Influence of human behaviors on the spread of an epidemic

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Outline

 Spatial heterogeneity and human mobilities:
 ~> complex networks of epidemic models joint work with Cristiana J. Silva

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Influence of human behaviors:

 ~> coupling with a discrete-probabilistic process
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On-going work:

 → continuous domains
 → abstraction and verification of hybrid dynamical systems

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Human behaviors

[Epstein et al. (2008). Coupled contagion dynamics of fear and disease : mathematical and computational explorations. PLoS One.]

A huge literature...

→ Numerous books, thousands of papers...





A huge literature...



mate individuals coupled with the coupled

Differential equations

► The SIR model (S: susceptible, I: infected, R: recovered):

$$\begin{cases} \frac{dS}{dt} = -\frac{\beta IS}{N}, \\ \frac{dI}{dt} = +\frac{\beta IS}{N} - \gamma I, \\ \frac{dR}{dt} = +\gamma I. \end{cases}$$

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∽→ the transmission of the disease is much faster than the dynamics of birth and death,

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► Multiple variants: additional compartments, reaction-diffusion, fractional diffusion, time delays, age structure...

▶ Agent-based models, cellular automata, transition systems...



Source: https://cloud.anylogic.com/models





► Existence of irregular oscillations



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- ▶ The environment is not necessarily periodic



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- ▶ The environment is not necessarily periodic
- \rightsquigarrow First step: provide an heterogeneous spatial structure
 - \rightarrow geographical network
- \rightsquigarrow Second step: integrate the impacts of human behaviors
 - \rightarrow hybrid dynamical system

Spatial heterogeneity and human mobilities: complex networks of epidemic models We consider a population affected by a HIV/AIDS epidemic. The SICA model [Silva & Torres (2017)] is given by

$$\begin{cases} \dot{S} = \Lambda - \beta \left(I + \eta_C C + \eta_A A \right) S - \mu S, \\ \dot{I} = \beta \left(I + \eta_C C + \eta_A A \right) S - \left(\rho + \phi + \mu \right) I + \omega C + \alpha A, \\ \dot{C} = \phi I - \left(\omega + \mu \right) C, \\ \dot{A} = \rho I - \left(\alpha + \mu + d \right) A. \end{cases}$$

S: number of susceptible individuals;

- I: HIV-infected individuals with no clinical symptoms of AIDS;
- C: HIV-infected individuals under ART treatment;
- A: HIV-infected individuals with AIDS clinical symptoms;
- N: total population.

Parameters of the SICA model

- Λ Recruitment rate
- μ Natural death rate
- β HIV transmission rate
- η_C Modification parameter
- η_A Modification parameter
- ϕ HIV treatment rate for I individuals
- ρ Default treatment rate for I individuals
- α AIDS treatment rate
- ω Default treatment rate for C individuals
- d AIDS induced death rate

► The SICA model admits a disease-free equilibrium (DFE) given by $\Sigma_0 = \left(\frac{\Lambda}{\mu}, 0, 0, 0\right)$.

▶ Its basic reproduction number R_0 (expected average number of new infections produced by a single infected individual) is given by

$$R_{0} = \frac{S^{0}\beta \left[\xi_{2} \left(\xi_{1} + \rho \eta_{A}\right) + \eta_{C} \phi \xi_{1}\right]}{\mu \left[\xi_{2} \left(\rho + \xi_{1}\right) + \phi \xi_{1} + \rho d\right] + \rho \omega d}$$

▶ The disease free equilibrium Σ_0 is globally asymptotically stable if $R_0 < 1$.

► The SICA model admits an endemic equilibrium Σ_+ , which is globally asymptotically stable if $R_0 > 1$.

▶ The SICA model can be rewritten:

$$\dot{x} = f(x, p), \quad x = (S, I, C, A)^T, \quad p = (\Lambda, \beta, \dots, \alpha, d).$$

Case study: Cape Verde archipelago



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► Ideas:

 \leadsto we can model the archipelago by a graph,

 \rightsquigarrow we can couple each vertex of the graph with an instance of the SICA model.

 \blacktriangleright We consider a graph ${\mathscr G}$ with n vertices.

▶ We divide the vertices into two subsets \mathscr{V}_1 , \mathscr{V}_2 .

► We couple:

 \leadsto the vertices of \mathscr{V}_1 with an instance of the SICA model for which $R_0 < 1$,

 \leadsto the vertices of \mathscr{V}_2 with an instance of the SICA model for which $R_0>1.$

▶ The complex network is determined by:

$$\dot{X} = F(X, P) + LHX,$$

where

$$X = (x_1, \dots, x_n)^T \in \left(\mathbb{R}^4\right)^n,$$

$$HX = (Hx_1, \dots, Hx_n)^T \in \left(\mathbb{R}^4\right)^n,$$

$$P = (p_1, \dots, p_n) \in \left(\mathbb{R}^{10}\right)^n,$$

and F determines the internal dynamic of each vertex:

$$F(X, P) = (f(x_1, p_1), \dots, f(x_n, p_n))^T.$$

Complex network of SICA models

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► Explicit equations of the complex network:

$$\begin{cases} \dot{S}_{j} = \Lambda_{j} - \beta_{j} (I_{j} + \eta_{C,j} C_{j} + \eta_{A,j} A_{j}) S_{j} - \mu_{j} S_{j} + \varepsilon_{S} \sum_{k=1}^{n} L_{j,k} S_{k}, \\ \dot{I}_{j} = \beta_{j} (I_{j} + \eta_{C,j} C_{j} + \eta_{A,j} A_{j}) S_{j} - (\rho_{j} + \phi_{j} + \mu_{j}) I_{j} \\ + \omega_{j} C_{j} + \alpha_{j} A_{j} + \varepsilon_{I} \sum_{k=1}^{n} L_{j,k} I_{k}, \\ \dot{C}_{j} = \phi_{j} I_{j} - (\omega_{j} + \mu_{j}) C_{j} + \varepsilon_{C} \sum_{k=1}^{n} L_{j,k} C_{k}, \\ \dot{A}_{j} = \rho_{j} I_{j} - (\alpha_{j} + \mu_{j} + d_{j}) A_{j} + \varepsilon_{A} \sum_{k=1}^{n} L_{j,k} A_{k}. \end{cases}$$

Connections

▶ L is the matrix of connectivity: for each edge $(k, j) \in \mathcal{E}$, $k \neq j$, we have $L_{j,k} > 0$. If $(k, j) \notin \mathcal{E}$, $k \neq j$, we set $L_{j,k} = 0$. The diagonal coefficients satisfy

$$L_{j,j} = -\sum_{\substack{k=1\\k\neq j}}^{n} L_{k,j}.$$

 \blacktriangleright Finally, H is the matrix of the coupling strengths and it is given by

$$H = \begin{bmatrix} \varepsilon_S & 0 & 0 & 0 \\ 0 & \varepsilon_I & 0 & 0 \\ 0 & 0 & \varepsilon_C & 0 \\ 0 & 0 & 0 & \varepsilon_A \end{bmatrix},$$

with non negative coefficients ε_S , ε_I , ε_C and ε_A .

► Theorem (Cantin & Silva 2019)

The complex network of SICA models admits a unique disease-free equilibrium Σ_0 , which is globally asymptotically stable in the region Ω defined by

$$\Omega = \left\{ (x_j)_{1 \le j \le 4n} \in (\mathbb{R}^+)^{4n} \ ; \ \sum_{j=1}^{4n} x_j \le \frac{\sum \Lambda_j}{\min \mu_j} \right\}$$

provided

$$\frac{\Lambda_0}{\mu_0} \frac{\mathcal{N}_i}{\mathcal{D}_i} < 1,$$

for all $i \in \{1, \ldots, n\}$, with known constants \mathcal{N}_i , \mathcal{D}_i .

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for all $i \in \{1, \ldots, n\}$, with known constants \mathcal{N}_i , \mathcal{D}_i .

 \sim Local basic reproduction number: $R_{0,i} = \frac{\Lambda_i}{\mu_i} \frac{\mathcal{N}_i}{\mathcal{D}_i}$.


Two-nodes network. Green node: $R_{0,1} < 1$. Red node: $R_{0,2} > 1$.

Example: simple two-nodes network



Two-nodes network. Green node: $R_{0,1} < 1$. Red node: $R_{0,2} > 1$.



Influence of the coupling strengths ε_S , ε_I , ε_C and ε_A on the basic reproduction numbers $R_{0,1}$ and $R_{0,2}$.

Randomly generated topologies

► We introduce the final level of infected individuals:

$$L_{f} = \sum_{j=1}^{n} \left[I_{j}(T) + C_{j}(T) + A_{j}(T) \right].$$

▶ Question: can we find a network topology that minimizes L_f ?

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▶ Question: can we find a network topology that minimizes L_f ?

▶ Idea: we generate a sample of randomly generated topologies, by choosing a random number of edges $1 \le |\mathscr{E}| \le 72$, and a random subset of $|\mathscr{E}|$ edges.



Optimal topologies



Numerical results for two samples of 1400 randomly generated topologies. Green dotted vertical line: level of infected individuals without coupling. Optimal topology: green circle. ► A near-optimal topology detected by the random simulation:

$$\mathscr{E} = \Big\{ [1,3], [2,9], [5,6], [3,7], [7,9], [2,7], [1,9], \\ [6,2], [6,4], [2,8], [5,2], [8,1], [1,5], [1,4] \Big\}.$$

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Influence of human behaviors: hybrid dynamical systems

Assume a population of individuals is subject to a complex evolution process which cannot be described at a single scale.
 We construct a hybrid model by coupling a system of ordinary differential equations and a discrete process, which can be derived from an agent-based model.

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$$X = (x_1, \ldots, x_n).$$

▶ We consider a discrete sequence of times (t_s).
 ▶ We introduce, for s ≥ 0, the abstract hybrid problem

$$\begin{cases} (\Im \mathfrak{C}) & X(t_0) = X_0, \quad \lambda_0 \in J, \\ (\mathfrak{M}_s) & \dot{X}(t) = F(X(t), \lambda_s), \quad t_s < t \le t_{s+1}, \\ (\mathfrak{m}_s) & \lambda_{s+1} = G(X(t_{s+1}), \lambda_s). \end{cases}$$

Construction of a class of abstract hybrid models

▶ F is a function defined in $E \times J$ with values in \mathbb{R}^n , where E is an open subset of \mathbb{R}^n and J is an open subset of \mathbb{R}^d .

- ▶ G is a function defined in $E \times J$ with values in J.
- ▶ (\mathfrak{IC}) determines the initial condition $(X_0, \lambda_0) \in E \times J$.

▶ (\mathfrak{M}_s) is an ordinary differential equation which determines the macroscopic part of the hybrid problem.

▶ (\mathfrak{m}_s) is a discrete mapping which determines the microscopic part of the hybrid problem.

Timeline of the hybrid model



Timeline of the hybrid model. At $t = t_0$, the initial condition (\mathfrak{IC}) gives $(X_0, \lambda_0) \in E \times J$. On each interval $[t_s, t_{s+1}]$, the macroscopic part (\mathfrak{M}_s) is determined by an ordinary differential equation. At each time step $t = t_s$, the microscopic part (\mathfrak{m}_s) follows from a discrete mapping which is derived from an agent-based model. ▶ Assumption 1. The function F involved in the macroscopic part (\mathfrak{M}_s) of the hybrid problem is $\mathscr{C}^1(E \times J)$.

▶ Assumption 2. There exists a compact set $K \subset E$ such that, for all $(X_0, \lambda_0) \in K \times J$, each local solution $X(t, X_0)$ of the Cauchy problem

$$X(t_0) = X_0, \quad \dot{X}(t) = F(X(t), \lambda_0)$$

defined on $[t_0, t_0 + T]$ with T > 0 satisfies

 $X(t, X_0) \in K,$

for all $t \in [t_0, t_0 + T]$.

▶ Assumption 3. The function G involved in the microscopic part (\mathfrak{m}_s) of the hybrid problem is continuous in $E \times J$.

► Theorem (Cantin Silva Banos, 2022)

Let the assumptions 1, 2 hold. Then for all $(X_0, \lambda_0) \in K \times J$, the hybrid problem admits a unique global solution $X(t, X_0, \lambda_0)$ defined on $[t_0, +\infty)$.

If moreover assumption 3 holds, then each global solution $X(t, X_0, \lambda_0)$ of the hybrid problem is continuous at (X_0, λ_0) , uniformly on each finite time interval $[t_0, t_0 + T]$ with T > 0, that is, for each T > 0 and each $\varepsilon > 0$, there exists $\delta > 0$ such that

$$\|X(t, X_0 + h, \lambda_0 + k) - X(t, X_0, \lambda_0)\|_{\mathbb{R}^n} < \varepsilon,$$

for all $t \in [t_0, t_0 + T]$, provided that $||(h, k)||_{\mathbb{R}^n \times \mathbb{R}^d} < \delta$.

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• What if G is discontinuous? \rightsquigarrow High sensitivity of the model.

Irregular oscillations

▶ We suppose that there exist two distinct parameters sets $\Lambda_1 \subset J$ and $\Lambda_2 \subset J$ with $\Lambda_1 \cap \Lambda_2 = \emptyset$.

• Assume Σ_1 is an equilibrium point of the equation

 $\dot{X} = F(X, \lambda_1),$

for each $\lambda_1 \in \Lambda_1$, and Σ_2 is an equilibrium point of the equation

$$\dot{X} = F(X, \lambda_2),$$

for each $\lambda_2 \in \Lambda_2$.

• We introduce the minimum step of the timeline $\{t_s\}$:

$$\tau = \min_{s \ge 0} \left| t_s - t_{s+1} \right|.$$

► Theorem

Suppose that assumptions 1, 2 hold. Assume that Σ_1 is globally asymptotically stable in $W_1 \subset K$ for each $\lambda_1 \in \Lambda_1$, Σ_2 is globally asymptotically stable in $W_2 \subset K$ for each $\lambda_2 \in \Lambda_2$. Assume moreover that $\Sigma_1 \in W_2$, $\Sigma_2 \in W_1$ and $G(Y, \lambda) \in \Lambda_2$ if Y is near Σ_1 and $\lambda \in \Lambda_1$, $G(Y, \lambda) \in \Lambda_1$ if Y is near Σ_2 and $\lambda \in \Lambda_2$.

Then every solution $X(t, X_0, \lambda_0)$ of the hybrid problem starting from $(X_0, \lambda_0) \in W_1 \times \Lambda_1$ admits irregular oscillations, that is, oscillations between a neighborhood \mathcal{N}_1 of Σ_1 and a neighborhood \mathcal{N}_2 of Σ_2 , provided the minimum step τ of the timeline is sufficiently large. ▶ We consider the *SAIRP* model with refractory behaviors [Silva *et al.* 2021]:

$$\begin{cases} \dot{S} = \Lambda - \beta (1 - p(1 - u)) \frac{(\theta A + I)}{N} S - \phi p(1 - u) S + \omega P - \mu S, \\ \dot{A} = \beta (1 - p(1 - u)) \frac{(\theta A + I)}{N} S - \nu A - \mu A, \\ \dot{I} = \nu A - \delta I - \mu I, \\ \dot{R} = \delta I - \mu R, \\ \dot{P} = \phi p(1 - u) S - \omega P - \mu P. \end{cases}$$

► S: susceptible individuals, A: asymptomatic infected individuals, I: active infected individuals, R: removed (including recovered and COVID-19 induced deaths); P: protected individuals.

- $\Lambda \quad {\rm Recruitment\ rate}$
- μ Natural death rate
- θ ~ Infectiousness of the asymptomatic infected individuals
- v Transfer rate from A to I
- q Fraction of A individuals that are confirmed to be infected
- ϕ ~ Transfer rate from S to P
- δ ~ Transfer rate from I to R
- ω $\;$ Transfer rate from P to S
- p Fraction of protected individuals
- u Refractory or opposition behaviors to the protection strategy

▶ We assume that the individuals are spatially distributed into a finite number of regions D_1, \ldots, D_m with $m \ge 1$; some of these regions are interconnected and individuals present a spatial mobility from one region to another.



► The dynamics of the epidemic is modeled at the macroscopic scale by a complex network of ordinary differential equations:

$$\frac{dx_{i,j}}{dt} = f_j(x_i, \alpha_i) + \sigma_j \sum_{k=1}^n L_{i,k} x_{j,k}, 1 \le j \le 5, 1 \le i \le m, t \ge 0.$$

Transition from the ODE to an agent-based model

► We cannot follow the trajectory of a single individual during the macroscopic process.

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▶ Assume X(t, X_s, λ_s) solves (M_s) on [t_s, t_{s+1}]. For each sub-population x_{ij} of type j in each region D_i, we evaluate x_{ij}(t_{s+1}) and we compute N_{ij}(t_{s+1}) = [x_{ij}(t_{s+1})]. We then introduce the agents: A_{ij} = {a¹_{ij}, a²_{ij}, ..., a^{N_{ij}}}.
▶ We generate a social network over the groups (A_{ij})_{1≤j≤5} of each region D_i by running a graph generation algorithm.



We assume that agents model citizens or decision makers and focus on two types of actions.

► Action 1. In each region D_i , $1 \le i \le m$, decision makers evaluate the rate $\rho_I(D_i, t_{s+1})$ of infected individuals.

- If the rate ρ_I(D_i, t_{s+1}) overcomes a given threshold T₁, that is ρ_I(D_i, t_{s+1}) > T₁, then decision makers decide to increase the fraction p_i of individuals.
- Else, the fraction of protected individuals is maintained.
- If at least one of the rates ρ_I(D_i, t_{s+1}), 1 ≤ i ≤ m, overcomes a second threshold T₂ > T₁, then decision makers decide to confine the individuals in their region.
- Else, then decision makers reestablish the mobilities.

► Action 2. In each region D_i , agents \mathfrak{a}_{ij}^g observe the types of their neighbors. Among these neighbors, each agent \mathfrak{a} evaluates the number $\mathfrak{N}(I, \mathfrak{a}, t_{s+1})$ of infected neighbors.

- If the rate of infected neighbors overcomes a given threshold *T*₃, then citizens decide to be in opposition with the protection strategy.
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- If the rate of infected neighbors overcomes a given threshold *T*₃, then citizens decide to be in opposition with the protection strategy.
- Else, then citizens accept to decrease their level of opposition.
- ▶ The two-actions protocol defines a discrete mapping

$$\lambda_{s+1} = G(X(t_{s+1}), \lambda_s),$$

which determines the microscopic part (\mathfrak{m}_s) of a hybrid model.

► Theorem (Cantin Silva Banos, 2022)

(1) For any $X_0 \in (\mathbb{R}^+)^{5m}$ and any $\lambda_0 \in J$, the hybrid model admits a unique solution denoted by $X(t, X_0, \lambda_0)$, defined on $[0, \infty)$, whose components are non-negative.

(2) Furthermore, the hybrid model admits a compact and positively invariant region K.

(3) The hybrid model admits solutions exhibiting irregular solutions between two equilibrium points (DFE and EE).

► Solutions exhibiting irregular solutions can easily be generated by forcing a variation of the parameter *p*.



 $\rightsquigarrow {\rm Roughly:} \ p=0.95 \Leftrightarrow {\rm confinement}, \ p=0.2 \Leftrightarrow {\rm end} \ {\rm of}$ confinement.

Sc. 3: postponed extinction of the disease by opposition behaviors



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On going work

Hybrid dynamical system with continuous domains

▶ We consider a reaction-diffusion epidemic model

$$\begin{aligned} \partial_t S &= d_1 \Delta S + \mu N - \mu S - \beta SI, \quad x \in \Omega, \quad t > 0, \\ \partial_t I &= d_2 \Delta I - (\mu + \nu)I + \beta SI, \quad x \in \Omega, \quad t > 0, \end{aligned}$$

in a bounded domain Ω , coupled with a discrete-probabilistic process along a timeline of step $\tau > 0$.

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Questions:

- well-posedness of the hybrid model?
- stability of the equilibrium points?
- bifurcation of cycles w.r.t τ?
- existence of an attractor?

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► We consider a continuous dynamical system $S_{\lambda}(t)$ depending on a parameter λ , with uniform phase space Φ , coupled with a discrete probabilistic process Θ along a timeline of step $\tau > 0$.

► How to verify dynamical properties of the hybrid system (S) resulting from the coupling?

 \rightsquigarrow We can abstract the dynamics of the hybrid system as a Markov decision process (\mathcal{M}) and verify relevant properties directly on (\mathcal{M}) , with *Model Checking* algorithmic techniques of theoretical computer science.

 \blacktriangleright The abstraction requires to consider a discretization of the hybrid model (S).

Abstraction and verification of piecewise deterministic Markov processes



▶ How to abstract a property of (S) as a property of (M)?

▶ Is the abstraction a "surjective" mapping?

▶ Can we "inverse" the verification of (\mathcal{M}) ?

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 \rightsquigarrow Joint work with Cristiana J. Silva, Arnaud Banos

[Mathematical analysis of a hybrid model: Impacts of individual behaviors on the spreading of an epidemic, Networks and Heterogeneous Media (2022)]

▶ and also: A. Tajani, B. Delahaye, G. Ardourel, D. Julien.

► It is difficult to model human behaviors and their influence on the spread of an epidemic.

- ▶ It is important to couple multiple formalisms and multiple scales.
- ► A hybrid model can reproduce complex epidemic waves.
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Thank you for your attention!