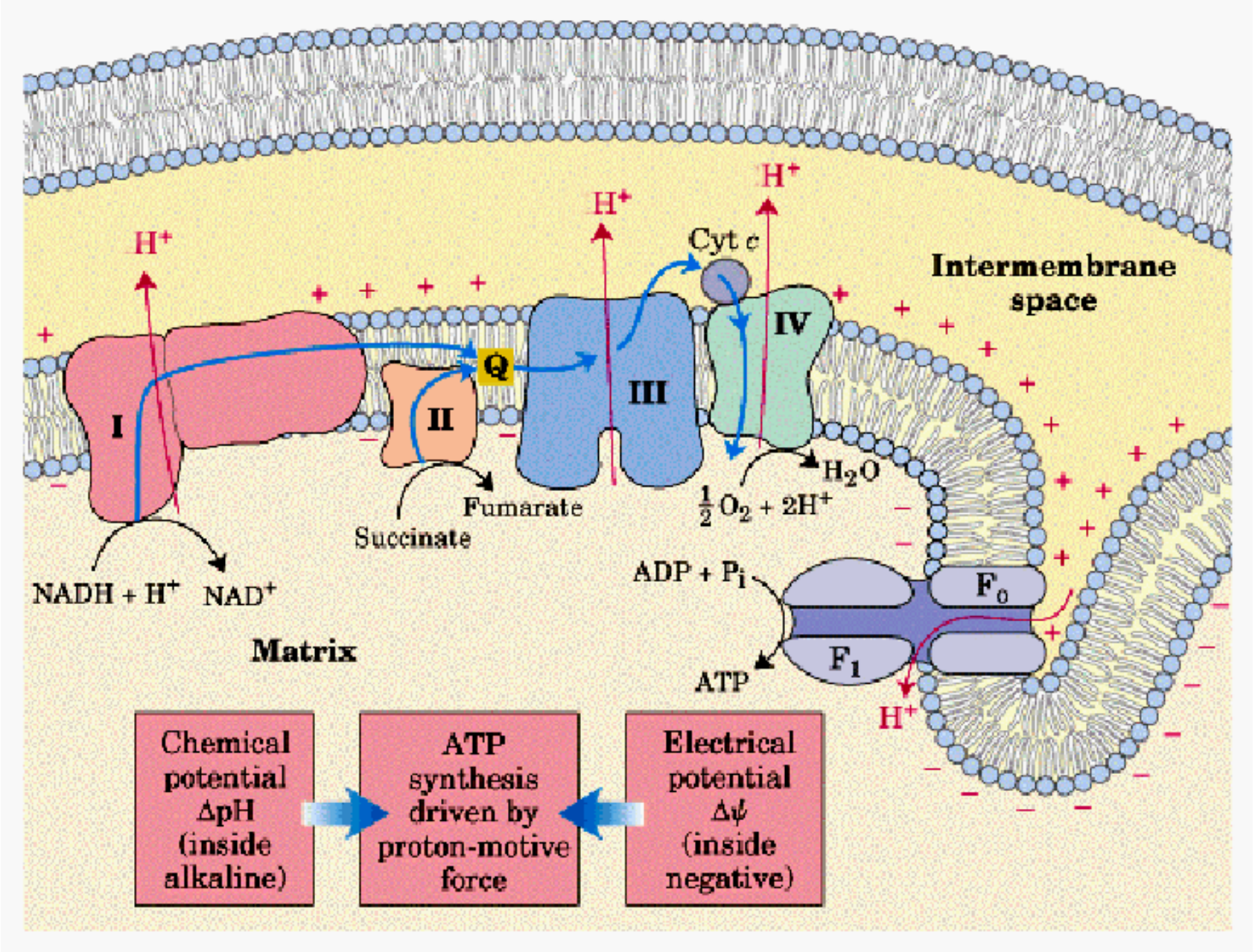
Regulação da Fosforilação Oxidativa

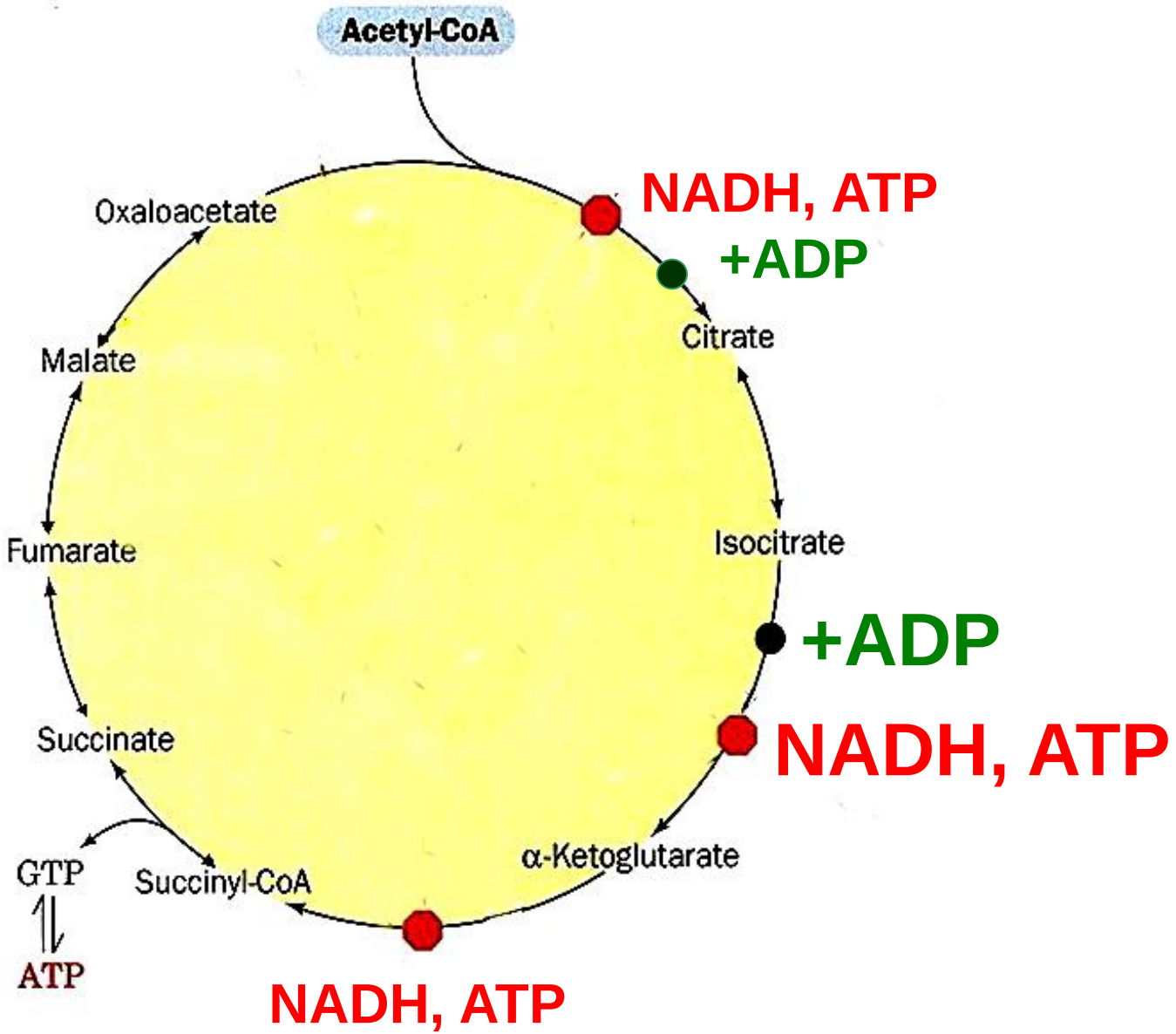
ATP sintase: - gradiente de prótons
- concentração de ADP, Pi

Gradiente de prótons: - ATPsintase
- transporte de elétrons
- outros transportadores (UCP, ANT...)

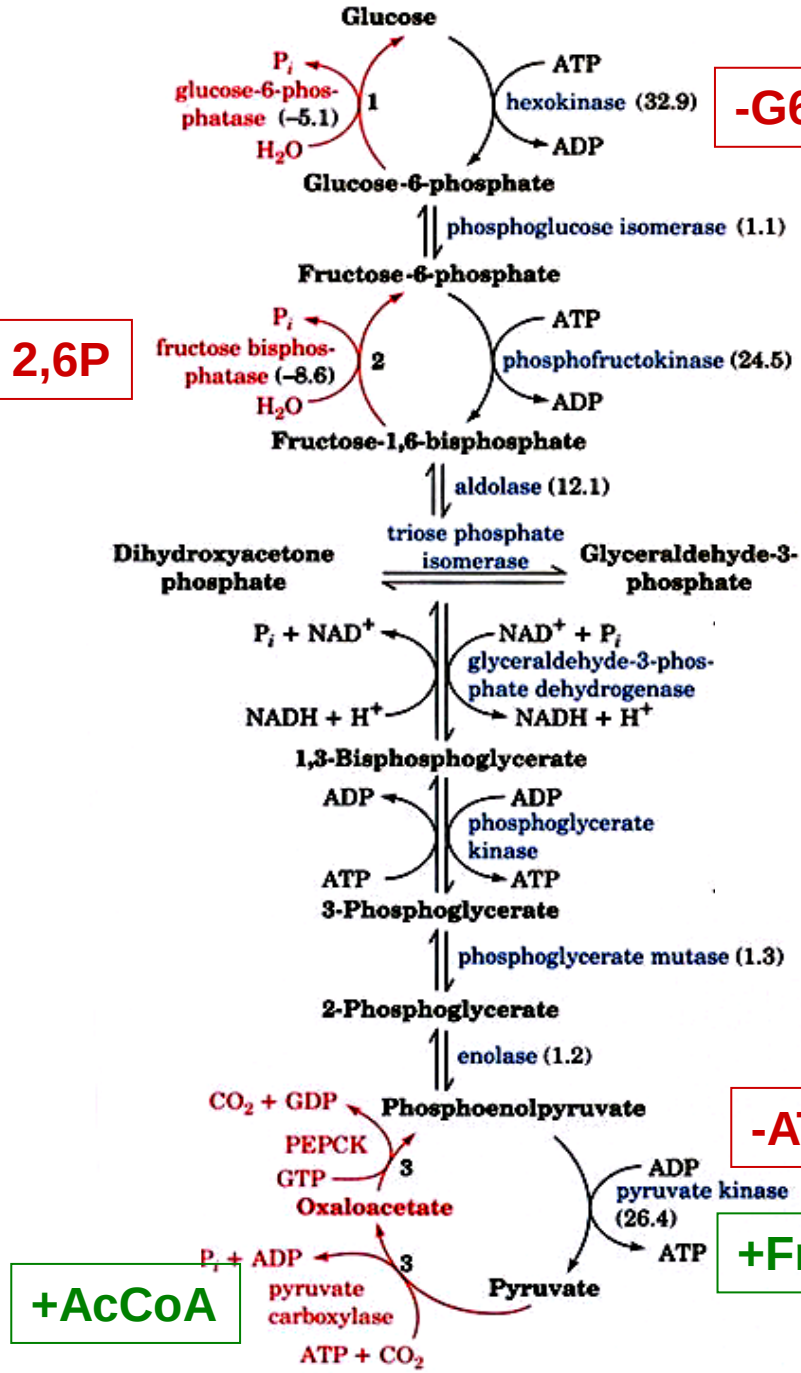
Cadeia de transporte de elétrons: - NADH, $FADH_2$, O_2
- gradiente de prótons


H+
H+
H+
Cyt c
Intermembrane space
IV
I
II
Q
III
H2O
½ O2 + 2H+
Fumarate
Succinate
NADH + H+
NAD+
ADP + Pi
F0
F1
ATP
Matrix
H+
Chemical potential ΔpH (inside alkaline)
ATP synthesis driven by proton-motive force
Electrical potential Δψ (inside negative)

↓ATP


Acetyl-CoA
Oxaloacetate
Citrate
Isocitrate
α-Ketoglutarate
Succinyl-CoA
Succinate
Fumarate
Malate
GTP
ATP
NADH, ATP
+ADP
+ADP
NADH, ATP
NADH, ATP

↓ ATP



-G6P

-Frutose 2,6P

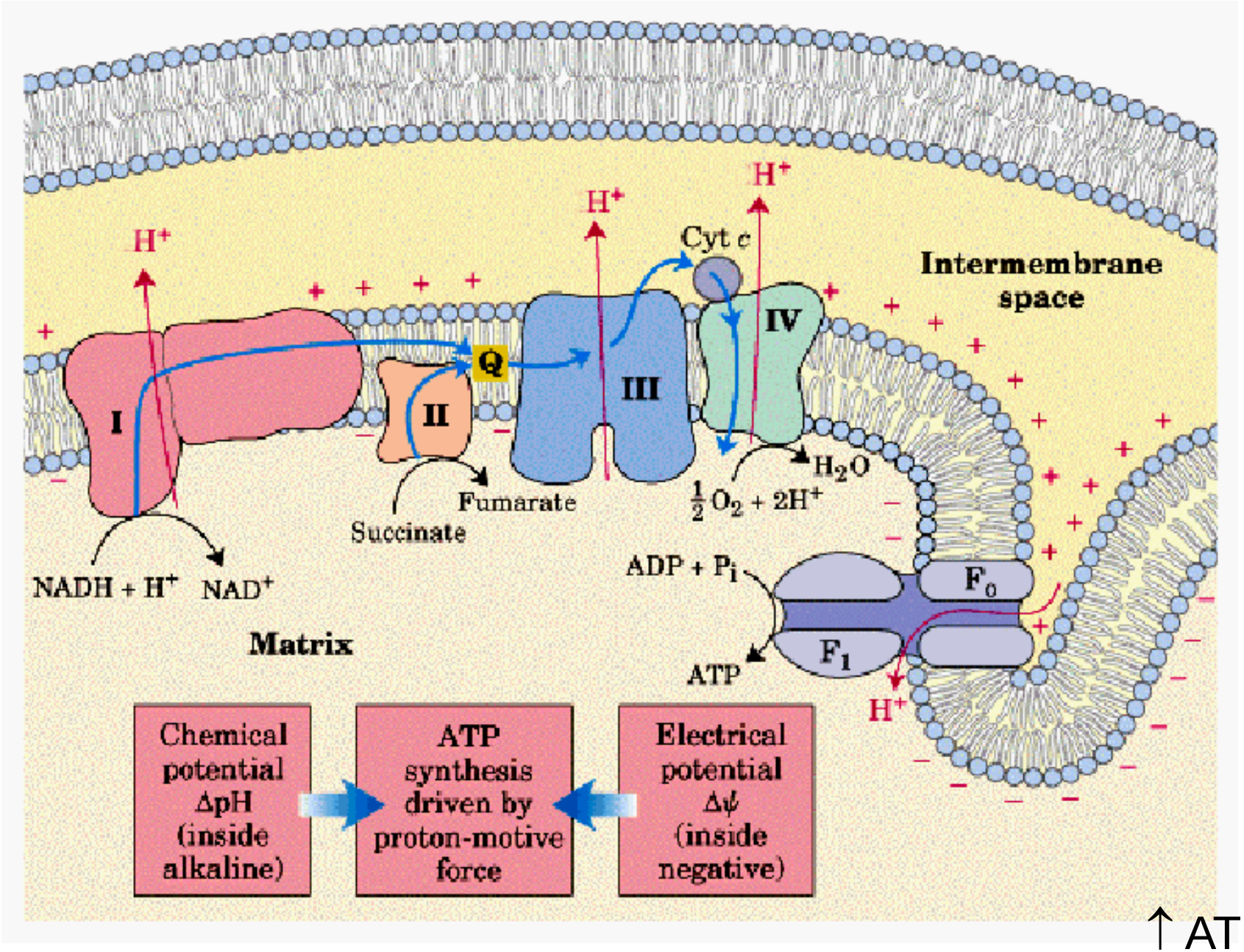
+Frutose 2,6P

-ATP, alanina

+Frutose 1,6P

+AcCoA

↓ ATP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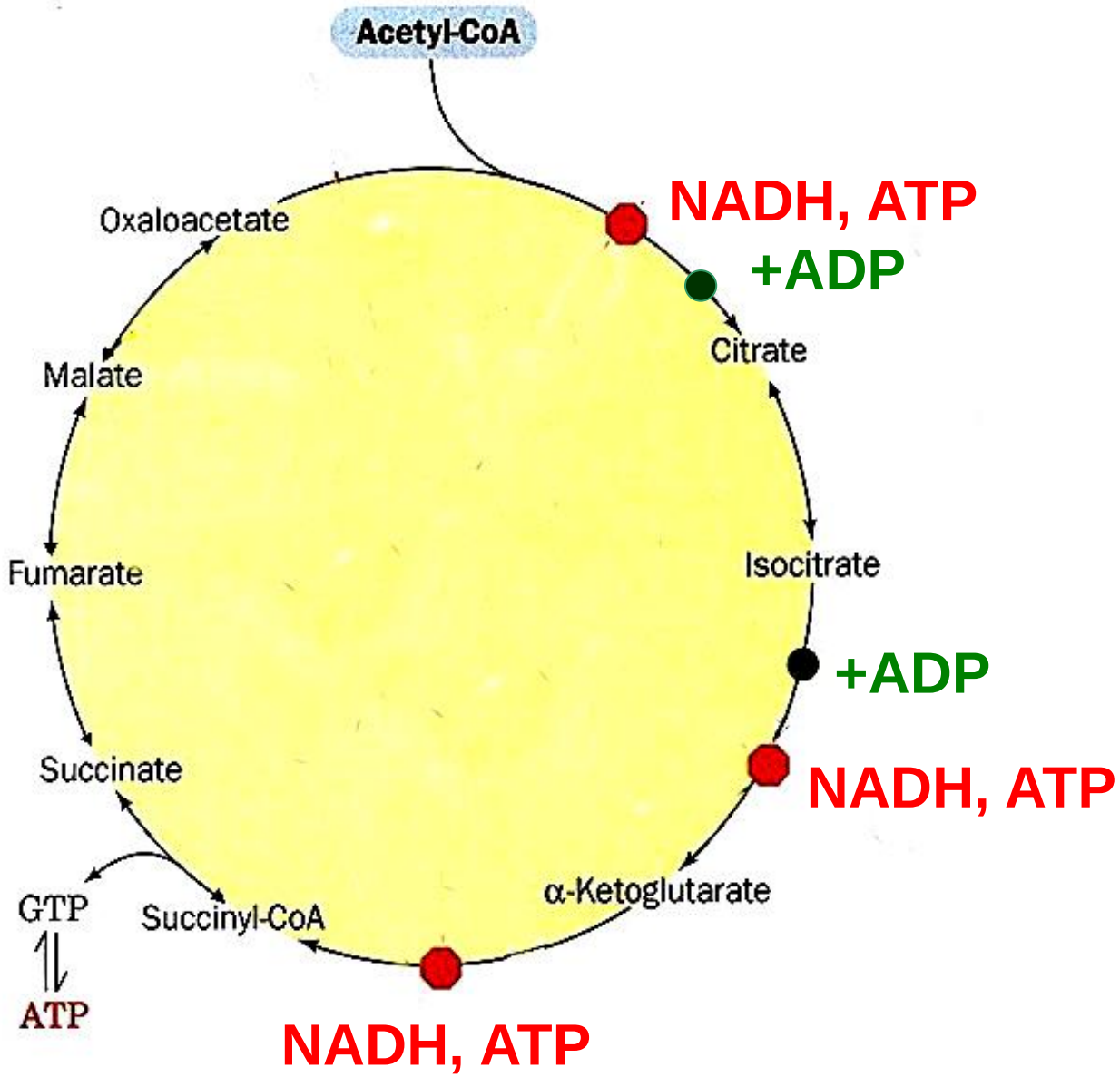
Electrical potential Δψ (inside negative)

↑ ATP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Succinate
Fumarate
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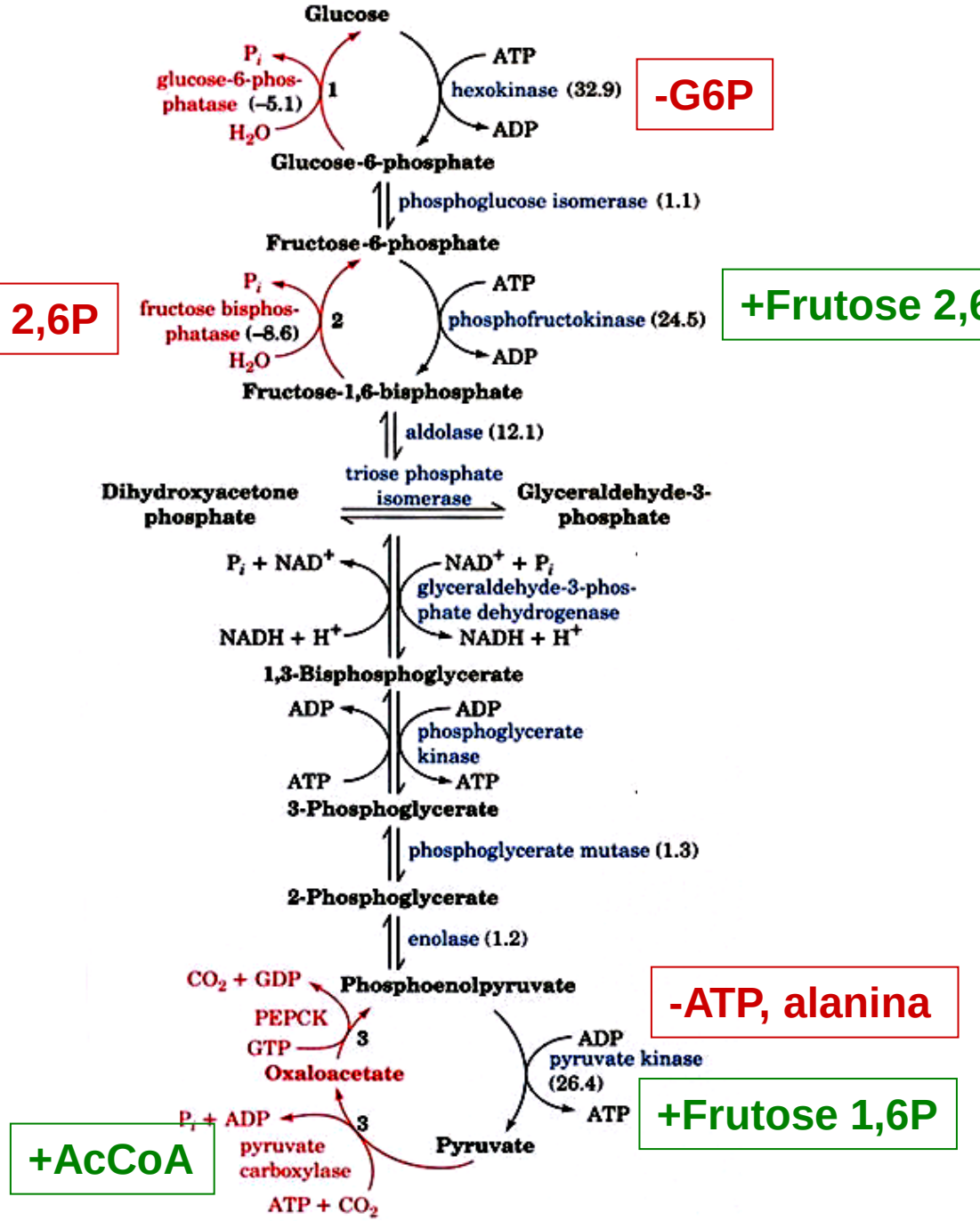
GTP
ATP
NADH, ATP
+ADP
+ADP
NADH, ATP
NADH, ATP

↑ ATP



-G6P

-Frutose 2,6P

+Frutose 2,6P

-ATP, alanina

+Frutose 1,6P

+AcCoA

↑ ATP

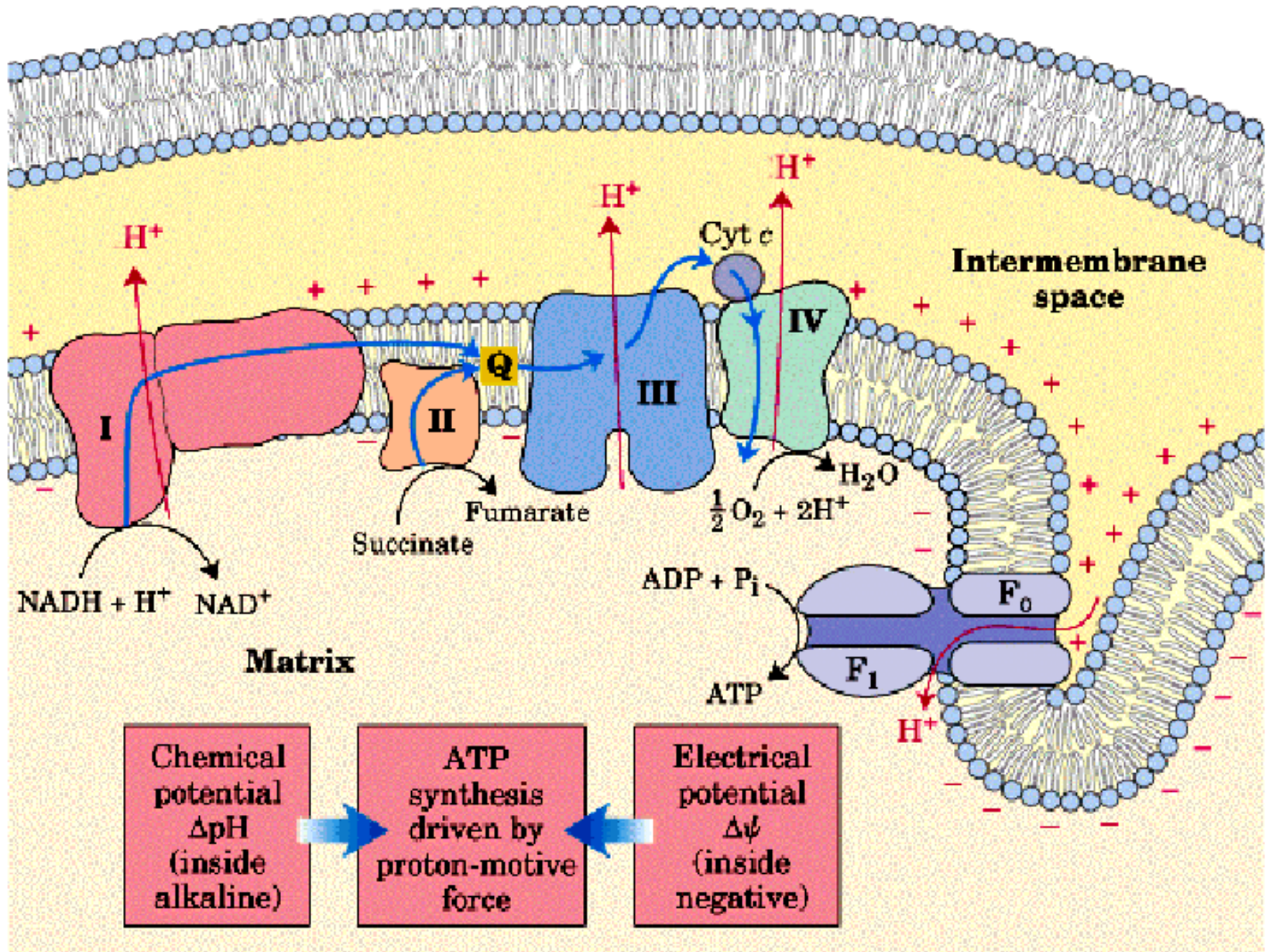
Inibição do Transporte de Elétrons

- Complexo I: - Oftalmopatia hereditária de Leber
  - Deficiência de riboflavina (B2)
  - Rotenona (*Lonchocarpus* ou *Derris*)
  - Doença de Parkinson

- Complexo II: - Malonato, metilmalonato

- Complexo III: - Mutações citocromo b, bc_1
  - Antimicina (*Rhodobacter*)

- Complexo IV: - MELAS, MERRF
  - Deficiência de Cobre, Ferro
  - CN^- e CO


H+
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Intermembrane space
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H2O
½ O2 + 2H+
Fumarate
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NADH + H+
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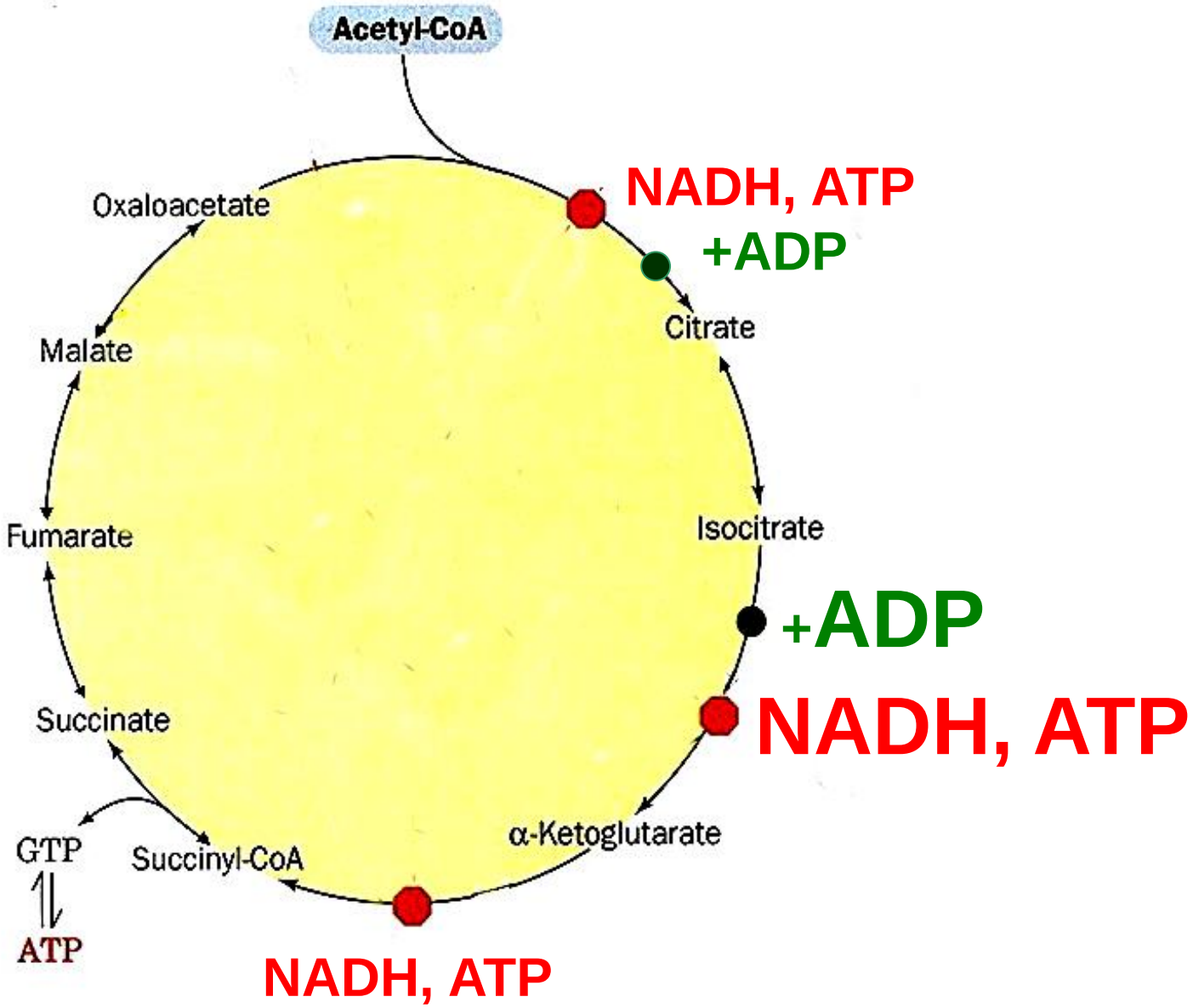
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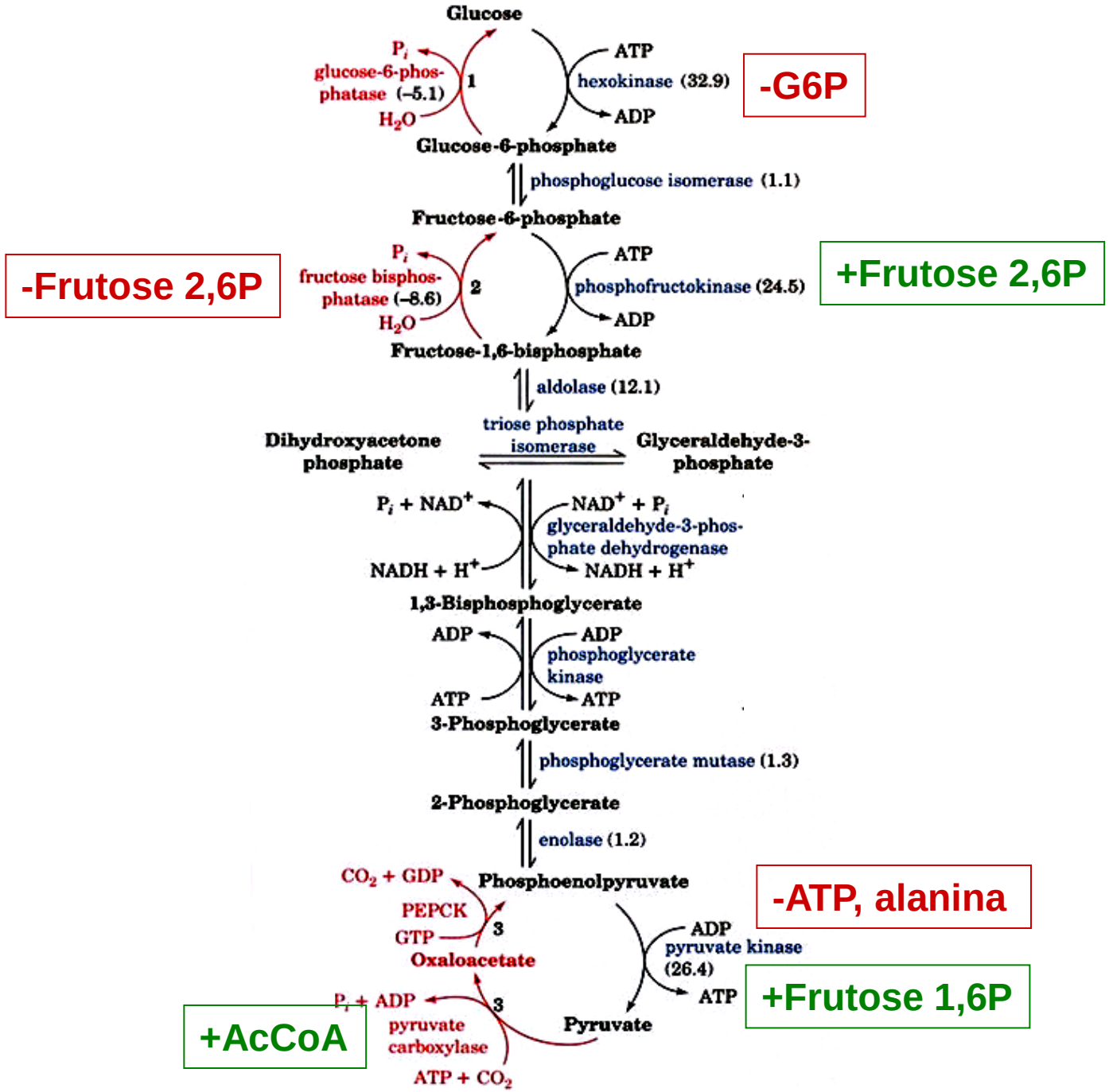
Glucose
P_i
glucose-6-phos-
phatase (–5.1)
H_2O
1
ATP
hexokinase (32.9)
ADP
-G6P
Glucose-6-phosphate
phosphoglucose isomerase (1.1)
Fructose-6-phosphate
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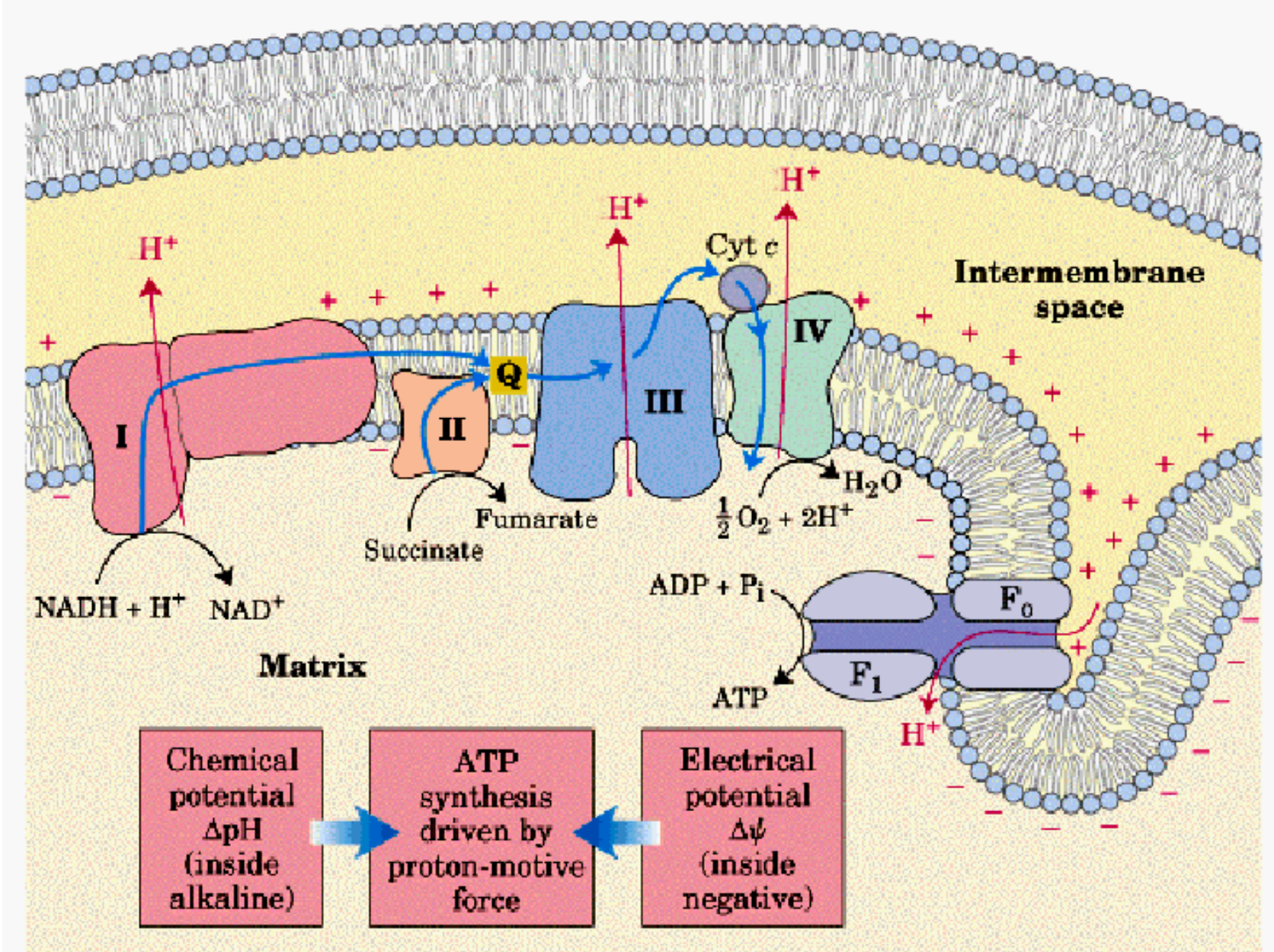
P_i
fructose bisphos-
phatase (–8.6)
H_2O
2
ATP
phosphofructokinase (24.5)
ADP
+Frutose 2,6P
Fructose-1,6-bisphosphate
aldolase (12.1)
Dihydroxyacetone
phosphate
triose phosphate
isomerase
Glyceraldehyde-3-
phosphate
P_i + NAD^+
NAD^+ + P_i
glyceraldehyde-3-phos-
phate dehydrogenase
NADH + H^+
NADH + H^+
1,3-Bisphosphoglycerate
ADP
ADP
phosphoglycerate
kinase
ATP
ATP
3-Phosphoglycerate
phosphoglycerate mutase (1.3)
2-Phosphoglycerate
enolase (1.2)
CO_2 + GDP
Phosphoenolpyruvate
-ATP, alanina
PEPCK
GTP
3
Oxaloacetate
ADP
pyruvate kinase
(26.4)
ATP
+Frutose 1,6P
P_i + ADP
pyruvate
carboxylase
ATP + CO_2
3
Pyruvate
+AcCoA

Anóxia/Reoxigenação, Isquemia/Reperfusão

- Falta de O_2, inibição de trans. de elétrons, fosforilação
- Inibição Krebs, inibição da formação de Acetil-CoA
- Aumento glicólise - acidose
  - hipoglicemia local
- Falta de ATP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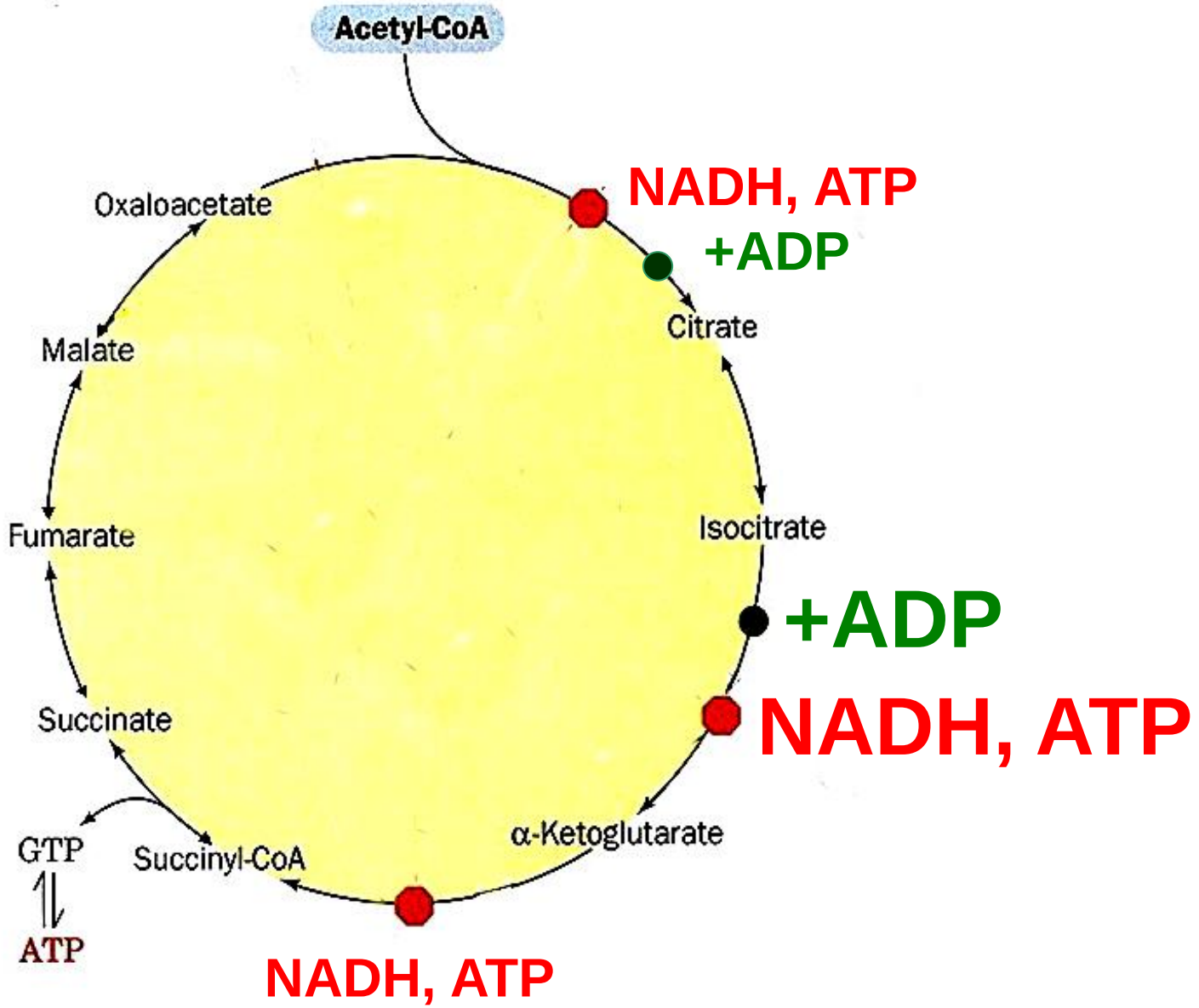
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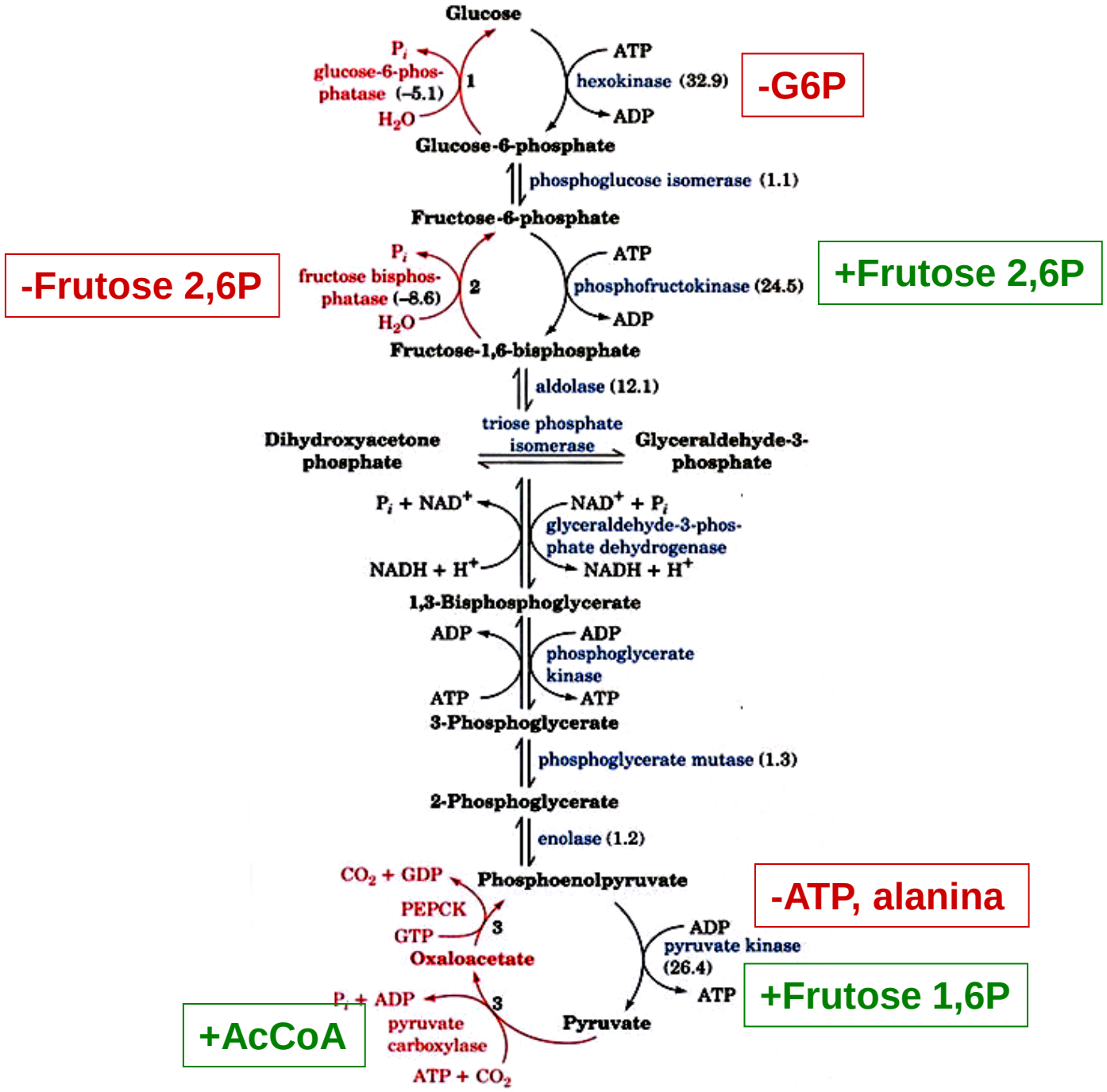
Fumarate
Malate
Oxaloacetate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-Frutose 2,6P
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-ATP, alanina
+Frutose 1,6P
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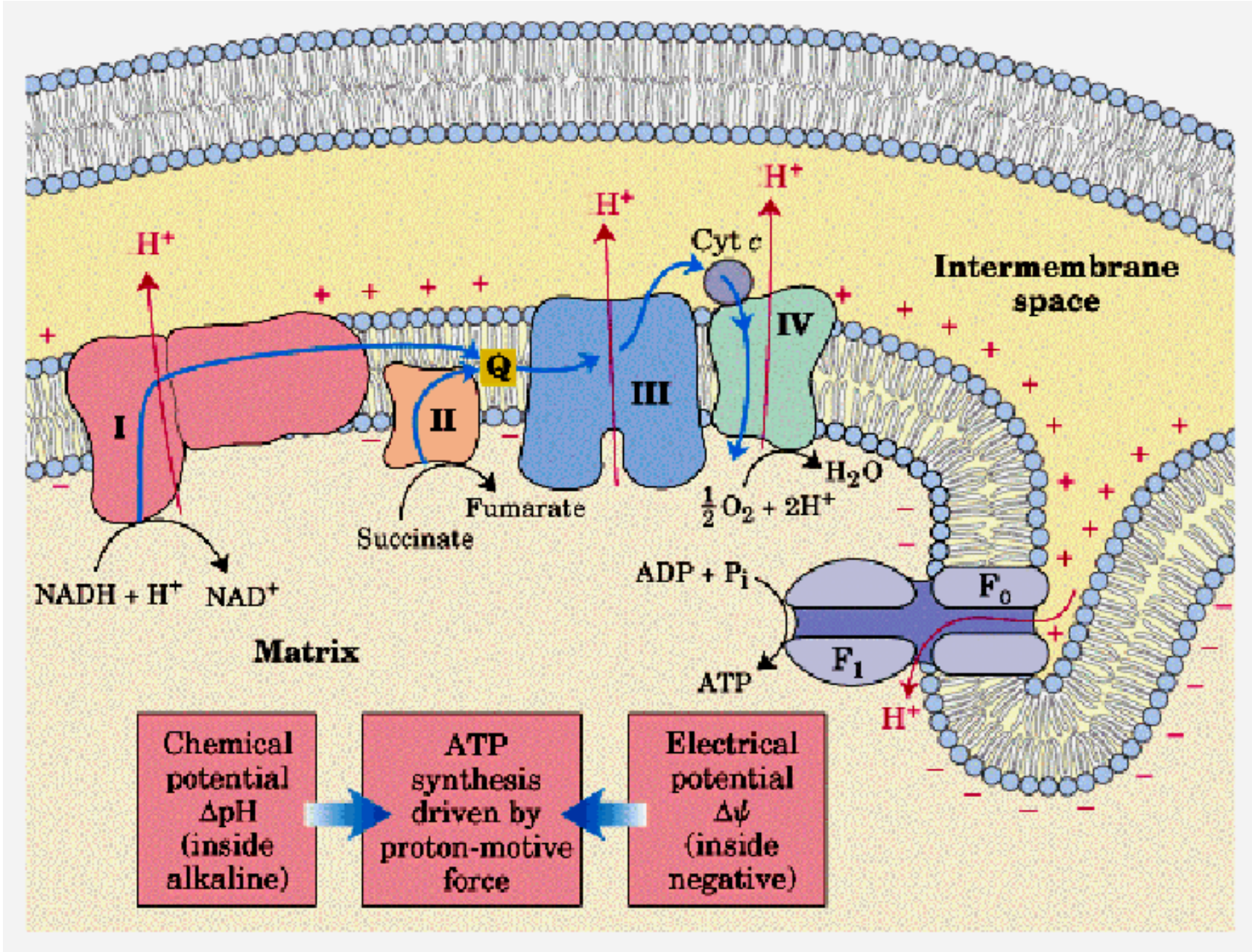
Regulação Farmacológica da Fosforilação Oxidativa

- Oligomicina: - inibidor da ATPsintase (porção F_O)
- produzido por bactérias *Streptomyces*
- não permite entrada de prótons por F_O

- Atractilosídeo: - inibidor do translocador ADP/ATP
- Produzido por *Atractylis gummifera*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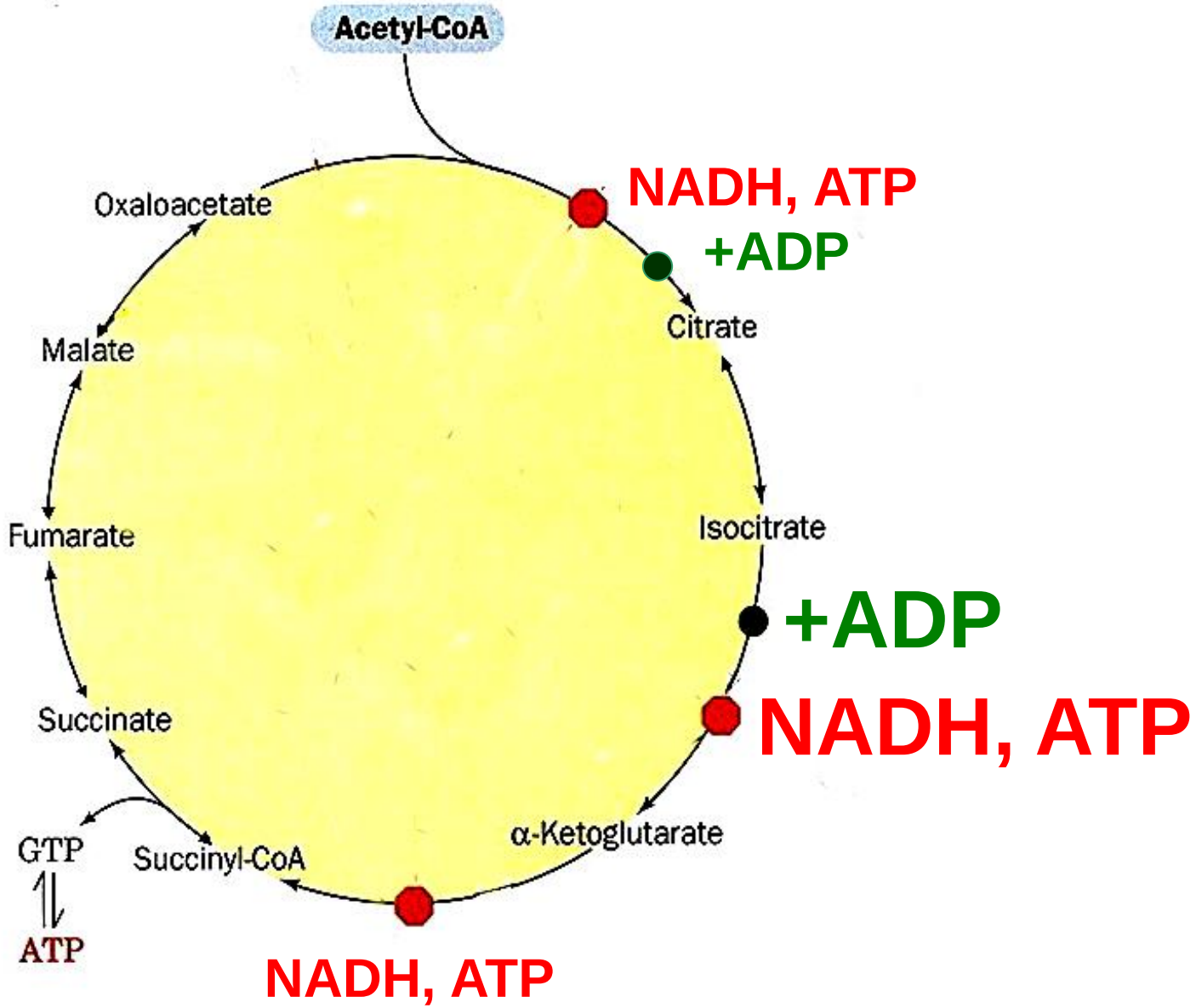
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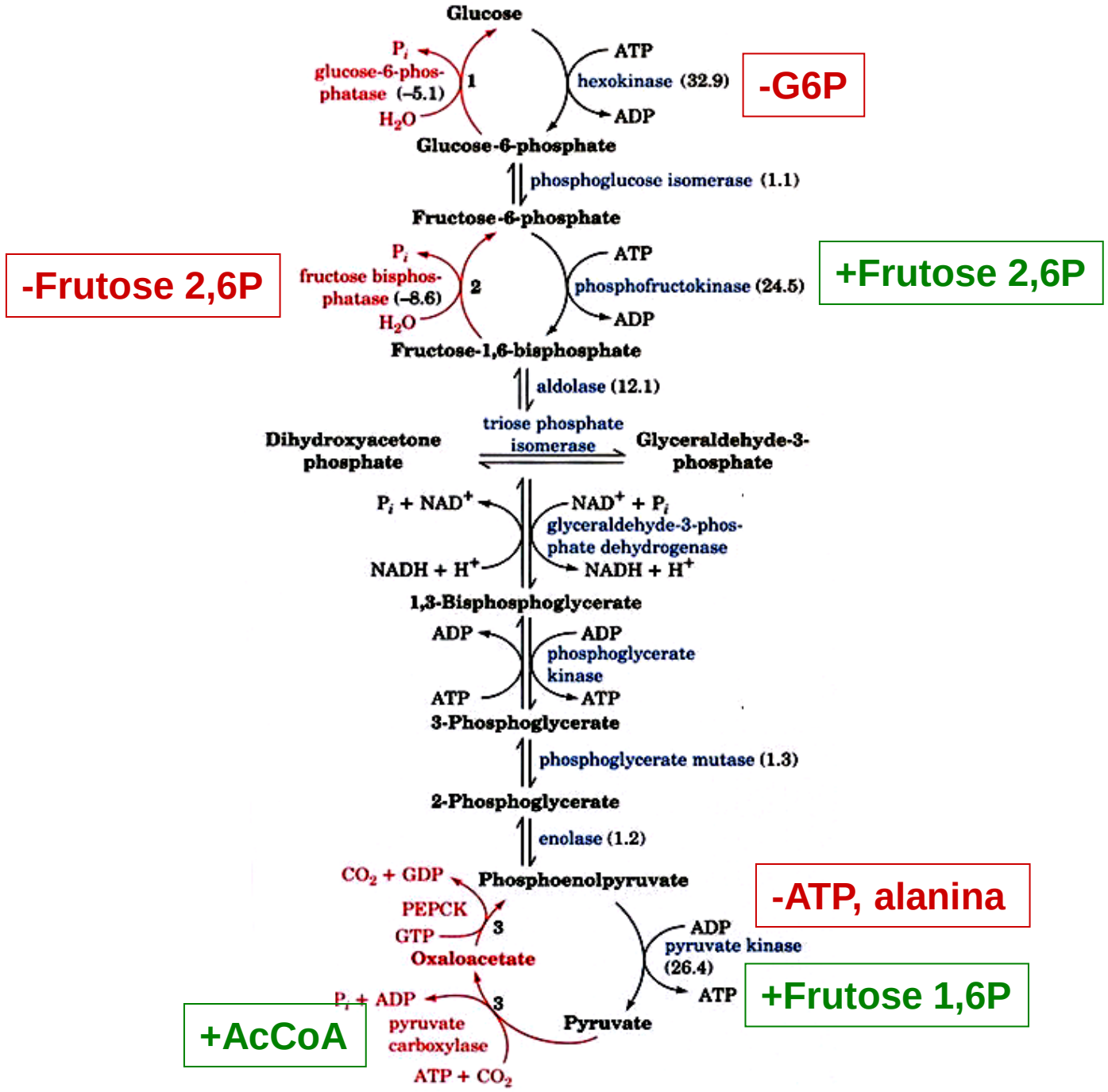
Succinate
Fumarate
Malate
Oxaloacetate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ATP + CO_2
Pyruvate
-G6P
-Frutose 2,6P
+Frutose 2,6P
-ATP, alanina
+Frutose 1,6P
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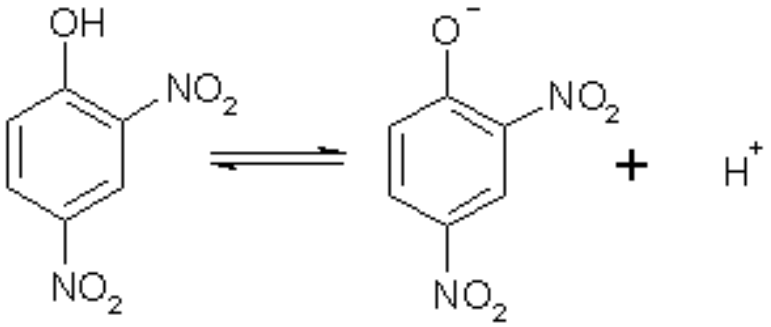
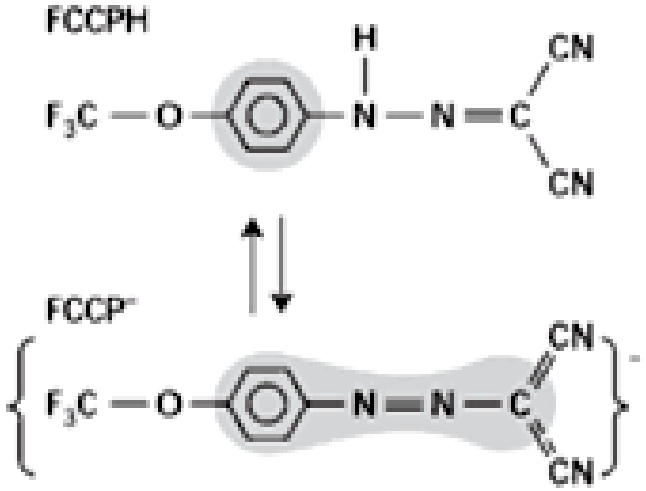
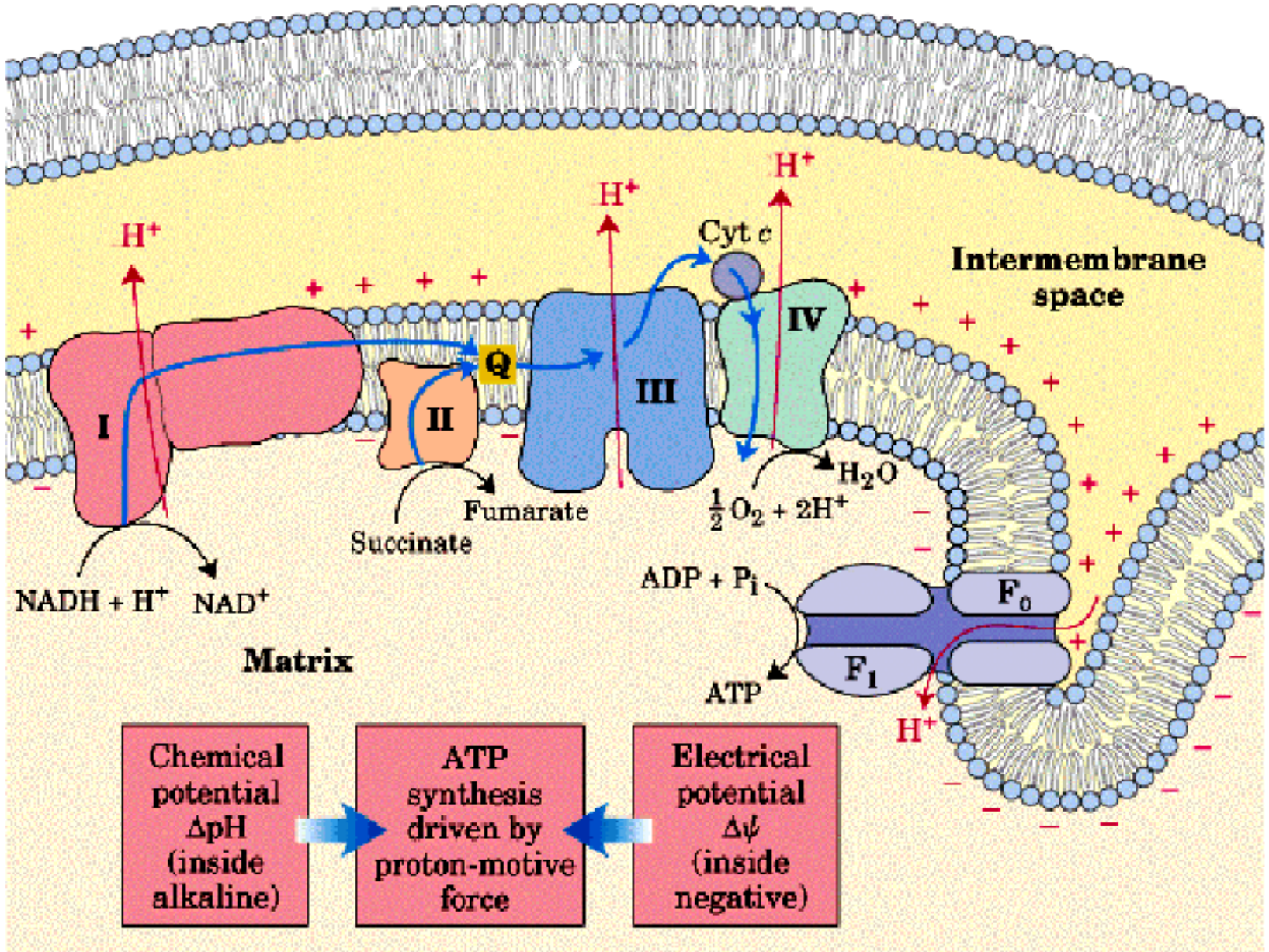
Regulação Farmacológica do $\Delta\Psi$

- Dinitrofenol e FCCP: - ionóforos de H^+
  - ácidos fracos, lipofílicos
  - “pílula da dieta”



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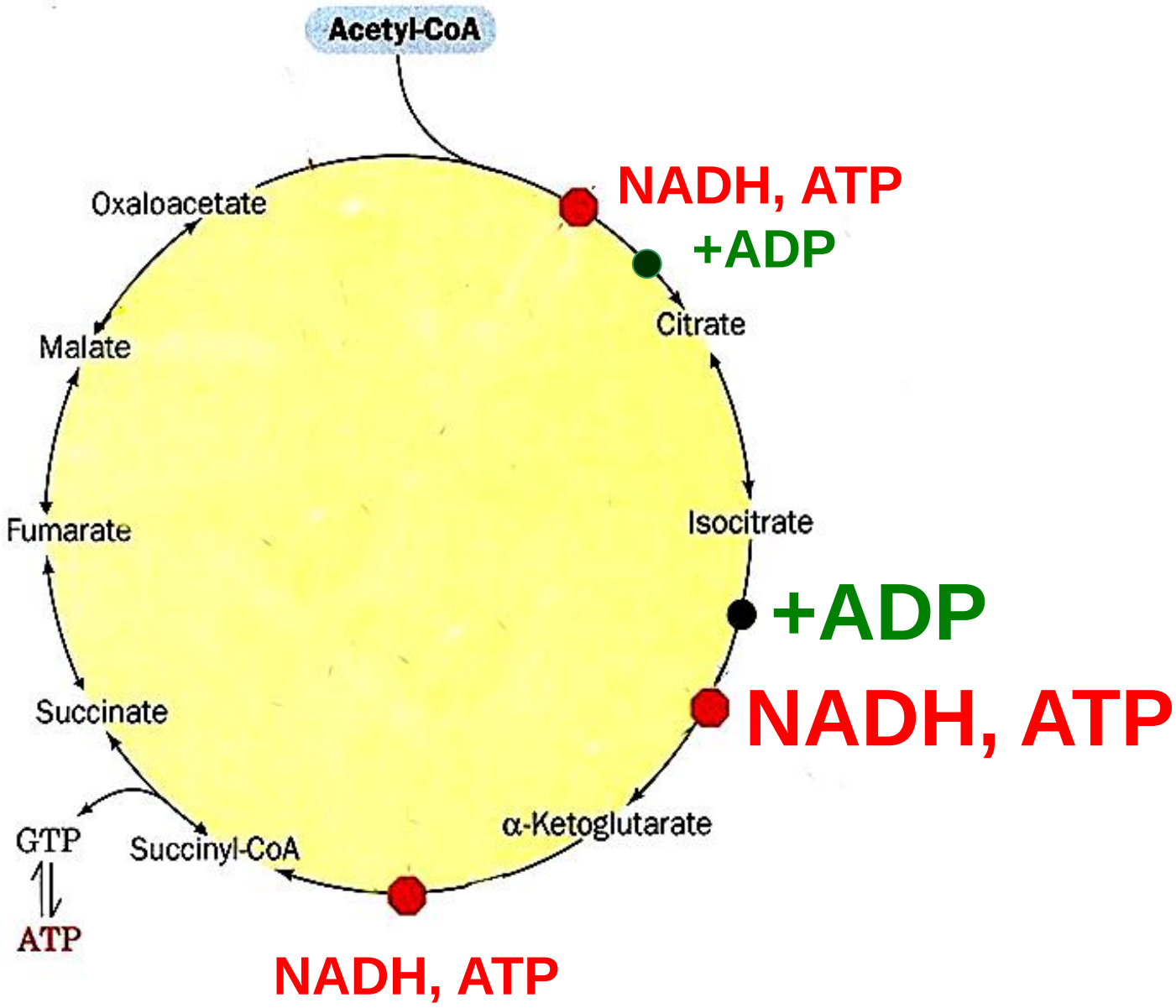
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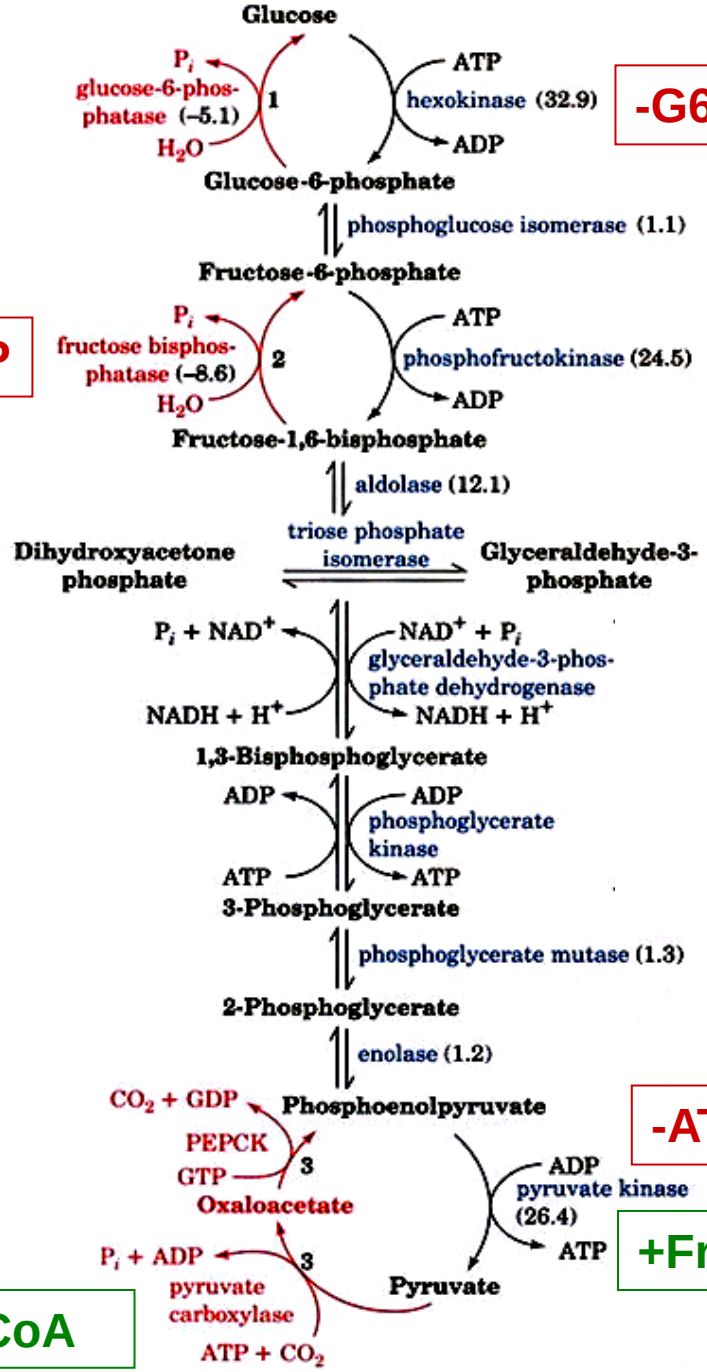

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