Notes 11/19

Monday, November 19, 2007

9:56 AM

Final Notes:

Glycolysis: Payoff Phase and Fermentation

Nov. 19, 2007

Glycolysis: Payoff Phase and Fermentation

Nov. 19, 2007

1

Overview

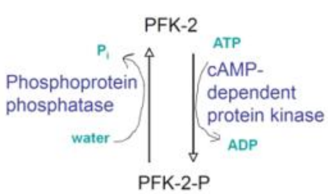
Overview

- Regulation and control of glycolytic enzymes
- Fermentation

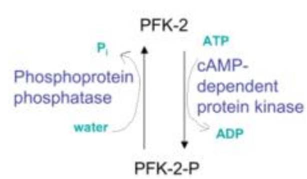
2

Step 3 in glycolysis

Coordinated regulation of kinase and phosphatase activities of PFK-2



Coordinated regulation of kinase and phosphatase activities of PFK-2



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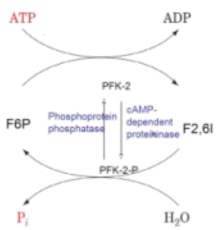
Regulation of PFK via F2,6P occurs in response to [glucose]

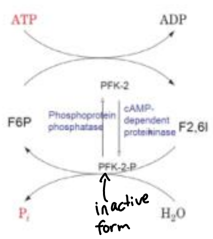
- When [glucose] is high
  - Phosphoprotein phosphatase hydrolyzes PFK-2-P into PFK-2
  - PFK-2 kinase activity converts F6P to F2,6P
  - F2,6P activates PFK <— in glycolysis pathway
  - Enhanced PFK kinase activity converts F6P to F1,6P

Phosphoprotein phosphatase takes inactive PFK-2-P to PFK-2.



Regulation of PFK via F2,6P occurs in response to [glucose]

- When [glucose] is low
  - cAMP-dependent protein kinase activity converts PFK-2 to PFK-2-P
  - PFK-2-P hydrolyzes F2,6P to F6P
  - PFK kinase activity is no longer enhanced (in glycolysis)



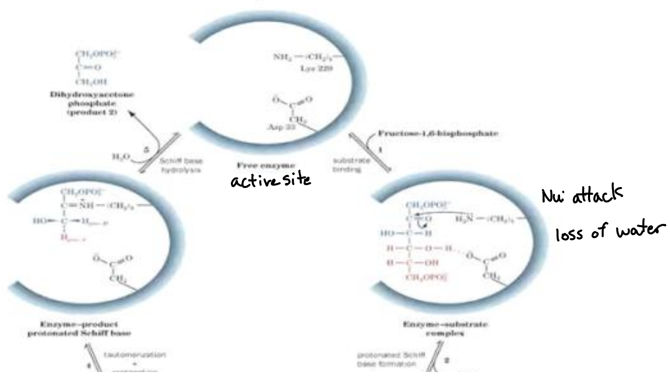
Step 4: Aldolase

- Cleavage of Fructose 1,6-bisphosphate into trioses (not F2,6 bisphosphate)
- Rxn
  F1,6P <--> dihydroxyacetone phosphate + glyceraldehyde 3-phosphate

Dihydroxyacetone phosphate

Aldolase

Figure 17-9



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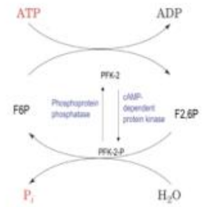

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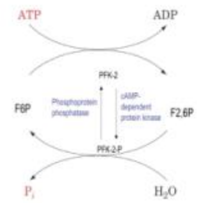

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Step 4: Aldolase

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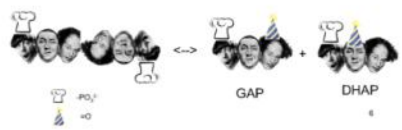

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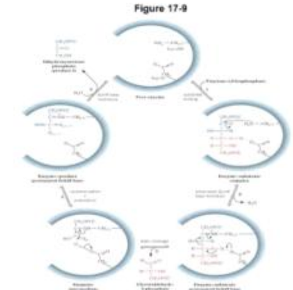
Figure 17-9



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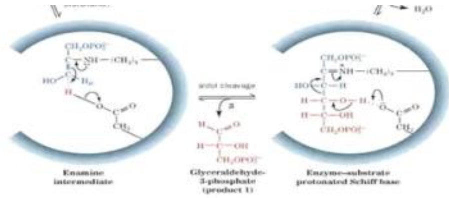

GAP

Step 5: Triose phosphate isomerase

- Isomerization of dihydroxyacetone phosphate to glyceraldehyde 3-phosphate
- Rxn

DHAP <--> GAP

DHAP — cannot undergo glucolysis

GAP — undergoes glycolysis

Score card for the preparatory phase of glycolysis

- Glucose + 2 ATP --> 2 G3P + 2 ADP + 2 H^+

Figure 17-3

Enzyme: GAPDH
Glyceraldehyde-3-phosphate dehydrogenase

Step 5: Triose phosphate isomerase

- Isomerization of dihydroxyacetone phosphate to glyceraldehyde 3-phosphate
- Rxn

DHAP <--> GAP

DHAP GAP

8

Score card for the preparatory phase of glycolysis

- Glucose + 2 ATP --> 2 GAP + 2 ADP + 2 H^+

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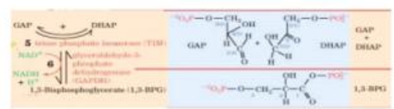
Figure 17-3



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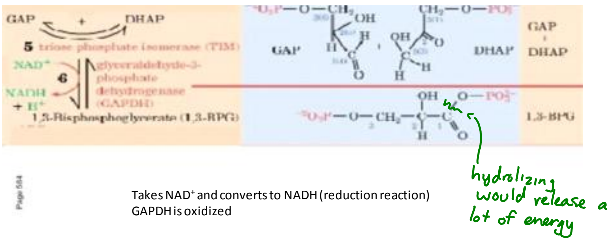

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Takes NAD^+ and converts to NADH (reduction reaction)
GAPDH is oxidized

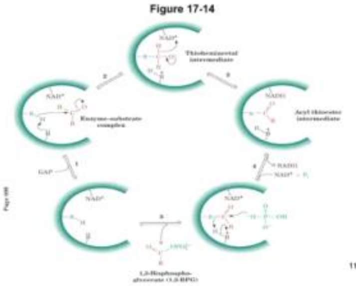

Figure 17-14

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Enzyme: GAPDH
Glyceraldehyde-3-phosphate dehydrogenase

Figure 17-14

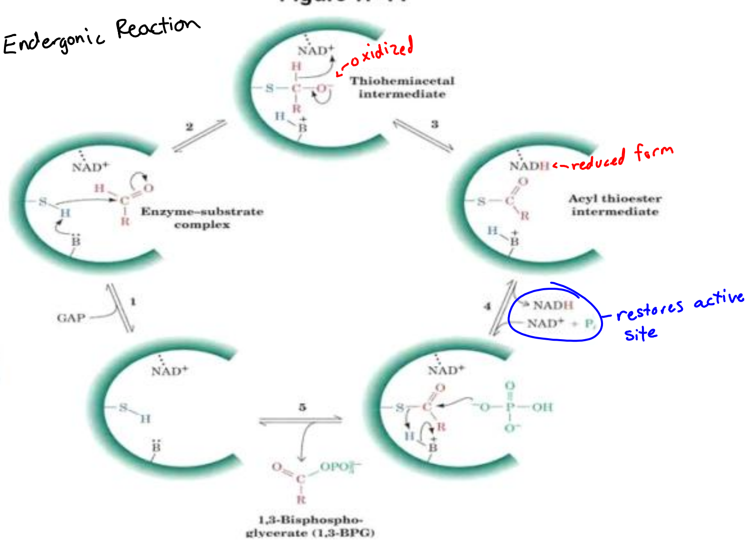

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Figure 17-3

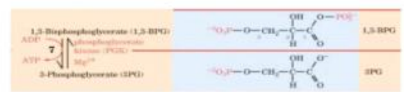

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Figure 17-3

Enzyme: PGK Phosphogylcerate kinease
Making ATP

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Figure 17-16

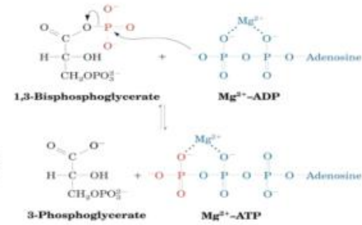

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Figure 17-3

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Figure 17-16

Enzyme: PGK Phosphogylcerate kinease
Making ATP

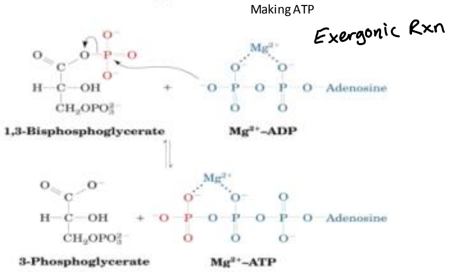

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Figure 17-18

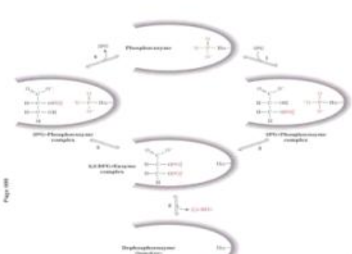

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Figure 17-3

Step 8
Enzyme :PGM

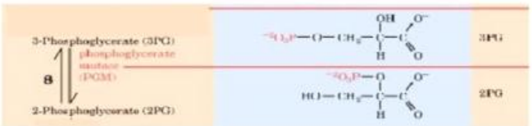


Figure 17-18

Step 8
Enzyme :PGM

Active site phosphoenzyme

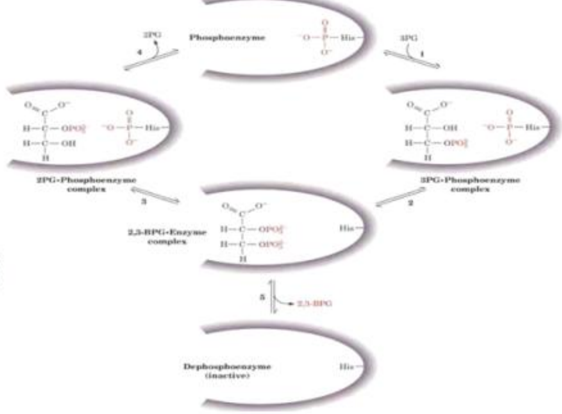
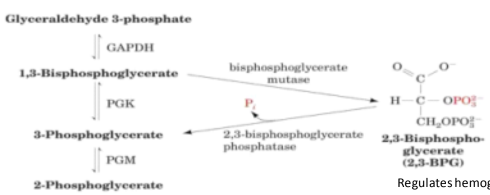


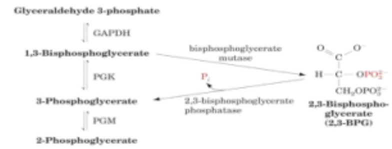
Figure 17-19

Detour off of glycolysis



Regulates hemoglobin and oxygen

Figure 17-19



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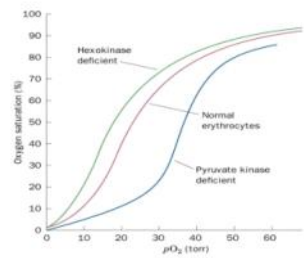

Figure 17-20

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Figure 17-3

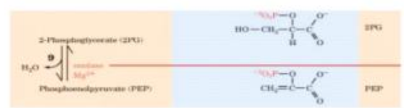

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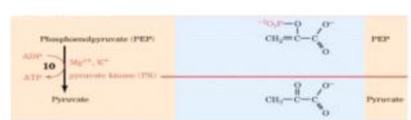
Figure 17-3



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Hemoglobin (sigmoidal shape)

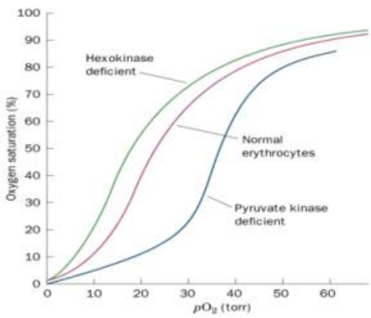


Figure 17-20

- Hexokinase increases binding strength of oxygen to hemoglobin
  - Less 2,3BPG is formed which affects affinity for hemoglobin for oxygen
- Pyruvate kinease decreases binding strength of oxygen to hemoglobin
  - Accumulation of 2,3BPG because pyruvate kinease catalyzes the final step of glycolysis and will accumulate intermediates of intermediates thus accumulation of 2,3BPG

Figure 17-22

Reaction Catalyzed by Pyruvate Kinase

Positive effectors	Negative effectors	Other
AMP, ADP	ATP	Reversible phosphorylation
F1,6P	Acetyl-CoA	
F2,6P	NADH	
	Alanine	
	Long-chain fatty acids	

Figure 17-3

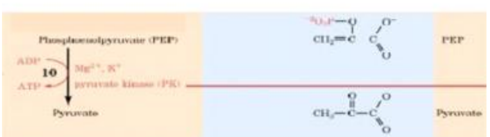
Step 9
Enzyme: Enolase
Enzyme class: Lyase

Overall Balance Sheet of Glycolysis

- We need to account for:
  - Carbon skeleton of glucose
  - Input of P_i and ADP
  - Output of ATP
  - Electrons in the redox rxns

Figure 17-3

Step 10
Enzyme: PK Pyruvate Kinase



Overall Balance Sheet of Glycolysis

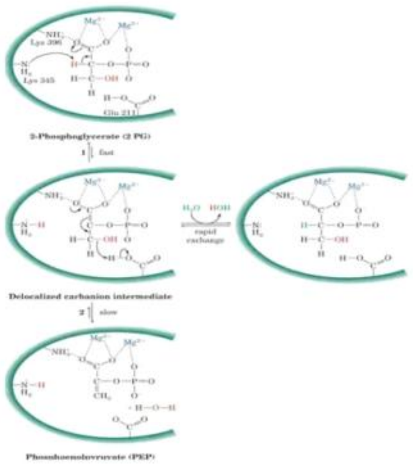
Glucose + 2ATP + $2NAD^+$ + 4ADP + $2P_i$ -->
2 pyruvate + 2 ADP + 2NADH + $2H^+$ + 4ATP + $2H_2O$

Cancel out common terms….

Glucose + $2NAD^+$ + 2ADP + $2P_i$ -->
2 pyruvate + + 2NADH + $2H^+$ + 2ATP + $2H_2O$

Step 10

Figure 17-21



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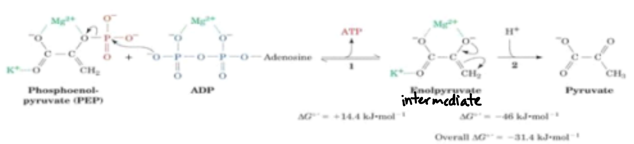
Step 10

Figure 17-22



Mg^{2+} helps stabilize negative charges

ATP needs 30.5kJ/mol so this is perfect energy to make ATP

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How can regulate?

Positive effectors	Negative effectors	Other
AMP, ADP Concentration effects	**ATP** Le'Chatier	**Reversible phosphorylation** dephosphorylated, pyruvate is active. Phosphorylated is inactive.
F1,6P Intermediate in glycolysis. If we have higher concentration then positive effector	**Acetyl-CoA** Is made from pyruvate Le'chatier	
F2,6P Same reason F1,6P	**NADH**	
	Alanine Pyruvate has anabolic and catabolic fates meaning pyruvate can be made to make other biomolecules (alanine is one of those)	
	Long-chain fatty acids Same reason as alanine	

Intermediates are Channeled

- Glycolytic enzymes likely exist as multienzyme complexes
- Complexes ensure efficient passage of metabolites

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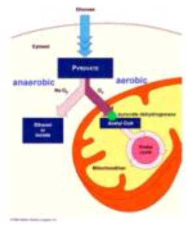
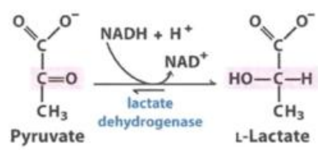
Fates of Pyruvate



- Aerobic respiration
  - Pyruvate --> acetyl-Coenzyme A --> CO_2
  - NADH to electron transport regenerates NAD+
  - We'll discuss this another time
- Anaerobic fermentation
  - Lactic acid fermentation:
    - Pyruvate to lactic acid regenerate NAD+
  - Ethanol fermentation:
    - Pyruvate to acetaldehyde
    - Acetaldehyde to ethanol regenerates NAD+

Homolactic Fermentation



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

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Homolactic Fermentation Balance Sheet

Glucose + 2ADP + $2P_i$ -->
2 lactate + 2ATP + $2H_2O$ + $2H^+$

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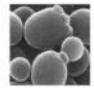
Overall Balance Sheet of Glycolysis

- We need to account for:
  - Carbon skeleton of glucose
  - Input of P_i and ADP
  - Output of ATP
  - Electrons in the redox rxns


Alcohol Fermentation

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Overall Balance Sheet of Glycolysis

Glucose + 2ATP + $2NAD^+$ + 4ADP + $2P_i$ --> 2 pyruvate + 2 ADP + 2NADH + $2H^+$ + 4ATP + $2H_2O$

Cancel out common terms….

Glucose + $2NAD^+$ + 2ADP + $2P_i$ --> 2 pyruvate + + 2NADH + $2H^+$ + 2ATP + $2H_2O$

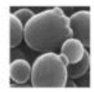
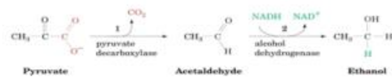


Figure 17-25

Alcohol Fermentation



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Enzymes are in cytisol
More efficient when enzymes are close together

Intermediates are Channeled

- Glycolytic enzymes likely exist as multienzyme complexes
- Complexes ensure efficient passage of metabolites

Fates of Pyruvate

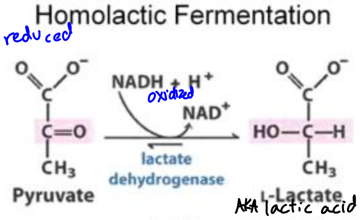
Picture missing

- Aerobic respiration
  - Pyruvate --> acetyl-Coenzyme A --> CO_2
  - NADH to electron transport regenerates NAD+
  - We'll discuss this another time
- Anaerobic fermentation
  - Lactic acid fermentation: occurs in animals
    - Pyruvate to lactic acid regenerate NAD+
  - Ethanol fermentation: occurs in yeast
    - Pyruvate to acetaldehyde
    - Acetaldehyde to ethanol regenerates NAD+

12.5% (2.5M) ethanol yeast can survive
most organisms can't survive >5% ethanol

Homolactic Fermentation

occurs in muscles



$\Delta G'^\circ = -25.1$ kJ/mol
Exergonic reaction

anaerobic

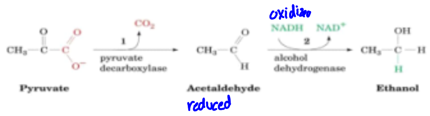
Soreness in muscles due to lactic acid

Slide Missing: Homolactic Fermentation Balance Sheet

Slide Missing: Alcohol Fermentation
- Occurs in wine, beer etc
- Occurs in bread making (bread rises)

Figure 17-25

Alcohol Fermentation



Alcohol dehyrogenase also takes methanol to formaldehyde which is toxic

No time, did not cover here and down

Figure 17-26

Thiamine pyrophosphate.

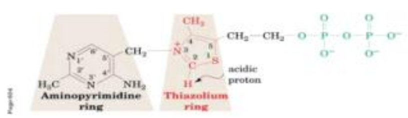


Figure 17-27