Stability Analysis Methodology for Epidemiological Models

Paola Lizarralde-Bejarano

Supervisor: María Eugenia Puerta
Co-supervisor: Sair Arboleda-Sanchéz
EAFIT University
Medellín, Colombia

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Objective

Figure: *Aedes aegypti*. Image taken from `https://goo.gl/tneEZY`

Determine the must relevant components of the mathematical models based on Ordinary Differential Equations (ODS) in order to understand the transmission of a infectious disease.

Epidemiological models

Figure: McKendrick (1876 - 1943) and Kermack (1898 - 1970).

Image taken from `https://goo.gl/GNOcAF`

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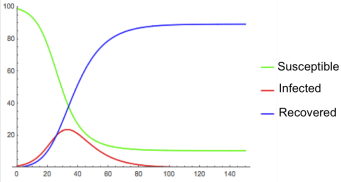

Figure: SIR Model

Threshold theorem (basic reproductive number, R_0)

R_0 for SIR model

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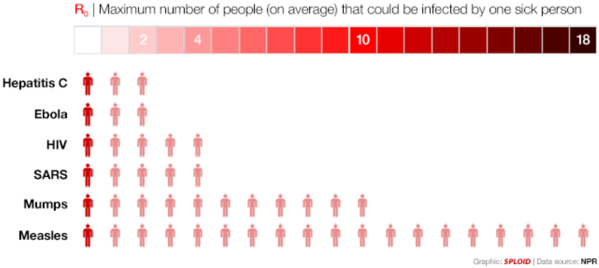

Figure: Basic reproductive number for some infectious disease. Image taken from `https://goo.gl/vDc70u`

Example: Dengue model, Bello's case

$$\frac{dA}{dt} = \delta\left(1-\frac{A}{C}\right)M-(\gamma_m+\mu_a)A$$

$$\frac{dM_s}{dt} = f\gamma_m A - b\beta_m\frac{H_i}{H}M_s-\mu_m M_s$$

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$$\frac{dH_s}{dt} = \mu_h H - b\beta_h\frac{M_i}{M}H_s-\mu_h H_s$$

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$$\frac{dH_r}{dt} = \gamma_h H_i-\mu_h H_r$$

Example: Dengue model, Bello's case

$$\begin{aligned} R_0 &= \frac{b^2\beta_m\beta_h\theta_h\theta_m}{(\theta_m+\mu_m)(\gamma_h+\mu_h)(\theta_h+\mu_h)\mu_m M}\cdot\frac{f\gamma_m}{\mu_m}\frac{\delta MC}{(\delta M+C(\gamma_m+\mu_a))} \\ &= \frac{b^2\beta_m\beta_h\theta_h\theta_m}{(\theta_m+\mu_m)(\gamma_h+\mu_h)(\theta_h+\mu_h)\mu_m}\cdot\frac{M_s^*}{M} \end{aligned}$$

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\end{aligned}
$$

The Basic Reproductive Number (R_0) of the epidemic occurred in Bello in 2010 was between 1.5 and 2.7.

Epidemiological data

The parameters used in the model, their biological descriptions, and their ranges of values.

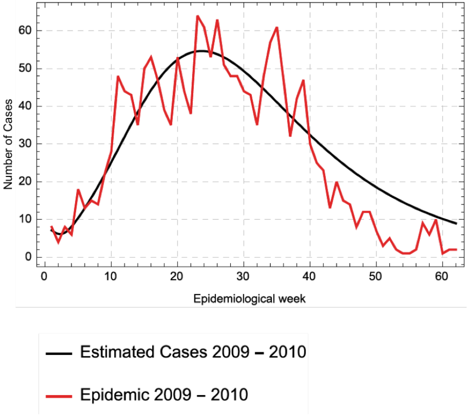
Param.	**Meaning**	**V. / day**	**V. / week**
b	Biting rate	$[0, 1]$	$[0, 4]$
δ	Per capita oviposition rate	$[8, 24]$	$[55, 165]$
γ_m	Transition rate from the aquatic phase to the adult phase	$[0.125, 0.2]$	$[0.875, 1.4]$
μ_a	Mortality rate in the aquatic phase	$[0.001, 0.5]$	$[0.007, 0.3]$
μ_m	Mortality rate in the adult phase	$[0.008, 0.03]$	$[0.06, 0.20]$
f	Fraction of female mosquitoes hatched from all eggs	$[0.42, 0.55]$	$[0.42, 0.55]$
C	Carrying capacity of the environment	$[6400, 95000]$	$[6400, 95000]$
μ_h	Birth and death rate of the human population	0.00006	0.0004
β_h	Transmission probability from mosquito to human	$[0, 1]$	$[0, 1]$
β_m	Transmission probability from mosquito to human	$[0, 1]$	$[0, 1]$
θ_m	Transition rate from exposed to infectious mosquitoes	$[0.08, 0.13]$	$[0.58, 0.88]$
θ_h	Transition rate from exposed to infectious humans	$[0.1, 0.25]$	$[0.7, 1.75]$
γ_h	Recovery rate	$[0.07, 0.25]$	$[0.5, 1.75]$

Initial conditions

The initial conditions used in the model, their descriptions, and their ranges of values.

Initial condition	**Meaning**	**Range**
$A(0)$	Initial condition for the aquatic phase	$[5755, 17265]$
$M_s(0)$	Initial condition for susceptible mosquitoes	$[0, 1200000]$
$M_e(0)$	Initial condition for exposed mosquitoes	$[0, 100]$
$M_i(0)$	Initial condition for infectious mosquitoes	$[0, 100]$
$H_s(0)$	Initial condition for susceptible humans	$[244402, 321734]$
$H_e(0)$	Initial condition for exposed humans	$[18, 72]$
$H_i(0)$	Initial condition for infectious humans	$[6, 24]$
$H_r(0)$	Initial condition for recovered humans	$[81405, 158809]$

The model fitted to the real biological data



Param.	Value
δ	65
γ_m	1.4
μ_a	0.1156
b	4
μ_m	0.12
θ_m	0.58
f	0.5
θ_h	0.7
C	10000
γ_h	1
β_m	0.6
β_h	0.15
μ_h	0.0004
$A(0)$	9000
$M_s(0)$	1199976
$M_e(0)$	18
$M_i(0)$	6
$H_s(0)$	321710
$H_e(0)$	18
$H_i(0)$	6
$H_r(0)$	81501

Stability analysis

Figure: Henri Poincaré (April 29, 1854 - July 17, 1912). Image taken from https://goo.gl/0I0qLJ

Figure: Aleksandr Lyapunov (June 6, 1857 - November 3, 1918). Image taken from https://goo.gl/dLNfwW

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Definition

A point $\mathbf{x}^*$ is called an *equilibrium point* of $\dot{\mathbf{x}} = \mathbf{f}(\mathbf{x})$, if $\mathbf{f}(\mathbf{x}^*) = 0$.

Definitions: stable, unstable and asymptotically stable

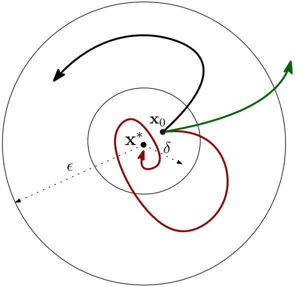


Figure: The **black** line shows the definition of *stable* point. The **green** line shows the definition of *unstable* point. The **red** line represents a definition of *asymptotically stable* point.

Definitions: stable, unstable and asymptotically stable

Definition

The equilibrium point $\mathbf{x}^*$ is

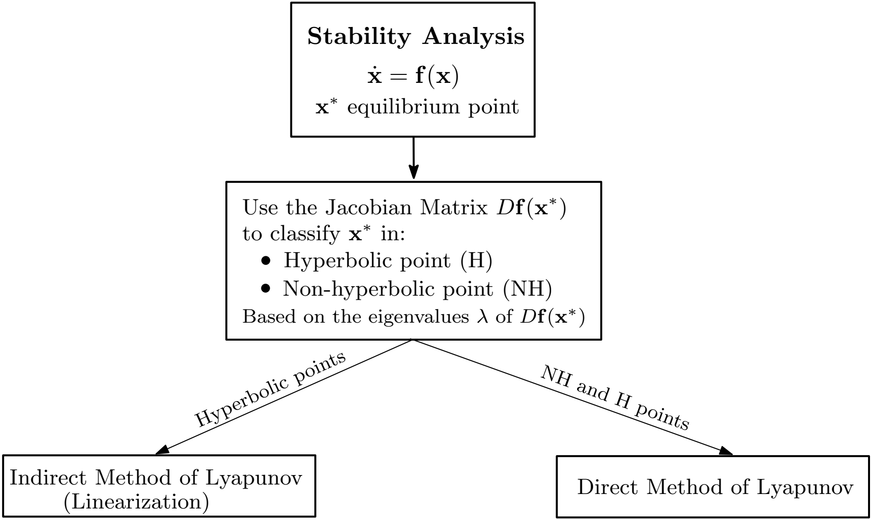
- *stable* if, for each $\epsilon > 0$, there is a $\delta = \delta(\epsilon) > 0$ such that,

$$||\mathbf{x}^0 - \mathbf{x}^*|| < \delta \Rightarrow ||\varphi(t, \mathbf{x}^0) - \mathbf{x}^*|| < \epsilon, \ \forall t \geq 0$$

- *unstable*, if not stable
- *asymptotically stable*, if it is stable, and δ can be chosen such that

$$||\mathbf{x}^0 - \mathbf{x}^*|| < \delta \Rightarrow \lim_{t \to \infty} ||\varphi(t, \mathbf{x}^0) - \mathbf{x}^*|| = 0$$

Stability diagram



Indirect method of Lyapunov

The following results were taken from (Hale and Koçak, 2012).

Theorem

Let $\mathbf{f}$ *be a* C^1 *function. If all eigenvalues of the Jacobian matrix* $D\mathbf{f}(\mathbf{x}^*)$ *have negative real parts, then the equilibrium point* $\mathbf{x}^*$ *of* $\dot{\mathbf{x}} = \mathbf{f}(\mathbf{x})$ *is asymptotically stable.*

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Theorem

Let $\mathbf{f}$ *be a* C^1 *function. If at least one of the eigenvalues of the Jacobian matrix* $D\mathbf{f}(\mathbf{x}^*)$ *has positive real part, then the equilibrium point* $\mathbf{x}^*$ *of* $\dot{\mathbf{x}} = \mathbf{f}(\mathbf{x})$ *is unstable.*

Indirect method of Lyapunov

Theorem

(Grobman (1959) - Hartman(1960)) If $\mathbf{x}^*$ *is a hyperbolic equilibrium point of nonlinear system* $\dot{\mathbf{x}} = \mathbf{f}(\mathbf{x})$, *then there is a neighborhood of* $\mathbf{x}^*$ *in which* $\mathbf{f}$ *is topologically equivalent to the linear vector field* $\dot{\mathbf{x}} = D\mathbf{f}(\mathbf{x}^*)\mathbf{x}$.

Direct method of Lyapunov

The following result was taken from (Khalil, 1996).

Theorem

Let $\mathbf{x}^* = \mathbf{0}$ *be an equilibrium point of* $\dot{\mathbf{x}} = \mathbf{f}(\mathbf{x})$. *Let* $V : D \to \mathbb{R}$ *be a continuously differentiable function on a neighborhood* D *of* $\mathbf{x}^* = \mathbf{0}$, *such that*

$$V(\mathbf{0}) = 0 \text{ and } V(\mathbf{x}) > 0 \text{ in } D - \{\mathbf{0}\}$$

$$\dot{V}(\mathbf{x}) \leq 0 \text{ in } D$$

then, $\mathbf{x}^* = \mathbf{0}$ *is stable. Moreover, if*

$$\dot{V}(\mathbf{x}) < 0 \text{ in } D - \{\mathbf{0}\}$$

then $\mathbf{x}^* = \mathbf{0}$ *is asymptotically stable.*

Exponentially stable

Definition

The equilibrium point $\mathbf{x}^* = 0$ of $\dot{\mathbf{x}} = \mathbf{f}(\mathbf{x})$ is said to be exponentially stable if

$$\|\mathbf{x}(t)\| \leq k\|\mathbf{x}(0)\|e^{-\lambda t}, \ \forall t \geq 0$$

$k \geq 1$, $\lambda > 0$, for all $\|\mathbf{x}(0)\| < c$.

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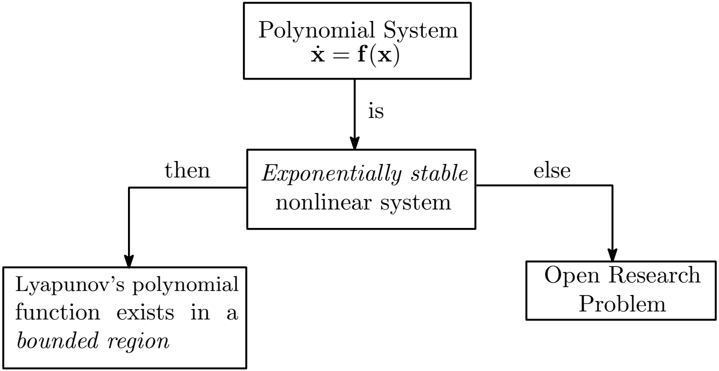
Theorem

The equilibrium point $\mathbf{x}^* = 0$ of $\dot{\mathbf{x}} = \mathbf{f}(\mathbf{x})$ is exponentially stable if and only if the linearization of $\mathbf{f}(\mathbf{x})$ at the origin is a Hurwitz matrix.

How to find a Lyapunov function?



For a deeper discussion of when a Lyapunov's polynomial function exists in a bounded region we refer the reader to (Peet, 2009).

Counterexample

The system (1) does not admit a polynomial Lyapunov function of any degree.

$$\begin{aligned} \dot{x} &= -x + xy \\ \dot{y} &= -y \end{aligned} \tag{1}$$

See (Ahmadi et al., 2011) for details of this result.

How to find a Lyapunov function?

Definition of Lyapunov function

$$V(x) \geq 0$$

$$\dot{V} = \sum_{i=1}^{n} \frac{\partial V}{\partial x_i} \dot{x}_i = \langle \frac{\partial V}{\partial x_i}, \dot{x}_i \rangle$$

$$\dot{V} \leq 0$$

Relaxation of constraints

$V(x)$ is a Sum of Squares (SOS)

$-\dot{V}(x)$ is a Sum of Squares (SOS)

Can we apply this results to epidemiological models?

Epidemiological Models

↓

- Disease free point
- Endemic equilibrium point

↓

R_0 depends on the parameters and the initial conditions of the model

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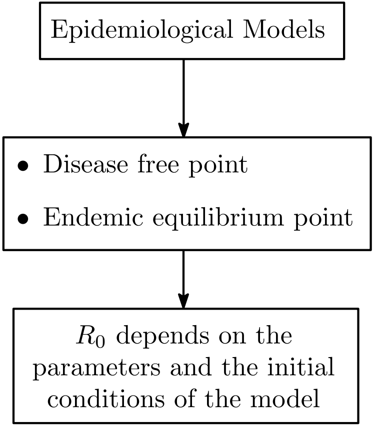

SIR Model

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\frac{dH_s}{dt} &= \mu_h H - b\beta_h\frac{M_i}{M}H_s-\mu_h H_s\\
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\frac{dH_i}{dt} &= \theta_h H_e-(\gamma_h+\mu_h)H_i\\
\frac{dH_r}{dt} &= \gamma_h H_i-\mu_h H_r
\end{aligned}
$$

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