V Stability analysis

Consider the following two coupled differential equations:

$$\dot{x} = f(x,y)$$
$$\dot{y} = g(x,y)$$

[V.1]

The nullclines are defined as:

$$\dot{x} = 0 \rightarrow f(x_o, y_o) = 0$$
$$\dot{y} = 0 \rightarrow g(x_o, y_o) = 0$$

[V.2]

in order to solve [V.2] we linearize around the fixed point (x_o, y_o):

$$\tilde{x} \equiv x - x_o$$
$$\tilde{y} \equiv y - y_o$$

[V.3]

If f(x,y) and g(x,y) are approximated by a first order Taylor expansion, [V.2] can be written as:

$$\dot{x} \approx \tilde{x} \left. \frac{\partial f}{\partial x} \right|_{(x_o, y_o)} + \tilde{y} \left. \frac{\partial f}{\partial y} \right|_{(x_o, y_o)} \equiv a\tilde{x} + b\tilde{y}$$

$$\dot{y} \approx \tilde{x} \left. \frac{\partial g}{\partial x} \right|_{(x_o, y_o)} + \tilde{y} \left. \frac{\partial g}{\partial y} \right|_{(x_o, y_o)} \equiv c\tilde{x} + d\tilde{y}$$

[V.4]

or in matrix notation:

$$\dot{\vec{X}} = A\vec{X}$$

$$A = \begin{bmatrix} a & b \\ c & d \end{bmatrix}$$

$$\dot{\vec{X}} = \begin{bmatrix} \dot{x} \\ \dot{y} \end{bmatrix}$$

$$\vec{X} = \begin{bmatrix} \tilde{x} \\ \tilde{y} \end{bmatrix}$$

[V.5]

The matrix A is characterized by its trace and the determinant:

$$\tau = trace(A) = a + d$$
$$\Delta = \det(A) = ad - bc$$

[V.6]

Let's try to find a solution of the convenient form:

$$\dot{\vec{v}} = \lambda\vec{v} = A\vec{v}$$

[V.7]

This vector is called the eigenvector, λ is the corresponding eigenvalue. [V.7] can be solved by:

$$\det\begin{bmatrix} a-\lambda & b \\ c & d-\lambda \end{bmatrix} = 0 \qquad \textbf{[V.8]}$$

leading to:

$$\lambda_1 = \frac{\tau + \sqrt{\tau^2 - 4\Delta}}{2}$$
$$\lambda_2 = \frac{\tau - \sqrt{\tau^2 - 4\Delta}}{2} \qquad \textbf{[V.9]}$$

or

$$\Delta = \lambda_1 \lambda_2$$
$$\tau = \lambda_1 + \lambda_2 \qquad \textbf{[V.10]}$$

For a stable fixed point both λ_1 and λ_2 should be negative. Therefore a stable fixed point is characterized by:

$$\Delta > 0$$
$$\tau < 0 \qquad \textbf{[V.11]}$$

Now let us use the evaluate the stability of the toggle switch (Chapter IV) as an example:

$$\dot{u} = f(u,v) = \frac{\alpha_1}{1+v^\beta} - u$$
$$\dot{v} = g(u,v) = \frac{\alpha_2}{1+u^\gamma} - v \qquad \textbf{[V.12]}$$

The fixed points are:

$$u = \frac{\alpha_1}{1+v^\beta}$$
$$v = \frac{\alpha_2}{1+u^\gamma} \qquad \textbf{[V.13]}$$

The matrix A is given by:

$$A = \begin{bmatrix} -1 & \dfrac{-\alpha_1\beta v^{\beta-1}}{(1+v^\beta)^2} \\[3mm] \dfrac{-\alpha_2\gamma u^{\gamma-1}}{(1+u^\gamma)^2} & -1 \end{bmatrix}$$

[V.14]

The trace of this matrix is always negative so the only requirement for stability is that the determinant of this matrix is larger than zero. Let us focus on the conditions for which the determinant equals zero. This would define the boundary in parameter space that separates the bistable from monostable region. Setting the determinant to zero gives:

$$\frac{\alpha_1\beta v^{\beta-1}}{(1+v^\beta)^2}\frac{\alpha_2\gamma u^{\gamma-1}}{(1+u^\gamma)^2} = 1$$

[V.15]

Using the conditions for the fixed points **[V.13]** gives:

$$\beta\gamma v^{\beta+1}u^{\gamma+1} = \alpha_1\alpha_2$$

[V.16]

To be able to solve [V.16] we have to make some assumptions. We assume that we are working with strong promoters and therefore α_1 and α_2 are large and that expression ratio between the ON and OFF state is large. In the case where $u \gg v$, the fixed points are approximated by:

$$u \approx \alpha_1$$

$$v \approx \frac{\alpha_2}{\alpha_1^\gamma}$$

[V.17]

Condition **[V.16]** now becomes:

$$\beta\gamma\alpha_2^\beta\alpha_1^{-\beta\gamma} = 1 \Leftrightarrow \log\alpha_1 \approx \frac{1}{\gamma}\log\alpha_2$$

[V.18]

Consistent with Fig. 2c-d in the toggle switch paper. The other boundary is obtained by realizing that the system is symmetry. By replacing α_1 by α_2 and γ by β, the other boundary is found:

$$\log\alpha_1 \approx \beta\log\alpha_2$$

[V.19]