Mathematical Oncology

A compact review of Linear Stability Analysis

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Consider the 2×2 system of ODEs

$$\begin{cases} \dfrac{du}{dt}(t) = F\left(u(t), v(t)\right) \\ \dfrac{dv}{dt}(t) = G\left(u(t), v(t)\right) \end{cases}, \quad (u(0), v(0)) = (u_0, v_0) \tag{1}$$

where $t \in [0, \infty)$, $u, v : [0, \infty) \to \mathbb{R}$, and where $F, G : \mathbb{R}^2 \to \mathbb{R}$ have continuous first derivatives. Let moreover (u^*, v^*) be one of the *steady states* (SS) of the system that satisfies

$$\begin{cases} F\left(u^*, v^*\right) = 0 \\ G\left(u^*, v^*\right) = 0 \end{cases}.$$

According to the behaviour of the solution (u, v) in the vicinity of the SS (u^*, v^*), we set the following definition(-s):

Definition 1 (Stable SS). *The SS (u^*, v^*) of (1) is called* stable *if a solution (u, v) that starts "close" the SS remains "close" to the SS for all times, i.e.*

$$\forall \varepsilon > 0 \ \exists \delta_\varepsilon > 0 \ : \ \| \left(u_0, v_0\right) - \left(u^*, v^*\right) \| < \delta_\varepsilon \Longrightarrow \| \left(u(t), v(t)\right) - \left(u^*, v^*\right) \| < \varepsilon \ \forall t \geq 0,$$

where $\| \cdot \|$ is a suitably chosen norm.

Note that the notion of stability *does not* imply the convergence of the solution (u, v) towards the SS (u^*, v^*); it merely implies boundedness. For the convergence of (u, v) towards the SS (u^*, v^*), and the implied "self-correction", we need the stronger notion of *asymptotic stability.*

Definition 2 (Asymptotically stable SS). *The SS (u^*, v^*) of (1) is called* asymptotically stable *if it is* stable *and*

$$\lim_{t \to \infty} \left(u(t), v(t)\right) = \left(u^*, v^*\right).$$

Complementary to the notion of stability is the notion of *instability*:

Definition 3 (Unstable SS). *The SS (u^*, v^*) of (1) is called* unstable *if it is not* stable*, i.e.*

$$\exists \varepsilon > 0 \ : \ \forall \delta > 0 \ \exists \tilde{t} \geq 0 \ : \| \left(u_0, v_0\right) - \left(u^*, v^*\right) \| < \delta \ \textit{and} \ \| \left(u(\tilde{t}), v(\tilde{t})\right) - \left(u^*, v^*\right) \| \geq \varepsilon$$

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Even more interesting (if that is ever possible!) is the fact that combinations of these complimentary notions of stability and instability are possible. For planar ($\mathbb{R}^2$) dynamical systems, an *asymptotically stable* SS is also called a *sink* or an *attractor*. An unstable SS can either be a *source*, if all trajectories lead away from the SS ("diverging"), or a *saddle*, if some trajectories lead to the SS ("converging") and others move away. Finally, a SS which is *stable* but not *asymptotically stable* is called a *center*.

Steady state characterisation based on the eigenvalues. The type of stability of the SSs can be deduced through analytical investigations of the eigenvalues of the Jacobian of the system (1), i.e. of

$$J(u,v) = \begin{pmatrix} F_u(u,v) & F_v(u,v) \\ G_u(u,v) & G_v(u,v) \end{pmatrix}, \tag{2}$$

evaluated at the SS (u^*, v^*)

$$A = J\left(u^*, v^*\right). \tag{3}$$

Let now $\lambda_{1,2}$ be the eigenvalues of A. Based on the sign of the real part of the eigenvalues we distinguish the following cases and sub-cases regarding the stability of the SS (u^*, v^*).

(R) Real eigenvalues $\lambda_{1,2} \in \mathbb{R}$.

- (a) If $\lambda_{1,2} < 0$ the SS (u^*, v^*) is asymptotically stable (a.k.a. focus or sink).
- (b) If $\lambda_1 < 0 = \lambda_2$ the SS (u^*, v^*) is a center.
- (c) If $\lambda_1 < 0 < \lambda_2$ the SS (u^*, v^*) is a saddle.
- (d) If $\lambda_1 = 0 = \lambda_2$ the SS (u^*, v^*) is a center.
- (e) If $\lambda_1 = 0 < \lambda_2$ the SS (u^*, v^*) is unstable.
- (f) If $0 < \lambda_{1,2}$ the SS (u^*, v^*) is unstable (a.k.a. source).

(C) Complex eigenvalues (which have to be conjugate) $\lambda_1 = \bar{\lambda}_2 \in \mathbb{C}$.

- (a) If $\mathrm{Re}(\lambda_1) = \mathrm{Re}(\lambda_2) < 0$ the SS (u^*, v^*) is asymptotically stable (a.k.a. spiral focus or spiral sink).
- (b) If $\mathrm{Re}(\lambda_1) = \mathrm{Re}(\lambda_2) = 0$ the SS (u^*, v^*) is a center.
- (c) If $\mathrm{Re}(\lambda_1) = \mathrm{Re}(\lambda_2) > 0$ the SS (u^*, v^*) is unstable (a.k.a. spiral source).

Steady state characterisation based on the Jacobian. An alternative approach is to calculate the eigenvalues through the characteristic equation

$$\lambda^2 - \mathrm{tr}(A)\lambda + \det(A) = 0,$$

where $\mathrm{tr}(A)$, $\det(A)$ are the trace and determinant, respectively, of A (3), to obtain

$$\lambda_{1,2} = \frac{\mathrm{tr}(A) \pm \sqrt{\mathrm{tr}(A)^2 - 4\det(A)}}{2} = \frac{\mathrm{tr}(A) \pm \sqrt{\Delta}}{2}, \tag{4}$$

where $\Delta = \mathrm{tr}(A)^2 - 4\det(A)$.

The stability of the SS (u^*, v^*) follows also from the trace and determinant of the Jacobian A. Namely, using (4), we distinguish the following cases

1. If $\det(A) < 0$ then $\lambda_{1,2} \in \mathbb{R}$ and $\lambda_1 < 0 < \lambda_2$ —corresponds to (R.c) in the above classification— the SS (u^*, v^*) is a saddle.
2. If $\det(A) > 0$ and $\Delta \geq 0$ then $\lambda_{1,2} \in \mathbb{R}$ and of the same sign and ...
   (a) if $\operatorname{tr} A > 0$ then $0 < \lambda_{1,2}$ —corresponds to (R.f) in the above classification— the SS (u^*, v^*) is unstable (source).
   (b) if $\operatorname{tr} A < 0$ then $\lambda_{1,2} < 0$ —corresponds to (R.a) in the above classification— the SS (u^*, v^*) is asymptotically stable (focus or sink).
3. If $\det(A) > 0$ and $\Delta < 0$ then $\lambda_1 = \bar{\lambda}_2 \in \mathbb{C}$ and ...
   (a) if $\operatorname{tr}(A) > 0$ then $\operatorname{Re}(\lambda_{1,2}) > 0$ —corresponds to (C.c) in the above classification— the SS (u^*, v^*) is unstable (spiral source).
   (b) if $\operatorname{tr}(A) < 0$ then $\operatorname{Re}(\lambda_{1,2}) < 0$ —corresponds to (C.a) in the above classification— the SS (u^*, v^*) is asymptotically stable (spiral focus or sink).
4. If $\det(A) > 0$ and $\operatorname{tr}(A) = 0$ then: $\lambda_{1,2} \in \mathbb{C}$ with $\operatorname{Re}(\lambda_{1,2}) = 0$ —corresponds to (C.a) in the above classification— the SS (u^*, v^*) is a center.

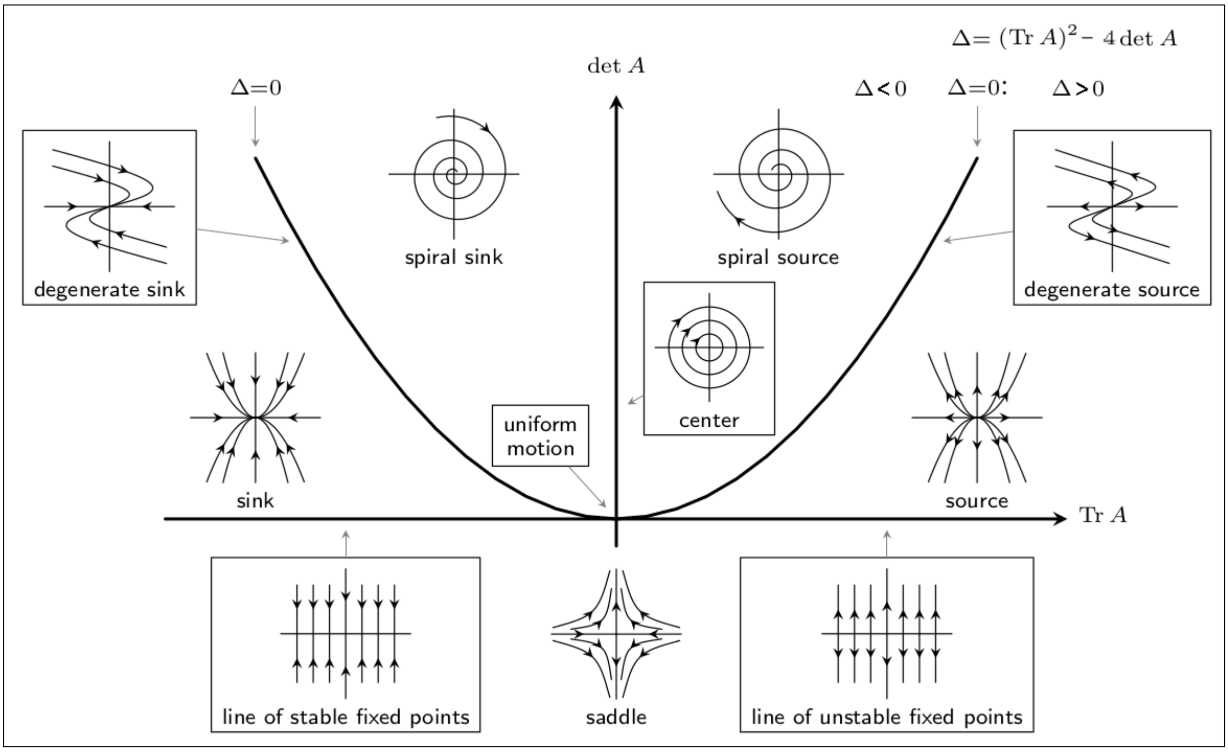

Figure 1: Stability diagram with respect to the trace tr and the determinant det of the Jacobian $A = J(u^*, v^*)$. The lines and arrows constitute a part of the phase plot and describe the expected local trajectory the solutions will follow in case of small perturbations around the steady state. (Figure: Elmer G. Weins)