Glycolysis (Sel’kov 1968)

Glycolysis, Krebs cycle and electron transport systems involved in oxidation of glucose which releases energy.

\[ \text{Glucose} \quad \xrightarrow{\text{ATP}} \quad \text{Glucose 6-P} \]
\[ \xrightarrow{\text{isomerization}} \]
\[ \text{Fructose 6-P} \quad \xrightarrow{\text{ATP}} \quad \text{Fructose 1,6-bisP} \]

chemical reaction equations (partial)

\[ 2S_1 + E \rightleftharpoons ES_1^\text{t} \]
\[ S_1 + ES_2 \rightleftharpoons S_1ES_2 \quad \text{=} \quad \text{complex} \]
\[ S_1ES_2 \rightarrow ES_2^\text{t} + S_1 \]
\[ S_2 \rightarrow \]
\[ \rightarrow S_1 \]

See Math Physiology by Keener & Sneyd for a complete discussion.
Dimensionless model equations

\[
\begin{align*}
\dot{x} &= -x + ay + x^2y \\
\dot{y} &= b - ay - x^2y
\end{align*}
\]

where

\[x = [\text{ATP}] \quad y = [\text{Fru 1-6}]\]

and \((a, b)\) are dimensionless constants that depend on (among other things) reaction rates.

Equilibria location and stability

1. \(\dot{x} > 0 \iff y > \frac{x}{a+x^2}\)
2. \(\dot{y} > 0 \iff y < \frac{b}{a+x^2}\)

Intersection of nullclines yields sole equilibrium

\[P = (\bar{x}, \bar{y}) = \left( \frac{b}{a+b^2} \right)\]

After some calculations

3. \(\det Df(x, y) = a + b^2 > 0\)
4. \(\text{Tr} Df(x, y) = \frac{2b^2}{a+b^2} - 1 - (a+b^2) = -1\)
Since $\det Df > 0$ for all $(a,b)$, the stability of the fixed point is determined solely by the sign of $\text{Tr} Df$.

Solve $T = 0$. Divides parameter space into regions where $T$ is positive and negative. $T = 0$ gives

$$b^2 = \frac{1}{2} (1 - 2a \pm \sqrt{1 - 8a})$$

Using software to plot these two curves:

For $(a, b) \in R_s$ the fixed point $P$ is stable since $T > 0$ there.

For $(a, b) \in R_u$ the fixed point $P$ is unstable and periodic orbits are possible.
Flow direction from nullclines

\[ \dot{x} > 0 \iff y > \frac{x}{a + x^2} \]

\[ \dot{y} > 0 \iff y < \frac{b}{a + x^2} \]

The flow on axes is inward on x-axis and y-axis below point A. These facts motivate a potential trapping region.
Trapping Region $M$

$\partial M_0 =$ outer boundary

$\partial M_1 =$ inner boundary

(1) For previous $(a, b)$ the fixed point $P$ is an unstable node hence flow on $\partial M_1$ is toward interior of $M$ if radius small enough.

(2) Flow along $\partial M_{OA}$ and $\partial M_{OB}$ is into $M$ as well on account of previous flow directions

Suffices to show flow in on $\partial M_{AB}$, and $\partial M_{AB'}$ $\partial M_{AB'}$ is easy since $y < 0$ and $x > 0$ on $\partial M_{AB}$.

Let $m =$ slope

$\vec{T} = (1, m)$

$\vec{N} = (m, -1)$
Compute $\mathbf{f} \cdot \mathbf{N}$ on $\partial M_{BB}$

$$\mathbf{f} \cdot \mathbf{N} = m f_1 - f_2$$

$$= m(-x+ay+x^2y) - (b-ay-x^2y)$$

$$= -(mx+b) + ay(m+1) + (m+1)x^2y$$

A simplifying choice $m = -1$ yields

$$\mathbf{f} \cdot \mathbf{N} = x - b > 0$$

only if $x > b$ ($x = b + B'$).

With these choices $M$ is a trapping region with no fixed points $\Rightarrow$ glycolytic oscillations.