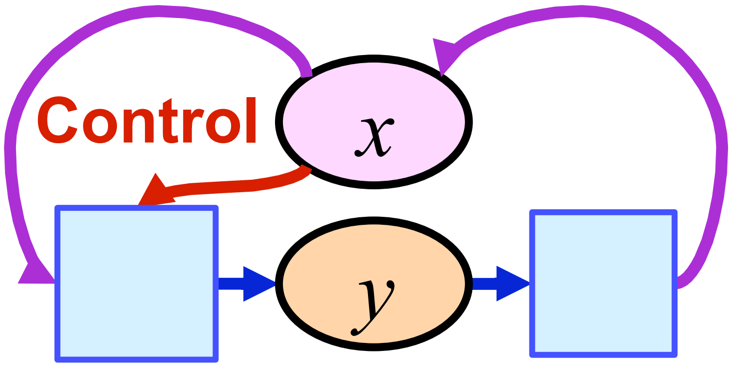
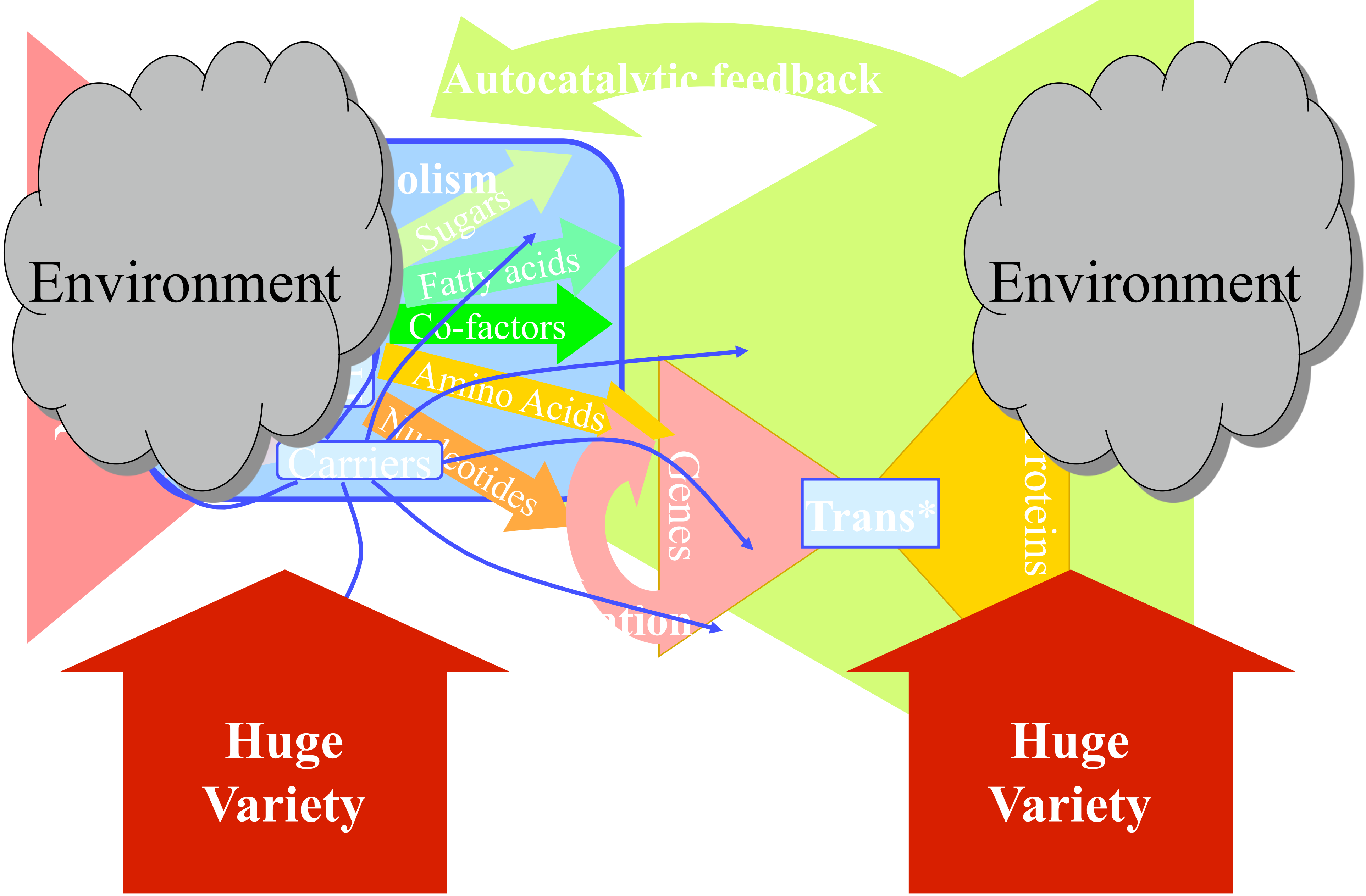
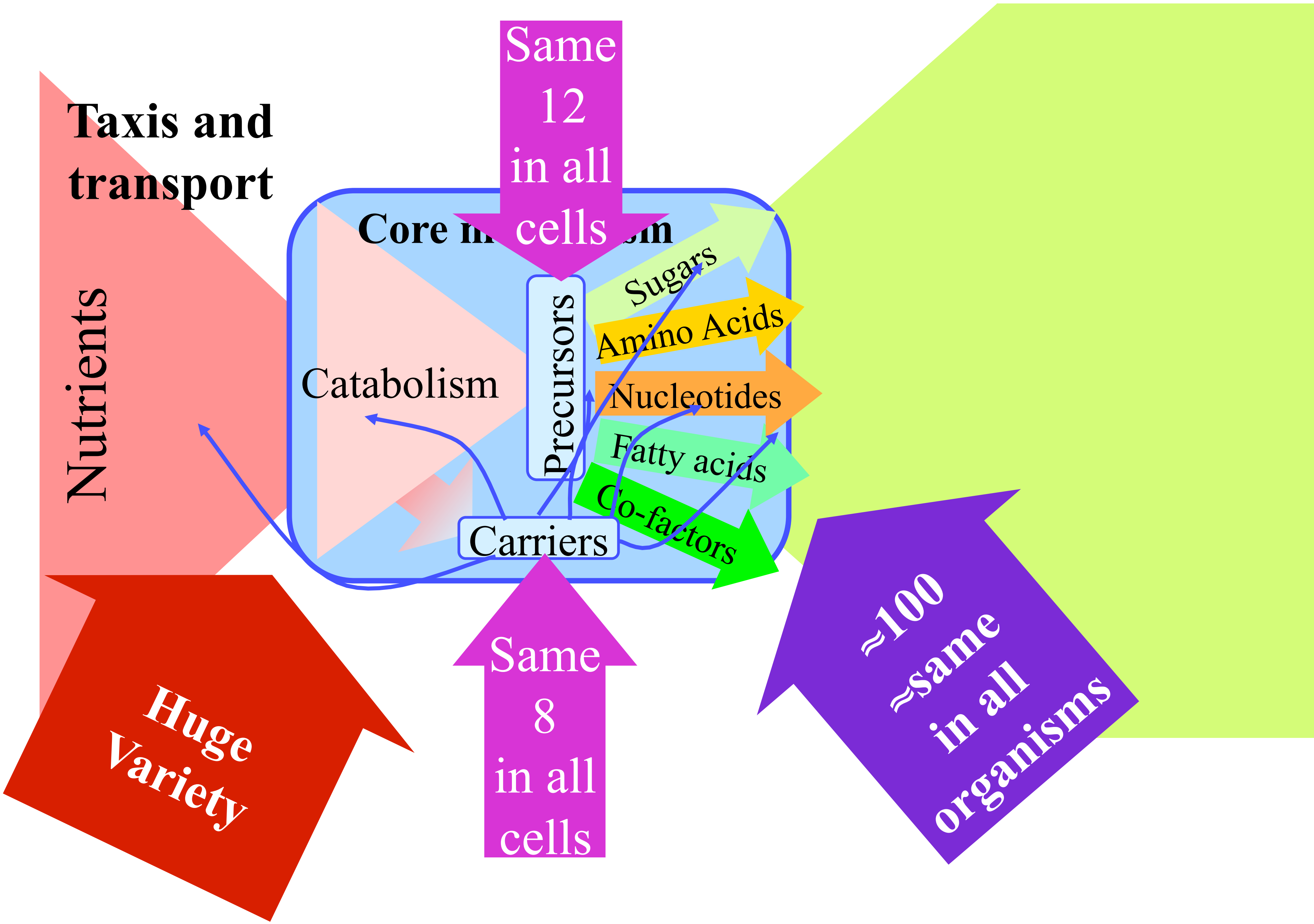


- How to get rid of the RHP zero?
- What are the new tradeoffs?

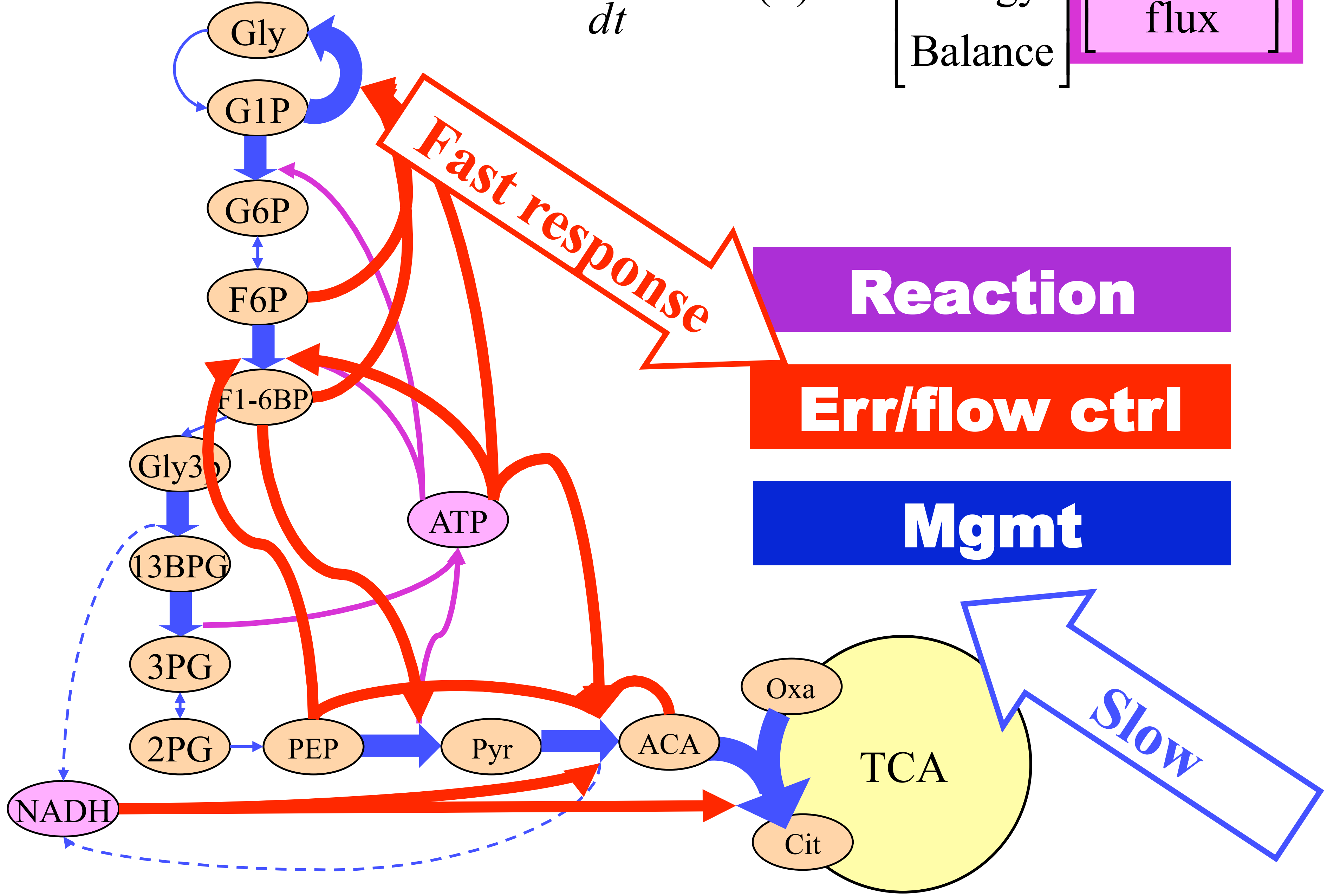
$$\frac{1}{\pi}\int_0^\infty \ln\left|S(j\omega)\right| \frac{z}{z^2+\omega^2}\,d\omega \geq \ln\left|\frac{z+p}{z-p}\right|$$

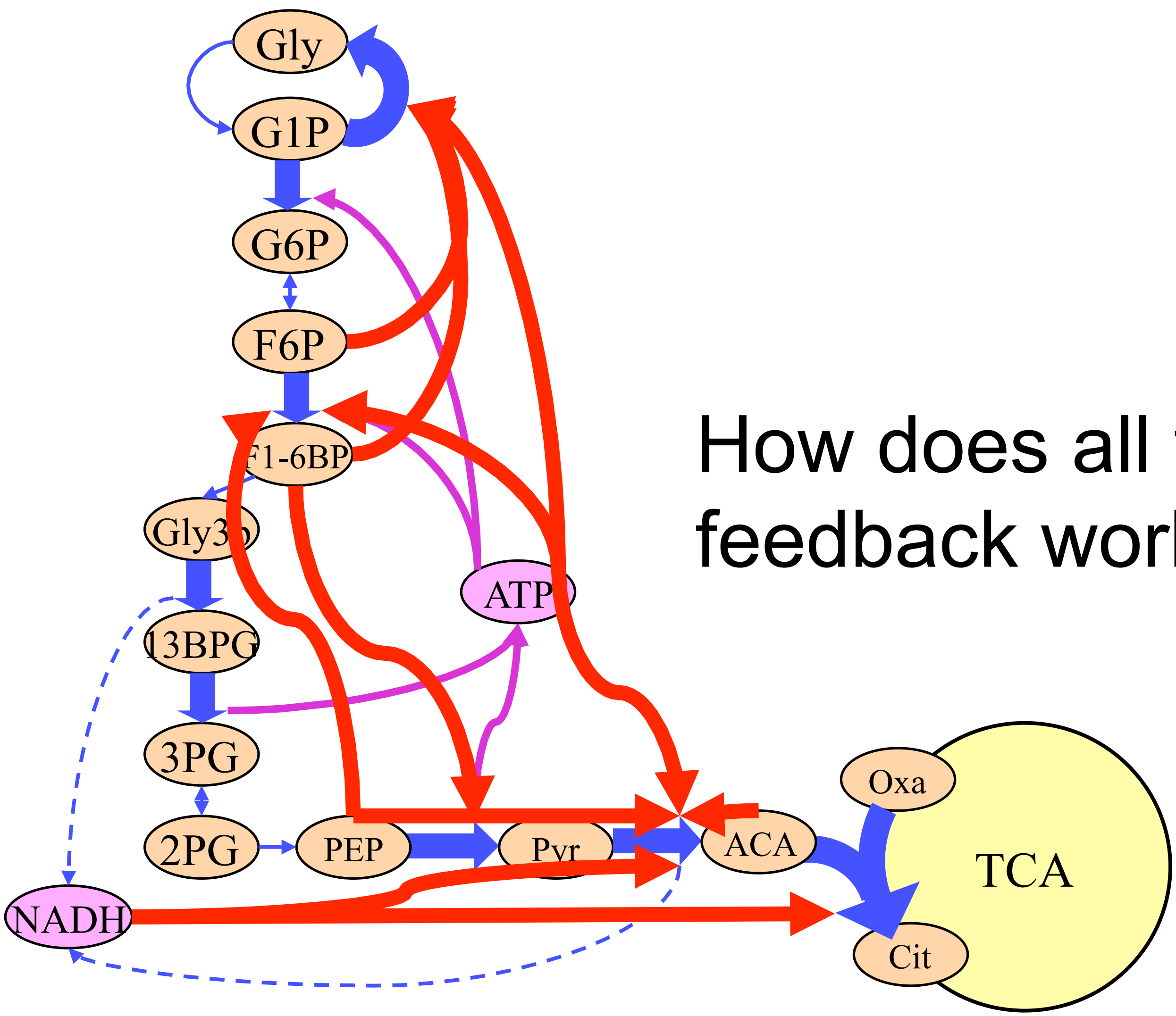
Bacterial cell



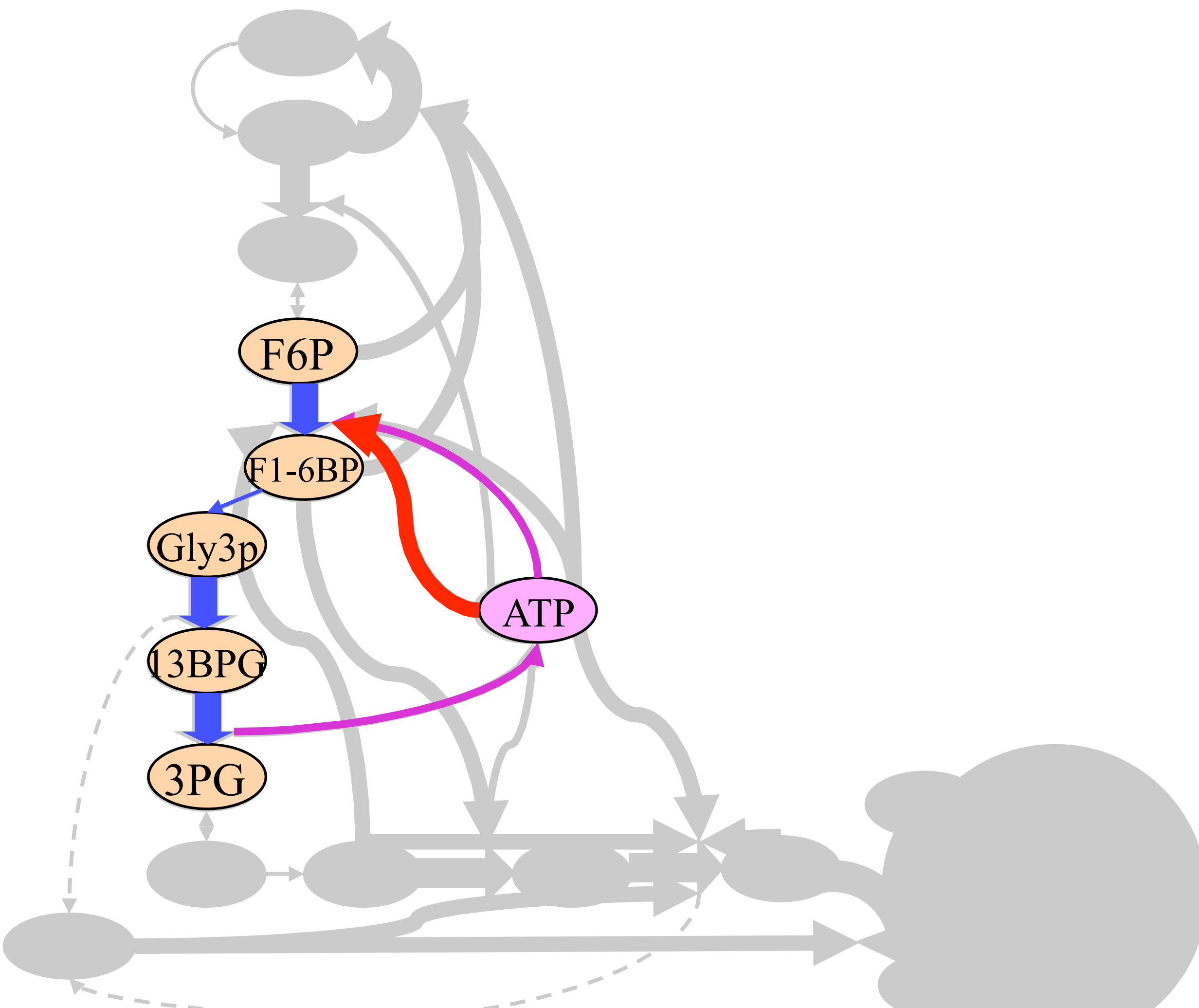

Same
12
in all
cells
Taxis and transport
Nutrients
Core metabolism
Catabolism
Precursors
Sugars
Amino Acids
Nucleotides
Fatty acids
Co-factors
Carriers
Huge Variety
Same
8
in all
cells
≈100
≈same
in all
organisms

$$\frac{dx}{dt} = Sv(x) = \begin{bmatrix} \text{Mass \&} \\ \text{Energy} \\ \text{Balance} \end{bmatrix} \begin{bmatrix} \text{Reaction} \\ \text{flux} \end{bmatrix}$$

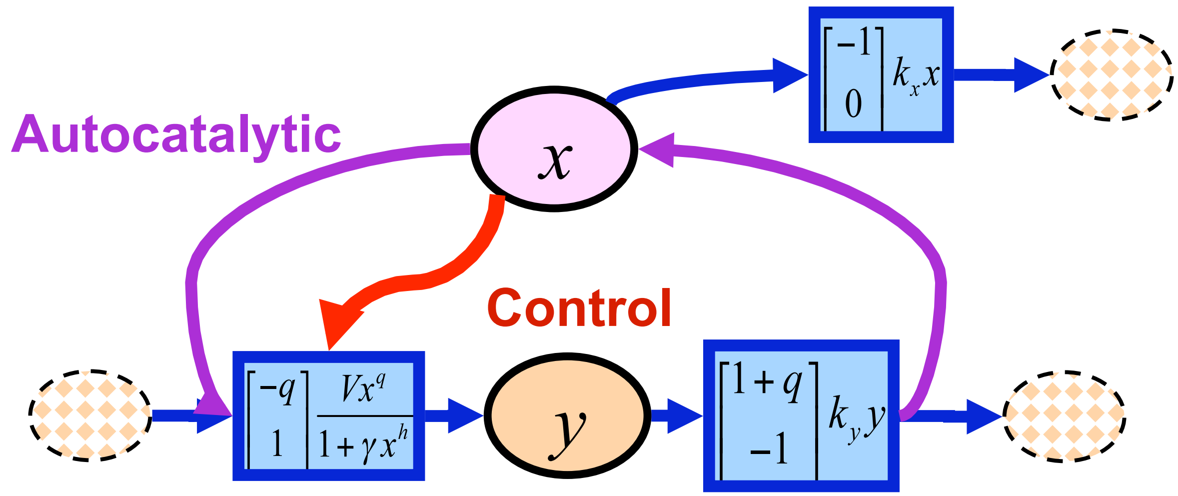




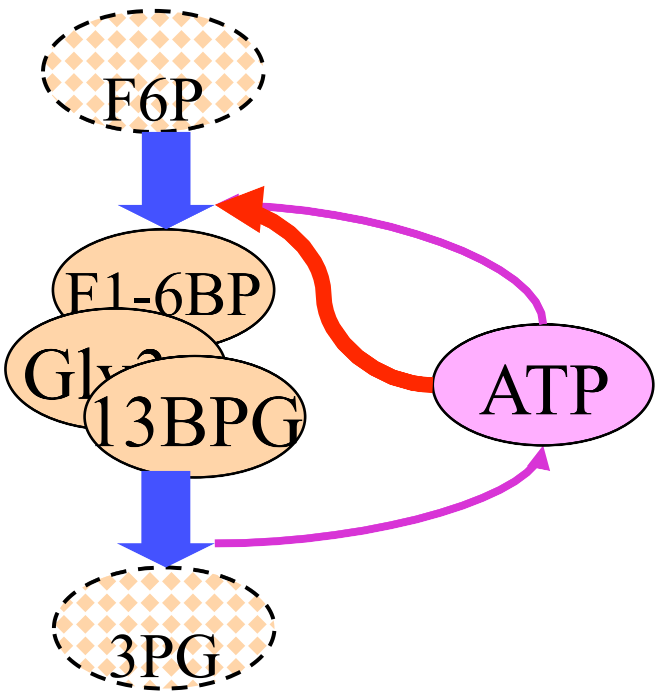
How does all this feedback work?



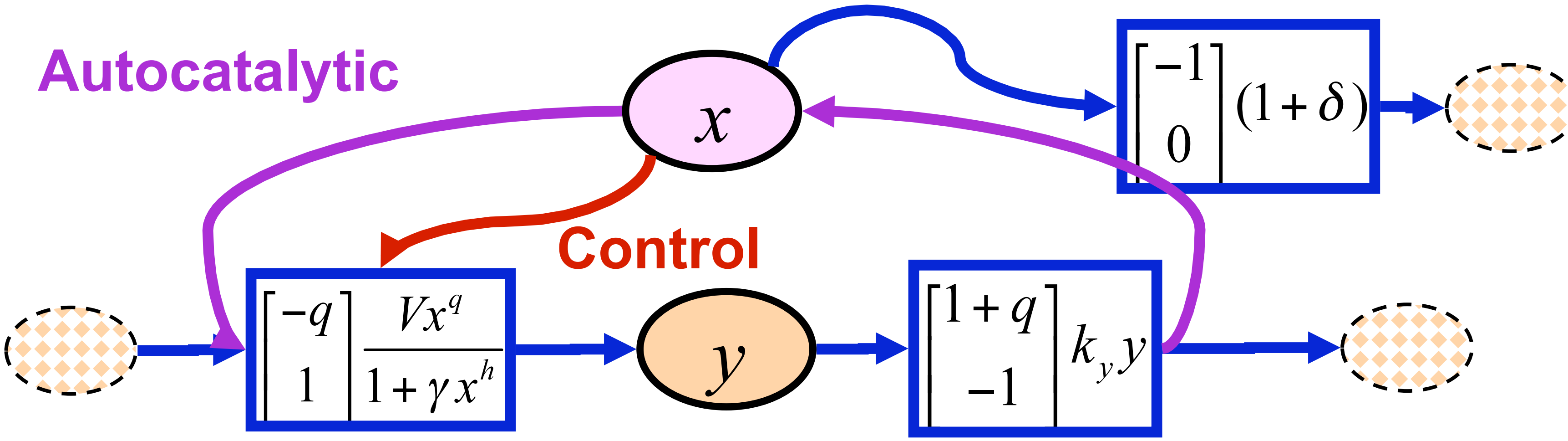
F6P
F1-6BP
Gly3p
13BPG
3PG
ATP



Autocatalytic
x
Control
y
$\begin{bmatrix}-1\\0\end{bmatrix} k_x x$
$\begin{bmatrix}-q\\1\end{bmatrix} \frac{Vx^q}{1+\gamma x^h}$
$\begin{bmatrix}1+q\\-1\end{bmatrix} k_y y$



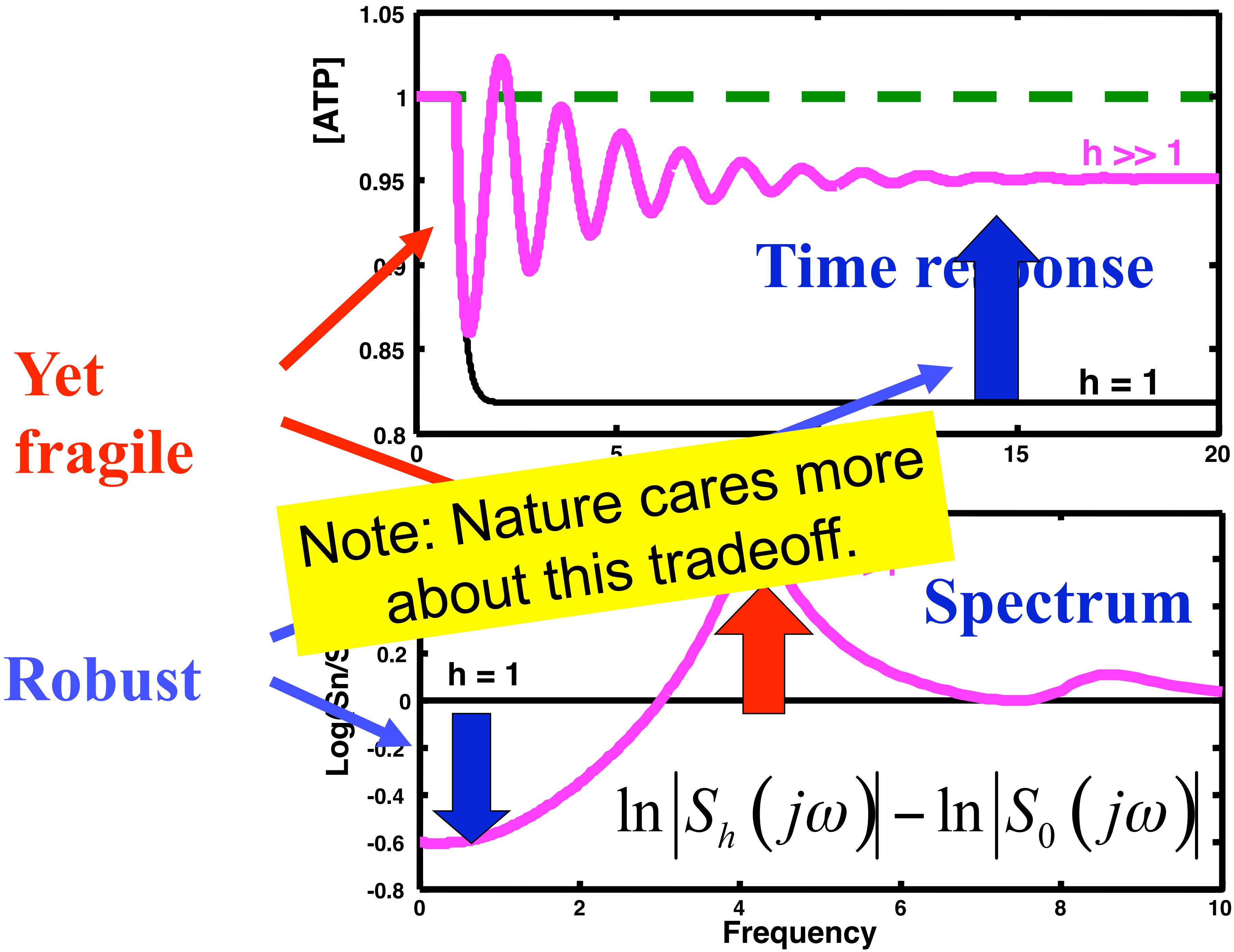
F6P
F1-6BP
13BPG
ATP
3PG



Autocatalytic

$$\begin{bmatrix}\dot{x}\\ \dot{y}\end{bmatrix} = \begin{bmatrix}-q\\ 1\end{bmatrix}\left(\frac{Vx^q}{1+\gamma x^h}\right) + \begin{bmatrix}1+q\\ -1\end{bmatrix}ky + \begin{bmatrix}-1\\ 0\end{bmatrix}(1+\delta)$$

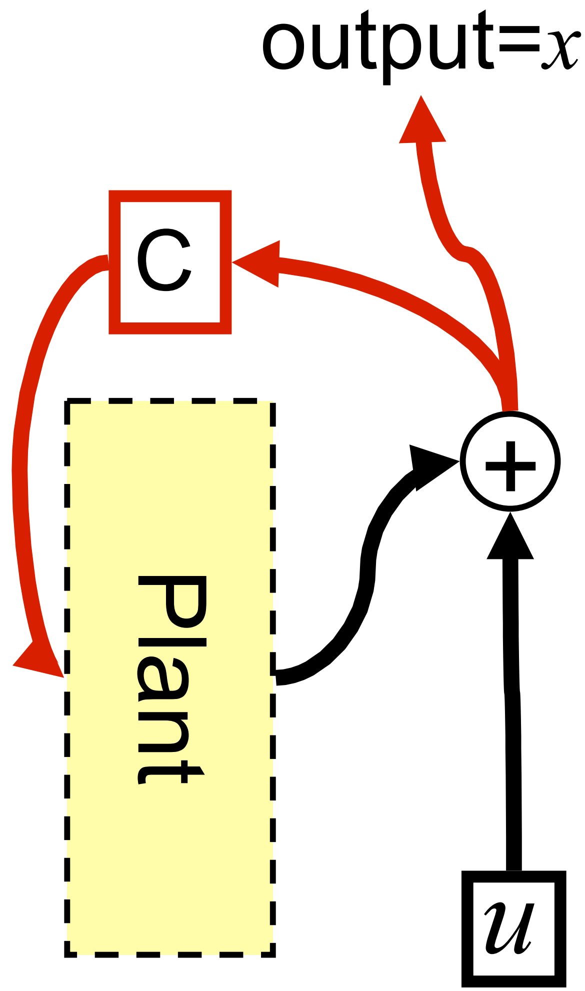
Control


Yet
fragile
Robust
[ATP]
1.05
1
0.95
0.9
0.85
0.8
0
5
15
20
h >> 1
h = 1
Time response
Note: Nature cares more about this tradeoff.
Spectrum
Log(Sn/S
0.2
0
-0.2
-0.4
-0.6
-0.8
h = 1
$\ln\left|S_h(j\omega)\right| - \ln\left|S_0(j\omega)\right|$
0
2
4
6
8
10
Frequency

$$S(j\omega) = \frac{X(j\omega)}{U(j\omega)}$$

$$\frac{1}{\pi}\int_0^{\infty} \ln\left|S(j\omega)\right| d\omega \geq 0$$

$$\frac{1}{\pi}\int_0^{\infty} \ln\left|S(j\omega)\right| \frac{z}{z^2+\omega^2} d\omega \geq \ln\left|\frac{z+p}{z-p}\right|$$



Small z is *bad*.

$$z = \frac{k}{q} \qquad p = RHPzero\left\{s^2 + (q\alpha + k)s - \alpha k\right\}$$

Small z is *bad* (oscillations and crashes)

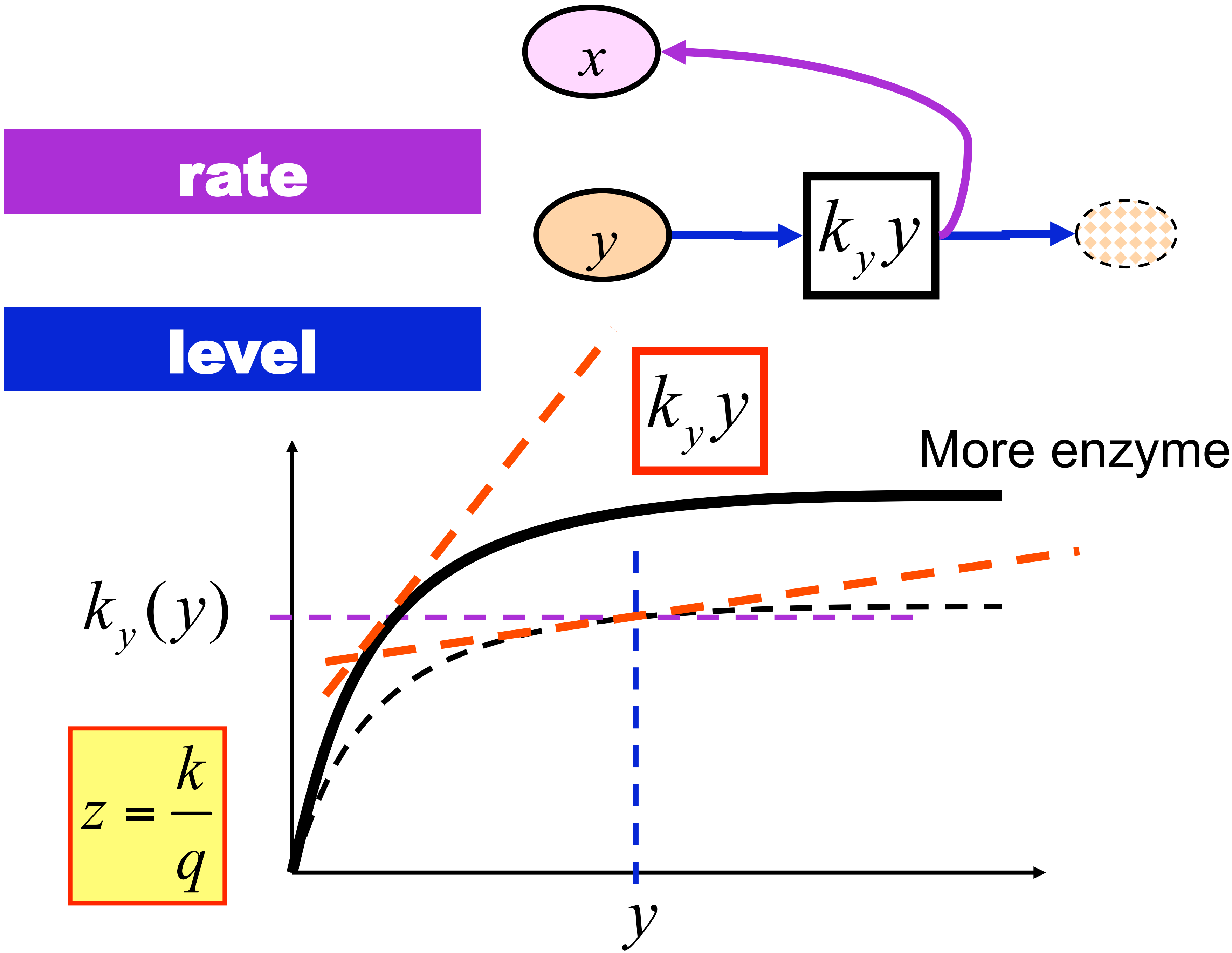
$$\frac{1}{\pi}\int_0^{\infty}\ln\left|S(j\omega)\right|\frac{z}{z^2+\omega^2}d\omega \geq \ln\left|\frac{z+p}{z-p}\right|$$

Small z =
- **small k and/or**
- **large q**

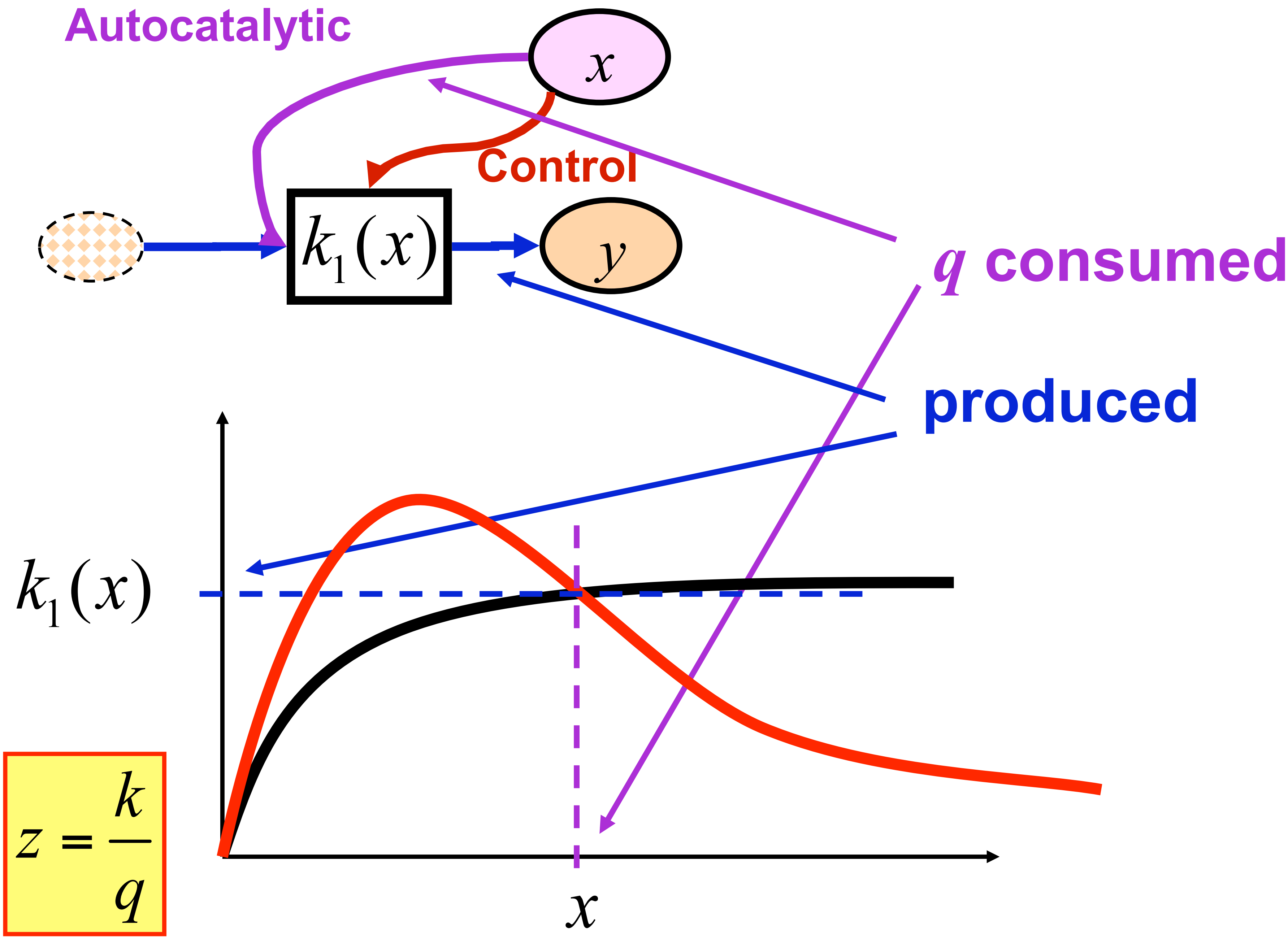
Efficiency =
- **small k and/or**
- **large q**

$$z = \frac{k}{q}$$

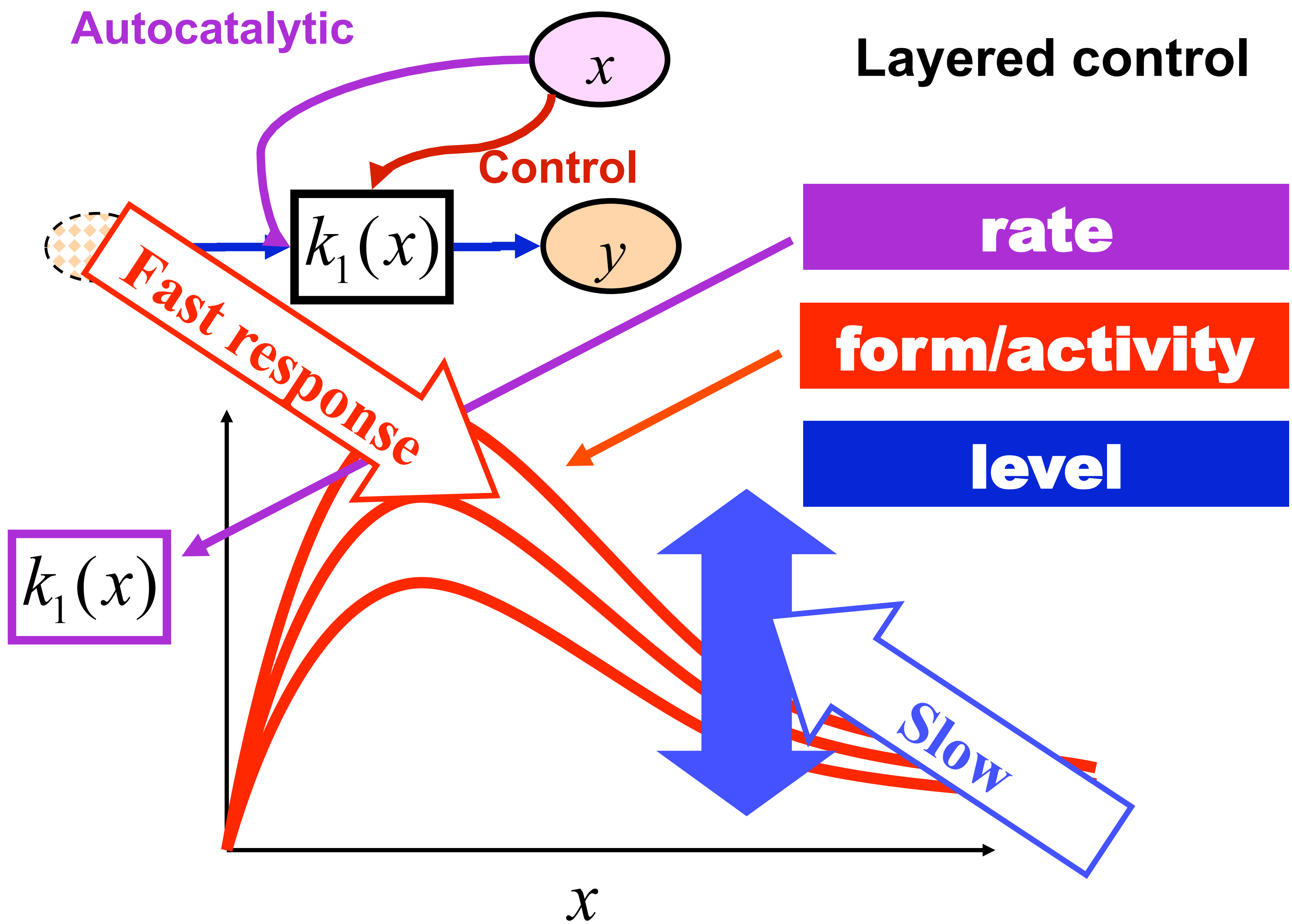
Correctly predicts conditions with "glycolytic oscillations"



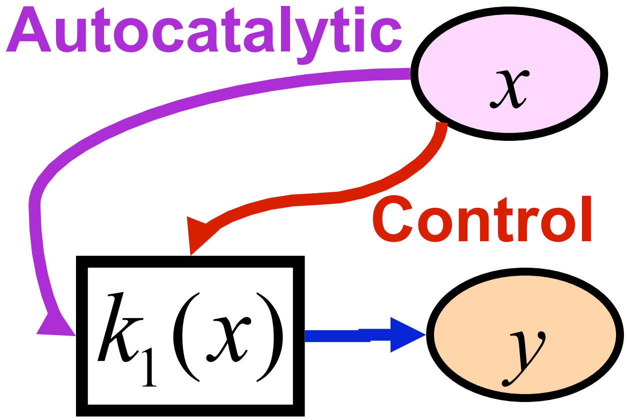
rate
level
x
y
$k_y y$
$k_y y$
More enzyme
$k_y(y)$
$z = \frac{k}{q}$
y



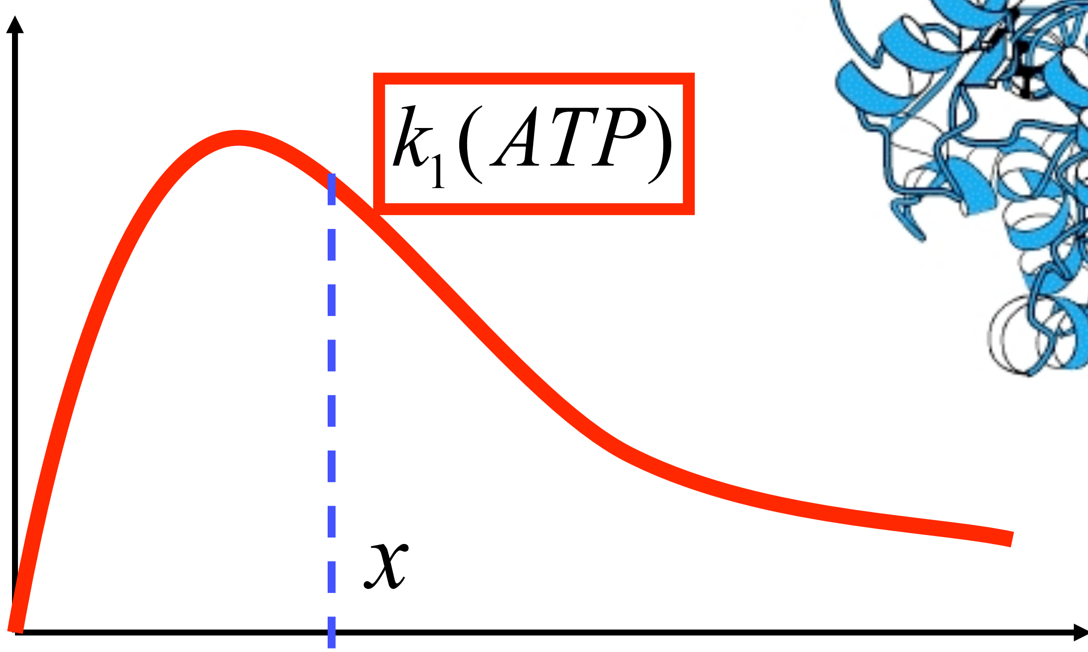
Autocatalytic
x
Control
$k_1(x)$
y
q consumed
produced
$k_1(x)$
x
$z = \frac{k}{q}$

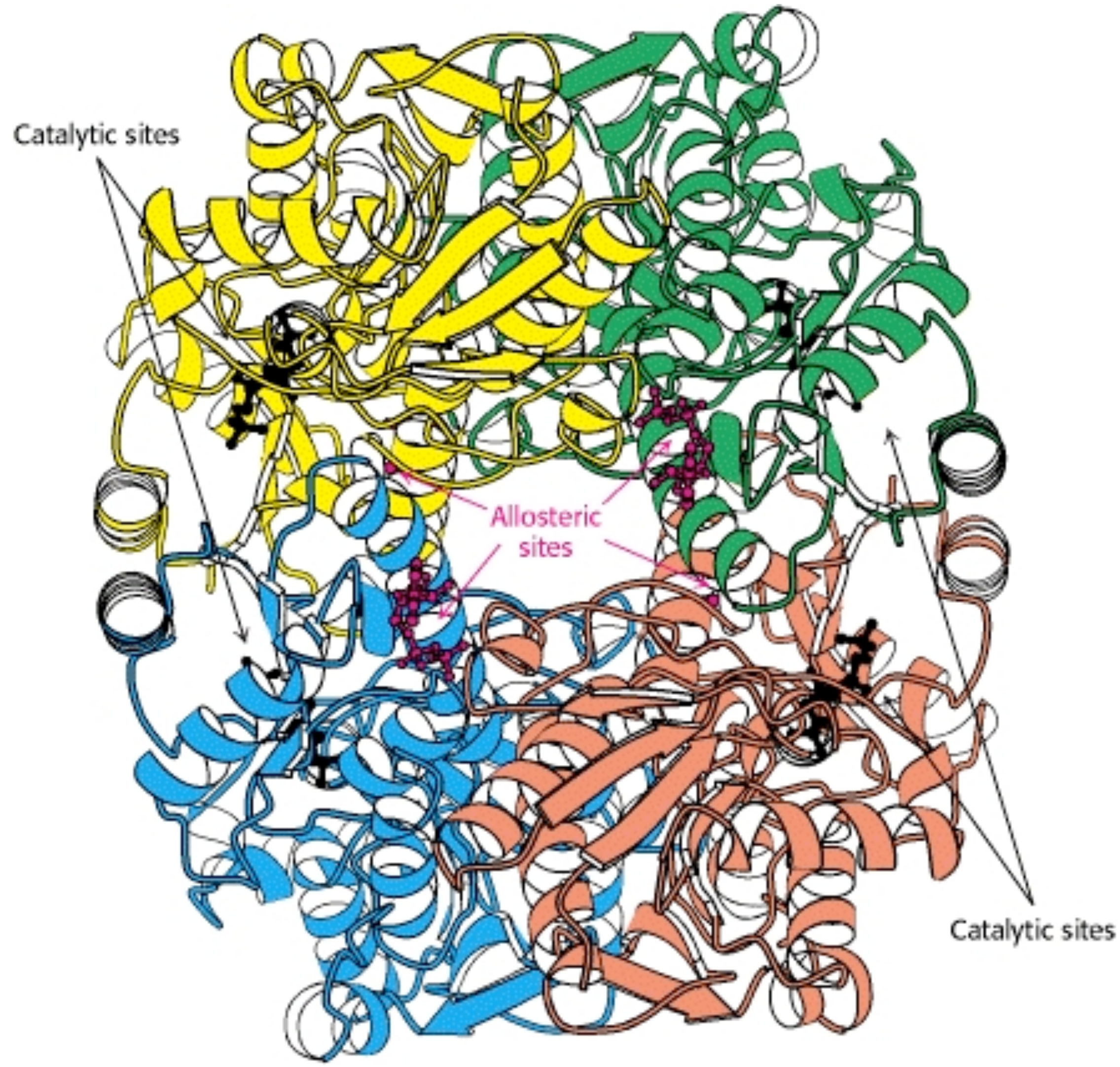


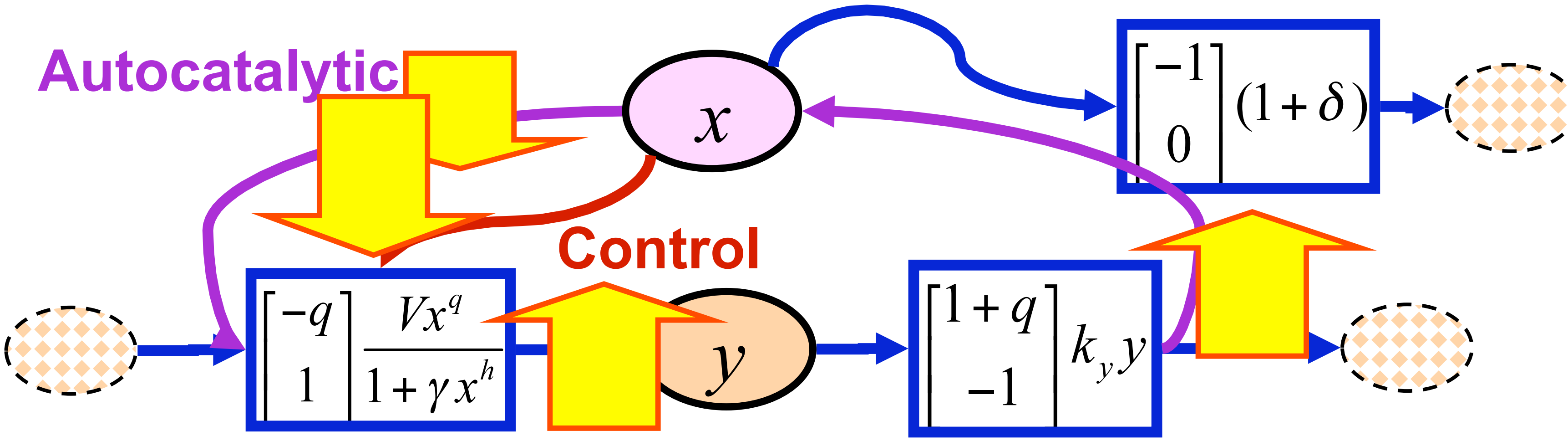
Autocatalytic
x
Control
Layered control
$k_1(x)$
y
rate
form/activity
level
Fast response
Slow
$k_1(x)$
x

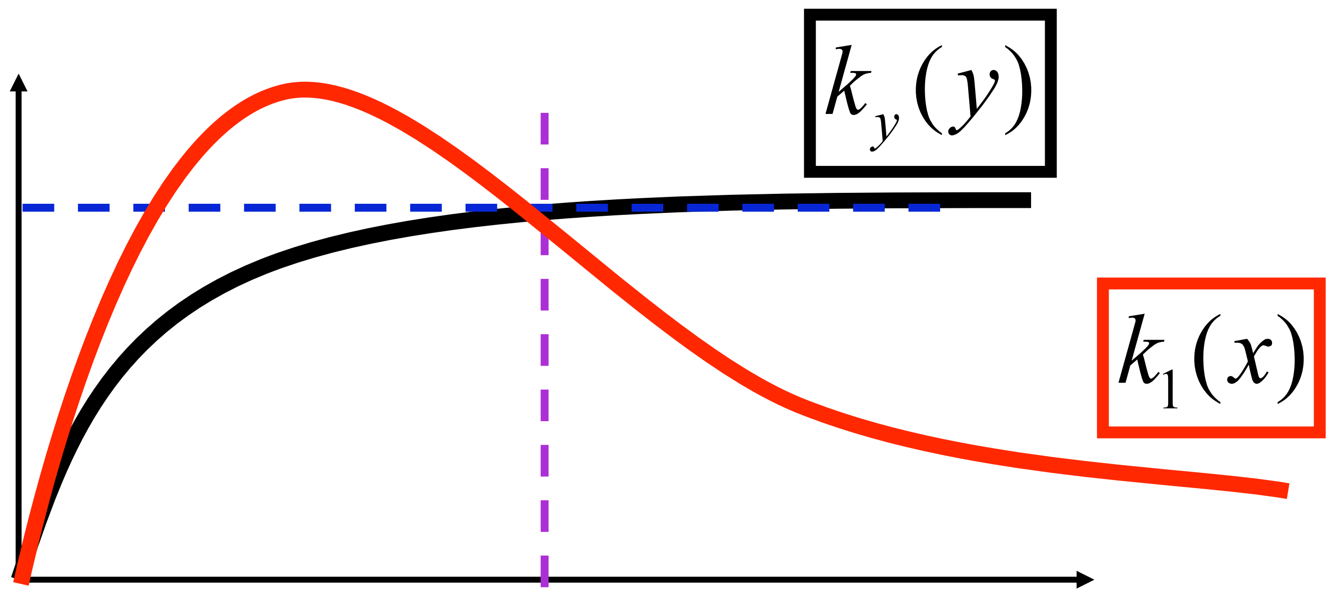


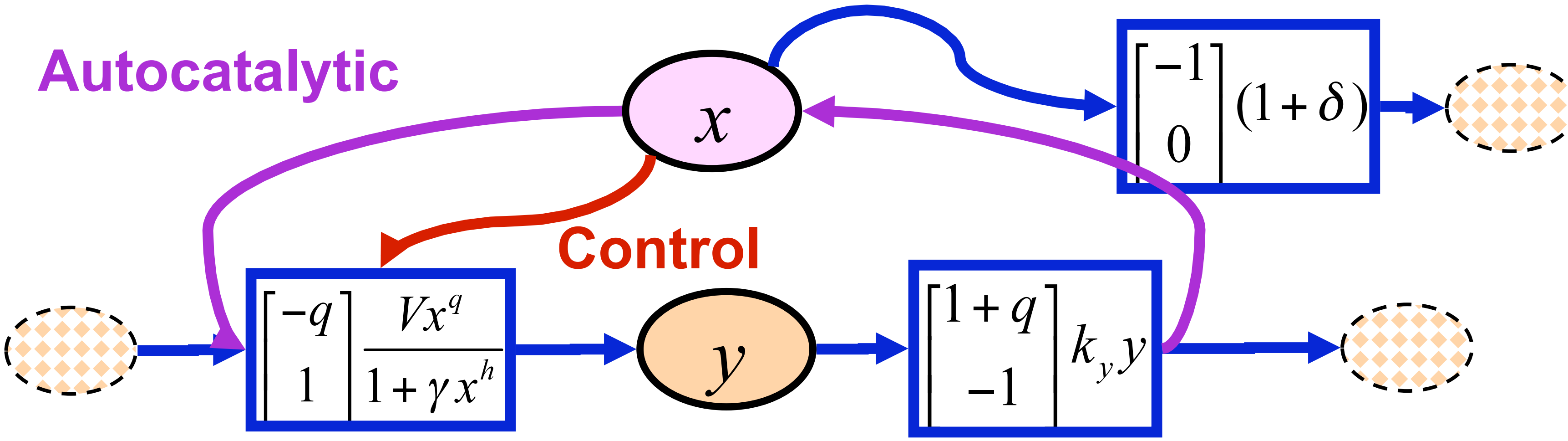
Enzyme complexity






Autocatalytic
Control
x
y
$\begin{bmatrix}-q\\1\end{bmatrix}\frac{Vx^q}{1+\gamma x^h}$
$\begin{bmatrix}1+q\\-1\end{bmatrix}k_y y$
$\begin{bmatrix}-1\\0\end{bmatrix}(1+\delta)$


$k_y(y)$
$k_1(x)$



$$\frac{1}{\pi}\int_0^\infty \ln\left|S(j\omega)\right|\frac{z}{z^2+\omega^2}d\omega \geq \ln\left|\frac{z+p}{z-p}\right|$$

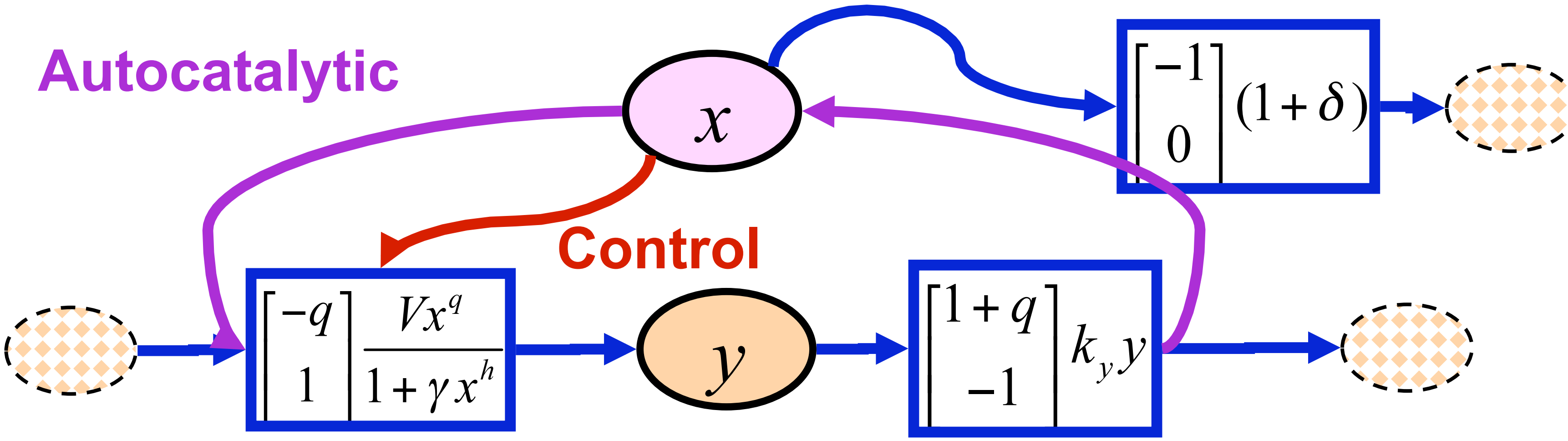
$$z = \frac{k}{q}$$

Small z =

- **small k and/or**
- **large q**

Efficiency =

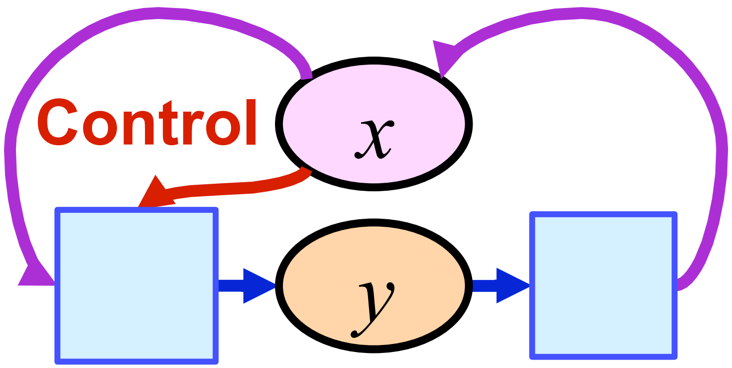
- **small k and/or**
- **large q**



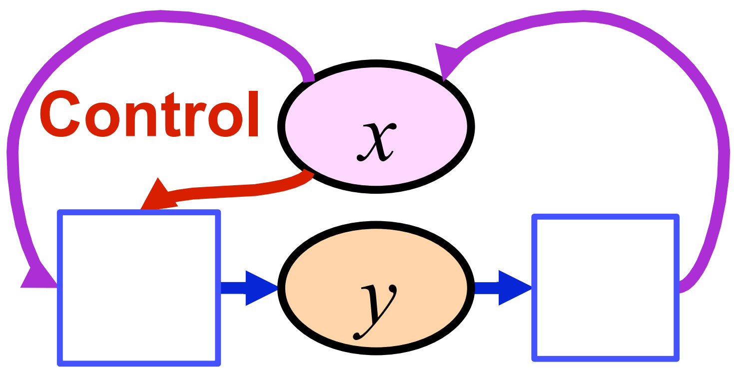
$$\frac{1}{\pi}\int_0^\infty \ln\left|S(j\omega)\right|\frac{z}{z^2+\omega^2}d\omega \geq \ln\left|\frac{z+p}{z-p}\right|$$

$$z=\frac{k}{q}$$

- How to get rid of the RHP zero?
- What are the new tradeoffs?

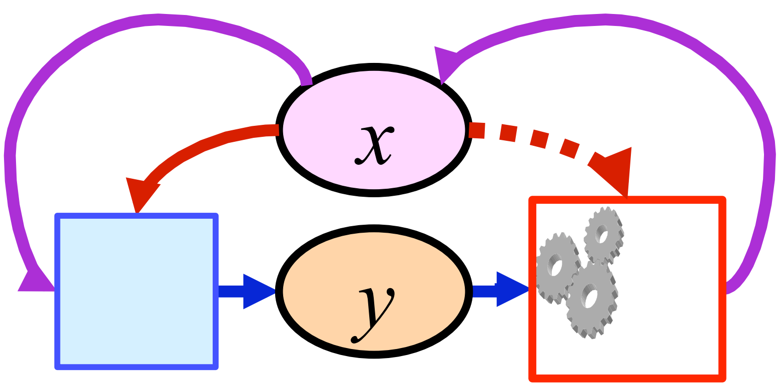


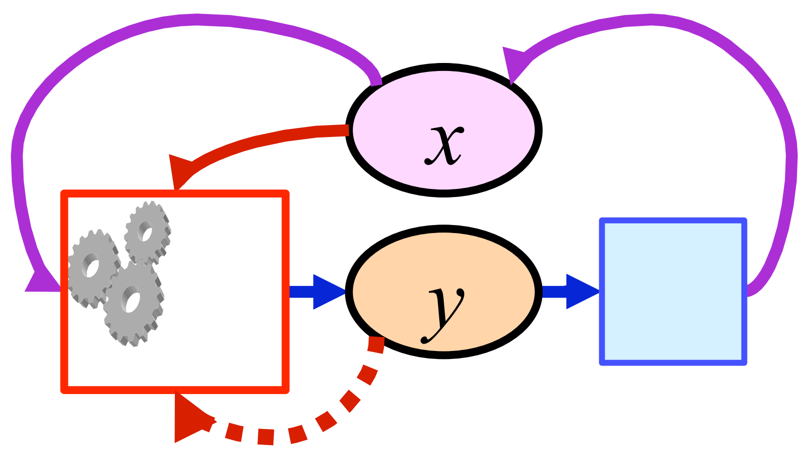
- How to get rid of the RHP zero?
- What are the new tradeoffs?



- How to get rid of the RHP zero?
- What are the new tradeoffs?

More control





More complex enzymes