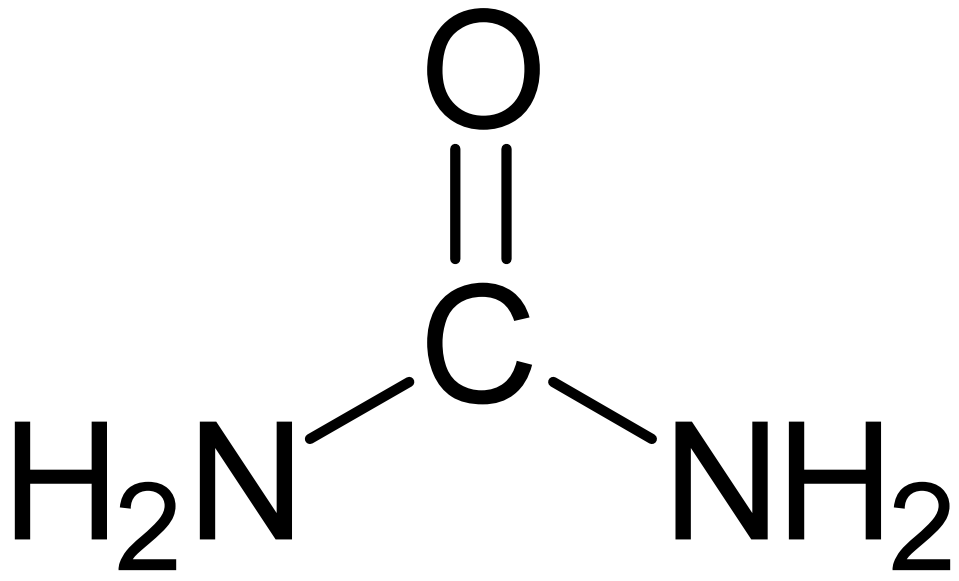
[a] Equivalent of 3 ATP (compare respiratory chain).

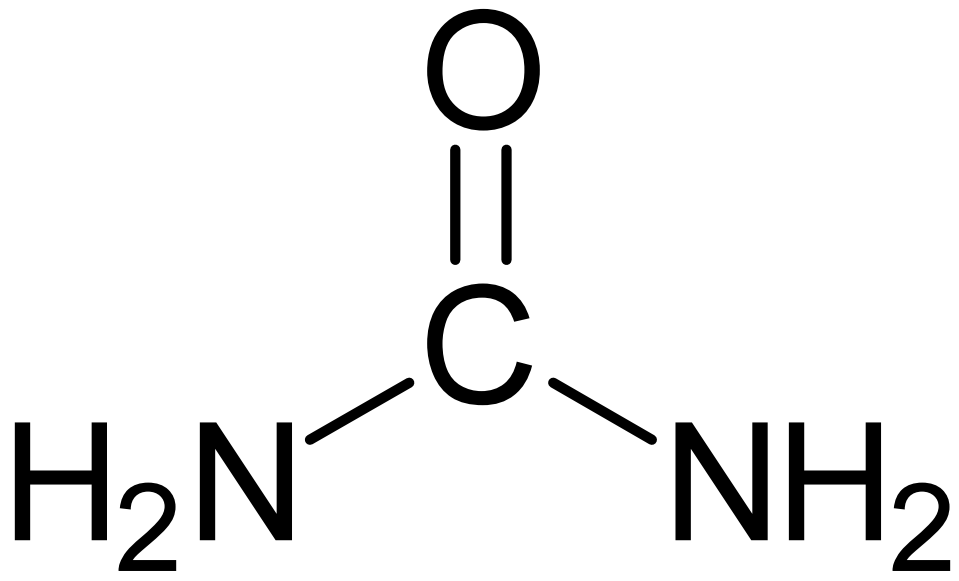
Hydrolysis of arginine provides urea



in urea cycle

What is metabolic origine of N atoms in urea?





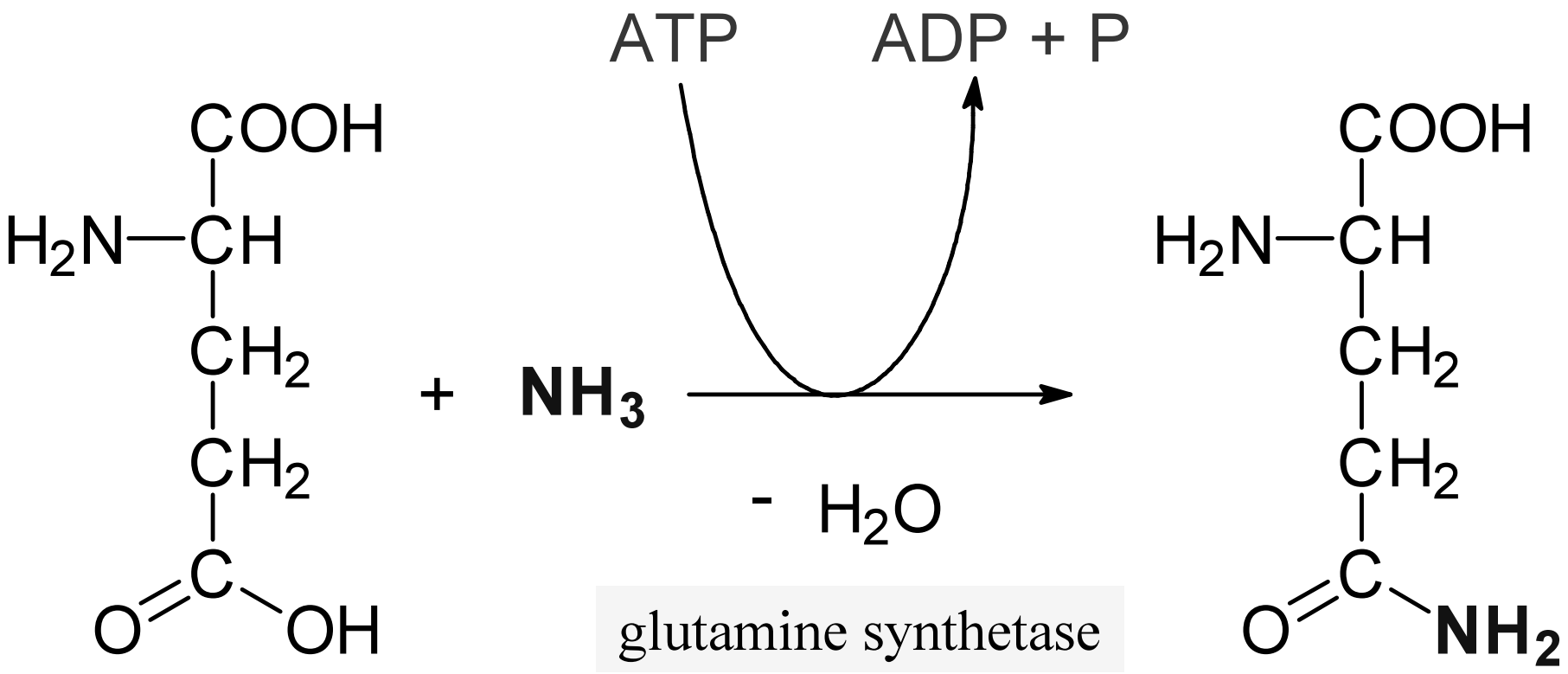
free ammonia

aspartate
(in urea cycle)

The properties of urea

- carbonic acid diamide
- perfectly soluble in water
- non-electrolyte $\Rightarrow$ neutral aq. solutions (pH = 7)
- produced in liver $\times$ excreted by kidneys
- difuses easily through all cell membranes

Glutamine synthesis requires ATP



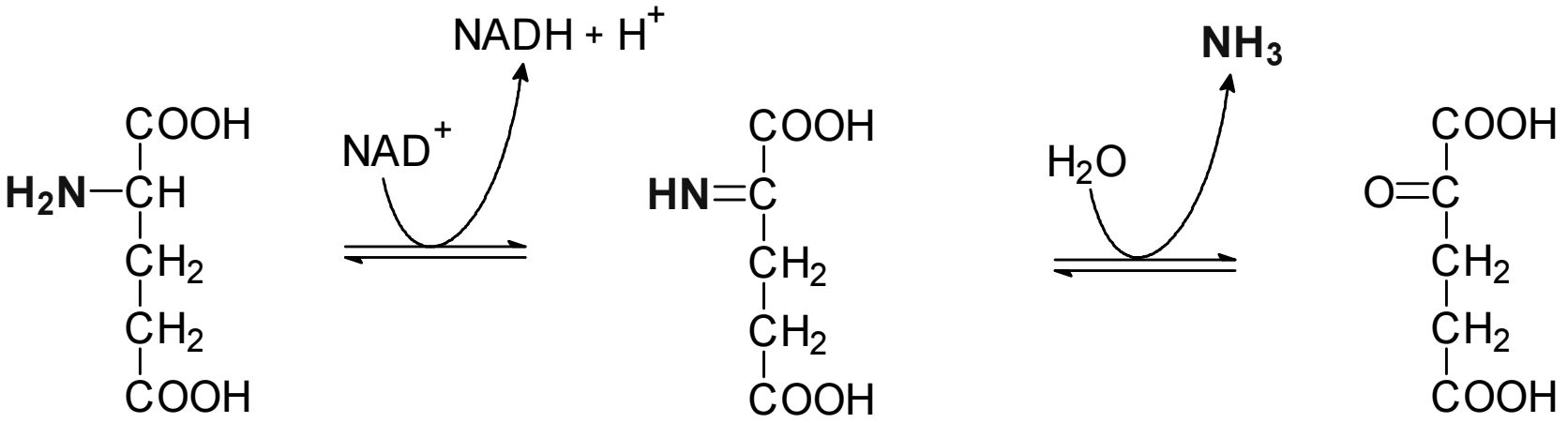
glutamate

glutamine

2nd way of NH_3 detoxication

Compare two reactions (GMD)

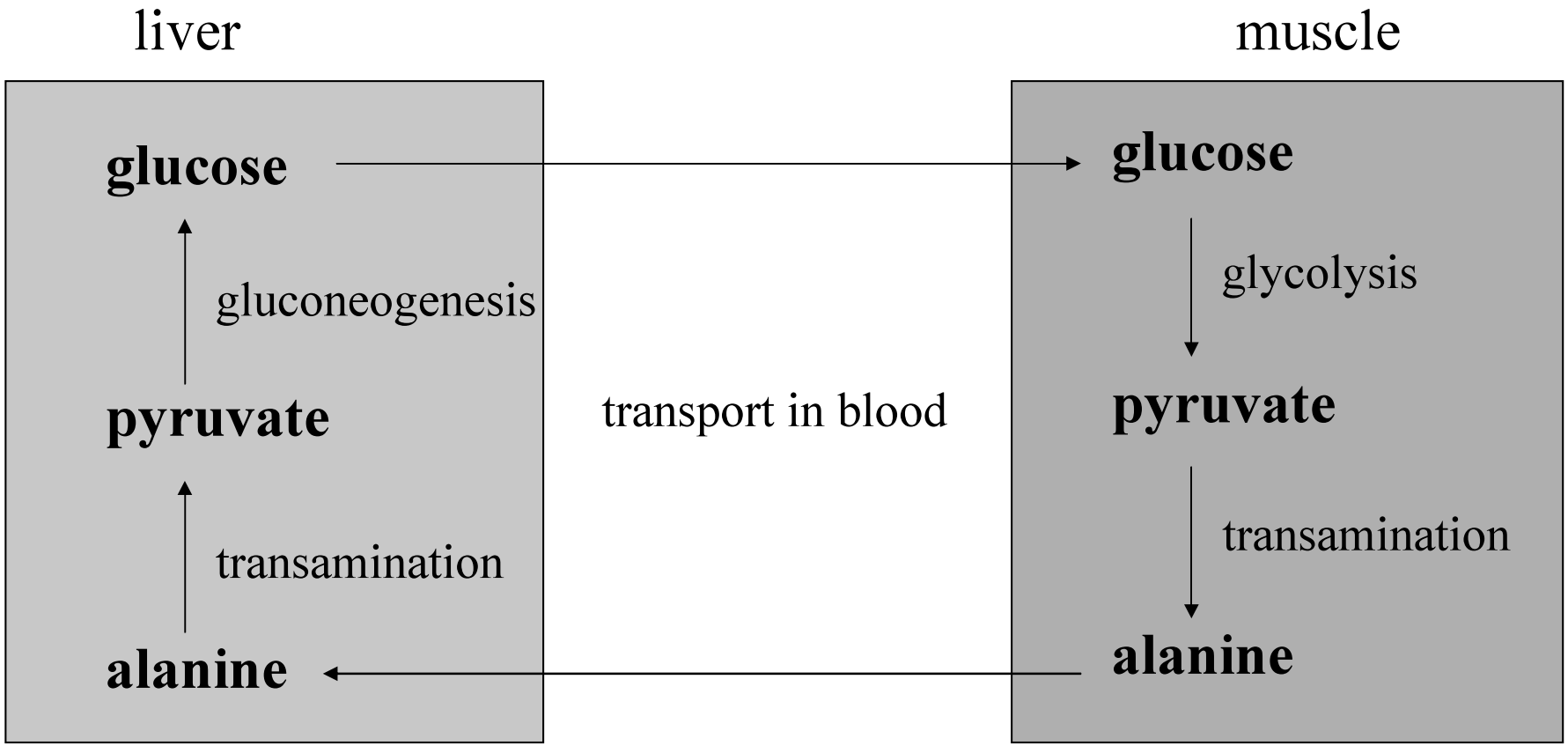
dehydrogenation **deamination** **of glutamate**



hydrogenation **amination** **of 2-oxoglutarate**

3rd way of NH_3 detoxication

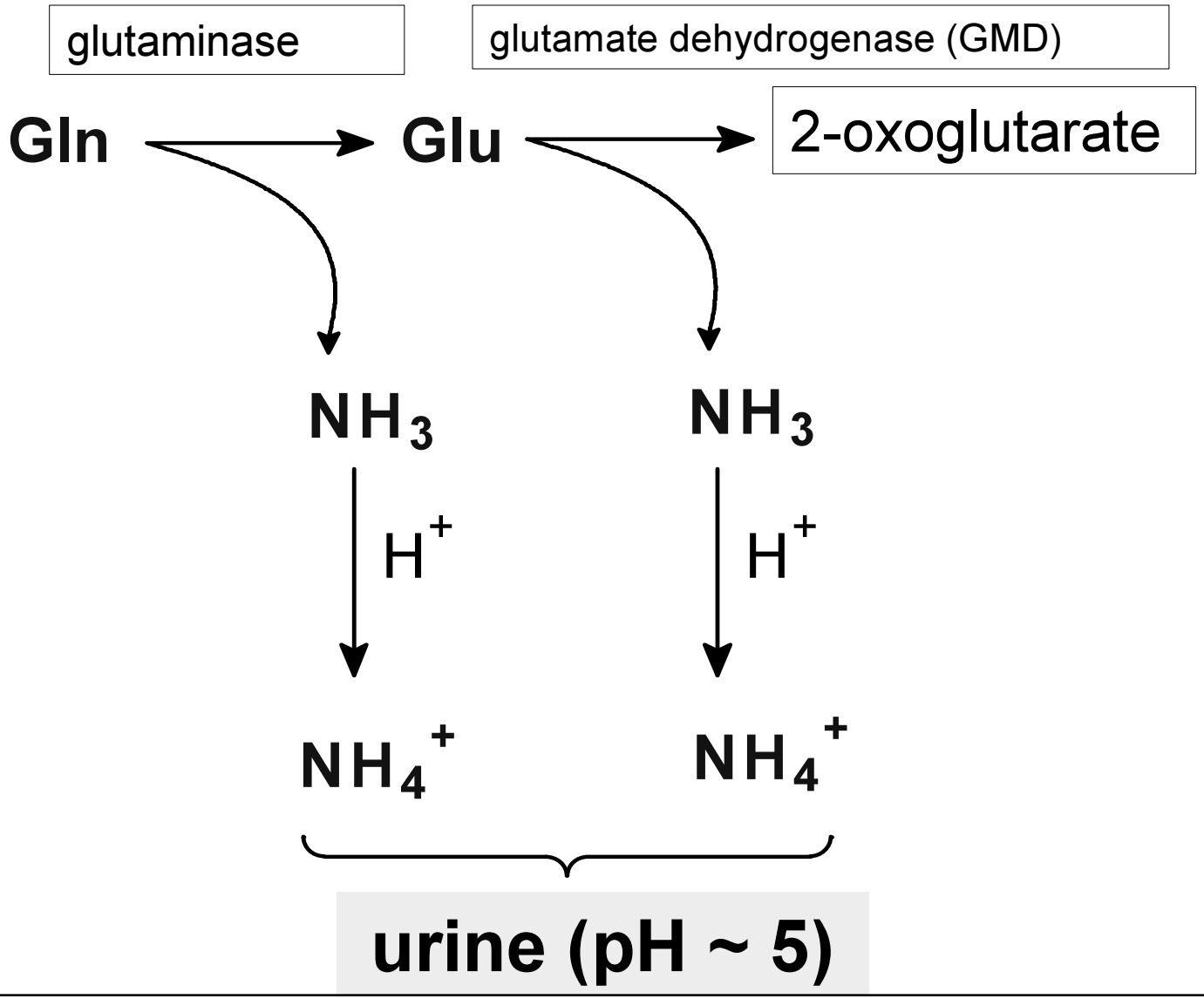
Glucose-alanine cycle



Glutamine cycle

- Gln carries $-NH_2$ group from muscles to liver (periportal hepatocytes) for detoxification
- in perivenous hepatocytes, Gln is made from glutamate to keep ammonia concentration low (Glu + $NH_3 \rightarrow$ Gln)
- Gln is exported from the liver to kidney where is deaminated, NH_4^+ ions are excreted by urine
- exogenous and endogenous Gln is the source of energy for intestinal mucosa: Gln $\rightarrow$ 2-OG $\rightarrow$ energy (CAC)

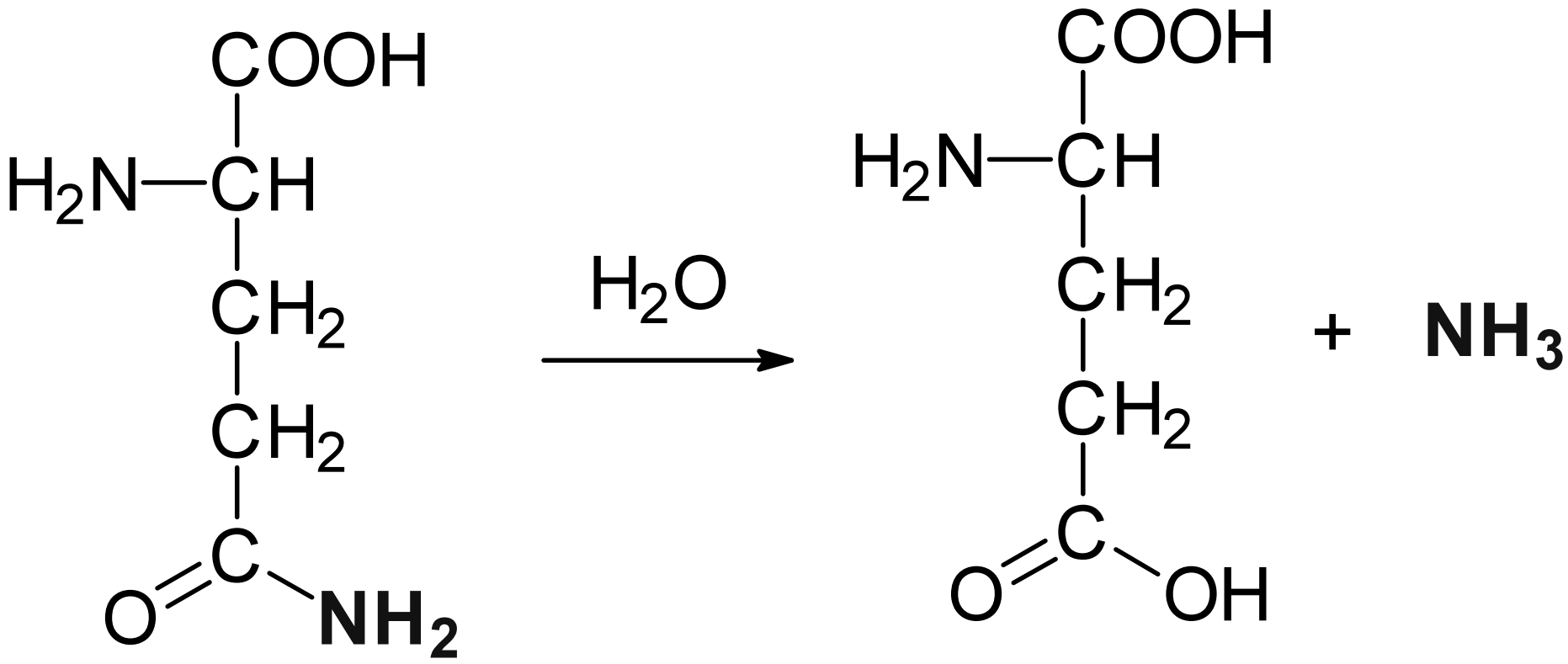
Glutamine deamination in kidney occurs stepwise



Q.

What reaction is catalyzed by glutaminase?

Glutaminase catalyses the hydrolysis of amide group in glutamine



glutamine

glutamate

Test results will be available on line

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Biochemistry II-s

Notebook