Summary of Glycogenolysis and Glycolysis

You have now studied a wealth of information about the central energy pathway of skeletal muscle – glycolysis. This small Topic exists to have you think about all this information and attempt to put the details in a broader context. You are also now armed with the knowledge to tally ATP regeneration from this pathway when starting from glycogen or glucose. Invest some time to understanding the process involved in tallying ATP. This is an effective method of studying, ensuring understanding and not memorization. Once you have completed the Topics on Mitochondrial Respiration you will be able to compare ATP yields from different substrates and pathways.

As expressed for the combined total of all reactions of glycogenolysis and glycolysis, these combined pathways are regulated at four key reactions; phosphorylase, hexokinase, PFK and PK. I add phosphorylase to glycolysis here, as glycogenolysis provides a rapid source of G6P for glycolysis during moderate to intense exercise. I hope you have noticed that such enzyme regulation shared common activators (AMP, ADP) and inhibitors (ATP, fatty acids, acetyl-CoA, G6P) so that either the presence of an activator and/or the removal of an inhibitor contributed to increased enzyme activity. Remember back to bioenergetics, for even if a reaction is highly exergonic, it will not occur at a meaningful rate of product formation without an active enzyme. Controlling enzymes literally means controlling reactions and metabolic pathways.

Another important point to reflect on is the pattern of standard free energy release as substrate progresses through glycolysis. Table 1 presents the standard and absolute free energy changes for the reactions of glycogenolysis and glycolysis. Note that the absolute delta G for these reactions reveals a pattern to all enzyme regulated reactions. Each of the phosphorylase, hexokinase, PFK, and PK reactions are highly exergonic. The only unregulated highly exergonic reaction is that of phosphoglycerate kinase. However, given that each of PFK and PK are regulated, spanning the start and end of glycolysis, respectively, there is really no additional regulation needed for the glycolytic pathway.

All the remaining glycogenolytic and glycolytic reactions are close to equilibrium. Thus, these reactions will change direction depending on changing substrate and product concentrations. When there is ample substrate for glycolysis, then product formation will increase the substrate for the next reaction, making it more exergonic and in the direction of substrate flux through glycolysis. Conversely, when PK is inhibited, substrate flux will be impaired, substrates will accumulate as the product of the prior reaction, and lower the delta G for prior reactions.

Added discussion will occur for the fate of pyruvate to lactate production in the Topic on Lactate Production.

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Table 1. The standard and absolute changes in free energy for the reactions of glycogenolysis and glycolysis.

Enzyme Reaction	ΔG°'	ΔG	Metabolite	μmol/L^
Phosphorylase*	**-4.5**	**-3.87**	**Glycogen**	200,000
Phosphogluco mutase	**-0.5**	**-0.98**	**Pi**	5000
Hexokinase	**-4.0**	**-6.72**	**G1P**	1800
Phosphoglucose isomerase	**-0.4**	**-1.18**	**Glucose**	550
Phosphofructokinase	**-3.4**	**-6.33**	**G6P**	3900
Aldolase	**5.7**	**6.38**	**F6P**	1100
Triose phosphate isomerase	**1.8**	**1.98**	**ATP**	10000
Glyceraldehyde-3-phosphate dehydrogenase	**1.5**	**-5.50**	**ADP**	60
Phosphoglycerate kinase	**-4.5**	**-3.65**	**F16P**	1580
Phosphoglyeromutase	**1.1**	**-0.32**	**DHP**	60
Enolase	**0.4**	**1.13**	**G3P**	80
Pyruvate kinase	**-7.5**	**-3.26**	**1,3BPG**	50
Lactate dehydrogenase	**-1.0**	**1.25**	**NAD^+**	540
			NADH	50
			3PG	200
			2PG	20
			PEP	65
			Pyr	380
			Lac	1350

* due to the structure of glycogen, bioenergetic calculations are not valid. ^Note that this unit expression is for umol/L of cell water, which would equate to being approximately 1.3 times higher than the concentration per kg of muscle wet weight (wt) (e.g. muscle lactate ~ 1 mmol/kg wet wt); 1 μmol = 1000 mmol.

The Tally of ATP Regeneration From Glycolysis

It is a useful exercise to sum the ATP regenerated from glycolysis. Historically, this used to be a mundane task for studying glycolysis, as the pathway was always presented as starting with glucose. Hopefully you are now convinced that this is erroneous, and that there needs to be clarification given to the proportion of G6P derived from glycogen vs. blood glucose. Anyway, Table 2 provides a table of ATP sums for glycolysis when starting with either glucose or glycogen. As shown, there are two ATP regenerated from glucose and 3 regenerated from glycogen. This is not a trivial difference when considering the rate of substrate flux through glycolysis. Although the 33% difference is obvious, you will be amazed how much more absolute ATP per unit time can be regenerated from glycolysis when glycogenolysis provides the bulk of the G6P.

Summary of Glycogenolysis and Glycolysis

Table 2. The ATP tally for glycogenolysis and glycolysis when starting from either glycogen or glucose.

Enzyme Reaction	Gluc	Glyc	NADH	ATP Eq
Enzyme Reaction	**ATP**	**ATP**	**NADH**	**ATP**
Phosphorylase*				
Phosphogluco mutase				
Hexokinase	**-1**			**-1 or 0**
Phosphoglucose isomerase				
Phosphofructokinase	**-1**	**-1**		**-1**
Aldolase				
Triose phosphate isomerase				
Glyceraldehyde-3-phosphate dehydrogenase			**2**	**4***
Phosphoglycerate kinase	**2**	**2**		**2**
Phosphoglyeromutase				
Enolase				
Pyruvate kinase	**2**	**2**		**2**
Glycolysis Totals	**2**	**3**	**2**	
Total ATP Equivalents - Aerobic				**8 or 9**
Total ATP Equivalents - Anaerobic				**2 or 3**

*assumes glycerol-3-phosphate shuttle