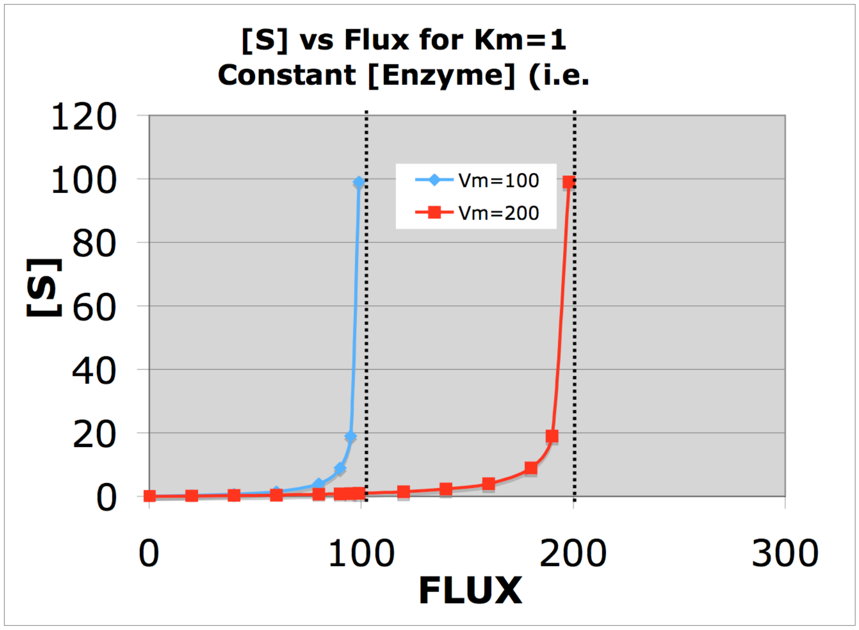
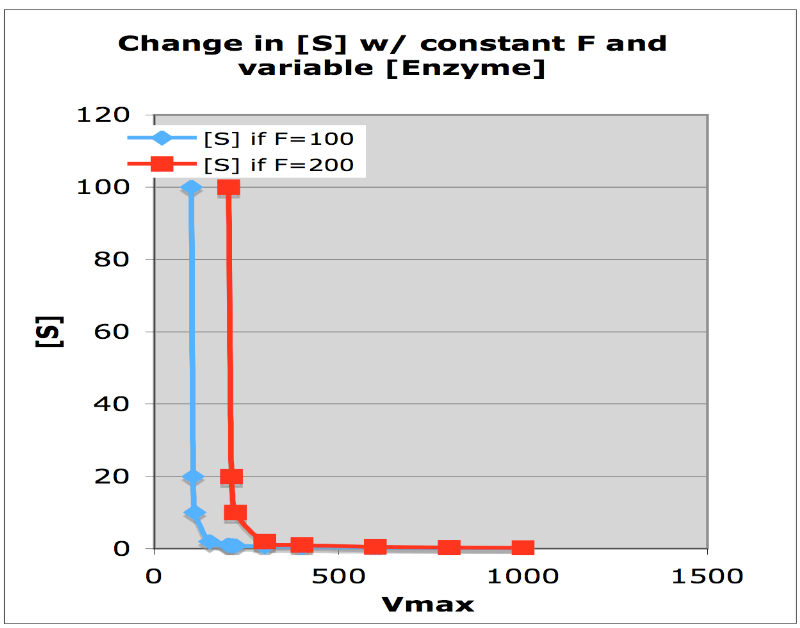
Key for Flux Problems-

Q1. As flux approaches Vmax, [S] rises catastrophically to maintain flow.



Q2. Remember Vmax is largely controlled by the amount of enzyme. So just as above when [enzyme] drops to where Vmax is almost the same as flux we again see catastrophic rise in [S]. Notice also how between F=150 to 1000 there is really not much change in [S]



Q3. A. [S] increases by ~ 230% (e.g. 100% x 13.3/5.7)
B. . [S] increases by ~ 20%

Flux =	85	Flux =	95
Vmax =	100	Vmax =	100
Km =	1	Km =	1
[S] =	5.7	[S] =	19

P1. 85% of Vmax

		50%	2X Substrate	5X Substrate
Flux =	85			
Vmax =	100	8.505	11.34	28.35
Km =	1	<89.5	<92	<96.6
[S] =	5.67			
	5.666666667			

P2. 35% of Vmax

		50%	2X Substrate	5X Substrate
Flux =	35			
Vmax =	100	0.81	1.08	2.7
Km =	1	<45	<52	<73
[S] =	0.54			
	0.54			

The message of these two problems is that an enzyme step at 35% Vmax can absorb much larger changes in flux without getting to dangerous [S] than can a step operating at 85 % Vmax. Notice for example that in Problem 1 only a 13.6% rise in flux leads to a 400% increase in [S] (going from F=85 to F=96.6). On the other hand, it takes a <u>108%</u> rise in flux (35 to 75) in a system operating at 35% Vmax to increase [S] by 400%.

P3. There is no real quantitative answer here, it's just a thought problem based on the previous questions. Recall that intermediate steps are at a steady state, often near $\Delta G'=0$, but NOT at equilibrium. Based on Problem 1 and 2 and Question 2 you can see that you can have enormous changes in flux without huge changes in [S], i.e. a steady state. This steady state in turn is enforced by flow from flux controlling points of entry (and to some extent also points of exit) which maintain [S] different from equilibrium. If flux-controlling steps were completely shut off, intermediate steps would quickly move to equilibrium. The [S] that is necessary to maintain a steady state, in turn, is also determined by Vmax (enzyme concentration and intrinsic activity) <u>and</u> Km. These factors can be controlled genetically and by allosteric control.

P5. From the answer to questions above it is clear that if the enzyme present were operating near Vmax a modest increase in flux would lead to big changes in [S] which could have toxicity and could be even more wasteful than synthesizing a little extra enzyme. In order to be responsive to the needs of the organism, metabolic fluxes need to be able to adjust quickly (think fight or flight). The slow reacting organism probably gets eaten!