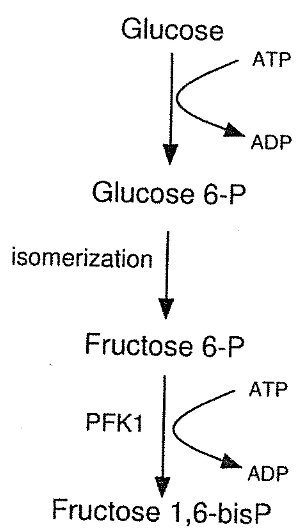
Glycolysis (Sel'kov 1968)

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



S_1 = ATP

S_2 = ADP

E = PFK1 (enzyme)

Chemical reaction equations (partial)

$$2S_2 + E \rightleftarrows ES_2^2$$

$$S_1 + ES_2^2 \rightleftarrows S_1ES_2^2$$

$$S_1ES_2^2 \rightarrow ES_2^2 + S_2$$

$$S_2 \rightarrow$$

$$\rightarrow S_1$$

$\smile$ = complex

See Math Physiology by Keener + Sneyd for a complete discussion.

Dimensionless model equations

$$\left\| \begin{aligned} \dot{x} &= -x + ay + x^2 y \\ \dot{y} &= b - ay - x^2 y \end{aligned} \right\| \qquad \begin{aligned} a &> 0 \\ b &> 0 \end{aligned}$$

where

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

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

Equilibria location and stability

(1) $\quad \dot{x} > 0 \iff y > \dfrac{x}{a + x^2}$

(2) $\quad \dot{y} > 0 \iff y < \dfrac{b}{a + x^2}$

Intersection of nullclines yields sole equilibria

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

After some calculations

(3) $\quad \det Df(\bar{x}, \bar{y}) = a + b^2 > 0$

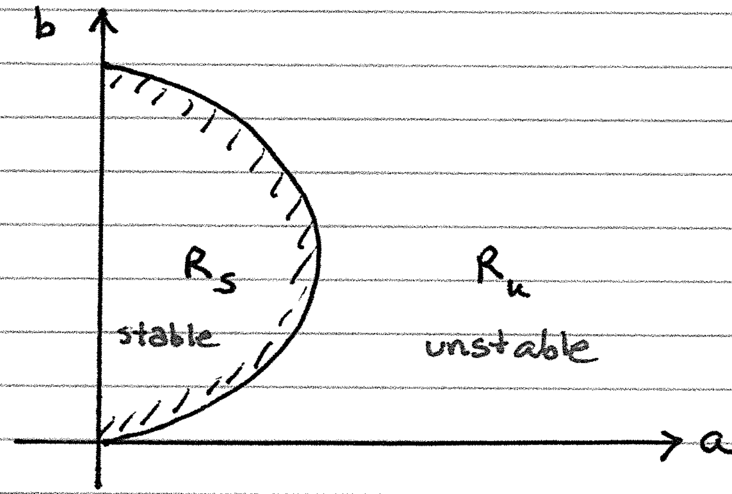
(4) $\quad \operatorname{Tr} Df(\bar{x}, \bar{y}) = \dfrac{2b^2}{a + b^2} - 1 - (a + b^2) \equiv T$

Since $\det Df > 0$ for all (a,b), the stability of the fixed point is determined solely by the sign of $\operatorname{Tr} Df$.

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

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

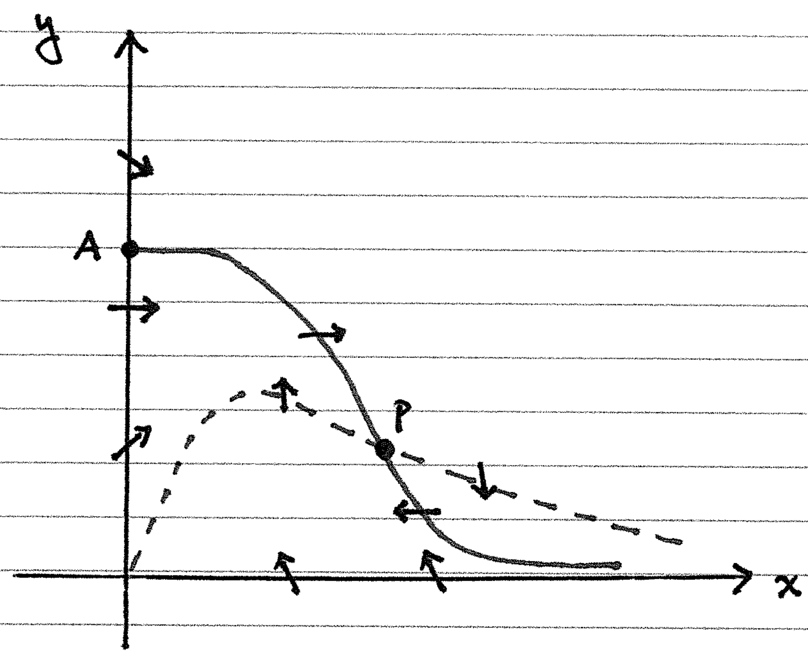
Using software to plot these two curves:



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

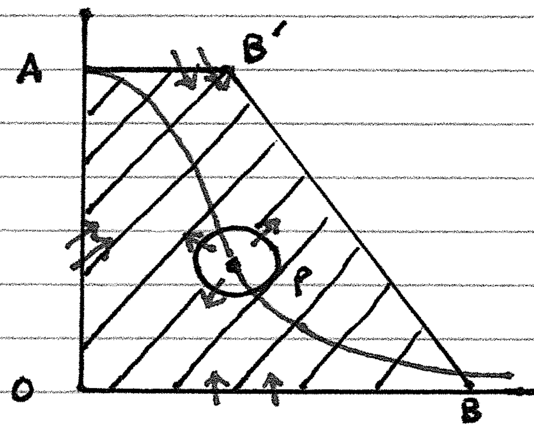


$\dot{x} > 0 \iff y > \dfrac{x}{a+x^2}$ - - - -

$\dot{y} > 0 \iff y < \dfrac{b}{a+x^2}$ ———

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



∂M_o = outer boundary

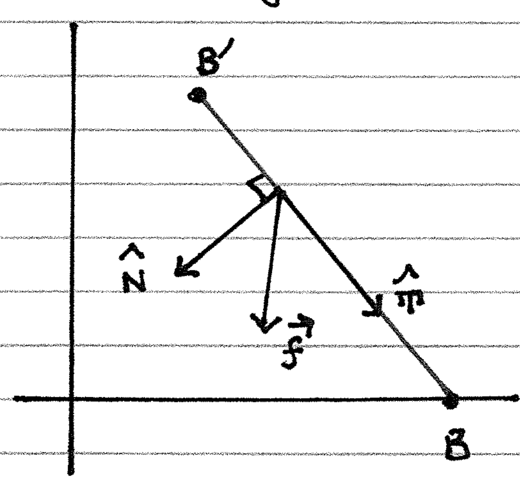
∂M_i = inner boundary

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

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

Suffices to show flow in on $\partial M_{AB'}$ and $\partial M_{B'B}$

$\partial M_{AB'}$ is easy since $\dot{y} < 0$ and $\dot{x} > 0$ on $\partial M_{AB'}$.



Let m = slope

$$\boxed{\begin{aligned} \vec{T} &= (1, m) \\ \vec{N} &= (m, -1) \end{aligned}}$$

Compute $\vec{f} \cdot \vec{N}$ on $\partial M_{B'B}$

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

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

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

A simplifying choice $m = -1$ yields

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

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

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