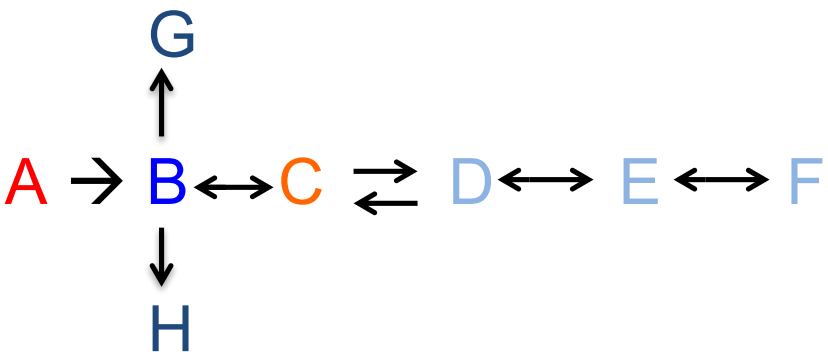
ANSC/FSTC 607
Physiology and Biochemistry of Muscle as a Food
CONTROL REACTIONS AND ENZYME KINETICS

I. Identification of control reactions in a pathway



A. Where is the regulatory reaction?

1. At unidirectional reactions (**A → B, B → G, B → H, C → D**).
2. Early in the sequence or pathway (**A → B, C → D**).
3. At branch points (**B → G, B → H**).
4. At steps where the reverse reaction is catalyzed by a different enzyme (**C ←→D**).

B. Kinetic considerations

1. Maximal reaction rate (i.e., number of binding sites), $\mathbf{V_{max}}$
2. Affinity of the enzyme for its substrate, $\mathbf{K_m}$ (or $K_{s.5}$)
3. Equilibrium constants and mass action ratios
4. Allosteric activators and inhibitors

C. Possible control reactions and respective controls

1. Hexokinase (**A → B**)	G-6-P (–)
2. Glycogen synthetase (**B → G**)	G-6-P (+)
3. Glycogen phosphorylase	AMP, Ca^{++} (+), ATP (–)
4. 6-Phosphofructokinase	ATP + citrate (–)), overcome by F-6-P, AMP, P_i, 6-PG, F-2,6-P_2 (+)
5. Glyceraldehyde-3-P-DH	NAD/NADH ratio
6. Pyruvate kinase	F-1,6-P_2, 6-PG, F-2,6- P_2 (+), ATP (–)

D. Equilibriium constants (K_{eq}) and Mass Action Ratio (MAR)

1. K_{eq} is measured under set conditions of concentration (1 M), temperature (20°C), and pressure (1 atmosphere).

2. MAR is calculated from actual intracellular concentrations of reactants and products.

e.g., the 6-PFK reaction: F-6-P + ATP → F-1,6-P_2 + ADP

$$K_{eq} = \frac{[\text{F-1,6-P}_2] \times [\text{ADP}]}{[\text{F-6-P}] \times [\text{ATP}]} \quad \textit{under set conditions}$$

and

$$\text{MAR} = \frac{[\text{F-1,6-P}_2] \times [\text{ADP}]}{[\text{F-6-P}] \times [\text{ATP}]} \quad \textit{actual cellular conditions}$$

Enzyme	Activities	K_{eq}	MAR
Hexokinase	1.5	4,000	0.08
Phosphoglucoisomerase	176	0.4	0.24
6-Phosphofructokinase	56	1,000	0.03
Aldolase	78	0.0001	0.00001
Triosephosphate isomerase	2,650	0.04	0.24
Glyceraldehyde-3-phosphate dehydrogenase plus phosphoglycerate kinase	440/169	1,000	9
Phosphoglycerate mutase	100	0.1	0.12
Enolase	158	3.5	1.4
Pyruvate kinase	387	2-20,000	40

II. Enzyme kinetics

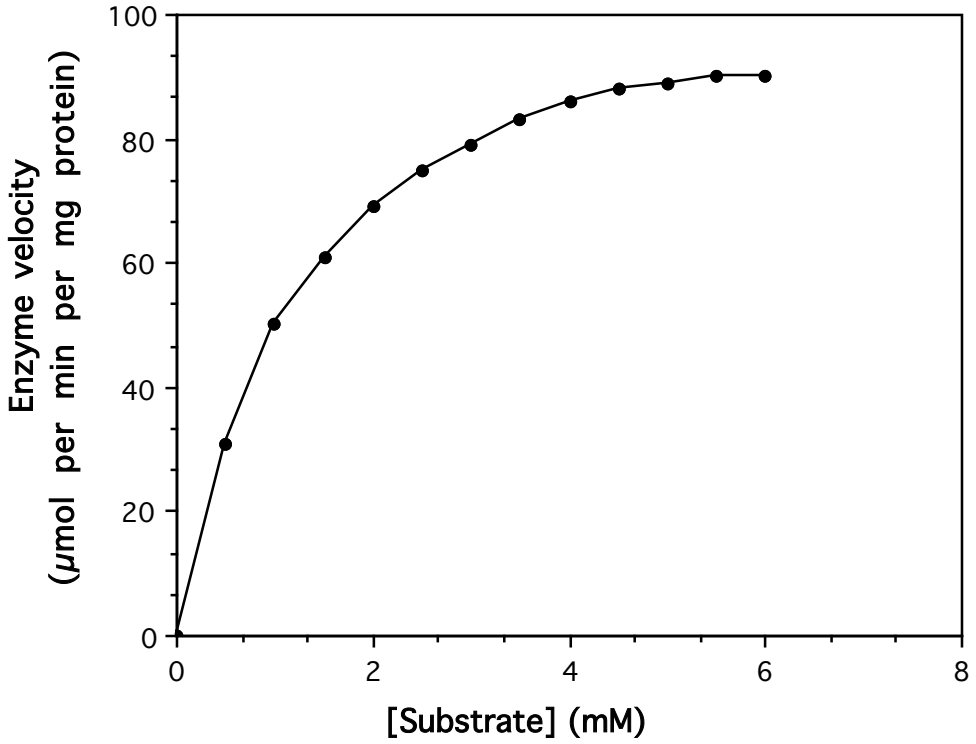
A. Reaction rates

1. Zero order
2. First order
3. Mixed order

B. Effect of substrate concentration

1. Michaelis-Menton hypothesis
2. Significance of K_m

3. Relationship of K_m, substrate concentration, and reaction order



III. Other kinetics

A. Sigmoidal kinetics -- K_s

1. Indicates cooperativity
2. Can be caused by allosteric effectors, pH, salts

B. Allosteric effectors

1. Inhibitors
2. Activators
3. Allows decision making between pathways.

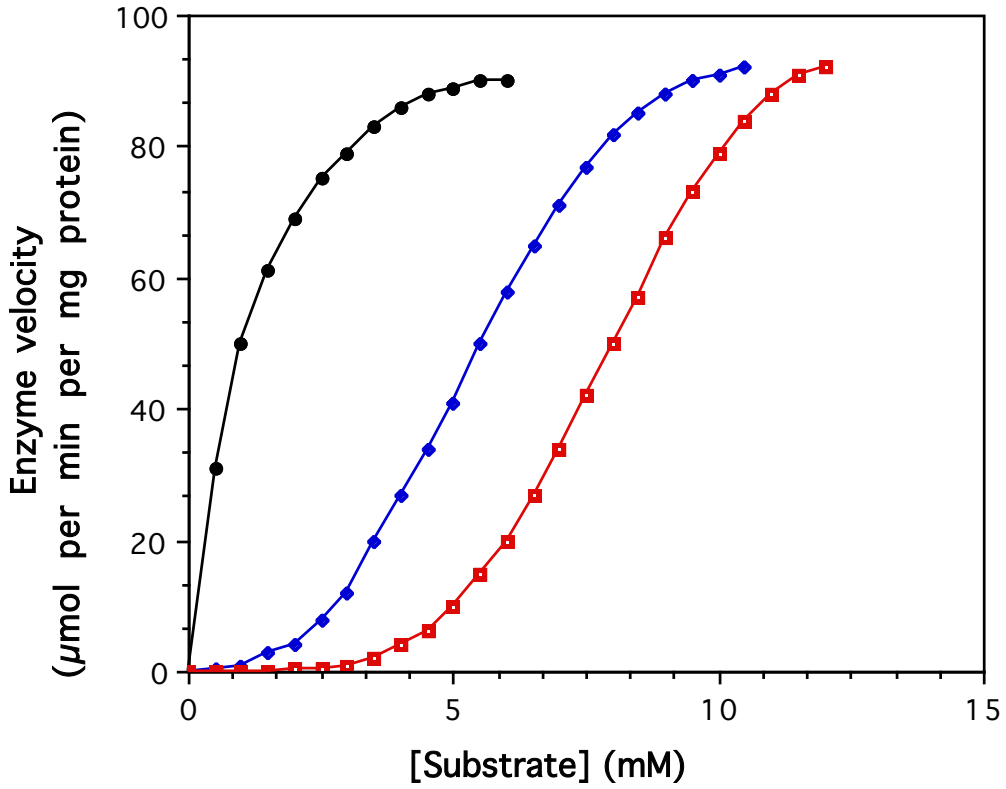
IV. Regulation of cellular processes

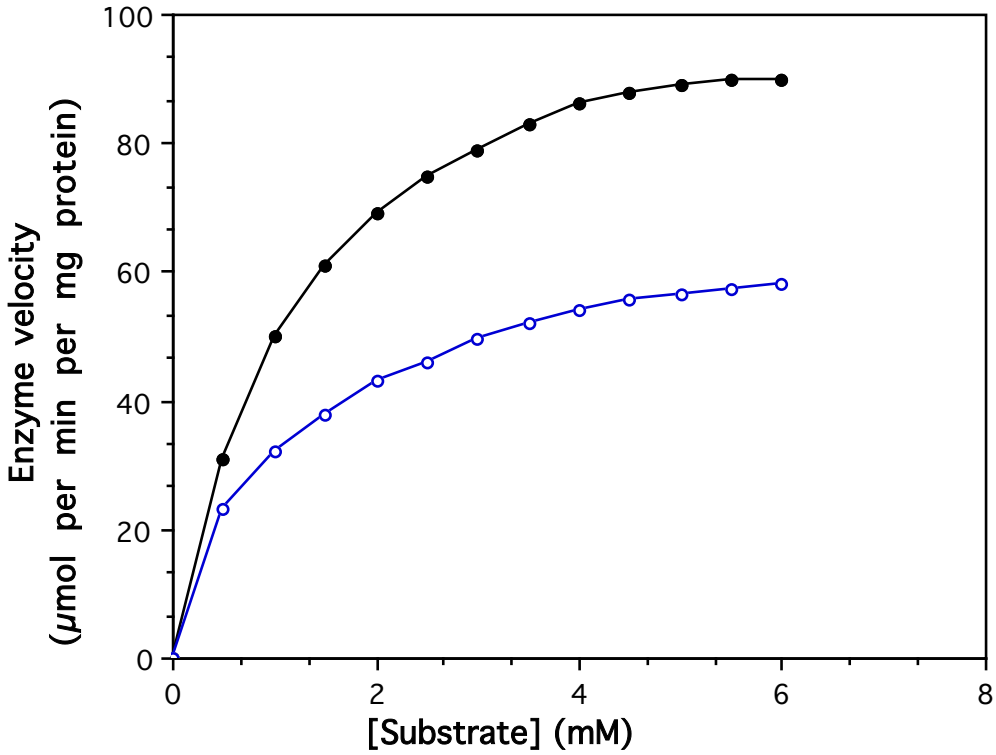
A. Change in amount of enzyme

1. Adaptive vs constuitive
2. Time required -- *slow*

B. Phosphorylation of enzymes

1. Glycogen metabolism
2. Lipid metabolism
3. *Fast*


Enzyme velocity
(μmol per min per mg protein)
100
80
60
40
20
0
0
5
10
15
[Substrate] (mM)


Enzyme velocity
(μmol per min per mg protein)
100
80
60
40
20
0
0
2
4
6
8
[Substrate] (mM)