Glycolysis

- Glucose is the major energy substrate in certain tissues like brain
- Glycolysis occurs in the cell's cytosol
- it takes place in all organisms both aerobic and anaerobic (mostly!)
- The intermediates either: ① Provide entry points to the cycle ② They are useful directly! (such as)

- phosphorylation goals: ① Priming / Activation ② Tricking the cell by changing the glucose's form. ③ Trapping the sugar inside the cell. | keep continous influx!

Glucose

(Step 1) ATP → ADP (phosphorylation) (Priming) (Activation)

Glucose 6-Phosphate

(Step 2) isomaraization

- mediated by ⇒ phosphoglucose isomerase
- mannose + Fructose ⇒ enters glycolytic pathway at this point!.
- Reversibile.

Fructose 6-phosphate

(Step 3) ATP → ADP (phosphorylation)

- Goal ? Destabalize the ring!
- mediated by ⇒ Phosphofructo Kinase (PFK-1)
- rate limiting step (key regulatory step) ⇒ slowest step that determines the speed of the reaction.
- Phosphorylation of (OH) at carbon #1

Fructose 1,6-Biphosphate

(Step 4) Cleavage between C3-C4

- mediated by ⇒ Aldose
- Cleavage into 2 triose phosphates at the bond between C3-C4.

Glyceraldehyde 3-phosphate ⇒ GAP (then ×2)
Dihydroxyacetone phosphate ⇒ DHAP

- Can't go further! → isomerization to GAP! (Step 5) By Triose phosphate isomeraze.
- Precursor for glycerol → used for the formation of triglycerol!!

(Step 6) 2P, 2NAD⁺ → 2 NADH + H⁺

- Super High energy molecule (Storing)
- oxidative phosphorylation.
- by → Glyceraldehyde 3-phosphate dehydrogenase. Goal → making high energy molecule.
- electron donors / Reductants (J ⇒ Jols)!

1,3-Biphosphoglycerate (2)

(Step 7) 2ADP → 2ATP

- First ATP forming reaction (Direct Energy) (Substrate level formation)
- by ⇒ phosphoglycerate Kinase!

3-phosphoglycerate (2)

(Step 8) Reversabile (internal shifting)

- Only terminal shifting → C3 to C2
- isomaraization by: phosphoglycerate mutase
- Activation of phosphate group

2-phosphoglycerate (2)

(Step 9) → 2H₂O (Dehydration Reaction)

- 2nd super high energy molecule
- by ⇒ Enolase
- increase in the energy stored in phosphate.
- OH from Carbon #3 is gone
- H from Carbon #2 is gone
- Double bond between C3 + C2

Phosphoenolpyruvate (2)

(Step 10) 2ADP → 2ATP

- 2nd ATP is generated
- Substrate level formation By pyruvate kinase.

Pyruvate (2)

⊛ Regarding the Enzyme used in Step 1 (Hexokinase)

Hexokinase ⇒ different versions/isoforms exist in the Heart, brain and liver. same gene but different expressions

Hexokinase I, II, III:
- non specific
- can phosphorylate variety of hexoses like: ① glucose ② Mannose ... etc
- type I ⇒ is involved in the Catabolic pathways
- type II + III ⇒ involved in anabolic pathways.
- all the time phosphorylation. - allosterically inhibited by G6P at high level (product control mechanism)

Hexokinase IV:
- expressed in the liver and β-cells of pancreas.
- Specific for D-glucose
- Specific phosphorylation only when the blood glucose is high.

Bi → 2 but not close
Di → 2 close (beside eachother)

⊛ Regarding Step 6: Nicotinoamide Adenine Dinucleotide (NAD)

- NAD ⇒ derivative? Vit B3 (Niacin)
- exist in 2 forms: → NAD⁺ (oxidized form) / → NADH (Reduced form)
- Coenzyme for dehydrogenases
- Energy rich molecule! indirect form of energy!

1 NADH = 2.5 ATP → only in aerobic conditions!

⊛ Net result of Glycolysis:

- 2 ATP (Steps 7, 10: 4 − 2 = 2; steps 1, 3)
- 2 Pyruvate → End result
- 2 NADH → step 6