

On the role of the basic reproduction number in systems modelling disease propagation

Written by: Noémi Gyúró

Supervisors: Dr. Sándor Kovács, Szilvia György

Eötvös Loránd University



1. Introduction: Linearized stability
 - 1.1 Linearized stability in systems of autonomous ordinary differential equations
 - 1.2 Linearized stability in systems of autonomous ordinary difference equations
 - 1.3 Linearized stability in systems of reaction-diffusion equations
2. The algorithm
 - 2.1 Ordinary differential equations
 - 2.2 Difference equations
 - 2.3 Reaction-diffusion equations
3. Applications
 - 3.1 A systems modelling disease propagation
 - 3.2 Discretizations
 - 3.2.1 Explicit Euler discretization
 - 3.2.2 Nonstandard discretization
 - 3.3 A reaction-diffusion version

Autonomous system of ordinary differential equations

$$\Omega \subset \mathbb{R}^d, \quad \mathbf{f} : \Omega \rightarrow \mathbb{R}^d : \mathbf{f} \in \mathcal{C}^1$$

$$\dot{\mathbf{x}} = \mathbf{f} \circ \mathbf{x}$$

$$\mathbf{f}(\mathbf{x}_*) = \mathbf{0}, \quad \sigma(\mathbf{f}'(\mathbf{x}_*)) \stackrel{?}{\subset} \mathbb{C}^- \quad /Hurwitz - stability/$$

- Routh-Hurwitz criterion,
- Liénard-Chipart criterion,
- Mikhailov criterion.

$$\mathbf{x}_* \in \partial\Omega^+ \quad \rightsquigarrow \quad \mathbf{x}_* \text{ is AS/US} \quad \iff \quad \mathcal{R}_0 \ll 1.$$

Autonomous system of ordinary difference equations

$$\Omega \subset \mathbb{R}^d, \quad \mathbf{f} : \Omega \rightarrow \mathbb{R}^d : \mathbf{f} \in \mathcal{C}^1$$

$$\mathbf{x}_{n+1} = \mathbf{f} \circ \mathbf{x}_n \quad (n \in \mathbb{N})$$

$$\mathbf{f}(\mathbf{x}_*) = \mathbf{x}_*, \quad \sigma(\mathbf{f}'(\mathbf{x}_*)) \stackrel{?}{\subset} \mathbb{T} := \{z \in \mathbb{C} : |z| < 1\} \quad /Schur\text{-stability}/$$

- Schur-Cohn criterion,
- Gerschgorin discs,
- Kakeya criterion;
- Möbius transformation.

$$\mathbf{x}_* \in \partial\Omega^+ \quad \rightsquigarrow \quad \mathbf{x}_* \text{ is AS/US} \quad \iff \quad \mathcal{R}_0 <> 1.$$

Reaction-diffusion equations

$$\mathbf{f} : \mathbb{R}^d \rightarrow \mathbb{R}^d, \quad \mathbf{f} \in \mathcal{C}^1, \quad \mathbf{f}(\mathbf{x}_*) = \mathbf{0},$$

$$D := [d_i \delta_{ij}] \in \mathbb{R}^{d \times d}, \quad \Omega \subset \mathbb{R}^d : \text{domain}, \quad \partial\Omega \text{ piecewise } \mathcal{C}^1$$

$$\mathbf{u}_t(\mathbf{r}, t) = D\Delta_{\mathbf{r}}\mathbf{u}(\mathbf{r}, t) + \mathbf{f}(\mathbf{u}(\mathbf{r}, t)) \quad (t > 0, \mathbf{r} \in \Omega)$$

$$(\mathbf{n} \cdot \nabla_{\mathbf{r}}\mathbf{u})(\mathbf{r}, t) = \mathbf{0} \quad ((\mathbf{r}, t) \in \partial\Omega \times \mathbb{R}_0^+),$$

$$\mathbf{0} \neq \mathbf{u}_0(\mathbf{r}) := \mathbf{u}(\mathbf{r}, 0) \geq \mathbf{0} \quad ((\mathbf{r}, t) \in \overline{\Omega} \times \{0\})$$

↓↓↓↓↓↓

$$\mathbf{v}_t(\mathbf{r}, t) \equiv D\Delta_{\mathbf{r}}\mathbf{v}(\mathbf{r}, t) + \mathbf{f}'(\mathbf{x}_*)\mathbf{v}(\mathbf{r}, t)$$

$$(\mathbf{n} \cdot \nabla_{\mathbf{r}}\mathbf{v})(\mathbf{r}, t) = \mathbf{0} \quad ((\mathbf{r}, t) \in \partial\Omega \times \mathbb{R}_0^+),$$

$$\mathbf{0} \neq \mathbf{v}_0(\mathbf{r}) := \mathbf{v}(\mathbf{r}, 0) \geq \mathbf{0} \quad ((\mathbf{r}, t) \in \overline{\Omega} \times \{0\})$$

Fourier method

$$\mathbf{v}(\mathbf{r}, t) = \sum_{n=0}^{\infty} \psi(\mathbf{r}) \exp(\mathfrak{A}_n t) \mathfrak{A}_n$$

where for $n \in \mathbb{N}_0$

$$\mathfrak{A}_n := \mathbf{f}'(\mathbf{x}_*) - \lambda_n D, \quad \mathfrak{A}_n := \int_{\Omega} \mathbf{v}_0(\mathbf{r}) \psi_n(\mathbf{r}) \, d\mathbf{r}$$

furthermore λ_n and ψ_n are solutions of

$$\Delta_{\mathbf{r}} \psi = -\lambda \psi, \quad \left. \frac{\partial \psi}{\partial \mathbf{n}} \right|_{\partial \Omega} = 0$$

\mathbf{x}_* is

asymptotically stable if $\forall n \in \mathbb{N}_0 : \mathfrak{A}_n$ is Hurwitz-stable

unstable if $\exists n \in \mathbb{N}_0 : \mathfrak{A}_n$ is unstable

$$\mathbf{x}_* \in \partial \Omega^+ \quad \rightsquigarrow \quad \mathbf{x}_* \text{ is AS/US} \quad \iff \quad \mathcal{R}_0 <> 1.$$

Ordinary differential equations

$$\dot{u}_i = f_i(\mathbf{u}) = f_i(\underbrace{u_1, \dots, u_m}_{\text{infected}}, u_{m+1}, \dots, u_d) =: \mathcal{F}_i(\mathbf{u}) - \mathcal{V}_i(\mathbf{u}) \quad (i \in \{1, \dots, d\})$$

$$\mathbf{f}(\mathbf{x}_*) = \mathbf{0},$$

$$J_{\mathcal{F}}(\mathbf{u}^*) = \begin{bmatrix} F & O \\ O & O \end{bmatrix} \quad \text{and} \quad J_{\mathcal{V}}(\mathbf{u}^*) = \begin{bmatrix} V & O \\ J_3 & J_4 \end{bmatrix}$$

where

$$F := [\partial_j \mathcal{F}_i(\mathbf{u}^*)]_{1 \leq i, j \leq m} \in \mathbb{R}^{m \times m} \quad \text{and} \quad V := [\partial_j \mathcal{V}_i(\mathbf{u}^*)]_{1 \leq i, j \leq m} \in \mathbb{R}^{m \times m}.$$

$$\mathcal{R}_0 := \rho(FV^{-1})$$

Difference equations

$$\mathbf{u}_{n+1} = \mathbf{f}(\mathbf{u}_n) \quad (n \in \mathbb{N}_0) \quad \mathbf{f}(\mathbf{x}_*) = \mathbf{x}_*$$

where

$$J_{\mathbf{f}}(\mathbf{u}^*) = \begin{bmatrix} F + T & O \\ A & C \end{bmatrix}$$

$$\mathcal{R}_0 := \rho(F(I_m - T)^{-1})$$

$$\rho(F + T) < 1 \quad \iff \quad \mathcal{R}_0 < 1$$

Reaction-diffusion equations

$$\mathbf{u}_t(\mathbf{r}, t) = D\Delta_{\mathbf{r}}\mathbf{u}(\mathbf{r}, t) + \mathbf{f}(\mathbf{u}(\mathbf{r}, t)) \quad (t > 0, \mathbf{r} \in \Omega), \quad f_i(\mathbf{u}) =: \mathcal{F}_i(\mathbf{u}) - \mathcal{V}_i(\mathbf{u})$$

$$(\mathbf{n} \cdot \nabla_{\mathbf{r}}\mathbf{u})(\mathbf{r}, t) = \mathbf{0} \quad ((\mathbf{r}, t) \in \partial\Omega \times \mathbb{R}_0^+),$$

$$\mathbf{0} \neq \mathbf{u}_0(\mathbf{r}) := \mathbf{u}(\mathbf{r}, 0) \geq \mathbf{0} \quad ((\mathbf{r}, t) \in \overline{\Omega} \times \{0\})$$

$$F := [\partial_j \mathcal{F}_i(\mathbf{u}^*)] \in \mathbb{R}^{m \times m} \quad \text{and} \quad V := [\partial_j \mathcal{V}_i(\mathbf{u}^*)] \in \mathbb{R}^{m \times m}$$

$$J_{\mathcal{F}}(\mathbf{u}^*) = \begin{bmatrix} F & O \\ O & O \end{bmatrix} \quad \text{and} \quad J_{\mathcal{V}}(\mathbf{u}^*) = \begin{bmatrix} V & O \\ J & -C \end{bmatrix}$$

$$-D_I \Delta_{\mathbf{r}} \boldsymbol{\phi} + V \boldsymbol{\phi} = \mu F \boldsymbol{\phi} \quad (\text{on } \Omega),$$

$$(\mathbf{n} \cdot \nabla_{\mathbf{r}}) \boldsymbol{\phi} = \mathbf{0} \quad (\text{on } \partial\Omega)$$

$$\mathcal{R}_0 = \rho(-FB^{-1}) = \rho(-B^{-1}F) = \frac{1}{\mu_0}.$$

A systems modelling disease propagation

$$\left. \begin{aligned} \dot{S} &= \lambda - \frac{aSI}{S+I} + \beta I - \psi S - \delta_S S =: f_1(S, E, I), \\ \dot{E} &= \psi S + \kappa I - \delta_E E =: f_2(S, E, I), \\ \dot{I} &= \frac{aSI}{S+I} - \kappa I - \beta I - \delta_I I =: f_3(S, E, I) \end{aligned} \right\} \quad (1)$$

Proposition: (KovácsGyörgyGyúró) All solutions of (1) which are initiated in \mathbb{R}_+^3 are uniformly bounded, more precisely

$$\Omega := \left\{ (S, E, I) \in \mathbb{R}^3 : 0 < S + E + I \leq \frac{K}{\mu} \right\}$$

is a positively invariant region for (1), where $K > 0$ is a suitable constant and $0 < \mu < \min\{\delta_S, \delta_E, \delta_I\}$.

$$(\dot{S}, \dot{E}, \dot{I}) =: \widehat{\mathcal{F}}(S, E, I) - \widehat{\mathcal{G}}(S, E, I)$$

$$\widehat{\mathcal{F}}(S, E, I) := \begin{bmatrix} 0 \\ 0 \\ \frac{aSI}{S+I} \end{bmatrix}, \quad \widehat{\mathcal{G}}(S, E, I) := \begin{bmatrix} -\lambda + \frac{aSI}{S+I} - \beta I + (\psi + \delta_S)S \\ -\psi S - \kappa I + \delta_E E \\ (\kappa + \beta + \delta_I)I \end{bmatrix}$$

$$\mathfrak{E}_b := (S_b, E_b, I_b) := \left(\frac{\lambda}{\delta_S + \psi}, \frac{\lambda\psi}{\delta_E(\delta_S + \psi)}, 0 \right)$$

$$D\widehat{\mathcal{F}}(\mathfrak{E}_b) := \begin{bmatrix} 0 & 0 & 0 \\ 0 & 0 & 0 \\ 0 & 0 & a \end{bmatrix}, \quad D\widehat{\mathcal{G}}(\mathfrak{E}_b) := \begin{bmatrix} \psi + \delta_S & 0 & a - \beta \\ -\psi & \delta_E & -\kappa \\ 0 & 0 & \kappa + \beta + \delta_I \end{bmatrix}.$$

$$D\widehat{\mathcal{F}}(\mathfrak{E}_b) =: \begin{bmatrix} \mathbf{0} & 0 \\ \mathbf{0} & F \end{bmatrix}, \quad D\widehat{\mathcal{G}}(\mathfrak{E}_b) =: \begin{bmatrix} J_1 & J_2 \\ \mathbf{0} & G \end{bmatrix}$$

$$F := \partial_3 \widehat{\mathcal{F}}_3(\mathfrak{E}_b) = a \quad \text{and} \quad G := \partial_3 \widehat{\mathcal{G}}_3(\mathfrak{E}_b) = \kappa + \beta + \delta_I.$$

$$\mathcal{R}_0 := \rho(FG^{-1}) = \frac{a}{\kappa + \beta + \delta_I}.$$

$$\kappa^* := a - \beta - \delta_I$$

$$\kappa \begin{cases} < \kappa^* & \iff & \mathcal{R}_0 > 1, \\ = \kappa^* & \iff & \mathcal{R}_0 = 1, \\ > \kappa^* & \iff & \mathcal{R}_0 < 1. \end{cases}$$

Proposition: If

1. $\kappa > \kappa^*$ then system (1) has only one equilibrium \mathfrak{E}_b on the boundary of the phase space $[S, E, I]$ which is locally asymptotically stable, and
2. the factor κ^* satisfies $\kappa^* \geq \kappa$, then a new (endemic) equilibrium \mathfrak{E}_e bifurcates from \mathfrak{E}_b (as κ crosses the value κ^*) and becomes the one locally asymptotically stable as $\kappa^* > \kappa$, whereas \mathfrak{E}_b is a repeller as $\kappa^* > \kappa$.

Explicit Euler discretization

$$\left. \begin{aligned} S_{n+1} &= S_n + h \left(\lambda - \frac{aS_n I_n}{S_n + I_n} + \beta I_n - \psi S_n - \delta_S S_n \right) =: f_1^{eE}(S_n, E_n, I_n), \\ E_{n+1} &= E_n + h (\psi S_n + \kappa I_n - \delta_E E_n) =: f_2^{eE}(S_n, E_n, I_n), \\ I_{n+1} &= I_n + h \left(\frac{aS_n I_n}{S_n + I_n} - \kappa I_n - \beta I_n - \delta_I I_n \right) =: f_3^{eE}(S_n, E_n, I_n). \end{aligned} \right\}$$

Proposition: Let $\delta := \min\{\delta_S, \delta_E, \delta_I\}$ and

$$h < h^* := \min \left\{ \frac{1}{a + \psi + \delta_S}, \frac{1}{\delta_E}, \frac{1}{\kappa + \beta + \delta_I}, \delta \right\}$$

Then

1. if $S_0, E_0, I_0 > 0$ then $S_n, E_n, I_n > 0$ for all $n \in \mathbb{N}$.
2. If $I_0 = 0$ but $S_0, E_0 > 0$ then $S_n, E_n > 0$ and $I_n = 0$ for all $n \in \mathbb{N}$;
3. $\Omega := \left\{ (S, E, I) \in \mathbb{R}^3 : 0 < S + E + I \leq \frac{\kappa}{\mu} \right\}$ is positively invariant.

$$F = \begin{bmatrix} ah & 0 \\ h(\beta - a) & 0 \end{bmatrix}, \quad T = \begin{bmatrix} 1 - h(\kappa + \beta + \delta_I) & 0 \\ 0 & 1 - h(\psi + \delta_S) \end{bmatrix}$$

⇓⇓⇓⇓⇓⇓

$$\begin{aligned} \mathcal{R}_0 &= \rho(F \cdot (I_2 - T)^{-1}) = \rho \left(F \cdot \begin{bmatrix} h(\kappa + \beta + \delta_I) & 0 \\ 0 & h(\psi + \delta_S) \end{bmatrix}^{-1} \right) = \\ &= \rho \left(\begin{bmatrix} ah & 0 \\ h(\beta - a) & 0 \end{bmatrix} \cdot \begin{bmatrix} 1/h(\kappa + \beta + \delta_I) & 0 \\ 0 & 1/h(\psi + \delta_S) \end{bmatrix} \right) = \\ &= \rho \left(\begin{bmatrix} \frac{a}{\kappa + \beta + \delta_I} & 0 \\ \frac{\beta - a}{\kappa + \beta + \delta_I} & 0 \end{bmatrix} \right) = \frac{a}{\kappa + \beta + \delta_I}. \end{aligned}$$

Proposition: Suppose that $d \in \mathbb{N}$, $A \in \mathbb{R}^{d \times d}$, $B := I_d + hA$, furthermore conditions

$$\lambda \in \sigma(A) \quad \text{and} \quad h < \frac{-\max^2(\mathcal{J}(\lambda)) - 2s(A)}{s^2(A)}$$

hold. Then $s(A) < 0$ implies $\rho(B) < 1$.

Proposition: Suppose that $d \in \mathbb{N}$, $A \in \mathbb{R}^{d \times d}$,

$$B := I_d + hA.$$

Then $s(A) > 0$ implies $\rho(B) > 1$ independent of h .

Nonstandard discretization

$$\left. \begin{aligned} S_{n+1} &= S_n + \varphi(h) \left(\lambda - \frac{aS_{n+1}I_n}{S_n + I_n} + \beta I_n - \psi S_n - \delta_S S_n \right), \\ E_{n+1} &= E_n + \varphi(h) (\psi S_n + \kappa I_n - \delta_E E_n), \\ I_{n+1} &= I_n + \varphi(h) \left(\frac{aS_{n+1}I_n}{S_n + I_n} - \kappa I_n - \beta I_n - \delta_I I_n \right) \end{aligned} \right\}$$

Proposition: Let $\delta := \min\{\delta_S, \delta_E, \delta_I\}$ and

$$\varphi(h) < h^{**} := \min \left\{ \frac{1}{\psi + \delta_S}, \frac{1}{\delta_E}, \frac{1}{\kappa + \beta + \delta_I}, \frac{1}{\delta} \right\}.$$

Then

1. if $S_0, E_0, I_0 > 0$ then $S_n, E_n, I_n > 0$ for all $n \in \mathbb{N}$;
2. if $I_0 = 0$ but $S_0, E_0 > 0$ then $S_n, E_n > 0$ and $I_n = 0$ for all $n \in \mathbb{N}$;
3. Ω is positively invariant.

$$F = \begin{bmatrix} a\varphi(h) & 0 \\ \varphi^3(h)(\delta_S a) + \varphi^2(h)\lambda(a - a\psi) + \varphi(h)\lambda(\beta - a) & 0 \end{bmatrix}$$

$$T = \begin{bmatrix} 1 - \varphi(h)(\kappa + \beta + \delta_I) & 0 \\ 0 & 1 - \varphi(h)(\psi + \delta_S) \end{bmatrix}.$$

⇓⇓⇓⇓⇓

$$\mathcal{R}_0 = \rho(F \cdot (I_2 - T)^{-1}) = \rho \left(F \cdot \begin{bmatrix} \varphi(h)(\kappa + \beta + \delta_I) & 0 \\ 0 & \varphi(h)(\psi + \delta_S) \end{bmatrix}^{-1} \right)$$

$$= \rho \left(F \cdot \begin{bmatrix} 1/\varphi(h)(\kappa + \beta + \delta_I) & 0 \\ 0 & 1/\varphi(h)(\psi + \delta_S) \end{bmatrix} \right) =$$

$$= \rho \left(\begin{bmatrix} \frac{a}{\kappa + \beta + \delta_I} & 0 \\ \frac{\varphi^2(h)(\delta_S a) + \varphi(h)\lambda(a - a\psi) + \lambda(\beta - a)}{\kappa + \beta + \delta_I} & 0 \end{bmatrix} \right) = \frac{a}{\kappa + \beta + \delta_I}.$$

A reaction-diffusion version

$$\begin{aligned}\partial_t S(\mathbf{r}, t) &= \partial_S \Delta_{\mathbf{r}} S(\mathbf{r}, t) + f_1(S, E, I), \\ \partial_t E(\mathbf{r}, t) &= \partial_E \Delta_{\mathbf{r}} E(\mathbf{r}, t) + f_2(S, E, I), \\ \partial_t I(\mathbf{r}, t) &= \partial_I \Delta_{\mathbf{r}} I(\mathbf{r}, t) + f_3(S, E, I)\end{aligned}\quad (\mathbf{r}, t) \in \Omega \times \mathbb{R}_0^+$$

↓↓↓↓↓↓

$$\begin{aligned}\partial_t S(\mathbf{r}, t) &= \partial_S \Delta_{\mathbf{r}} S(\mathbf{r}, t) - (\psi + \delta_S)S + (\beta - a)I, \\ \partial_t E(\mathbf{r}, t) &= \partial_E \Delta_{\mathbf{r}} E(\mathbf{r}, t) + \psi S - \delta_E E + \kappa I, \\ \partial_t I(\mathbf{r}, t) &= \partial_I \Delta_{\mathbf{r}} I(\mathbf{r}, t) + (a - \kappa - \beta - \delta_I)E\end{aligned}\quad (\mathbf{r}, t) \in \Omega \times \mathbb{R}_0^+$$

$$C = \begin{bmatrix} -\psi - \delta_S & 0 \\ \psi & -\delta_E \end{bmatrix} \quad \text{and} \quad J = \begin{bmatrix} a - \beta \\ -\kappa \end{bmatrix},$$

resp.

$$F = a \quad \text{and} \quad V = \kappa + \beta + \delta_I.$$

$$\phi'' = \frac{\mu a - (\kappa + \beta + \delta_I)}{\partial_I} \cdot \phi \quad (\text{on } (0, 1)), \quad \phi'(0) = 0 = \phi'(1). \quad (2)$$

The solutions of (2) are clearly

$$\phi(x) = \cos\left(\sqrt{\lambda}x\right) \quad (x \in [0, 1]),$$

where

$$\lambda = \frac{\kappa + \beta + \delta_I - \mu a}{\vartheta_I}$$

provided that

$$\sqrt{\lambda} = k\pi \quad (k \in \mathbb{N}_0)$$

The values

$$\lambda_k = (k\pi)^2 \quad \longleftrightarrow \quad \mu_k = \frac{\kappa + \beta + \delta_I - k\pi\vartheta_I}{a}$$

are the eigenvalues. Thus

$$\mathcal{R}_0 = \frac{1}{\mu_0} = \frac{a}{\kappa + \beta + \delta_I}.$$

Thank you very much for your
attention!