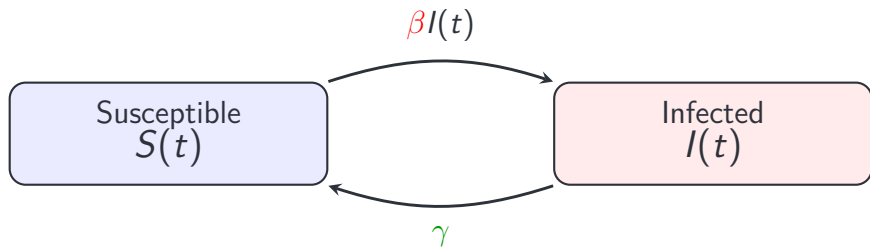


Spectral analysis and global dynamics of a structured SIS model with mutation

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Classical SIS dynamics

$$\begin{cases} S'(t) = \gamma I(t) - \beta S(t)I(t), \\ I'(t) = \beta S(t)I(t) - \gamma I(t). \end{cases}$$

Interpretation

$S(t)$: proportion of susceptible individuals;

$I(t)$: proportion of infected individuals;

$\beta > 0$: transmission rate;

$\gamma > 0$: recovery rate.

Conservation

$$S'(t) + I'(t) = 0 \quad \implies \quad S(t) + I(t) = 1.$$

Closed equation

Using $S(t) = 1 - I(t)$, the system becomes

$$I'(t) = (\beta - \gamma)I(t) - \beta I(t)^2.$$

Explicit solution

For $I(0) = I_0$ and $\beta \neq \gamma$,

$$I(t) = \frac{(\beta - \gamma)I_0}{\beta I_0 + (\beta - \gamma - \beta I_0)e^{-(\beta - \gamma)t}}.$$

If $\beta = \gamma$,

$$I(t) = \frac{I_0}{1 + \beta I_0 t}.$$

Equilibria

$$I_0^* = 0, \quad I_e^* = 1 - \frac{\gamma}{\beta} \quad (\beta > \gamma).$$

Numerical simulation

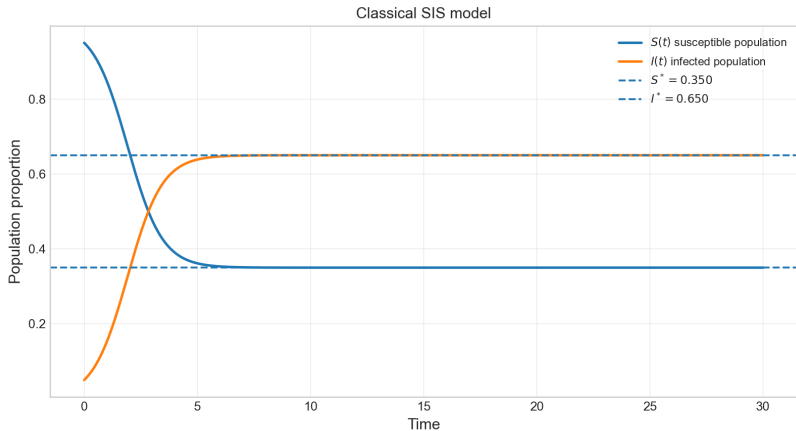


Figure: Convergence to the endemic equilibrium

Why introduce structure?

Classical SIS

$$I(t)$$
$$\beta, \gamma \text{ constant}$$

all infected individuals are treated identically

Structured SIS

$$I(t, x), \quad x \in \Omega$$
$$k(x, y), \quad \gamma(x)$$

different strains may transmit, mutate and recover differently



Evolution equation

$$\partial_t I(t, x) = S(t) \int_{\Omega} k(x, y) I(t, y) dy - \gamma(x) I(t, x).$$

Interpretation

- $k(x, y)$: transmission from trait y to trait x , including mutation;
- $\gamma(x)$: recovery rate of individuals infected by trait x ;
- $S(t)$: proportion of susceptible individuals,
- $I(t, x)$: proportion of infected by trait x individuals.

Normalized equation

Since the total population is conserved, we normalize

$$S(t) + \int_{\Omega} I(t, x) dx = 1.$$

Closed equation on I

$$\partial_t I(t, x) = (1 - m(t)) \int_{\Omega} k(x, y) I(t, y) dy - \gamma(x) I(t, x),$$

where

$$m(t) := \int_{\Omega} I(t, x) dx.$$

$$S(t) = 1 - m(t).$$

Definition

For each fixed infected mass $m \in [0, 1]$, define

$$L_m \varphi = (1 - m)K\varphi - \Gamma\varphi,$$

that is

$$L_m \varphi(x) = (1 - m) \int_{\Omega} k(x, y) \varphi(y) dy - \gamma(x) \varphi(x).$$

Interpretation

The operator L_m describes the linear infection dynamics when the total infected mass is fixed at level m .

Endemic equilibrium

An endemic equilibrium $I^* \geq 0$, $I^* \neq 0$ satisfies

$$0 = (1 - m^*)KI^* - \Gamma I^*, \quad m^* = \int_{\Omega} I^*(x) dx.$$

Equivalently,

$$L_{m^*} I^* = 0.$$

Definition

$$s(L_m) := \sup\{\operatorname{Re}(\lambda) \text{ for } \lambda \text{ in the spectrum of } L_m\}.$$

Possible equilibrium masses are selected by $s(L_m) = 0$.

Monotonicity and saturation

The map

$$m \mapsto s(L_m)$$

is continuous, non-increasing and may saturate at the level $-\underline{\gamma}$.

Regular case

If $\underline{\gamma} > 0$, a plateau may occur, but only below zero:

$$s(L_m) = -\underline{\gamma} < 0.$$

Thus $s(L_m) = 0$ still selects a unique mass.

Singular case

If $\underline{\gamma} = 0$, the saturation level is zero:

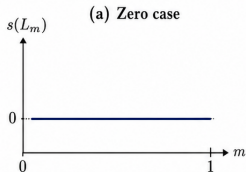
$$s(L_m) = 0 \quad \text{for } m \in [\underline{m}, 1].$$

Hence several endemic masses may be admissible.

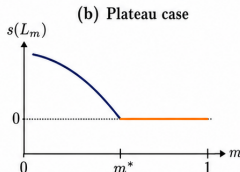
Illustration of the possible map $m \mapsto s(L_m)$

Possible shapes of $m \mapsto s(L_m)$

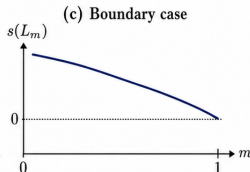
1) Singular case: $\gamma = 0$



$s(L_m) = 0$ for all m

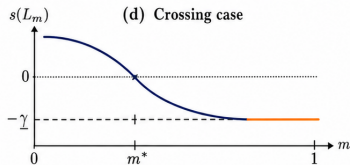


$s(L_m) = 0$ on $[m^*, 1]$

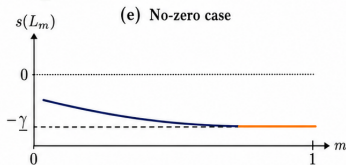


$s(L_m) \downarrow 0$ only at $m = 1$

2) Regular case: $\gamma > 0$



unique zero m^*



no endemic equilibrium

Numerical illustration: spectral plateau

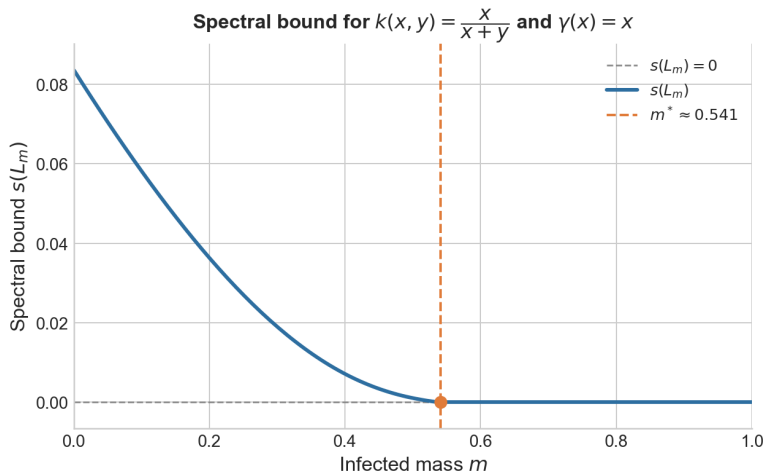


Figure: A spectral plateau may appear in the singular case.

Linearization

The disease-free equilibrium is

$$I \equiv 0.$$

The linearized operator is

$$L_0 = K - \Gamma.$$

Threshold principle

$$s(L_0) < 0 \implies \text{extinction,}$$

$$s(L_0) > 0 \implies \text{persistence.}$$

Epidemiological meaning of \mathcal{R}_0

Basic reproduction number

Average number of secondary infections from one individual in a fully susceptible population.

$\mathcal{R}_0 < 1$ — extinction

Each infection produces *less than one* new case on average.
 \implies disease dies out.

$\mathcal{R}_0 > 1$ — invasion

Each infection produces *more than one* new case on average.
 \implies epidemic spreads.

SIS classic model

In the first model we define \mathcal{R}_0 by the formula $\mathcal{R}_0 := \frac{\beta}{\gamma}$.

Structured populations

When infections are distributed over traits $x \in \Omega$, the quantity \mathcal{R}_0 is no longer a scalar rate ratio, but the **spectral radius of a positive operator**:

$$\mathcal{R}_0 = r(K\Gamma^{-1}) \quad \text{with} \quad K\Gamma^{-1}[f](x) = \int_{\Omega} \frac{k(x,y)}{\gamma(y)} f(y) dy.$$

Structured populations and singular case

If $\underline{\gamma} = 0$, the operator $K\Gamma^{-1}$ may not be well defined. We use instead the generalized quantity

$$\mathcal{R}_0 := \lim_{\lambda \downarrow 0} r \left(K(\lambda I + \Gamma)^{-1} \right).$$

Regular case (Horst R Thieme, 2009).

If $\underline{\gamma} > 0$, the next-generation operator $\mathcal{R}_0 = r(K\Gamma^{-1})$ is well defined. Then

$$s(L_0) \geq 0 \iff \mathcal{R}_0 \geq 1.$$

Singular case

If $\underline{\gamma} = 0$, the generalized reproduction number give us the following result :

$$s(L_0) = 0 \iff R_0 \leq 1, \quad \text{and} \quad s(L_0) > 0 \iff R_0 > 1.$$

Long-time dynamics according to $s(L_0)$

$$m(t) := \int_{\Omega} I(t, x) dx.$$

Regime	Assumption	Conclusion
Subcritical	$s(L_0) < 0, \underline{\gamma} > 0$	$m(t) \rightarrow 0$ exponentially
Critical	$s(L_0) = 0, \underline{\gamma} > 0$	$m(t) = O(t^{-1})$
Supercritical	$s(L_0) > 0$	$\liminf_{t \rightarrow +\infty} m(t) > 0$

Singular subcritical case

When $\underline{\gamma} = 0$, the extinction result for $s(L_0) = 0$ is not obtained by the present argument.

A spectral Lyapunov functional

Let $\Phi > 0$ satisfy $L_0^* \Phi = s(L_0) \Phi$ and set $Y(t) := \langle \Phi, I(t) \rangle$. Then

$$Y'(t) = s(L_0)Y(t) - m(t)\langle K^* \Phi, I(t) \rangle.$$

Subcritical case

If $s(L_0) < 0$, then

$$Y'(t) \leq s(L_0)Y(t),$$

hence

$$Y(t) \rightarrow 0, \quad m(t) \rightarrow 0.$$

Supercritical case

If $s(L_0) > 0$, then

$$Y'(t) \geq (s(L_0) - Cm(t))Y(t).$$

Therefore the infection cannot vanish.

In the singular case, some strains may have no recovery:

$$Z := \{x \in \Omega : \gamma(x) = 0\}.$$

Main difficulty

When $\underline{\gamma} = 0$, endemic equilibria may no longer be regular densities in $L^1(\Omega)$. They may appear as measures:

$$\mu^* \in \mathcal{M}_+(\Omega).$$

Vanishing recovery may produce concentration phenomena.

Let

$$\mu^* = \mu_{ac}^* + \mu_{sing}^*$$

be the Lebesgue decomposition of an equilibrium measure.

Localization of the singular part

Any singular part must be supported on the zero-recovery set:

$$\text{supp}(\mu_{sing}^*) \subset Z.$$

Singularities can only occur on incurable strains.

Zero-recovery set

The theory predicts that singular components can only concentrate on Z .

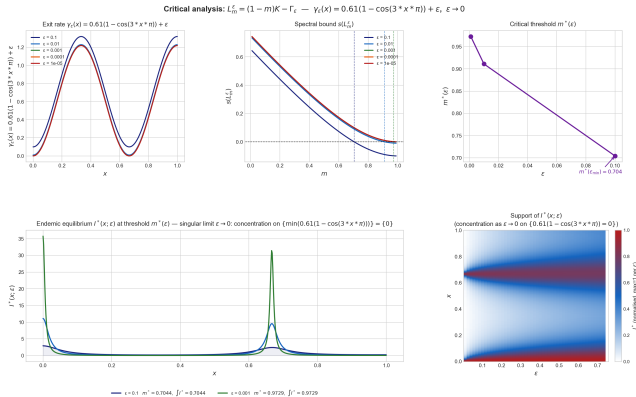


Figure: Concentration of the equilibrium near the zero-recovery set.

Stationary equation

An equilibrium measure μ^* satisfies

$$(1 - m)K\mu^* = \Gamma\mu^*.$$

Regularizing effect

Since $K\mu^*$ is absolutely continuous, the measure $\Gamma\mu^*$ is also absolutely continuous.

Consequence

On $\Omega \setminus Z$, one has $\gamma(x) > 0$, so μ^* is absolutely continuous there. Therefore

$$\text{supp}(\mu_{\text{sing}}^*) \subset Z.$$

Define the infectious potential

$$B(y) := \int_{\Omega \setminus Z} \frac{k(x, y)}{\gamma(x)} dx, \quad \bar{B} := \sup_{y \in \Omega} B(y).$$

Dichotomy

- $B(y) = +\infty$ for all $y \in Z \implies \int_Z d\mu^* = 0.$
- $0 < \bar{B} < +\infty \implies$ for $m > \frac{\bar{B} - 1}{\bar{B}}, \int_Z d\mu^* > 0.$

Regular approximation of the singular regime

$$\gamma_\varepsilon(x) = \gamma(x) + \varepsilon, \quad \varepsilon \downarrow 0.$$

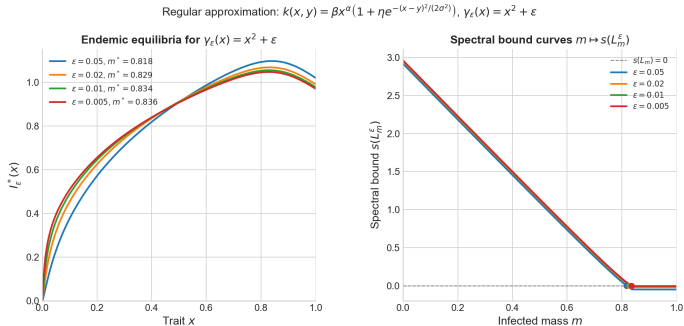


Figure: Regularized equilibria and spectral bounds as $\varepsilon \rightarrow 0$.

Main message

$s(L_0)$ is the relevant epidemic threshold.

- The nonlinear SIS dynamics is governed by the spectral bound of L_0 .
- In the regular case, this recovers the classical \mathcal{R}_0 -threshold.
- In the singular case, spectral plateaus and measure-valued equilibria may appear.
- Singular components concentrate on the zero-recovery set

$$Z = \{\gamma = 0\}.$$

Further directions

- Prove convergence of the total infected mass $m(t)$ toward an endemic mass m^* .
- Prove convergence of the infected distribution toward an endemic equilibrium:

$$I(t, \cdot) \longrightarrow I^*.$$

- Perturbations of mutation-selection operators.
- Extension to co-infection system.

Thank you for your attention

Questions?