Biological Nanomechanics: ATP Synthesis and Deuterium Depletion

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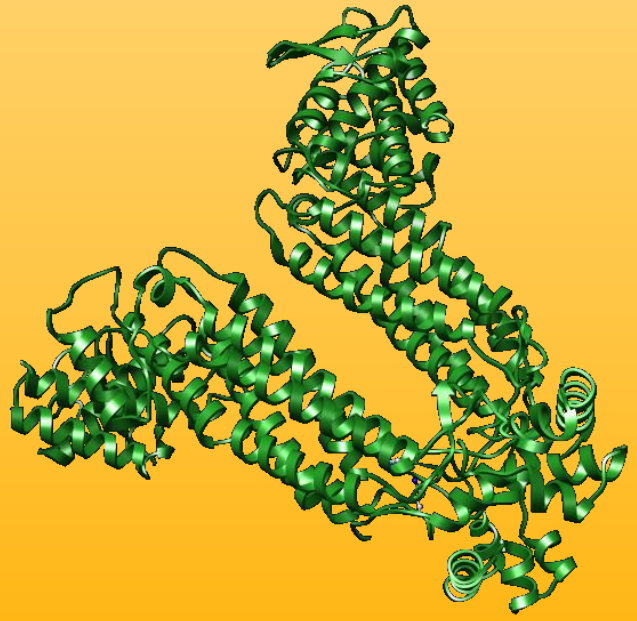

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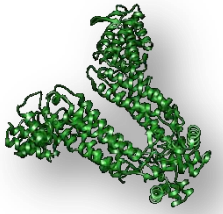
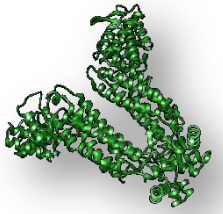


Biological Nanomechanics: ATP Synthesis and Deuterium Depletion

Jo Anne Brasel Basic Science Seminar – Los Angeles Biomedical research Institute at the Harbor-UCLA Medical Center
August 23, 2016

László G. Boros, M.D., Adjunct Professor of Pediatrics (Endocrinology & Metabolism), Harbor-UCLA Medical Center, Torrance, California, USA

https://youtu.be/6P8gqB4zLGQ

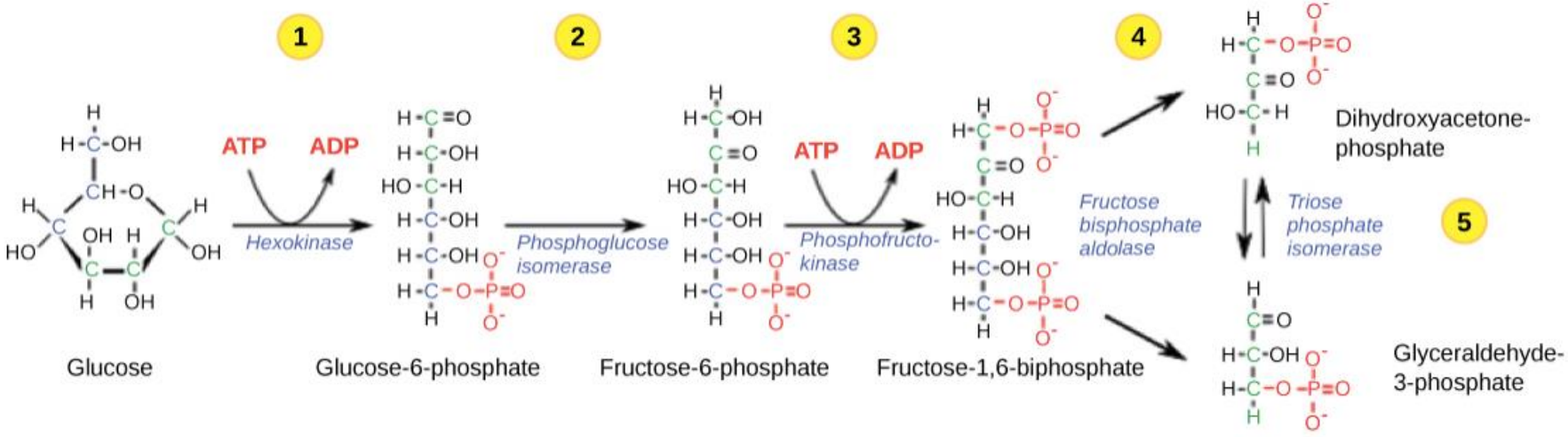


Common questions in biochemistry

- **Why does it take 10 enzymatic steps to cleave the six carbon glucose into two three carbon products, pyruvate, during glycolysis?**

- **Why does it take 9 enzymatic steps to cut two CO_2 molecules off in the TCA cycle?**

Glycolysis (I)



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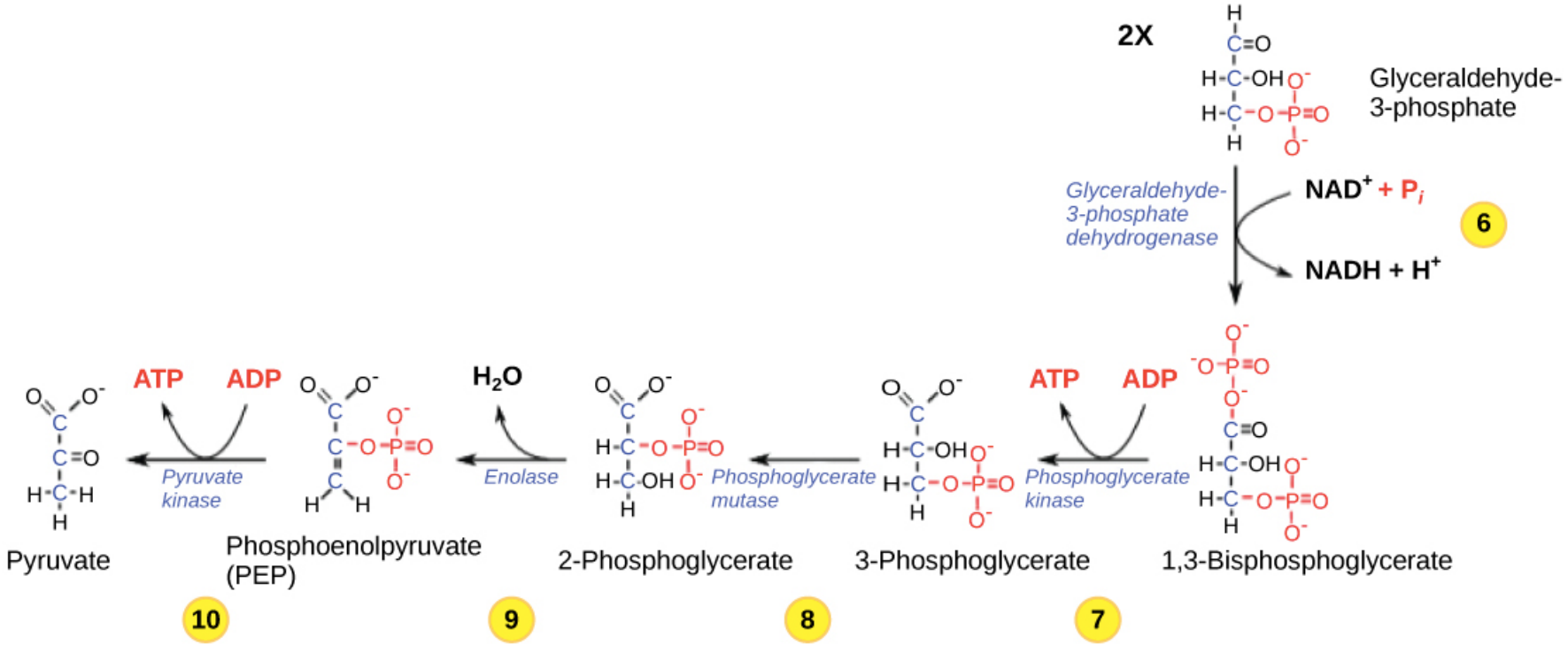
Glycolysis (II)



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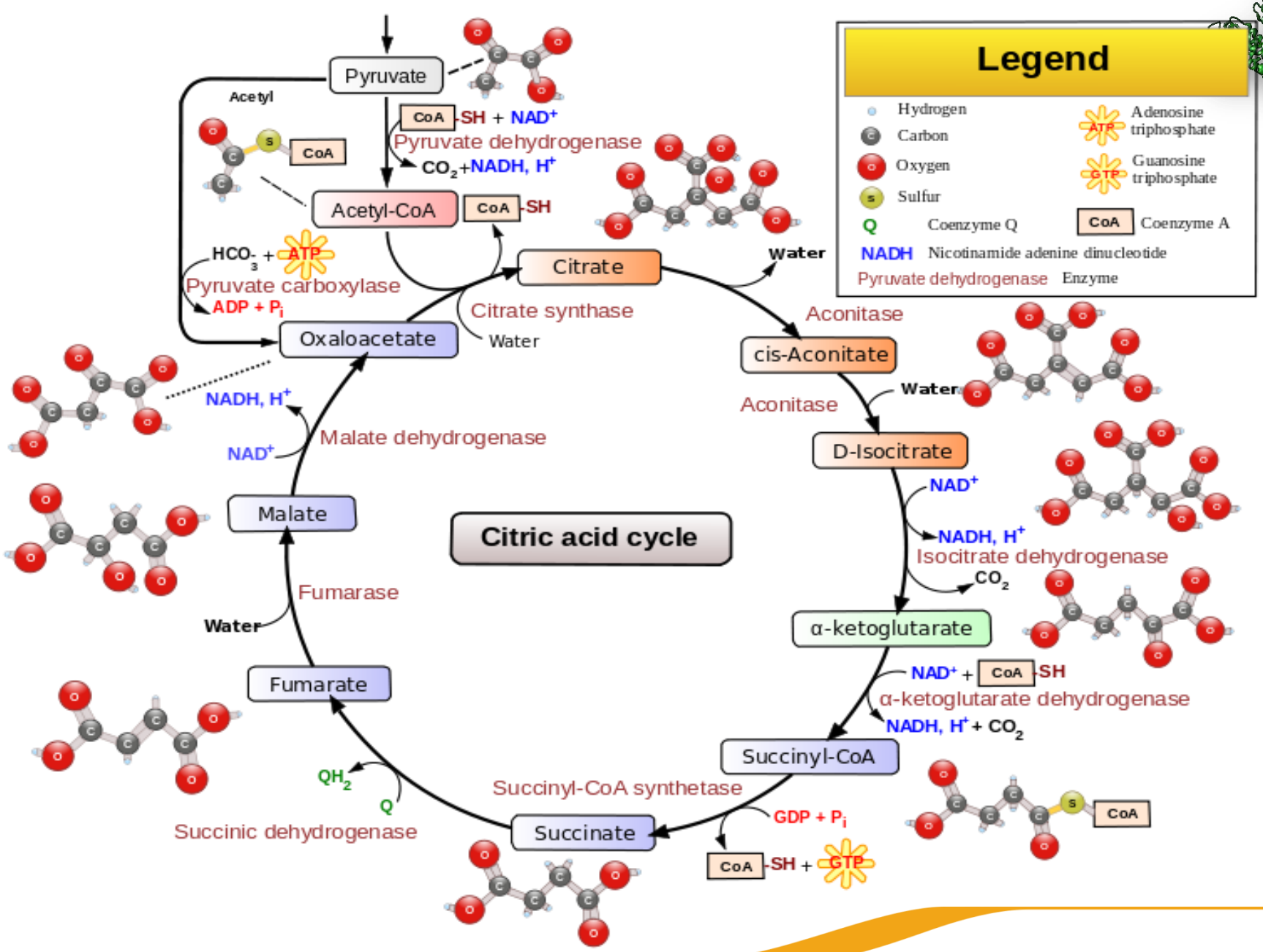
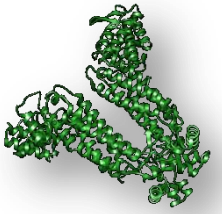

Legend
Hydrogen
Carbon
Oxygen
Sulfur
Adenosine triphosphate
Guanosine triphosphate
Coenzyme Q
Coenzyme A
NADH Nicotinamide adenine dinucleotide
Pyruvate dehydrogenase Enzyme
Pyruvate
Acetyl
CoA
Acetyl-CoA
Pyruvate dehydrogenase
Pyruvate carboxylase
Citrate
Citrate synthase
Water
Oxaloacetate
Aconitase
cis-Aconitate
D-Isocitrate
Isocitrate dehydrogenase
α-ketoglutarate
α-ketoglutarate dehydrogenase
Succinyl-CoA
Succinyl-CoA synthetase
Succinate
Succinic dehydrogenase
Fumarate
Fumarase
Malate
Malate dehydrogenase
Citric acid cycle

Hydrogen Loading & Deuterium Depletion

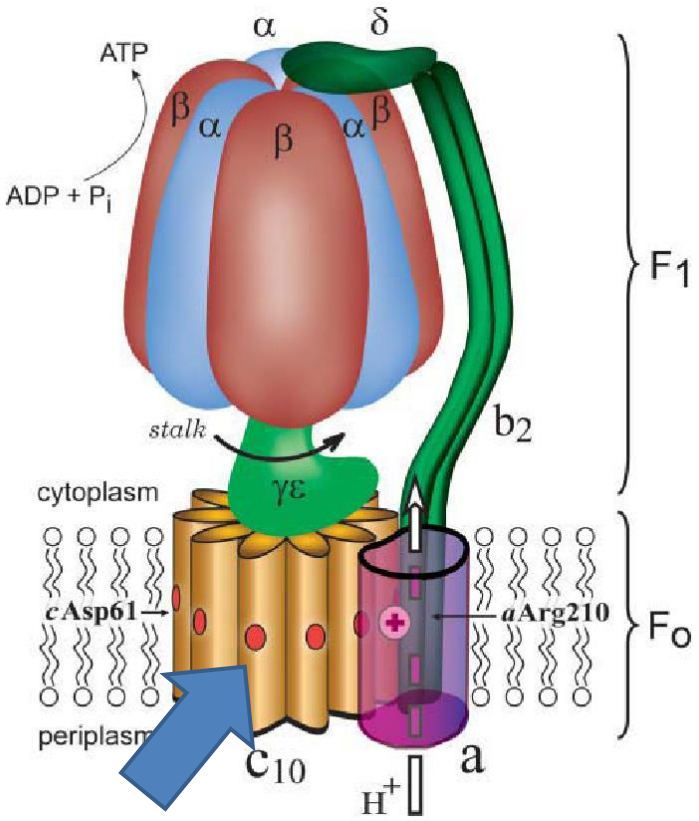


Movie from VCell animations - Gradients

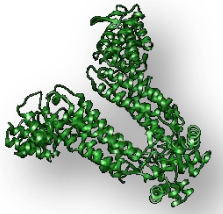

COMPUWARE
63


RPM / 1000
HEADLAMPS SUGGESTED

ATP Synthesis



ATP synthesis occurs with the continuous turning of proton (P) loading positions of the membrane rotor - arrow - C_{10} with about 9000 revolutions per minute [Aksimentiev et al., (2004) Biophys. J.]



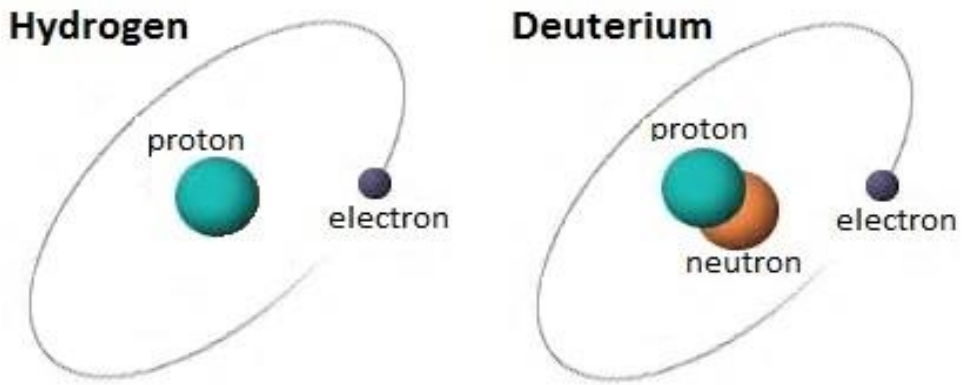
Normal Proton Loading and ATP

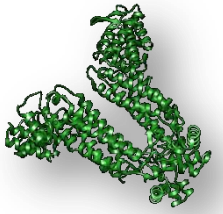
- At 9,000 revolutions per minute the ATP synthase C_{10} subunit transfers approximately 90,000 protons per minute

- That means 1,500 protons are released into the mitochondrial matrix in each second

Proton – Deuterium Biochemistry

- **ATP synthase is jammed by deuterium's isotope effect, which is the heavy stable isotope of hydrogen**

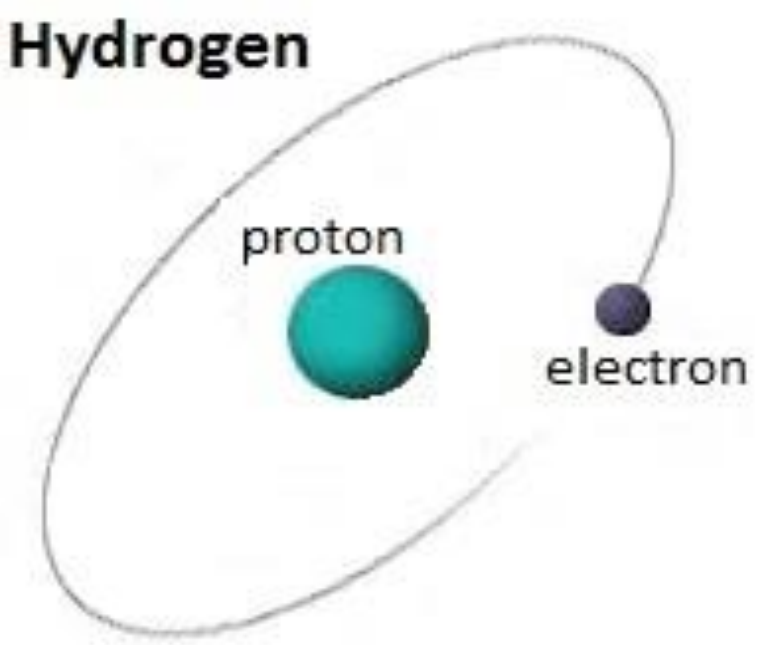


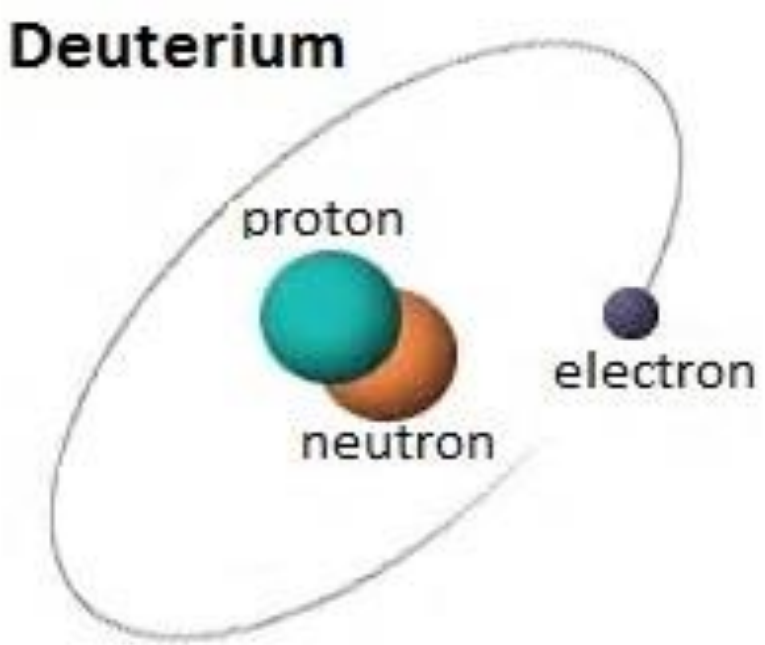


Hydrogen – Deuterium Physics

- Deuterium has a mass of 2.01 unified atomic mass unit with a charge radius of 2.14 femtometer (fm; 10^{-15} m)
- Proton's charge radius is 0.88 fm with a mass of 1.008 Da
- Physics.nist.gov.; Retrieved on 2016-01-JUL

Hydrogen – Deuterium Physics

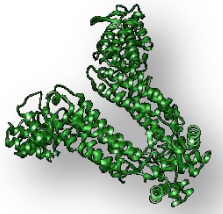




Hydrogen
mass=1Da

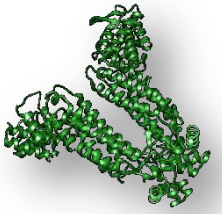
Deuterium
mass=2Da

Deuterium Plasma Chemistry



IONS BLOOD

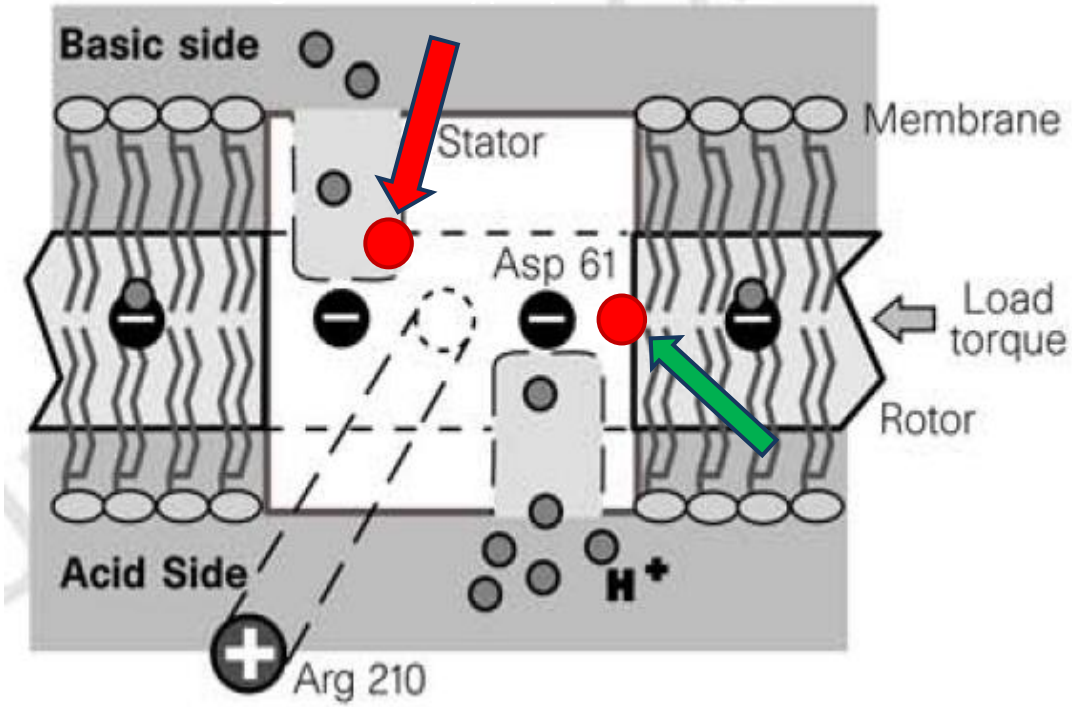
Test	*Lower limit*	*Upper limit*	*Unit*
Calcium	2.24	2.74	mmol/L
Magnesium	0.75	1.2	mmol/L
Potassium	3.5	5.1	mmol/L
Glucose	3.3	6.1	mmol/L
Deuterium	12	14	mmol/L



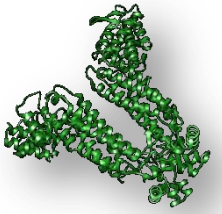
ATPase - Proton – Deuterium

https://goo.gl/K5dRVW - *VCell* animations

Displacement of protons by deuterons



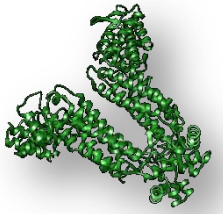
due to increased weight (mass) and slow acid dissociation constant ($\Delta pKa_{Asp61}=0.35$) there is a stutter with shaking [Olgun (2007)]



Abnormal Deuterium Loading

- There is one deuterium for every ~6,600 proton transfers in nature

- At 1,500 protons/second transfer velocity the nanomotor would break down every ~4.4 seconds (6600/1500) in environmental water

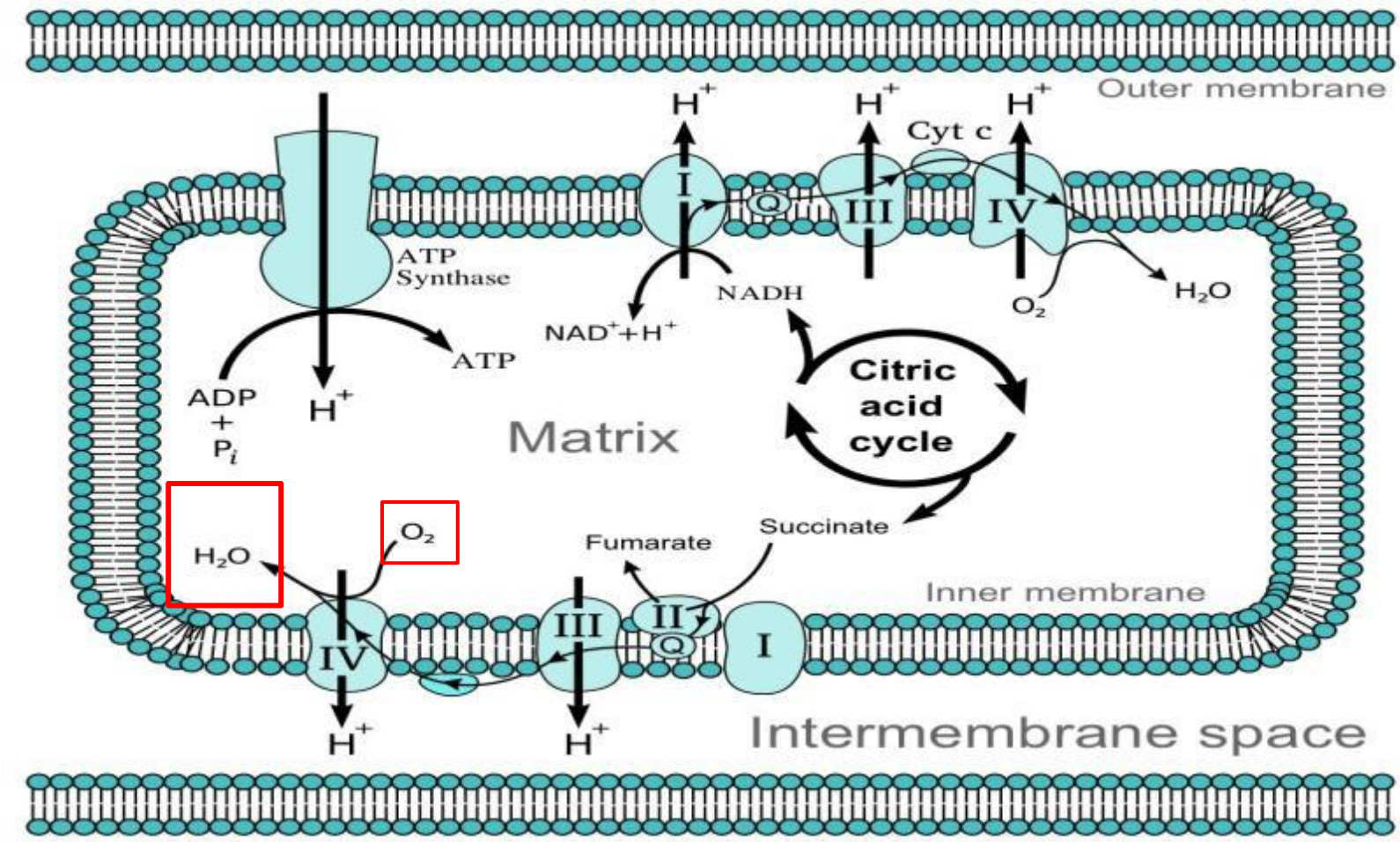


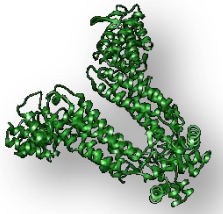
Deuterium Depletion (1)

- **Is a natural biochemical process starting in glycolysis to preserve mitochondrial health**

- **Failing of the body's natural deuterium depleting processes results in cancer, metabolic and neurodegenerative diseases**

Metabolic water (1)



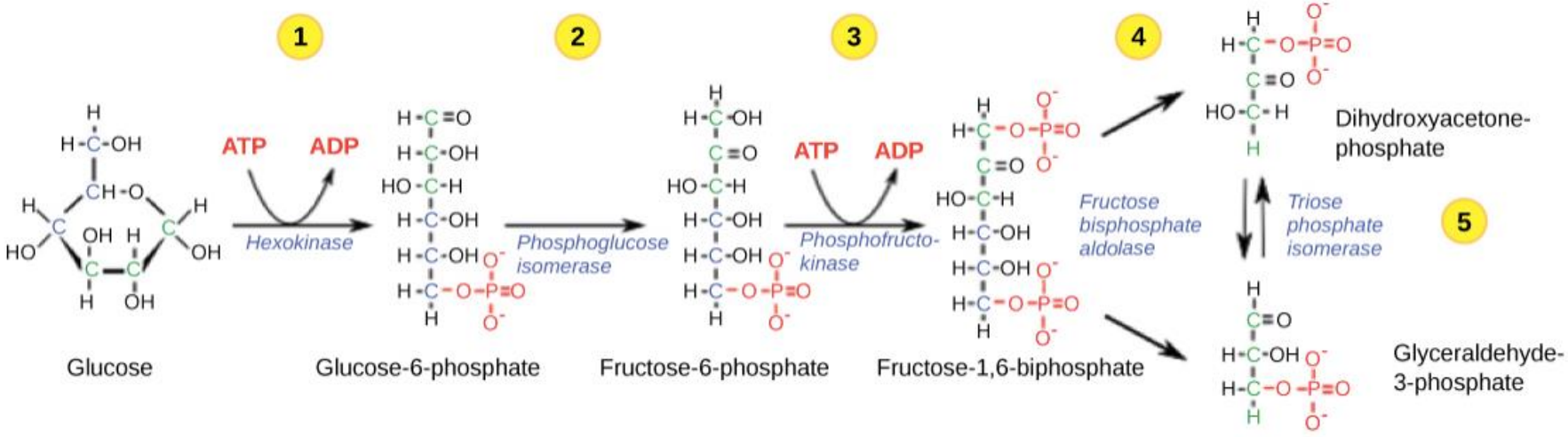


Deuterium Depletion (3)

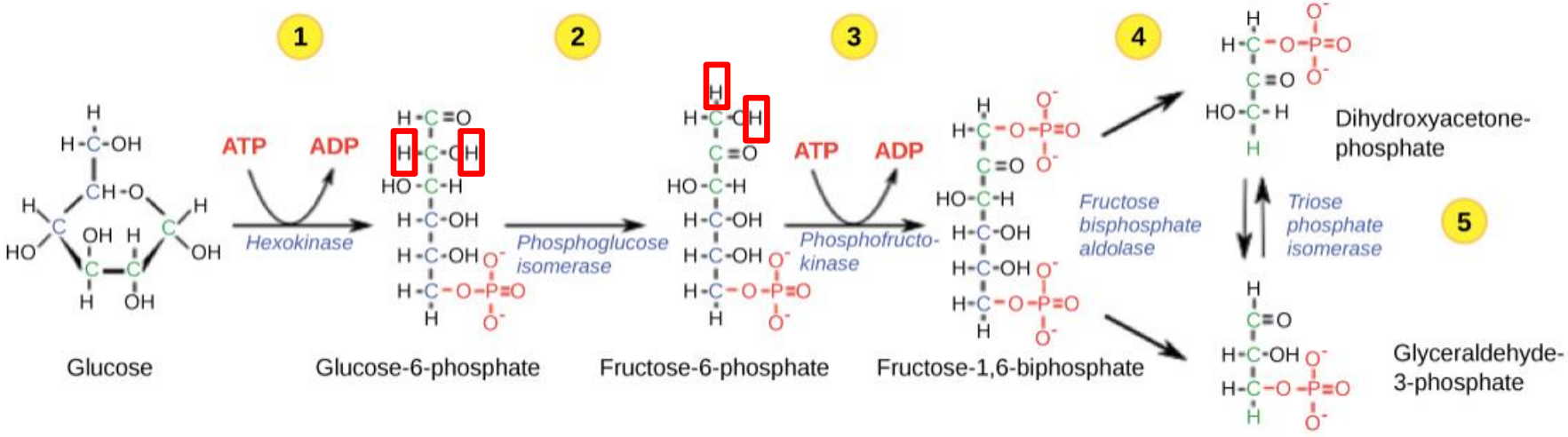
- **Metabolic disease epidemics and obesity are the result of excessive deuterium extraction from sugars by carbohydrate oxidation**

- **Nutritional ketosis and health benefits by deuterium depletion**

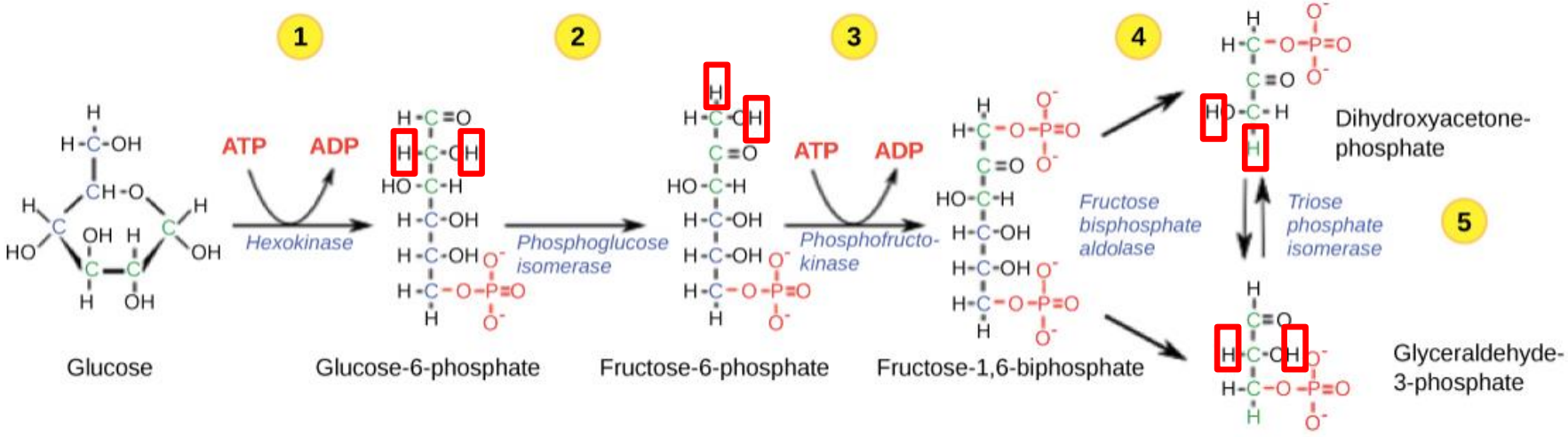
Glycolysis (I) – deuterium depleting steps



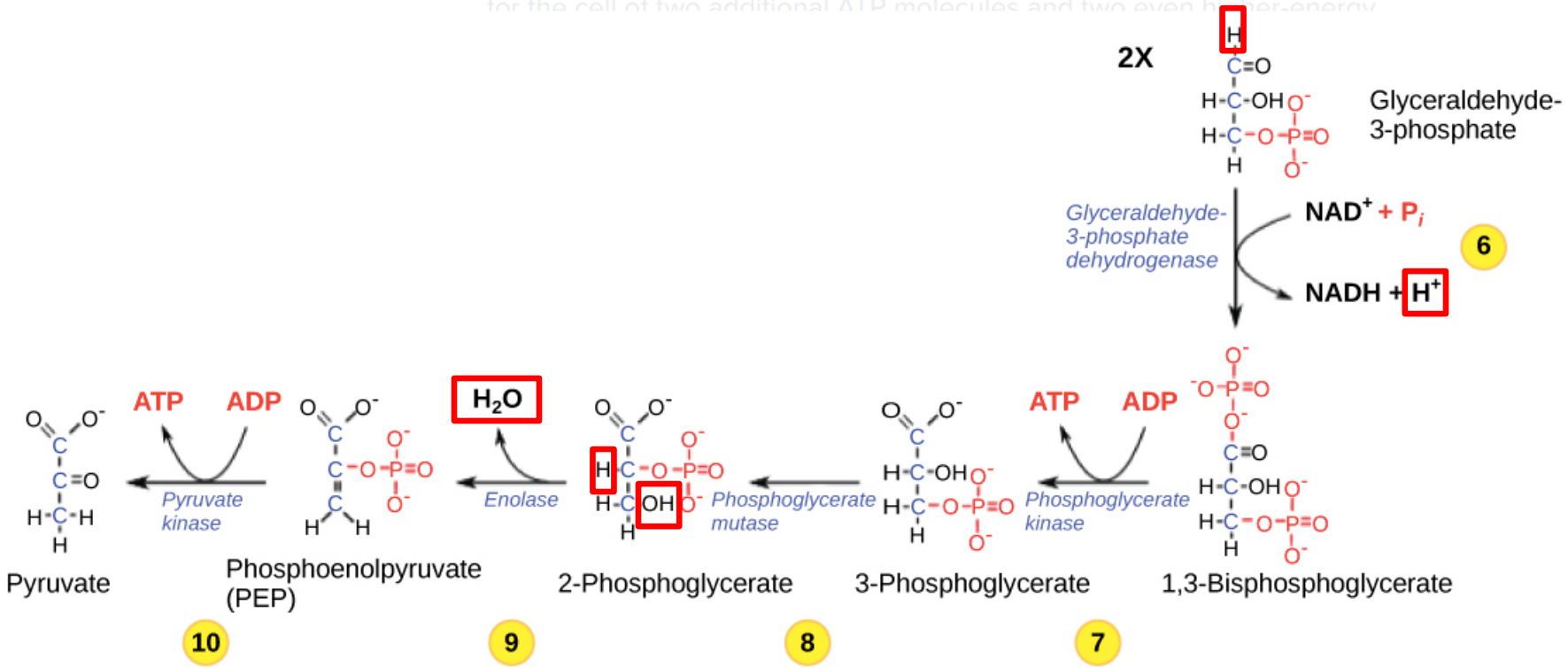
Glycolysis (I) – deuterium depleting steps

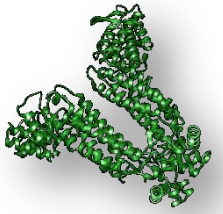


Glycolysis (I) – deuterium depleting steps



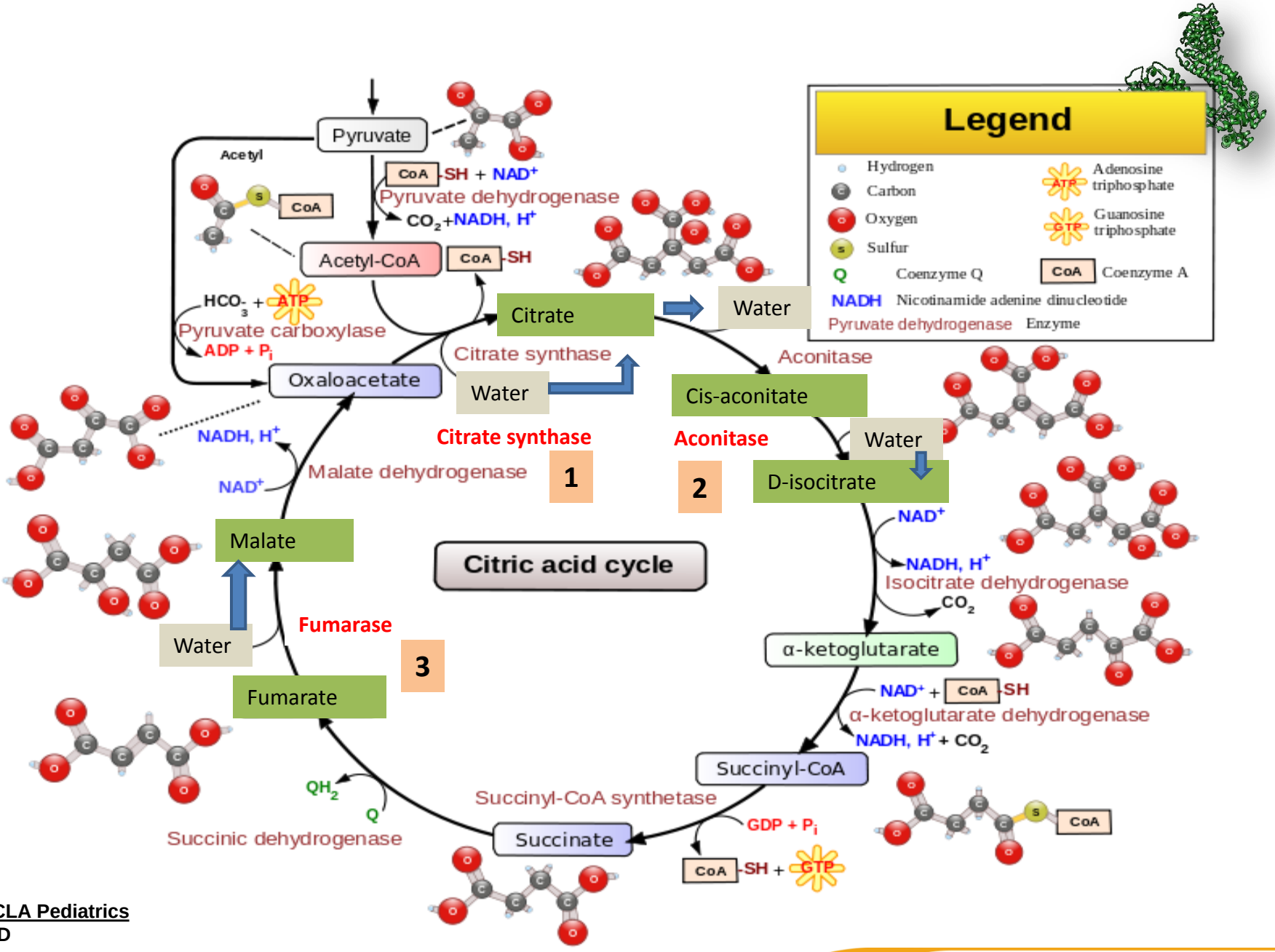
Glycolysis (II) – metabolic drying





Glycolysis is a metabolic "dryer"
It rips extracellular hydrogens off from glucose

TCA cycle is a metabolic "washer"
Adds metabolic water to TCA cycle intermediates



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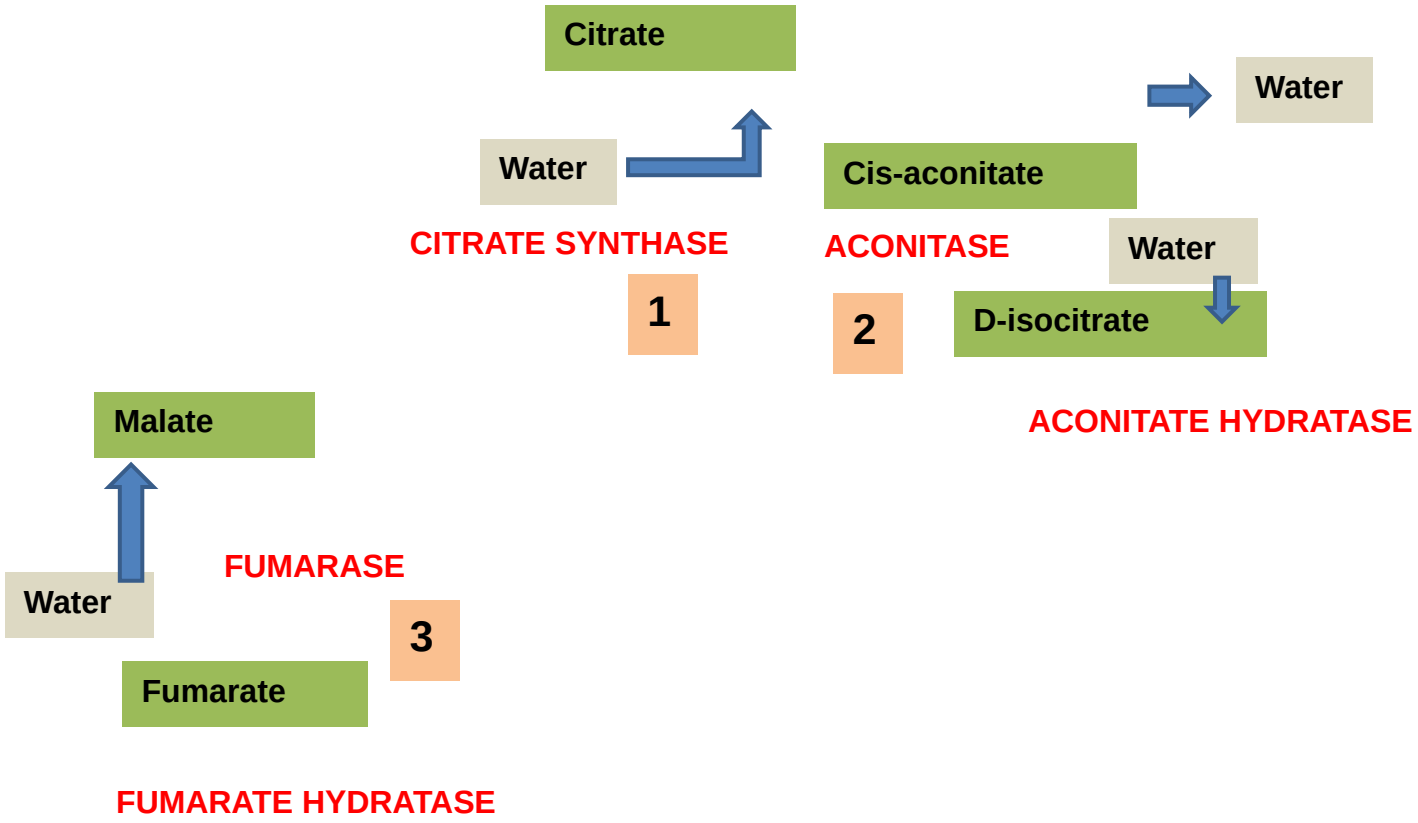
LABIOMED
HYD, LLC
SiDMAP,LLC

http://en.wikipedia.org/wiki/File:Citric_acid_cycle_with_aconitate_2.svg

WATER EXCHANGE/CONSUMPTION IN THE CITRIC ACID CYCLE



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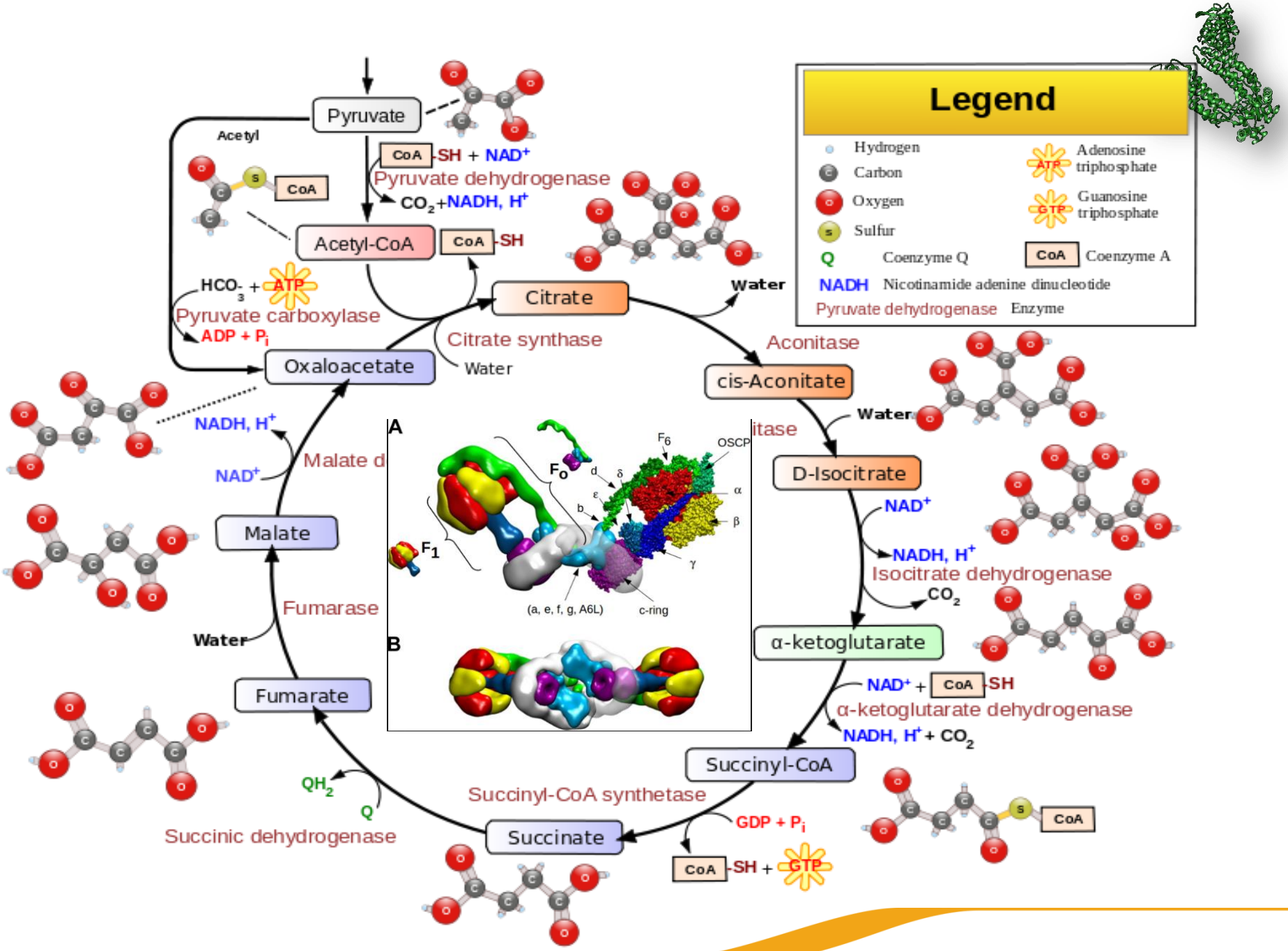
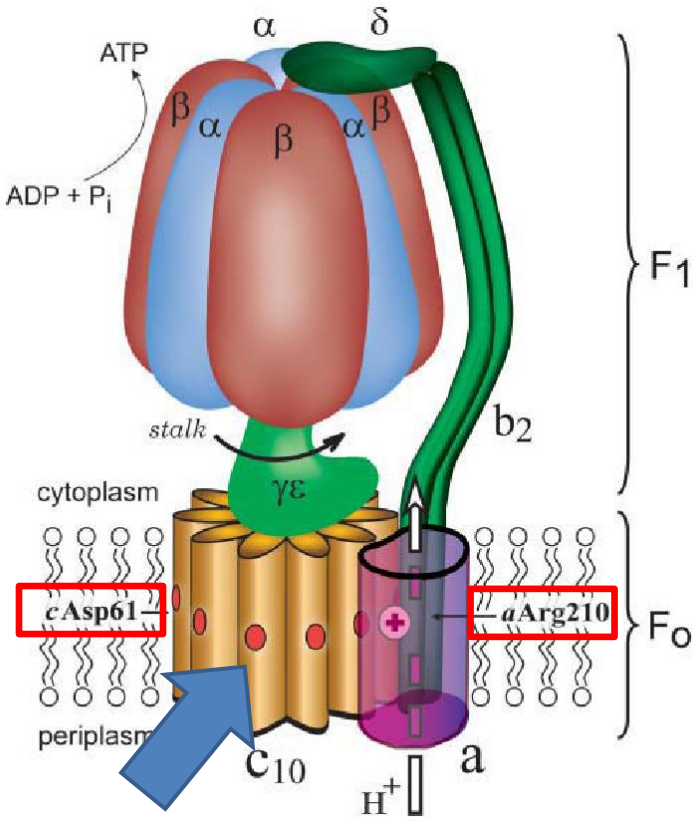
LABIOMED
HYD, LLC
SiDMAP,LLC


Legend
Hydrogen
Carbon
Oxygen
Sulfur
Adenosine triphosphate
Guanosine triphosphate
Coenzyme Q
Coenzyme A
Nicotinamide adenine dinucleotide
Enzyme
Pyruvate
Acetyl
CoA
Pyruvate dehydrogenase
Acetyl-CoA
Citrate
Water
Citrate synthase
Aconitase
cis-Aconitate
D-Isocitrate
Isocitrate dehydrogenase
α-ketoglutarate
α-ketoglutarate dehydrogenase
Succinyl-CoA
Succinyl-CoA synthetase
Succinate
Succinic dehydrogenase
Fumarate
Fumarase
Malate
Malate d
Oxaloacetate
Pyruvate carboxylase
A
B
F1
Fo
F6
OSCP
(a, e, f, g, A6L)
c-ring

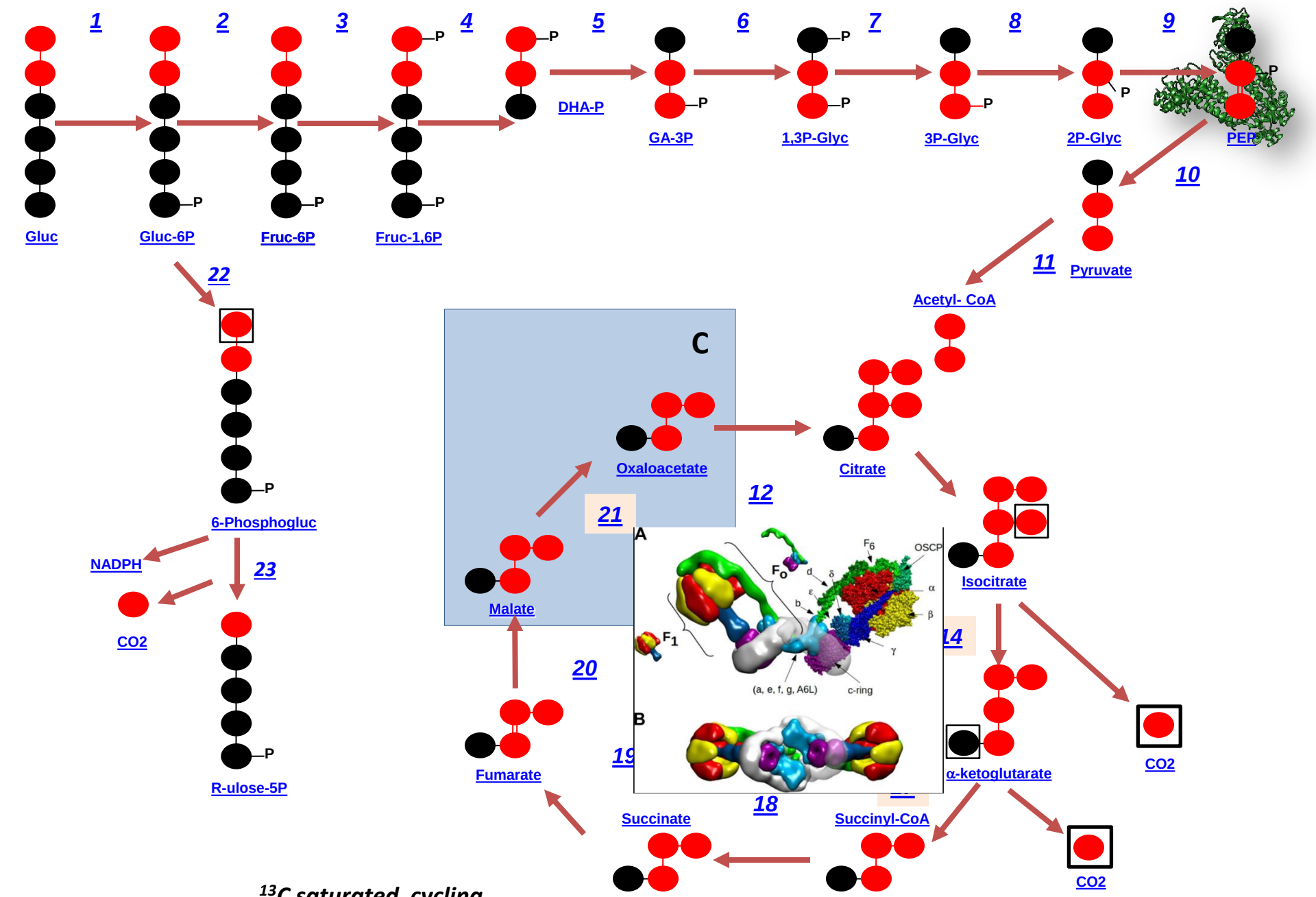
The Mitochondrial Gear

- **How are the TCA cycle and ATP synthase connected by proton/deuterium loading?**

ATP Synthesis



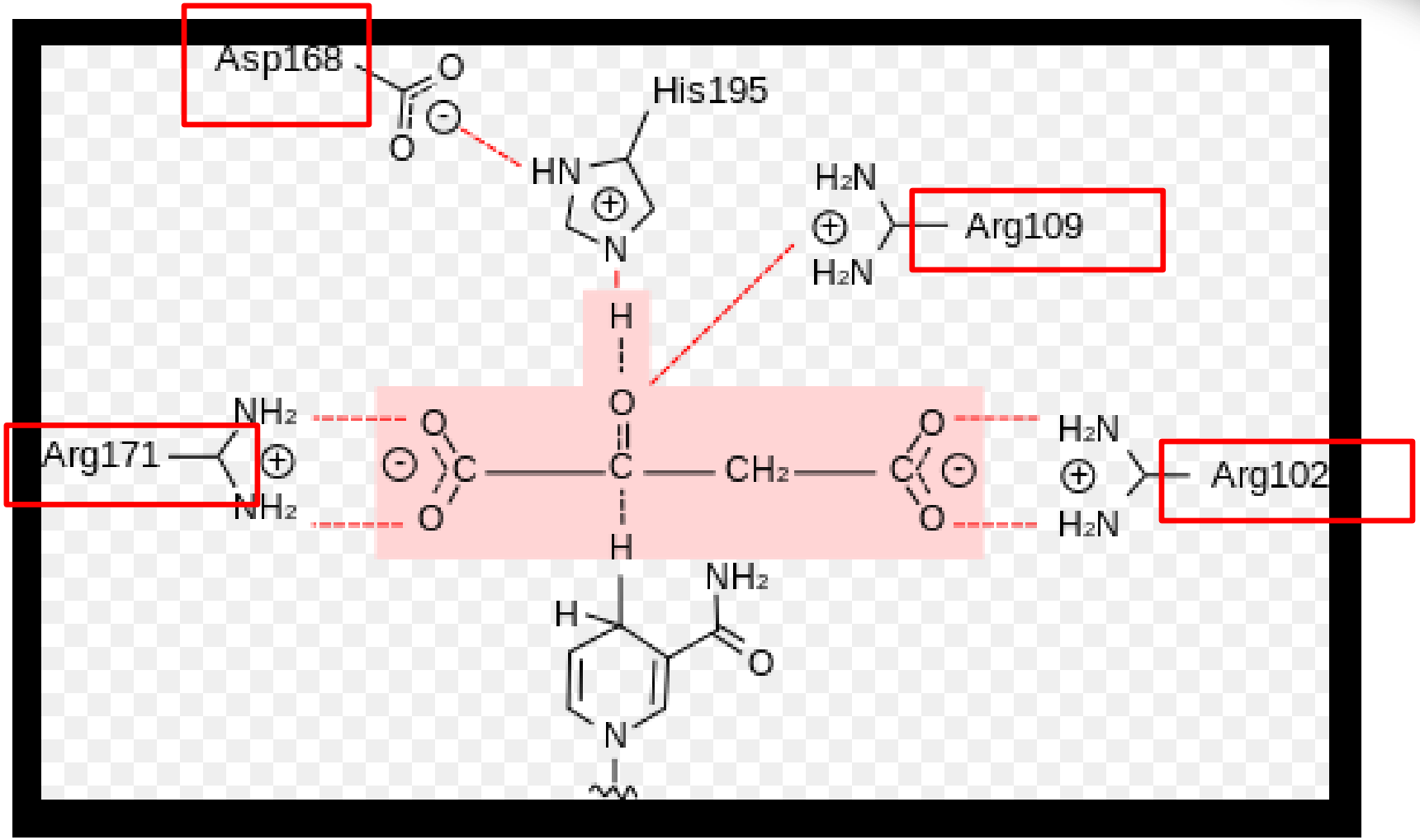
The aspartate and arginine amino acid residues transfer protons also in malate dehydrogenase (EC 1.1.1.37) to form oxaloacetate, which regulates citrate formation



^{13}C saturated cycling mitochondria by acetate

Figure 1

Laszlo G. Boros, MD



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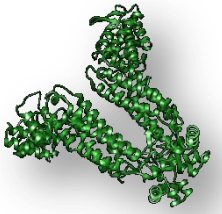
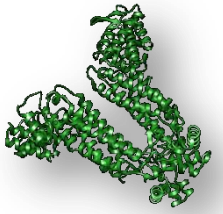


Simple answers for biochemistry

- It takes 10 enzymatic steps to exchange and remove 12 hydrogens from glucose before entering the TCA cycle as pyruvate

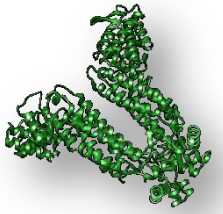
- Cleaving the six carbon glucose into two three carbon products, pyruvate, during glycolysis is not the prime purpose of glycolysis



Simple answers in biochemistry

- **It takes 9 enzymatic steps to replace 3 hydrogens with water and cut two CO_2 molecules off in the TCA cycle**

- **ATP synthase needs to operate in a deuterium depleted interfacial metabolic water environment**



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