

Il metabolismo ossidativo



13.3.2010
Ore 14:00

Riposare...stanca !

Respirare (muscoli, cuore)

Pensare/sognare (cervello, cuore)

Digerire (apparato gastroenterico, cuore, reni)

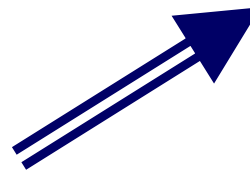
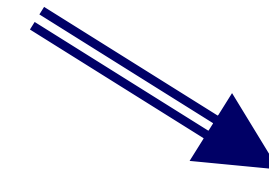
Controllo termico (cuore, circolazione periferica)

Controllo posizione (cervelletto, labirinto, muscoli)

Tutto questo richiede energia !

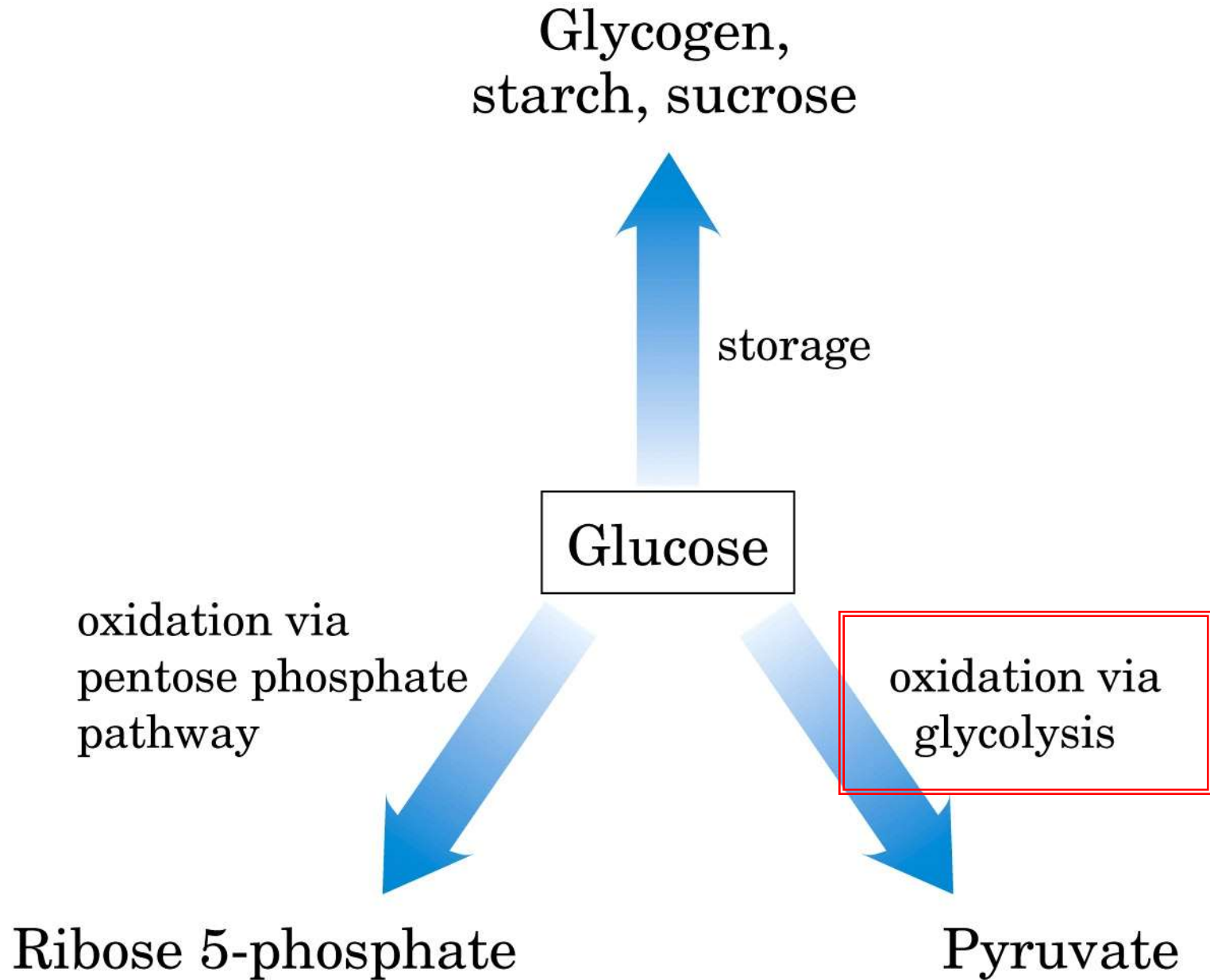
Il glucosio e gli altri carboidrati
sono una fonte **primaria** di energia

DEGRADAZIONE di
polisaccaridi (glicogeno epatico,
amido o glicogeno dalla dieta)

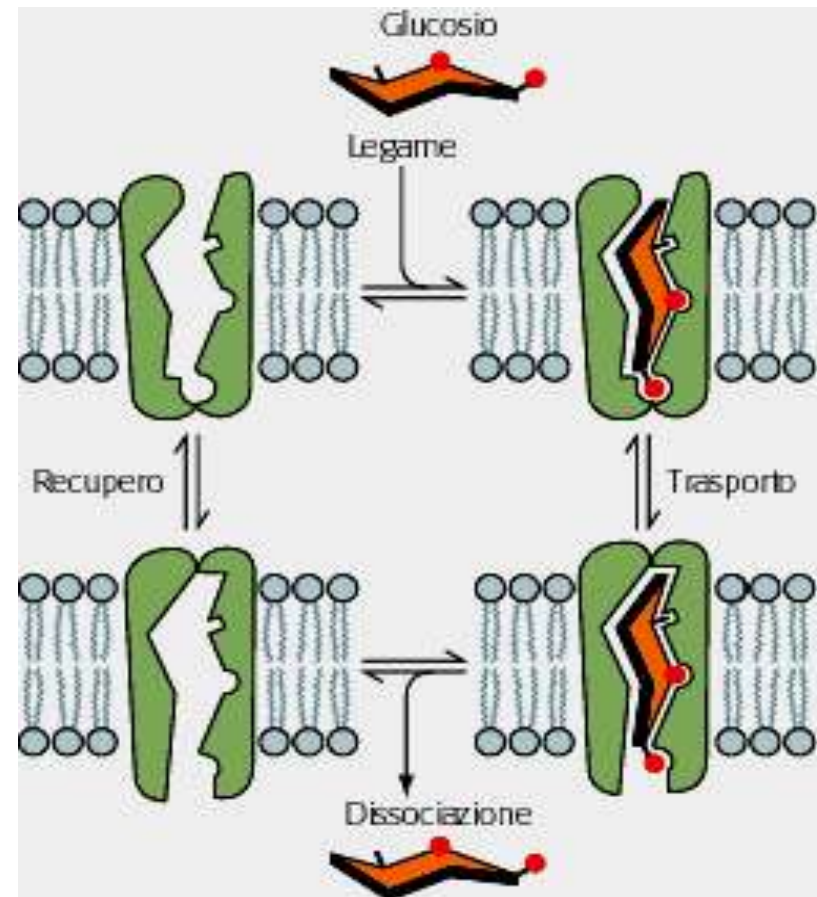


Glucosio

GLUCONEOGENESI (sintesi
da precursori non glucidici)



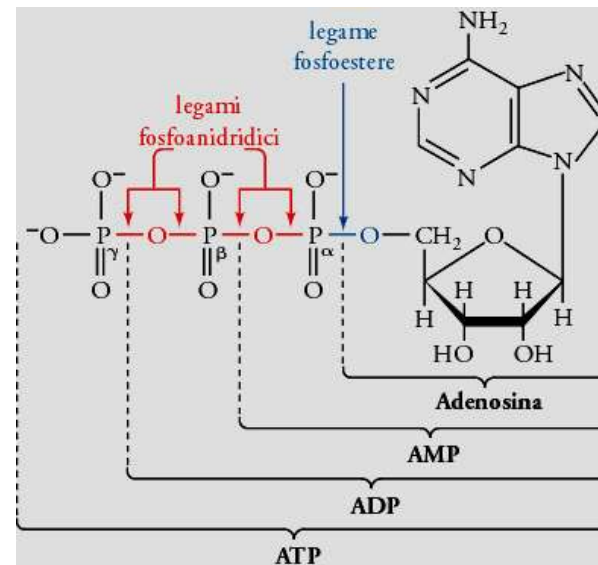
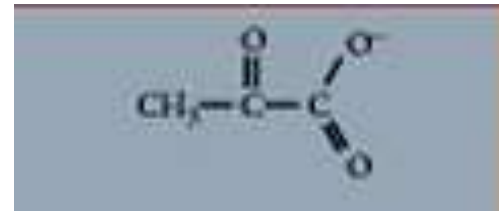
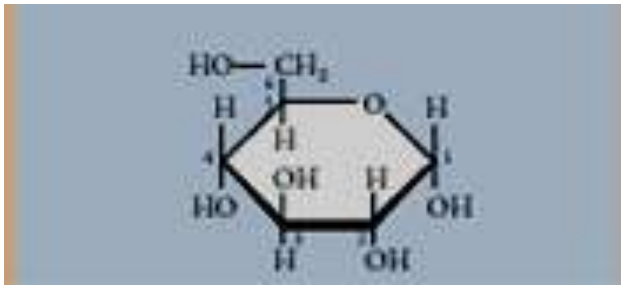
Il glucosio viene trasportato all'interno della cellula da uno specifico trasportatore di membrana



La glicolisi
avviene nel citosol

La GLICOLISI è una sequenza di 10 reazioni enzimatiche attraverso le quali una molecola di glucosio viene convertita in due molecole dello zucchero a tre atomi di C piruvato con la concomitante produzione di 2 ATP

Glucosio $\longrightarrow$ 2 piruvato + 2 ATP



(a)

first
priming
reaction

Glucose

①

ATP

ADP

Glucose 6-phosphate

②

Fructose 6-phosphate

second
priming
reaction

③

ATP

ADP

Fructose 1,6-bisphosphate

cleavage
of 6-carbon
sugar
phosphate to
two 3-carbon
sugar
phosphates

④

Glyceraldehyde 3-phosphate

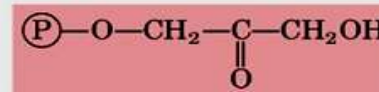
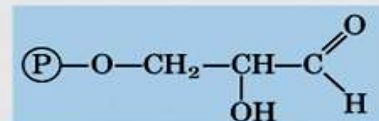
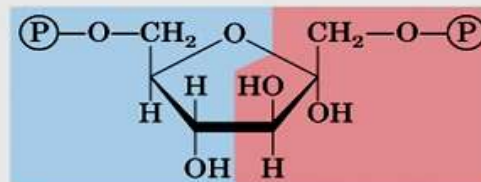
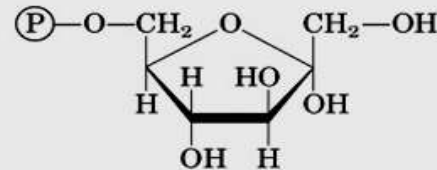
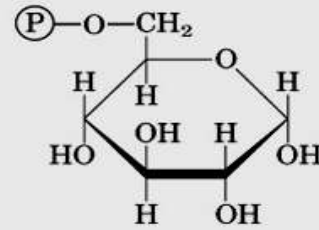
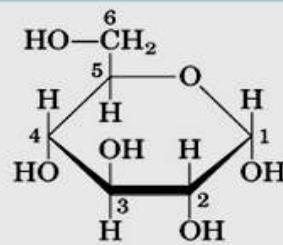
+

Dihydroxyacetone phosphate

⑤

Preparatory phase

Phosphorylation of glucose
and its conversion to
glyceraldehyde 3-phosphate



(b)

Payoff phase

Oxidative conversion of glyceraldehyde 3-phosphate to pyruvate and the coupled formation of ATP and NADH

oxidation and phosphorylation

⑥

Glyceraldehyde 3-phosphate (2)

2P_i
 2NAD^+

$2 \text{ NADH} + \text{H}^+$

first ATP-forming reaction (substrate-level phosphorylation)

⑦

1,3-Bisphosphoglycerate (2)

2ADP

2 ATP

3-Phosphoglycerate (2)

⑧

2-Phosphoglycerate (2)

⑨

$2\text{H}_2\text{O}$

Phosphoenolpyruvate (2)

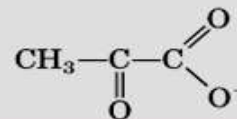
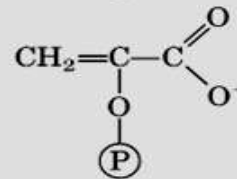
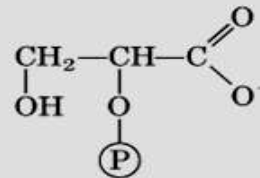
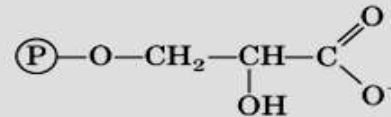
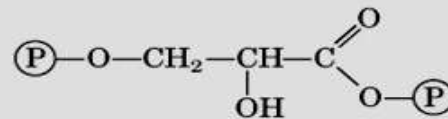
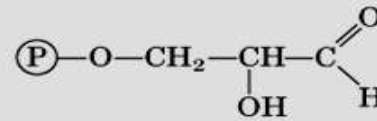
⑩

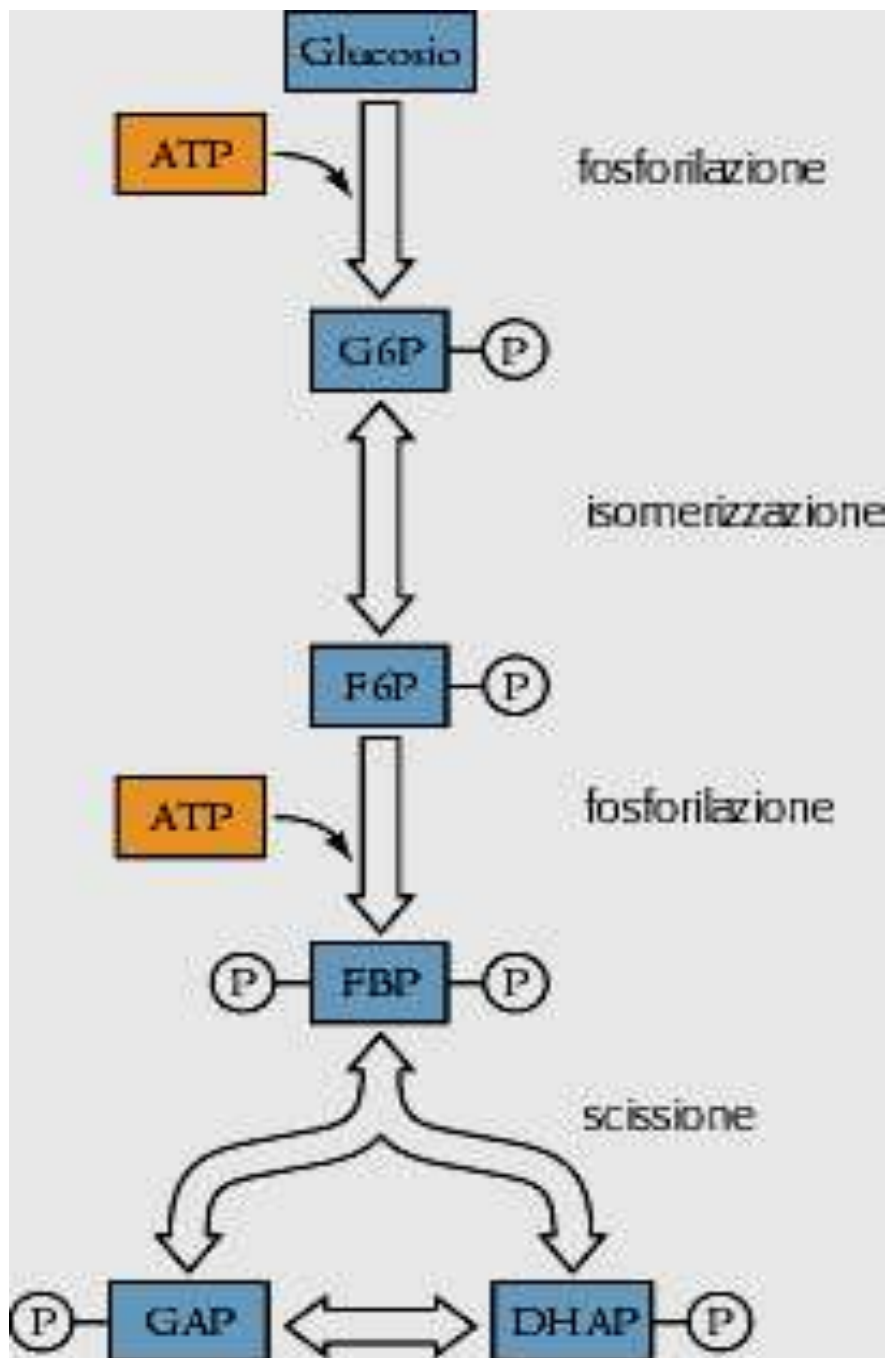
second ATP-forming reaction (substrate-level phosphorylation)

2ADP

2 ATP

Pyruvate (2)

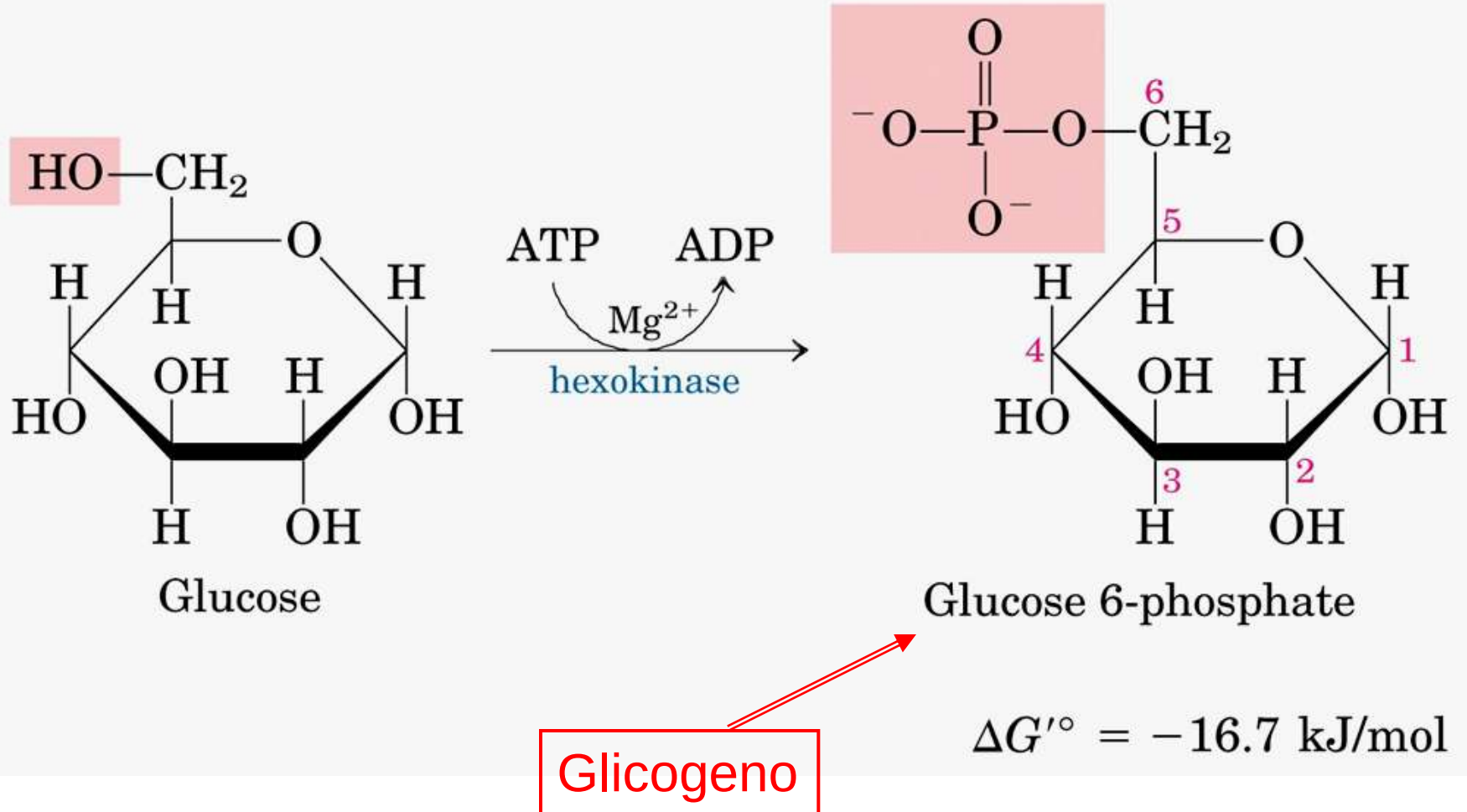




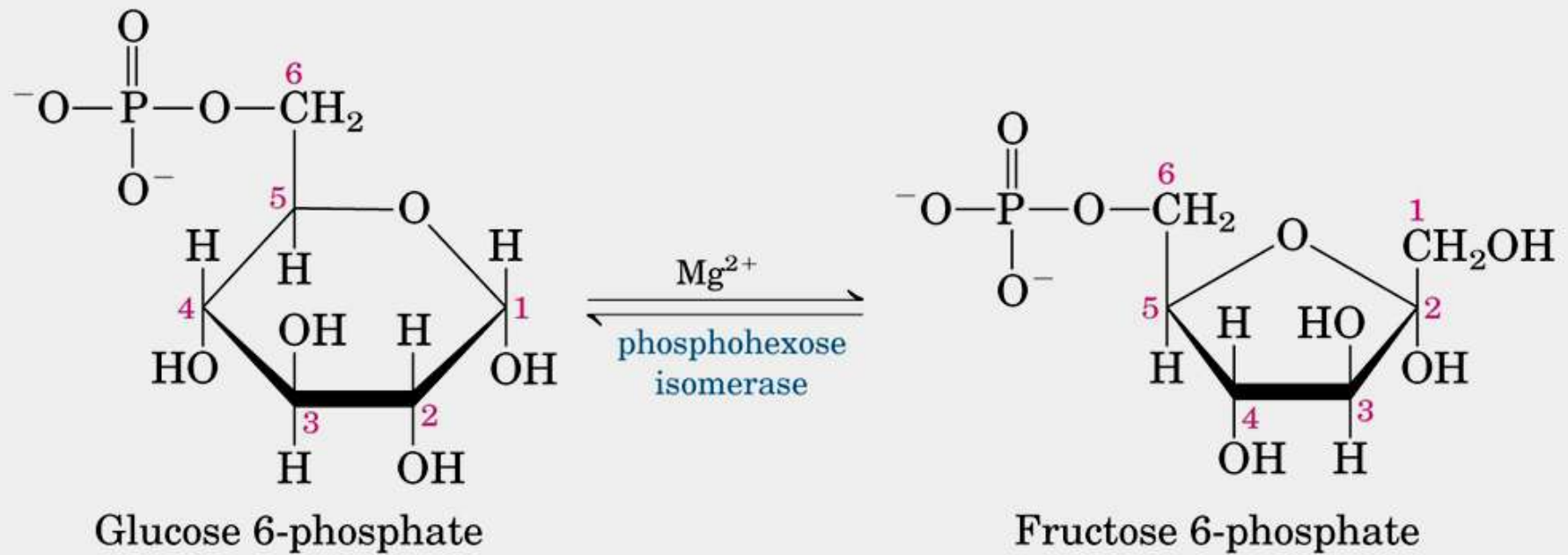
Fase I

1 molecola di glucosio viene convertita in 2 molecole di gliceraldeide-3-fosfato con consumo di 2 molecole di ATP

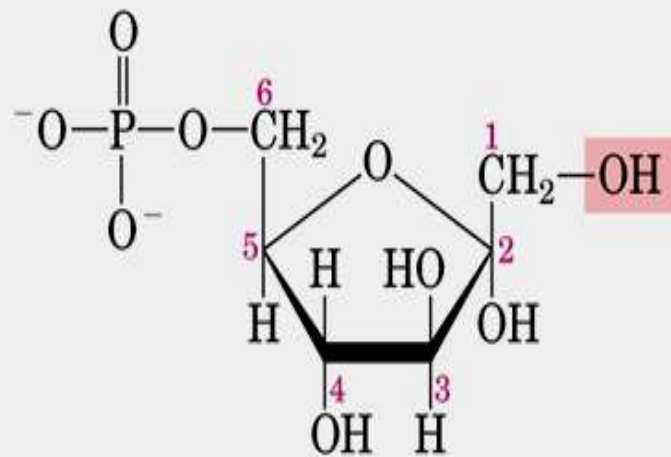
Reazione 1



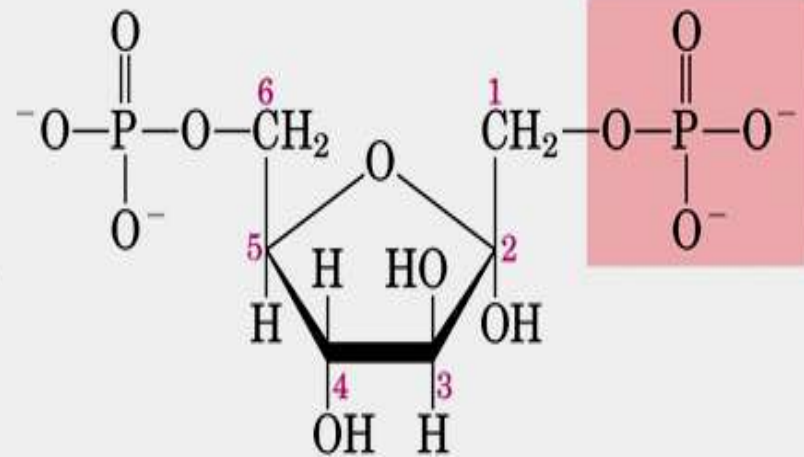
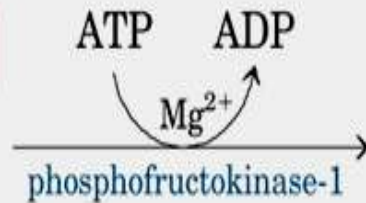
Reazione 2



Reazione 3



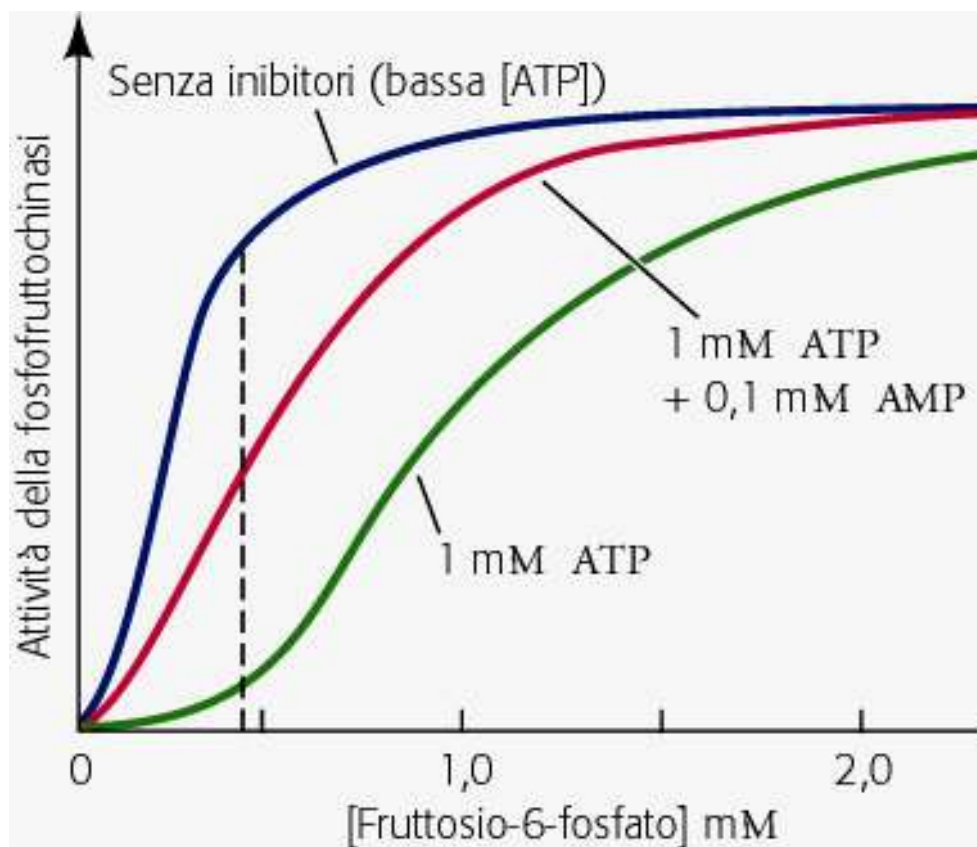
Fructose 6-phosphate



Fructose 1,6-bisphosphate

$$\Delta G'^{\circ} = -14.2 \text{ kJ/mol}$$

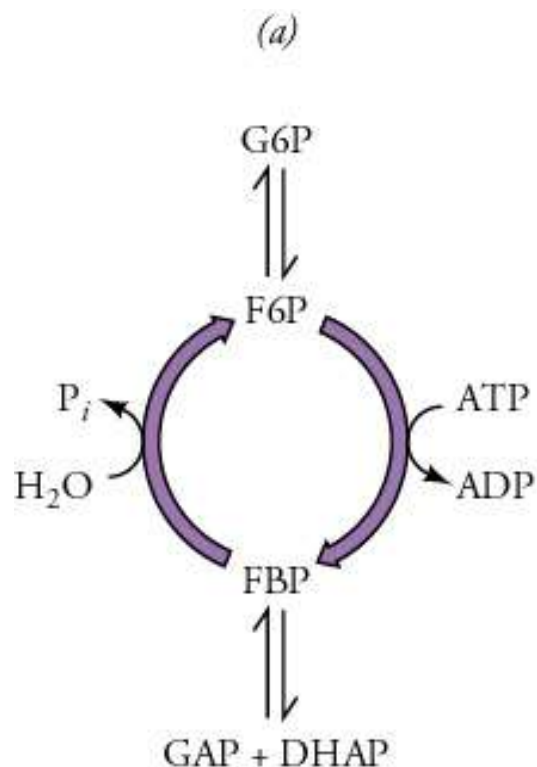
La Fosfofruttochinasi controlla la via glicolitica (nel muscolo scheletrico)



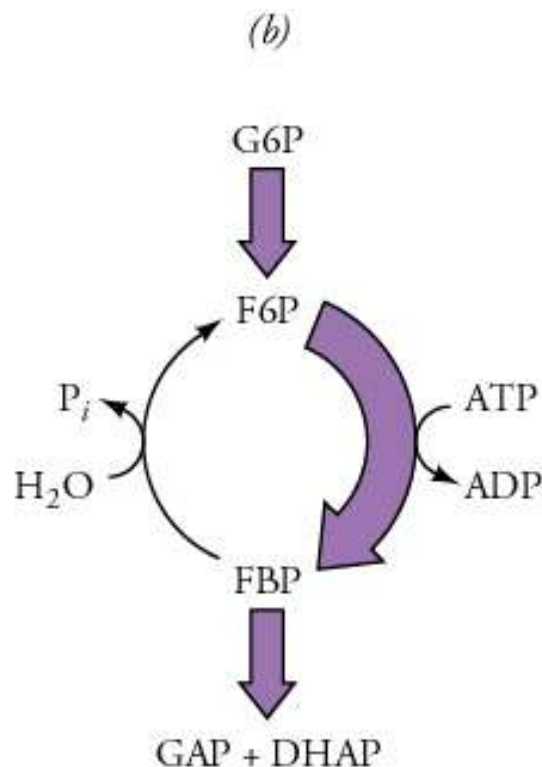
1.

- PFK è un tetramero con due stati conformazionali (T e R) in equilibrio tra loro
- L'ATP è sia substrato che inibitore (2 siti di legame diversi)
- AMP, ADP e fruttosio-2,6-bifosfato sono attivatori

La Fosfofruttochinasi controlla la via glicolitica (nel muscolo scheletrico)



Muscolo a riposo



Muscolo in contrazione

2.

- PFK è regolata nel ciclo del substrato dalla attività della fruttosio-1,6,-bifosfatasi (FBPasi)

Fructose 6-phosphate

Glycolysis

ATP

PFK-1

ADP

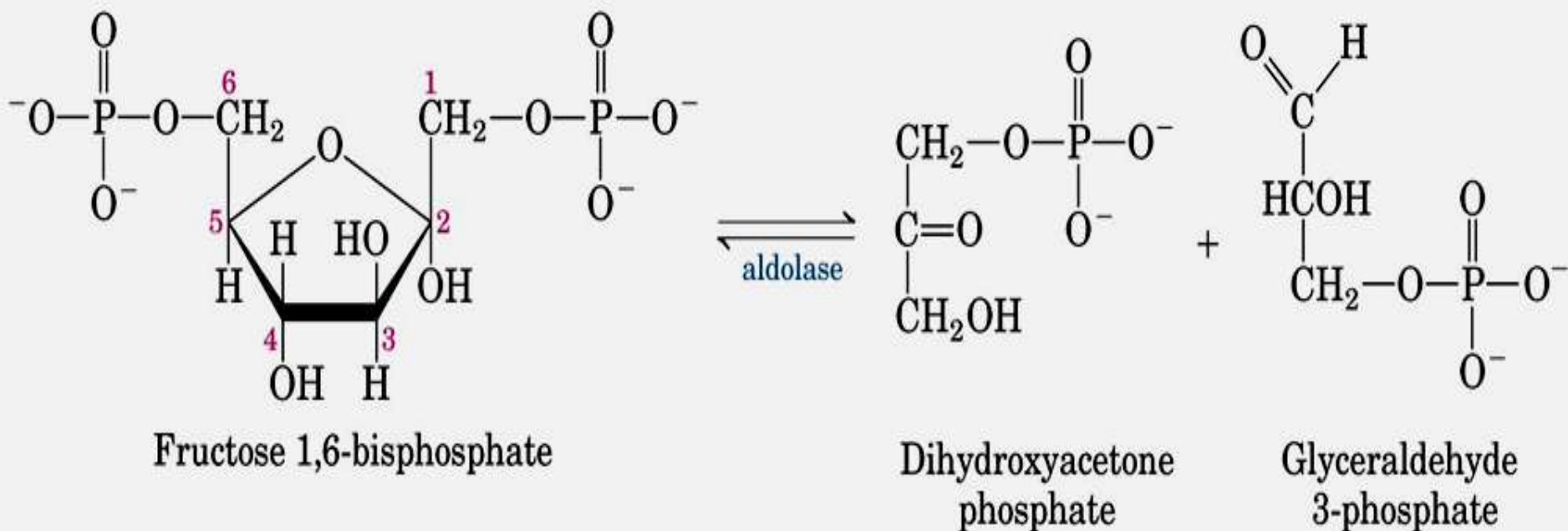
Gluconeogenesis

P_i

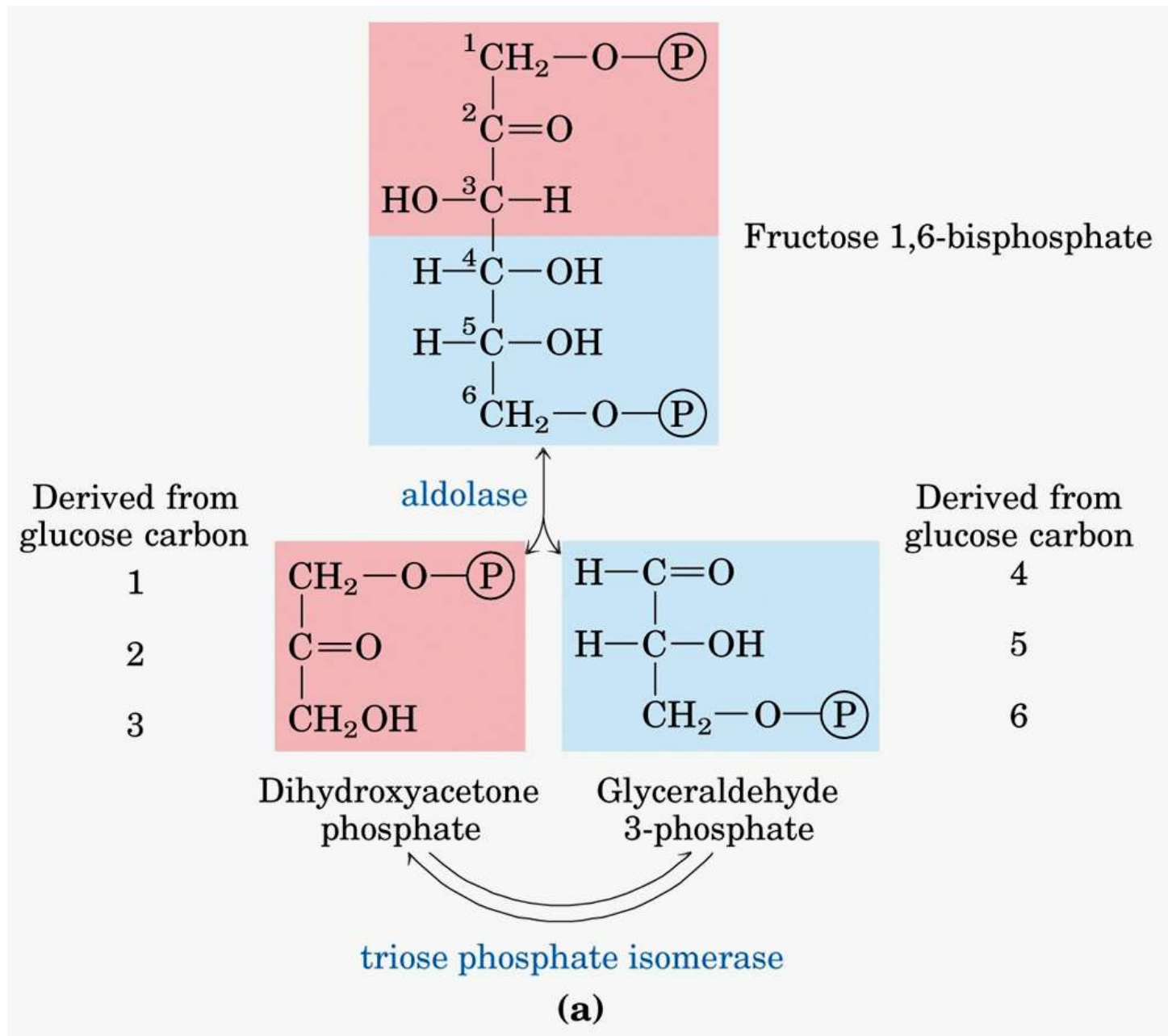
FBPase-1

Fructose 1,6-bisphosphate

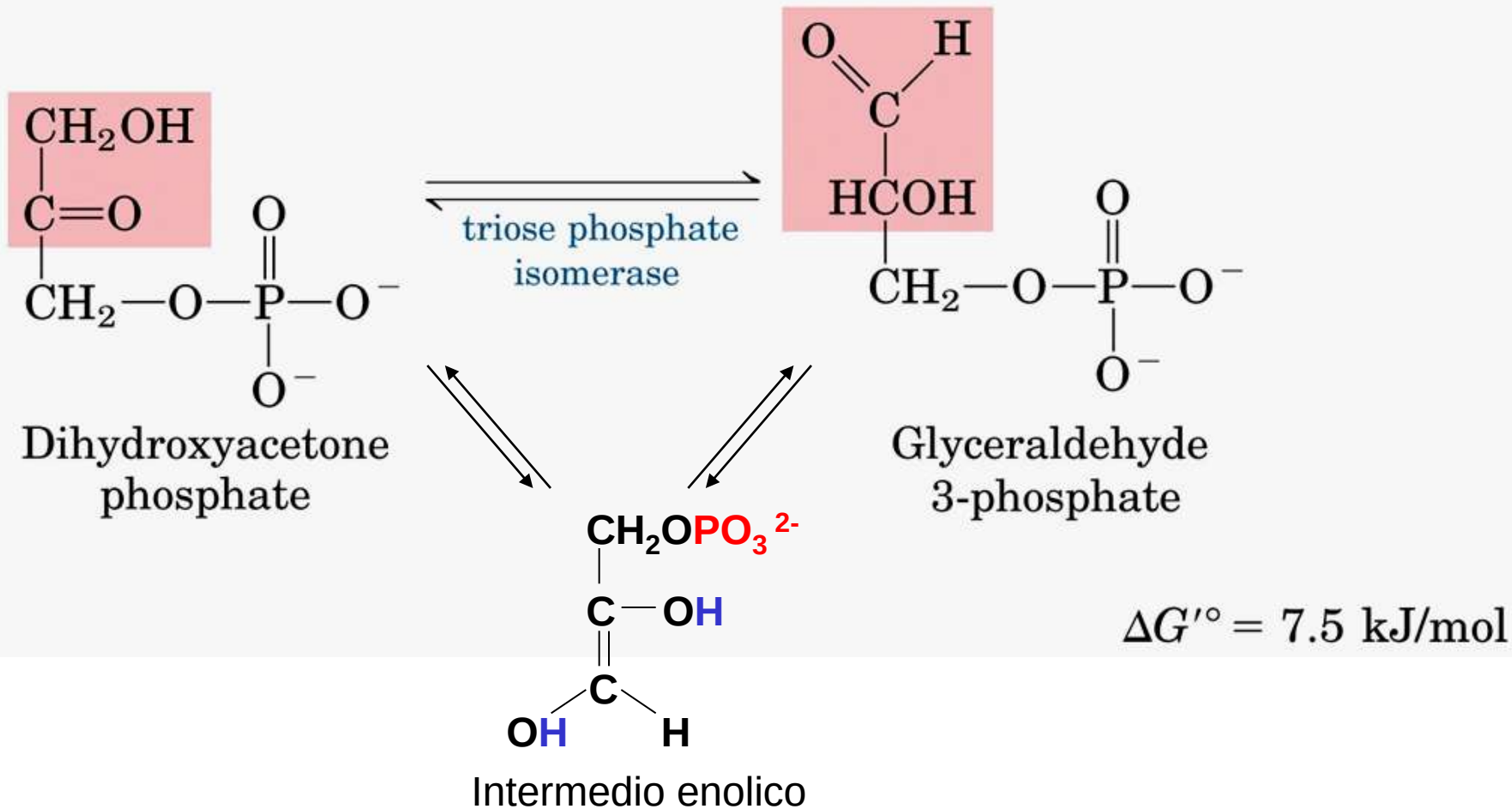
Reazione 4



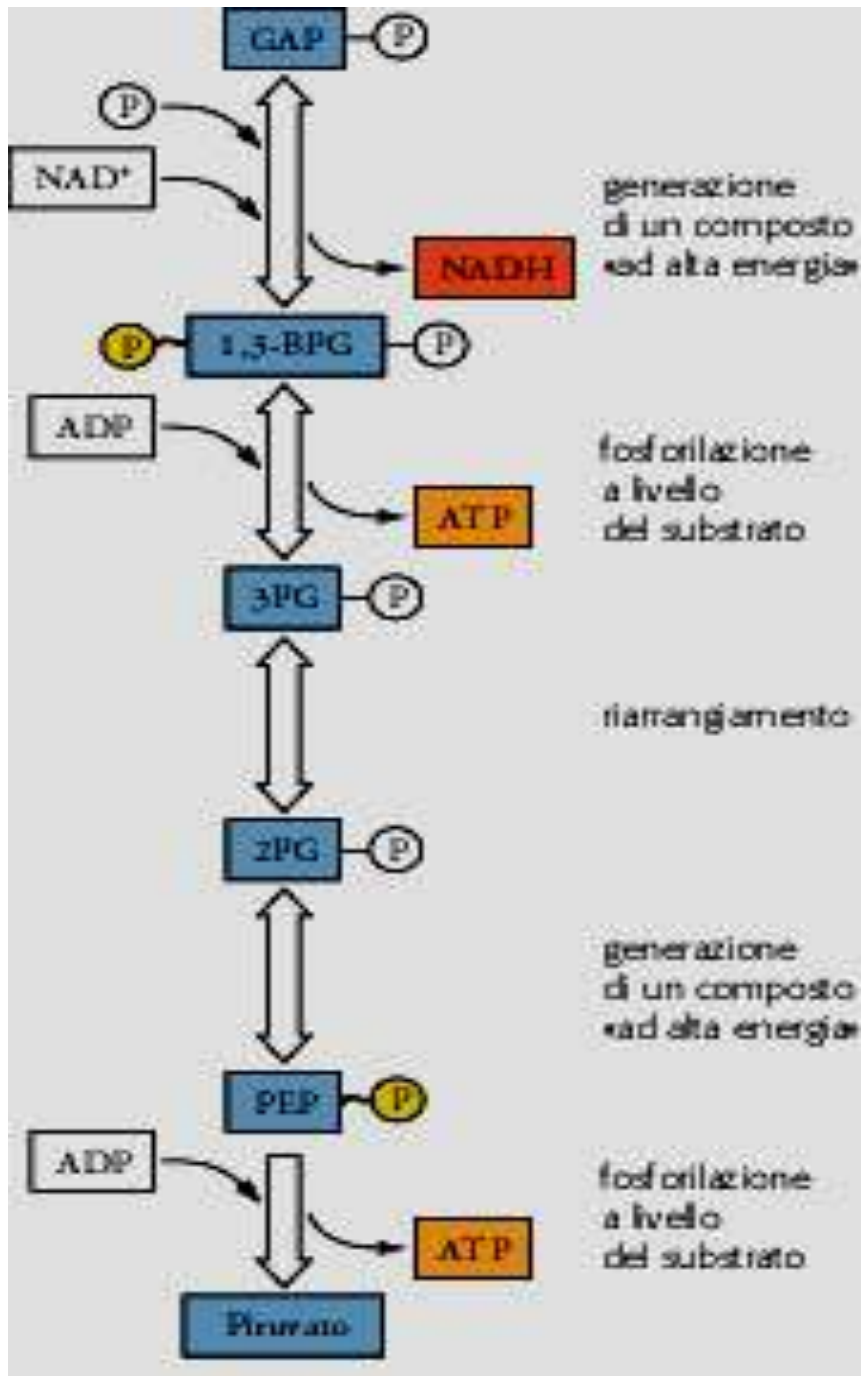
$$\Delta G'^{\circ} = 23.8 \text{ kJ/mol}$$



Reazione 5

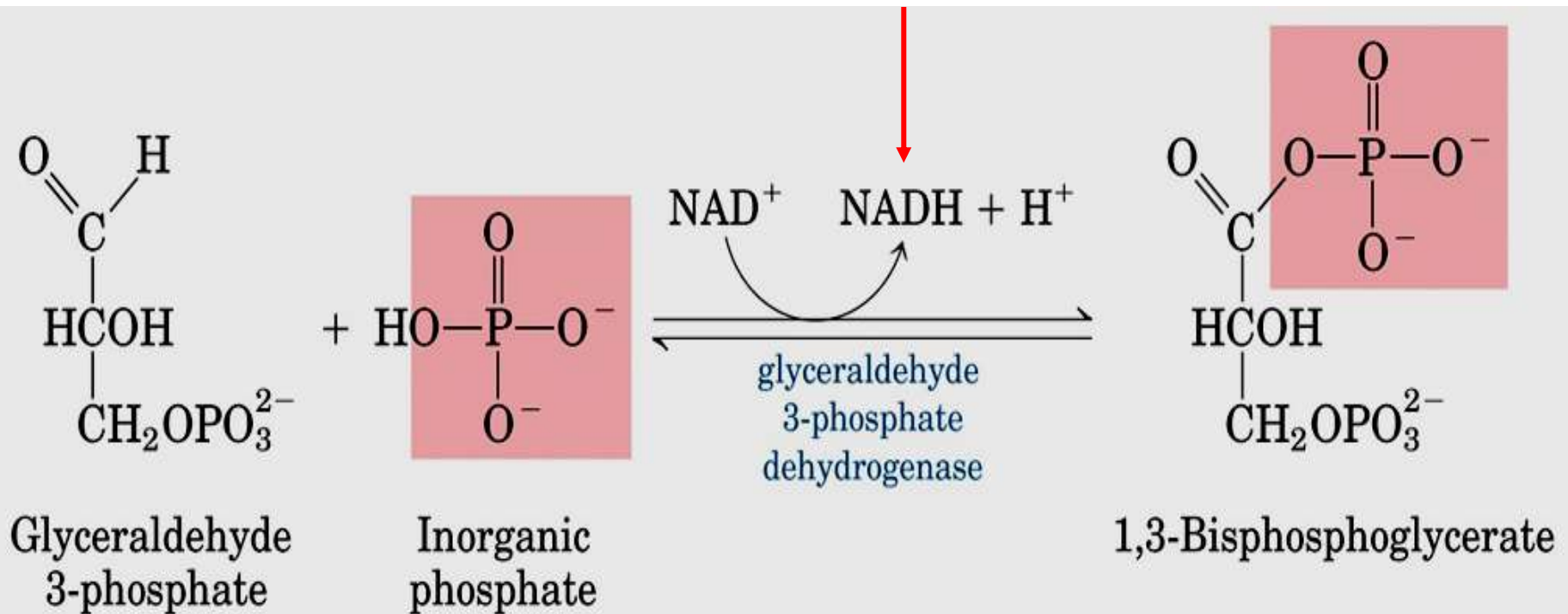


Fase II



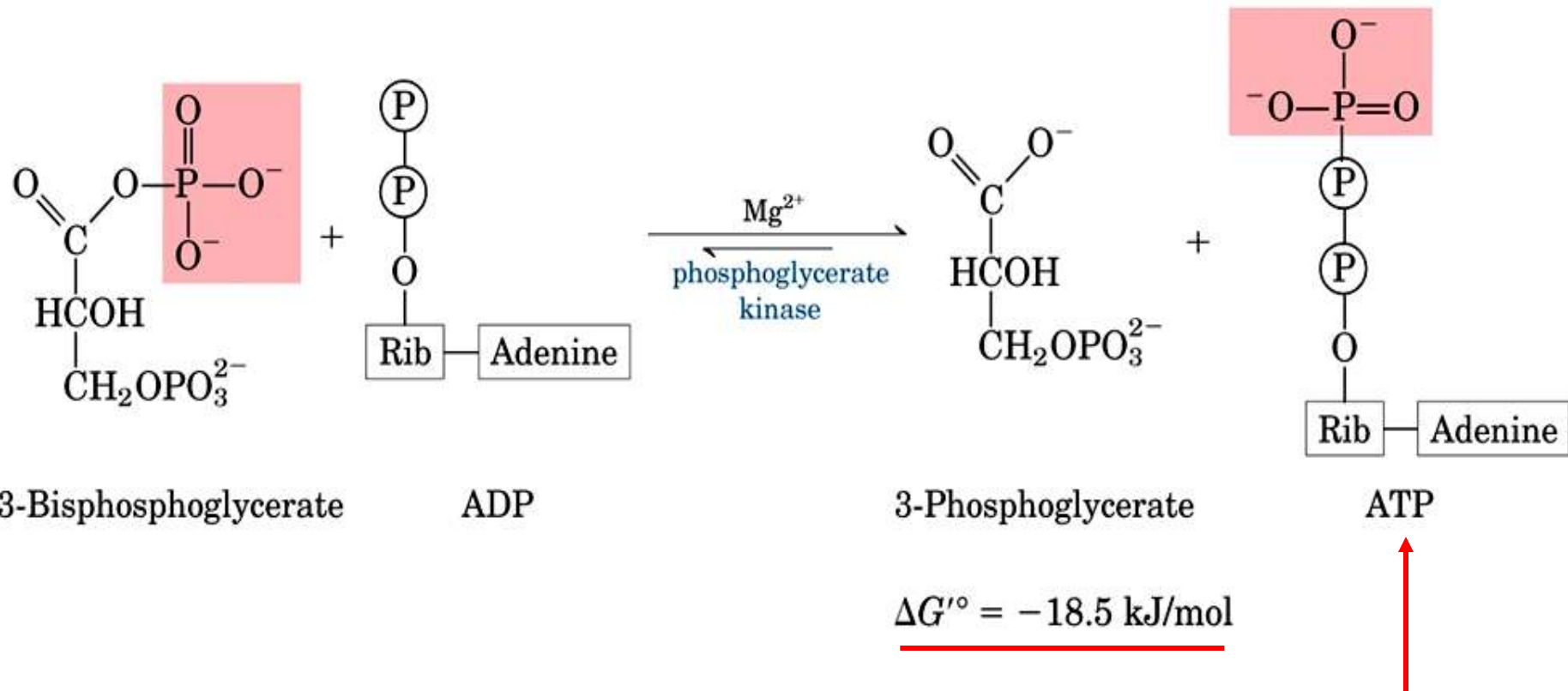
Le 2 molecole di gliceraldeide-3-fosfato vengono convertite in 2 molecole di piruvato con formazione di 4 molecole di ATP e 2 di NADH

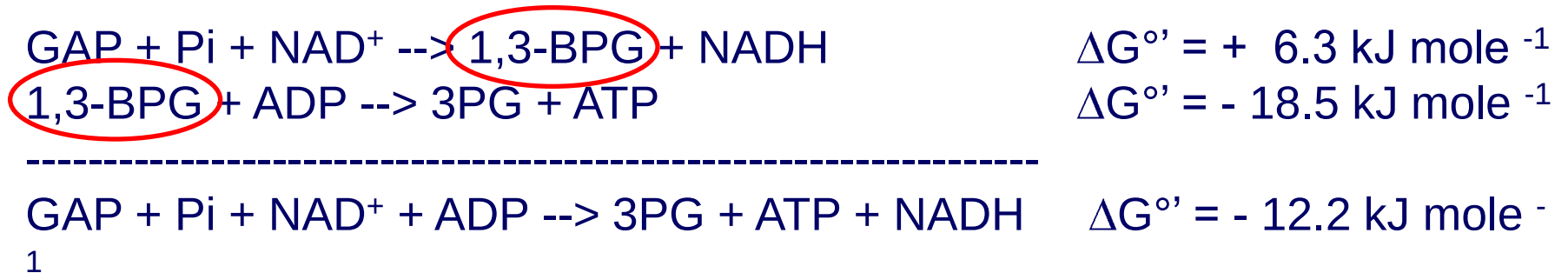
Reazione 6



$$\Delta G'^{\circ} = 6.3 \text{ kJ/mol}$$

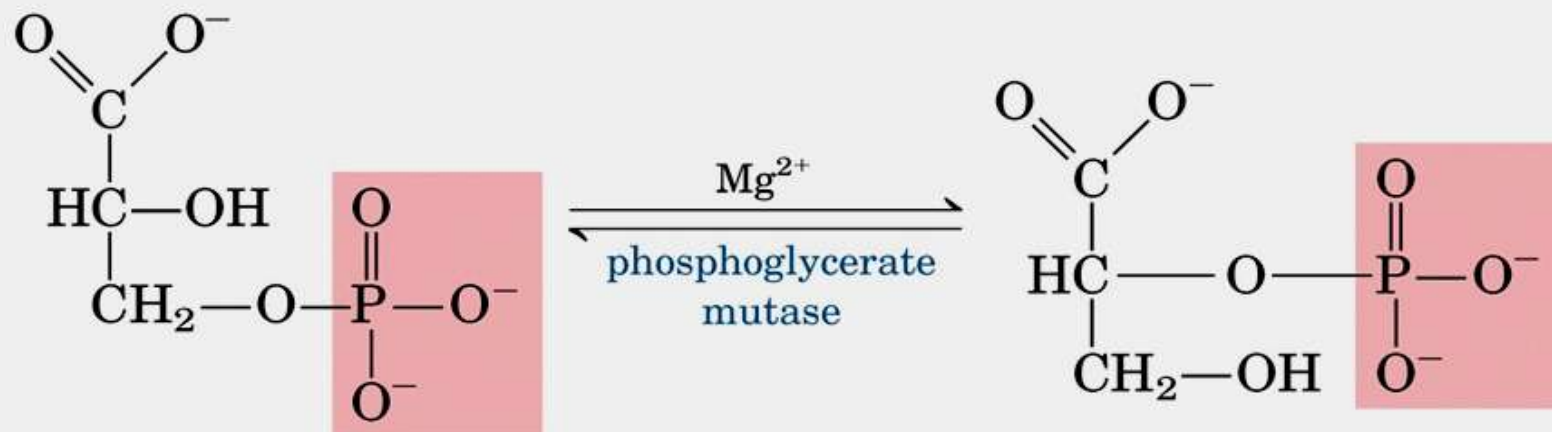
Reazione 7





L'accoppiamento tra la reazione della GAPDH (endoergonica) e la reazione della PGK (fortemente esoergonica) rende possibile la sintesi di NADH e di ATP.

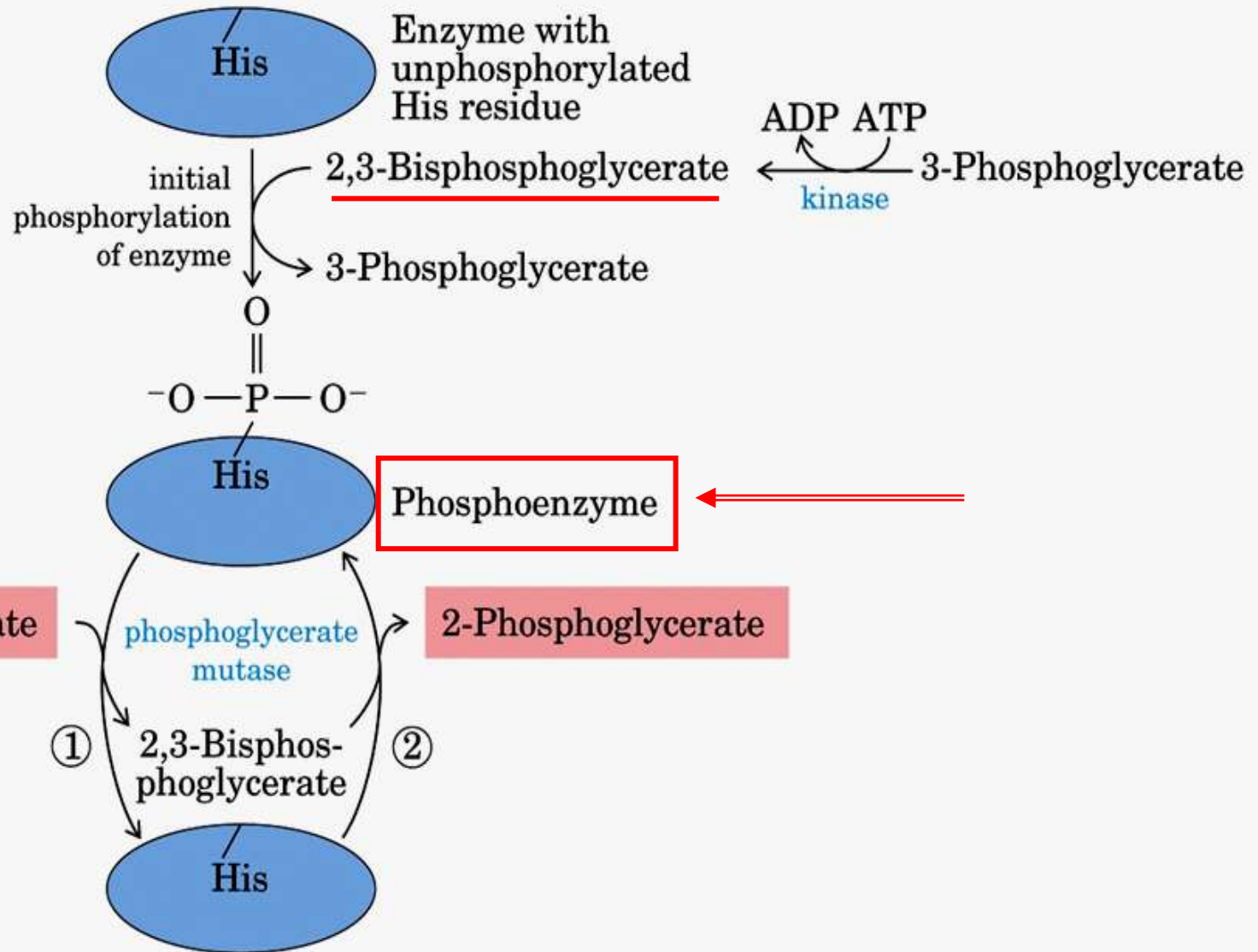
Reazione 8



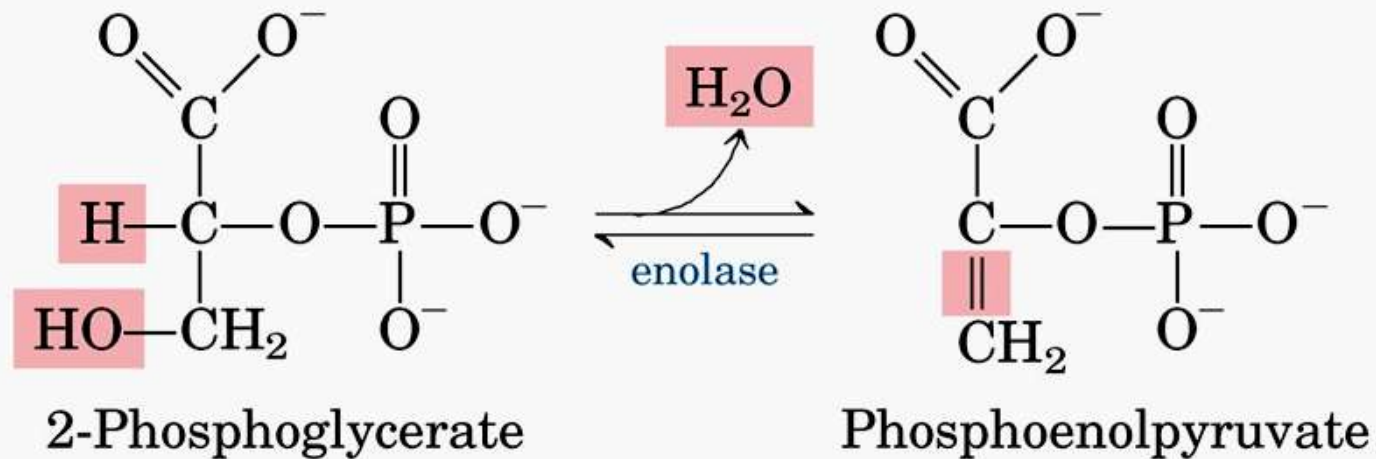
3-Phosphoglycerate

2-Phosphoglycerate

$$\Delta G'^{\circ} = 4.4 \text{ kJ/mol}$$

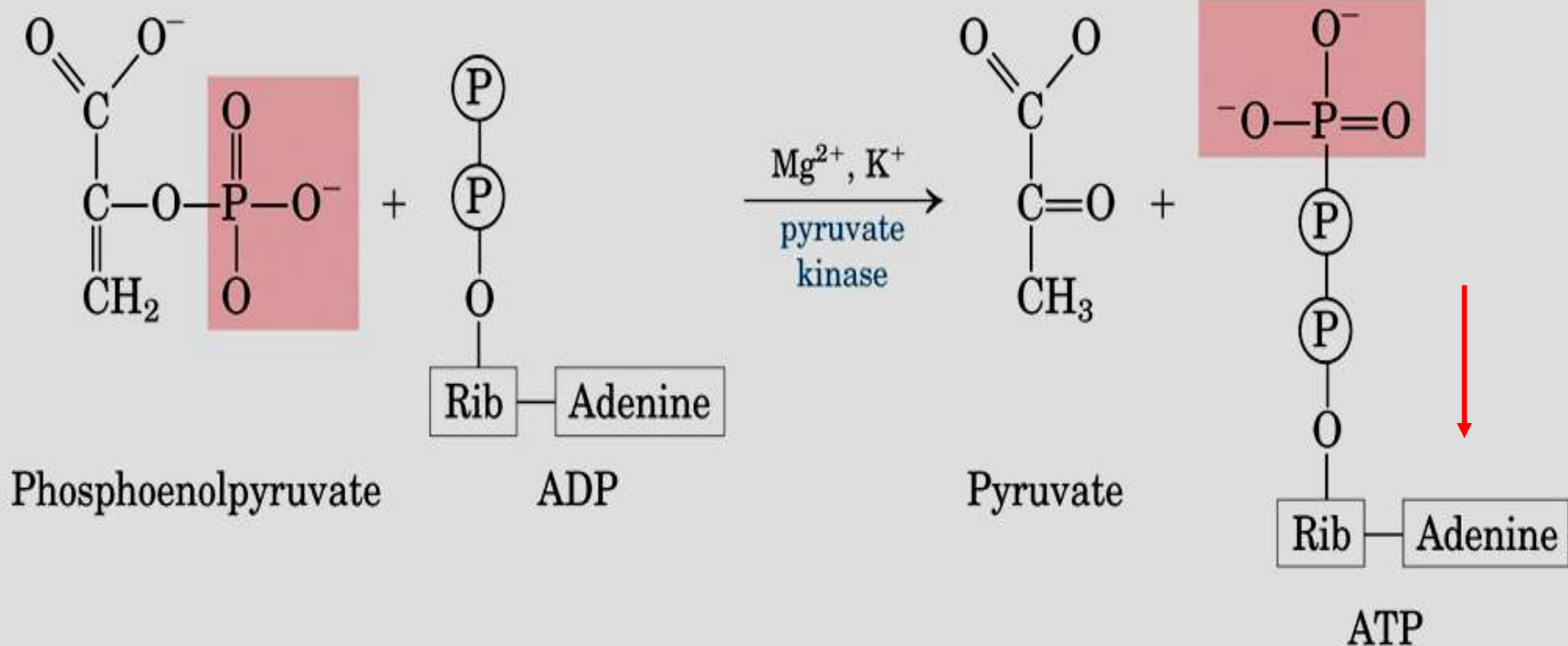


Reazione 9



$$\Delta G'^{\circ} = 7.5 \text{ kJ/mol}$$

Reazione 10



$$\Delta G'^{\circ} = -31.4 \text{ kJ/mol}$$

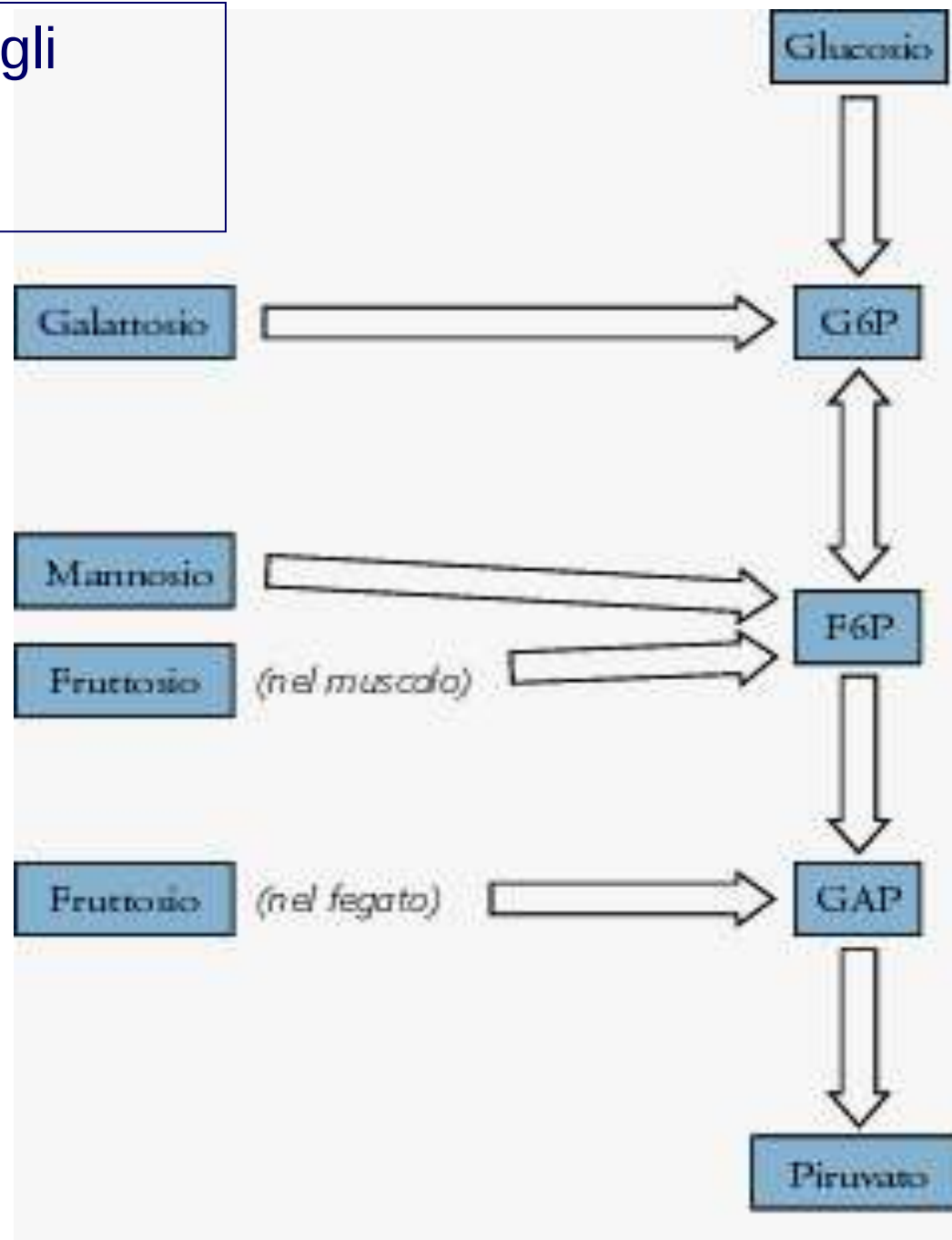
Resa energetica :

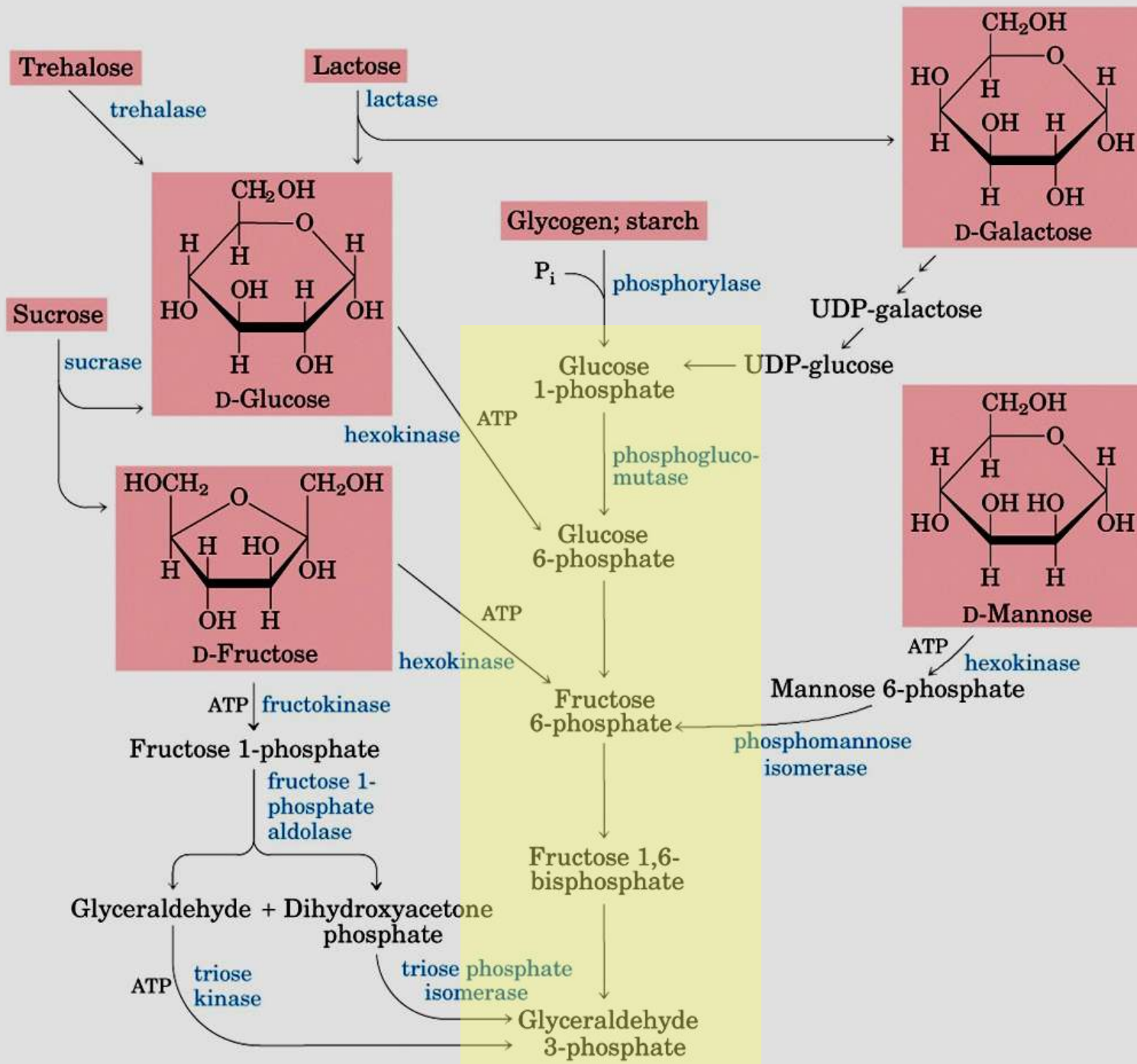
1 Glucosio + 2 ATP (Fase I) →

2 gliceraldeide 3' fosfato → 2 x (2 ATP + 1 NADH) (Fase II)

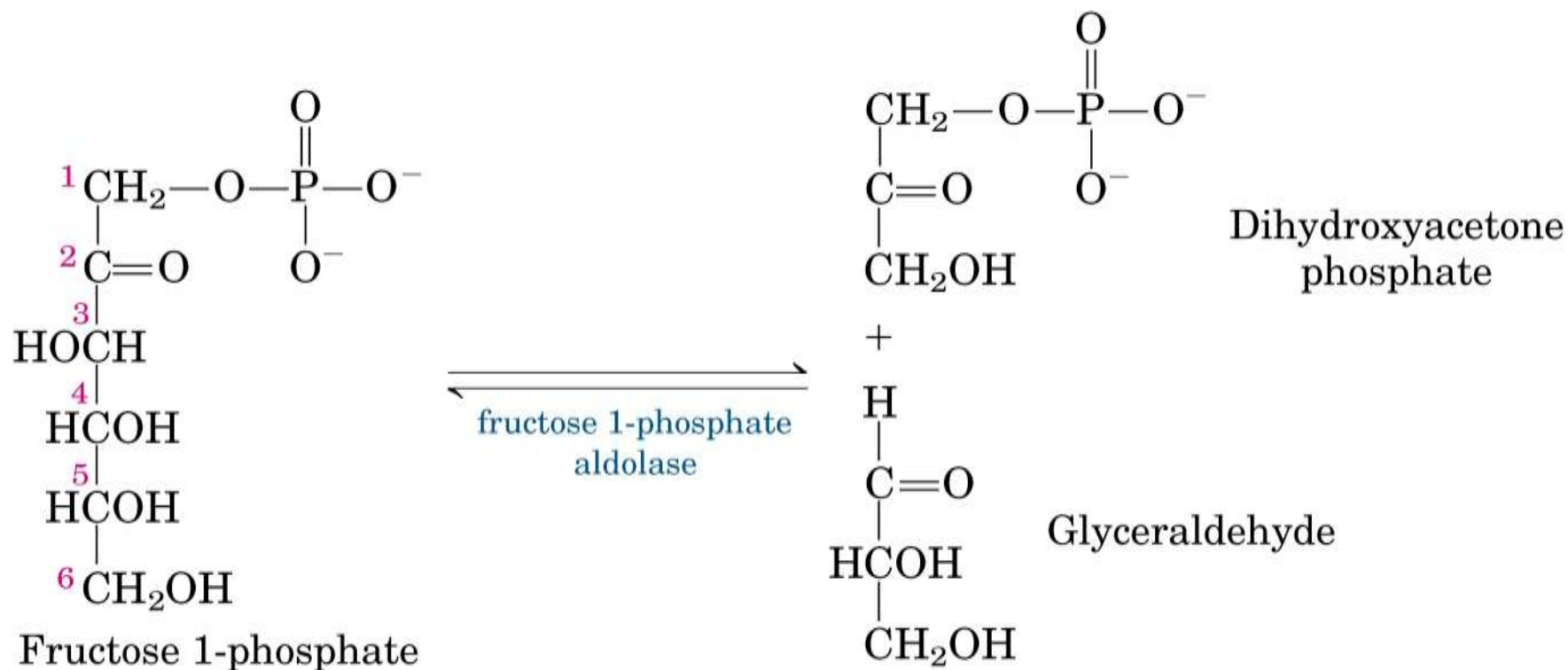
Totale : 2 ATP + 2 NADH / 1 glucosio

Metabolismo degli esosi diversi dal glucosio

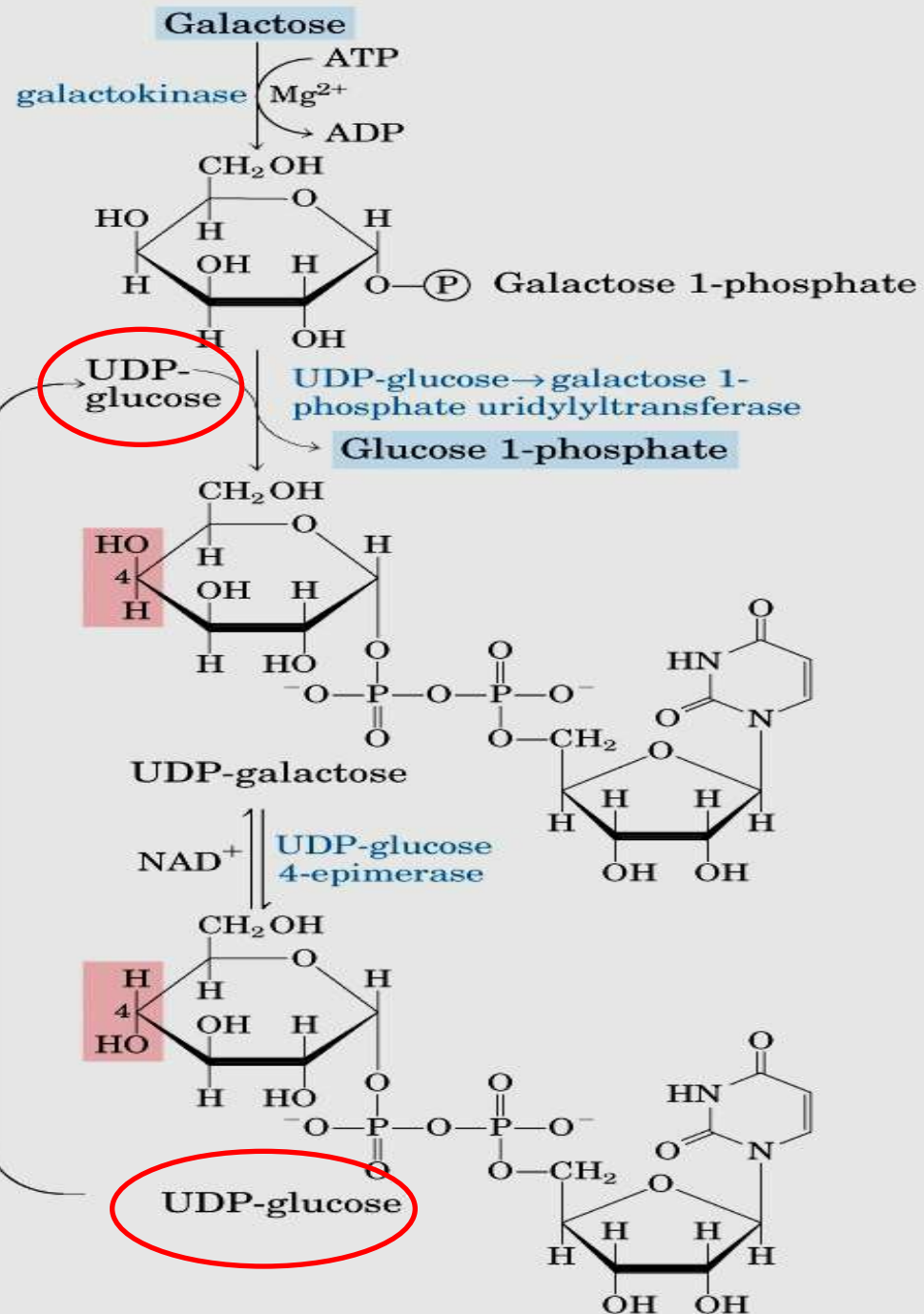


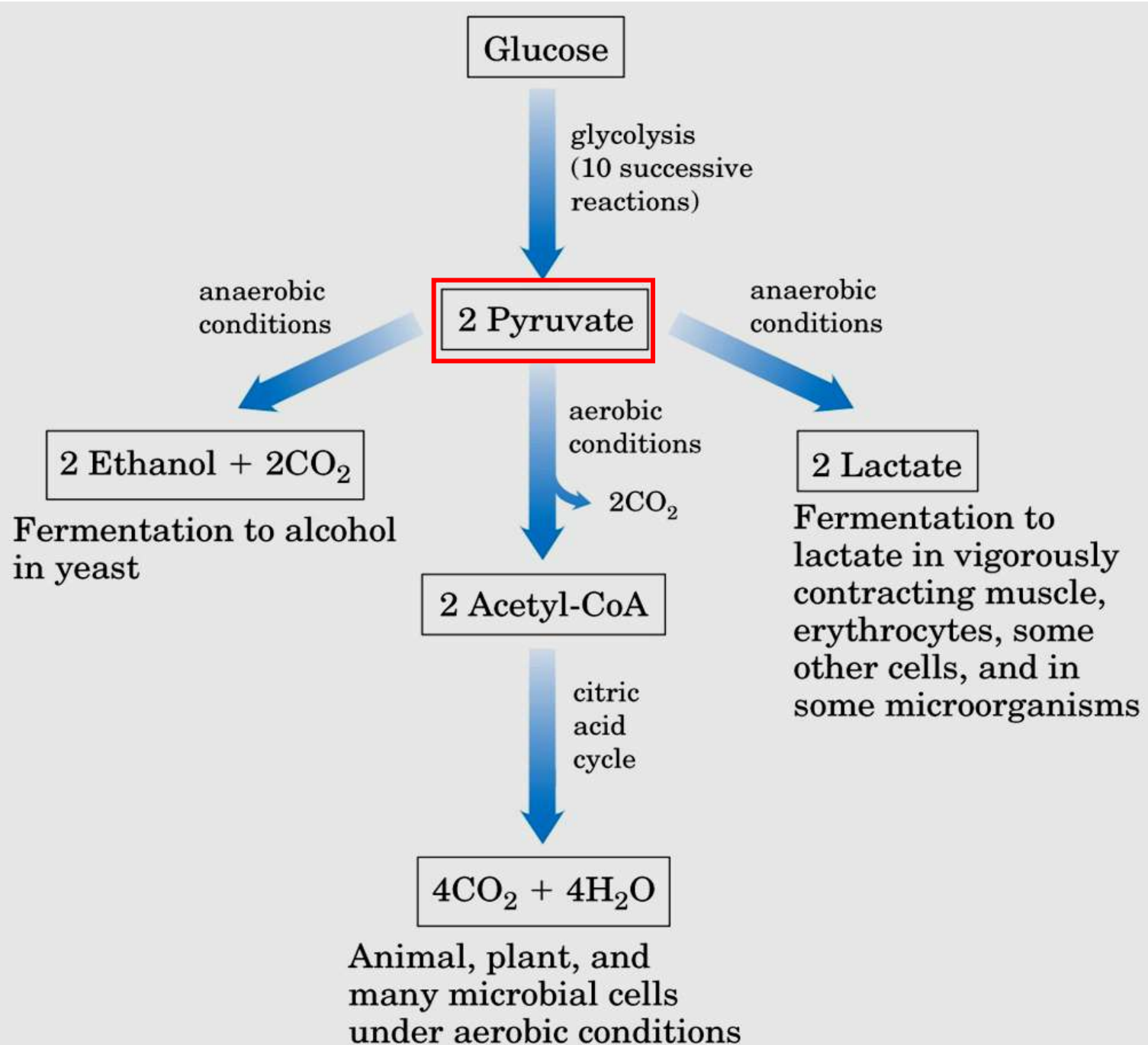


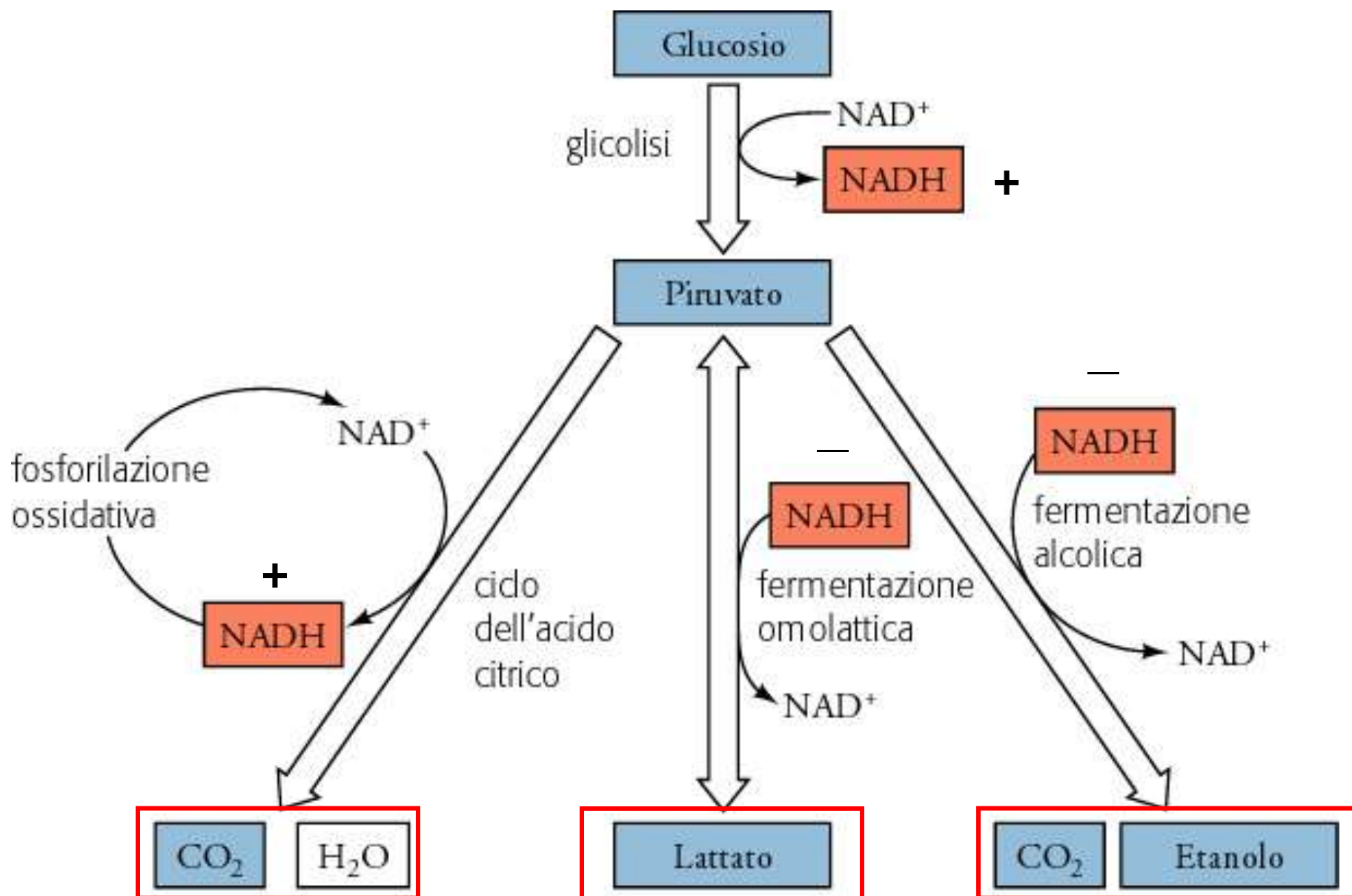
Fruttosio 1-fosfato



Galattosio



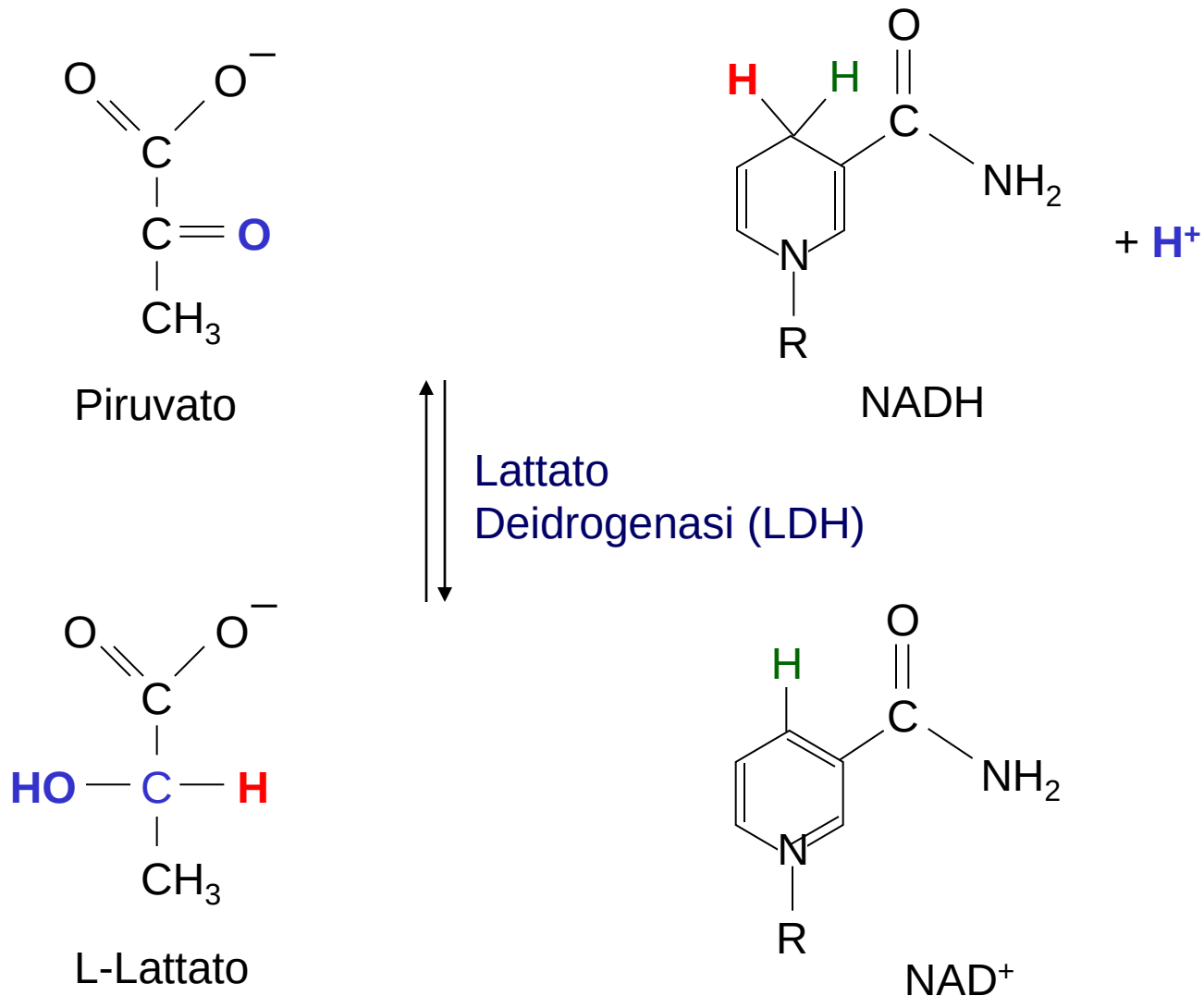


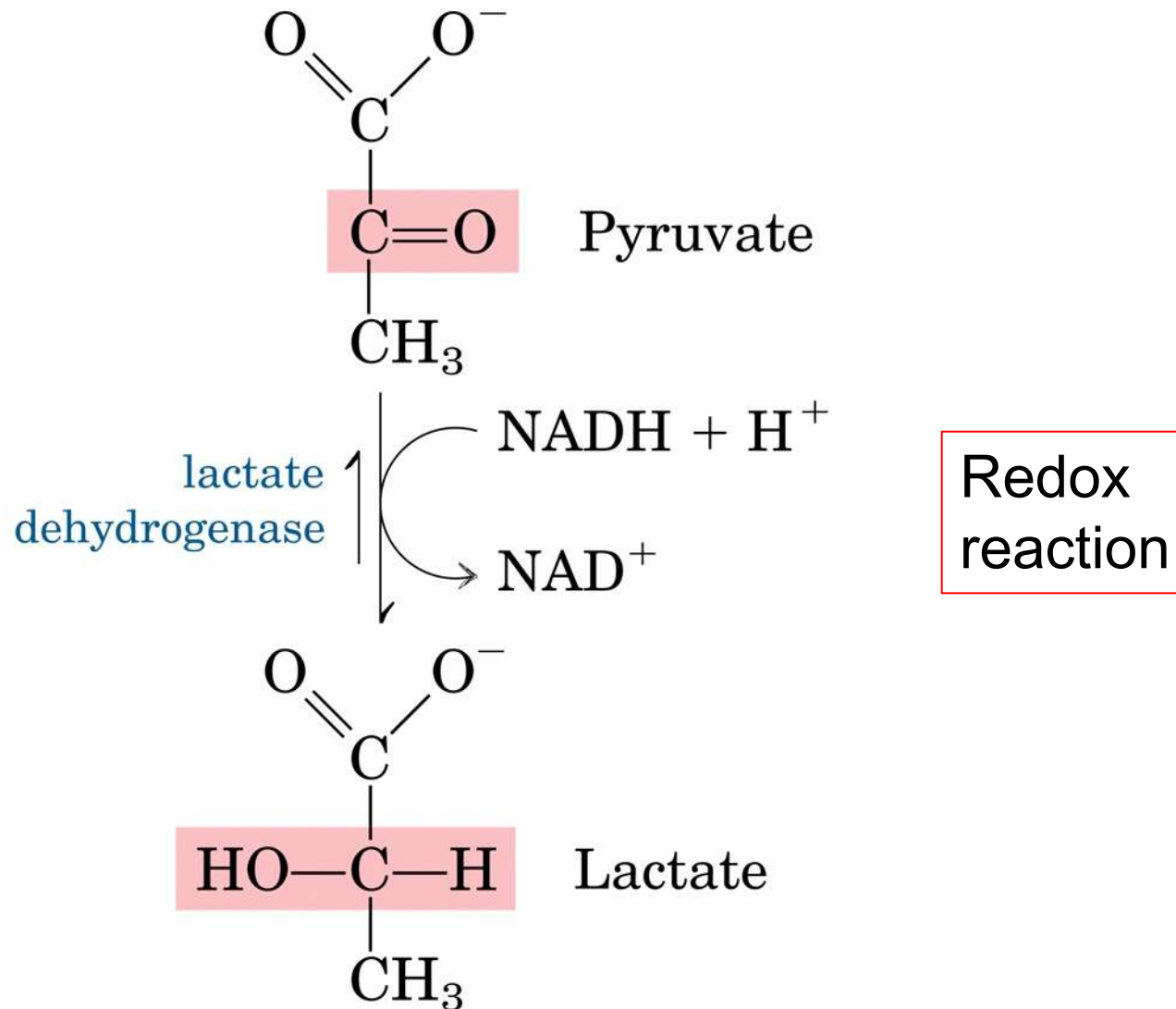


La **fermentazione** è un processo con cui si ottiene energia ossidando composti organici (come i carboidrati) usando un **accettore di elettroni endogeno**, che di solito è anch'esso un composto organico.

Fermentazione omolattica (nel muscolo)

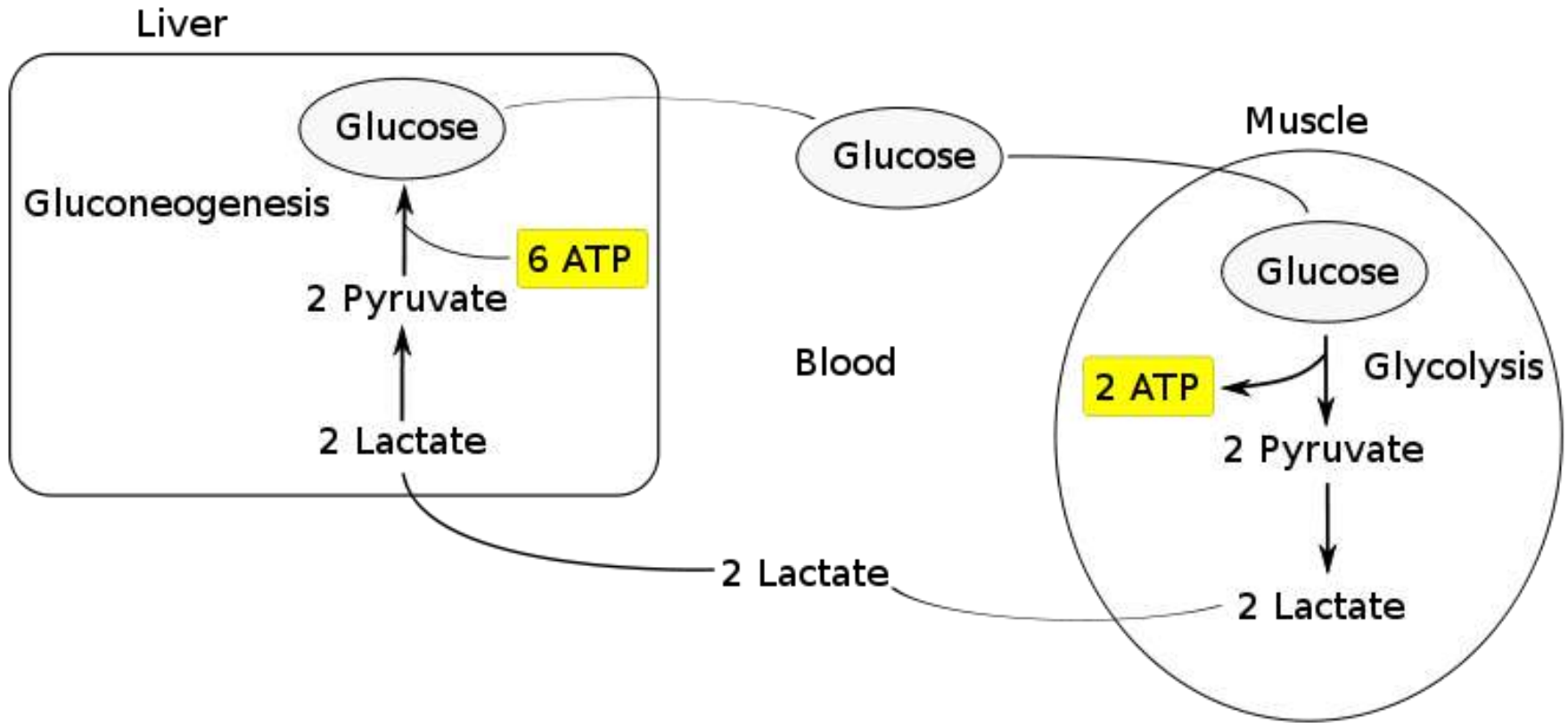
Reazione 11a





$$\Delta G'^{\circ} = -25.1 \text{ kJ/mol}$$

Il ciclo di Cori (Carl e Gerti, Nobel 1948)



Prevention of lactic acidosis in the muscle under anaerobic conditions.
Production of ATP, an energy source, during muscle activity

La fermentazione omolattica avviene anche in alcuni funghi e in alcuni batteri come i lattobacilli

Piruvato $\rightarrow$ Lattato

Yogurt

Lattosio + H_2O $\rightarrow$ 4 Lattato

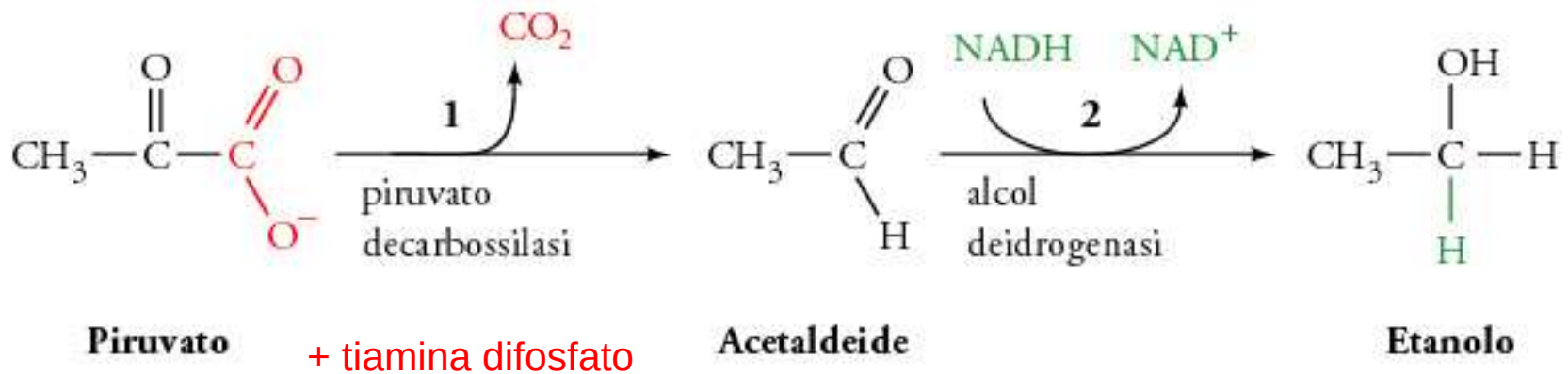
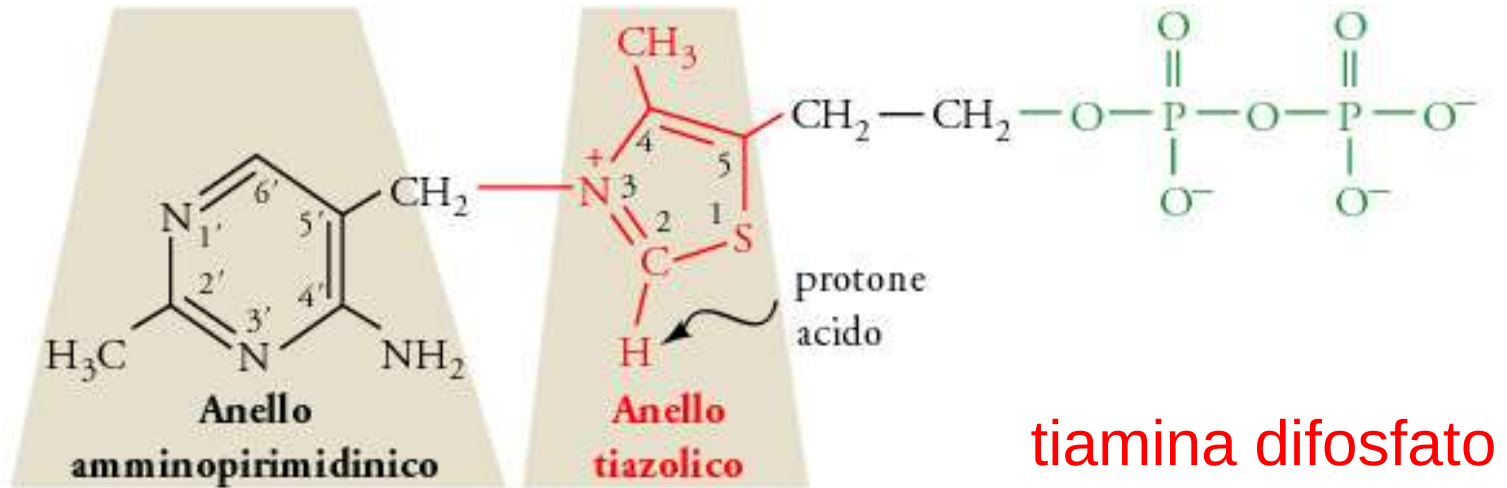
Yogurt
formaggio

... nel parmigiano tutto il lattosio è stato convertito !

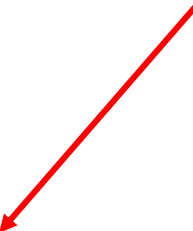
Fermentazione alcolica

(in condizioni anaerobie – lievito, alcuni batteri)

Reazione 11b



Piruvato $\rightarrow$ etanolo + CO₂



vino
birra

La CO₂ viene rilasciata
nell'aria o usata per rendere
la bevanda frizzante



pane

L'etanolo viene rilasciato
durante la cottura

La tiamina (**Vitamina B1**) si ritrova sia negli alimenti di origine animale e vegetale. In genere negli alimenti vegetali si trova per lo più in forma libera mentre in quelli animali si trova anche in quella fosforilata sia a mono- che a difosfato.

Particolarmente ricchi di tale vitamina sono i legumi ed il germe ed il pericarpo dei cereali. Negli alimenti animali le maggiori concentrazioni sono nel fegato, nel rene, nel cervello e nell'intestino. Un'altra fonte importante di tiamina è inoltre il **lievito di birra**.

Energetica della fermentazione

Fermentazione omolattica :



Fermentazione alcolica:



→ **Rendimento** in condizioni standard ~ 30 %
in condizioni fisiologiche > 50 %

E' **altamente inefficiente** rispetto alla fosforilazione ossidativa (in cui vengono prodotti 38 ATP / 1 glucosio), tuttavia in condizioni anaerobie la velocità di produzione di ATP è anche 100 volte maggiore.