

# Modèles structurés multi-niveaux de dynamiques épidémiques

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# Motivation and goals

School and/or workplace closures: efficient non-pharmaceutical interventions for mitigating epidemics, e.g. COVID-19 and influenza (Mendez-Brito et al., 2021; Luca et al., 2018).

⇒ Models with several levels of mixing: explicitly distinguish different types of contact.

## ⇒ Aim of the present study:

1. Better understanding of the epidemic impact of small contact structures: indicators capturing this impact?
2. Propose reduced models = approximate models that are more prone to mathematical analysis / numerical exploration.

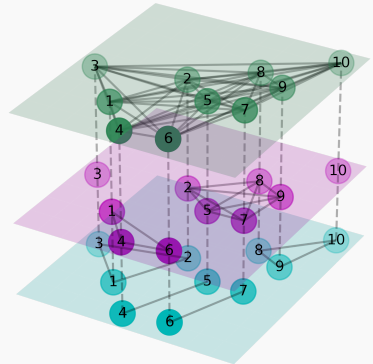
# **A multilayer model with households and workplaces**

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# Population structure

Model introduced by Pellis et al., 2009.

1. **Global** level of mixing → homogeneously mixing **general population**.
2. **Local** level of mixing → **households** and **workplaces**:
  - Structure size distributions  $\pi^H$  and  $\pi^W$ , maximal size  $n_{\max} < \infty$ .
  - Each individual is attributed to a household and workplace independently from one another and from other individuals.



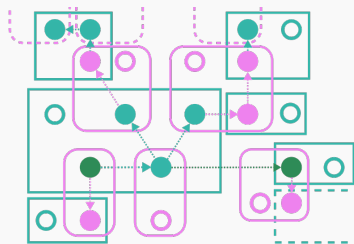
# Epidemic process

Modified *SIR* model  $\rightarrow$  three ways of contamination in a population of size  $K$ :

- **General population:** total of  $S$  susceptible and  $I$  infected individuals  $\rightarrow$  infections at rate  $\frac{\beta_G}{K} SI$ .
- **Intra-household** or **intra-workplace:**  $s$  susceptible and  $i$  infected members  $\rightarrow$  infections at rate  $\lambda_X si$  for  $X \in \{H, W\}$ , respectively.

Duration of infectious periods

$\sim \text{Exp}(\gamma)$

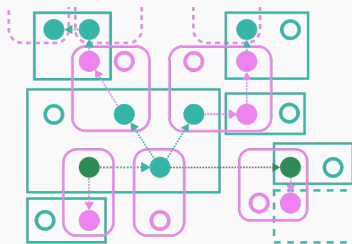


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⇒ **Stochastic model of parameters**

$$(K, \underbrace{\pi^H, \pi^W}_{\text{social structure}}, \underbrace{\lambda_h, \lambda_w, \beta_g, \gamma}_{\text{epidemic}}).$$

# $R_0$ and exponential growth rate

Reproduction number  $R_0$ : outbreak criterion (threshold = 1).

- Intuition: average number of contaminations caused by a 'typical' infected at the beginning of the epidemic.
- Several possible definitions → most of them use the fact that some correlations can be neglected at the beginning of the epidemic.
- $R_0$  introduced by Pellis et al., 2009 → associated to the proportions  $(p_H, p_W, p_G)$  of infection in each layer.

Exponential growth rate  $r$ : characterised by an implicit equation (Pellis et al., 2011) → can only be solved numerically.

# The epidemiological footprint of contact structures

Bansaye, Deslandes, Kubasch and Vergu (2023)

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# Simulation scenarios

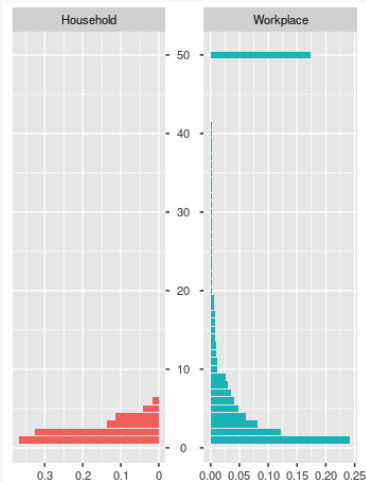
## 1. Population structure:

- Large population ( $K = 100,000$ ).
- Fixed household size distribution.
- Varied workplace size distributions (sizes 1 to 50).

↔ Teleworking.

## 2. Epidemic parameters: scenarios differ in terms of

- Epidemic intensity ( $R_0, r$ ).
- Proportions of infection between layers ( $p_G, p_H, p_W$ ).



# The influence of the variance of workplace size distribution of fixed average on key features of the epidemic

We are going to focus on a setting where the size of the population and the number of workplaces are fixed, considering that the latter is given by logistic constraints.

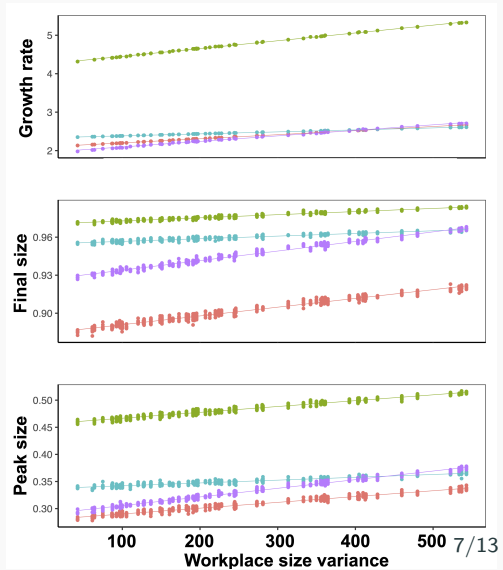
⇒ This implies that **the average workplace size is fixed**.

We are going to focus on the influence of the **workplace size variance** on the exponential growth rate  $r$ , the peak size and the final size of the epidemic.

# The influence of the variance of workplace size distribution of fixed average on key features of the epidemic

For each epidemic scenario  $\rightarrow$  simulate epidemics for a variety of workplace distributions, of fixed mean and different variances.

$\Rightarrow$  Linear dependence on the variance: good proxy for the impact of  $\pi^W$ .



## Approximation using a uniformly mixing SIR model

**Proposed approach:** approximate our model by a classical *SIR* model:

$$\begin{cases} S' = -\beta SI \\ I' = \beta SI - \gamma I \\ R' = \gamma I. \end{cases}$$

⇒ How to fit the parameters?

- Removal rate  $\gamma$  usually known (epidemiological expertise).
- Two natural candidates for calibrating  $\beta$ :  $\beta = \gamma R_0$  or  $\beta = r + \gamma$ .

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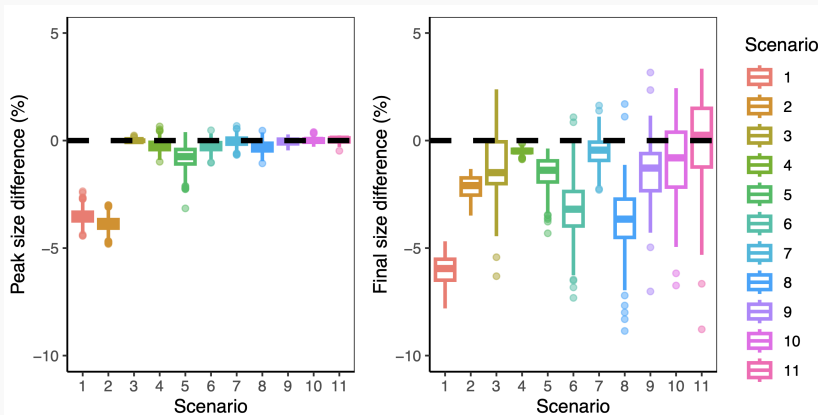
$$\begin{cases} S' = -(r + \gamma)SI \\ I' = (r + \gamma)SI - \gamma I \\ R' = \gamma I. \end{cases}$$

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- Removal rate  $\gamma$  usually known (epidemiological expertise).
- Two natural candidates for calibrating  $\beta$ :  $\beta = \gamma R_0$  or  $\beta = r + \gamma$ .

# The growth rate allows to capture the epidemic footprint of social structures

Comparison of simulation outputs and reduced model predictions  
⇒ satisfying results on key features of the epidemic:



# Large population approximation

Kubasch (2023)

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## General idea

**Large graph limit:** well understood for epidemics on configuration models (Volz, 2008; Decreusefond et al., 2012) → no small closed structures.

Reduced models suggested in similar settings (House and Keeling, 2008; Volz et al., 2011) → epidemic at the level of **structures** characterised by a **type**  $x$ :

$$x = (n, s, i)$$

structure size      number of susceptibles      number of infected

The diagram shows the equation  $x = (n, s, i)$  with three arrows pointing from the text below to the variables  $n$ ,  $s$ , and  $i$ . The text below is arranged in two lines: 'structure size' under  $n$ , 'number of susceptibles' under  $s$ , and 'number of infected' under  $i$ .

**Problem:** infected individuals correlate the epidemic states of their household and workplace.



## General idea

**Large graph limit:** well understood for epidemics on configuration models (Volz, 2008; Decreusefond et al., 2012)  $\rightarrow$  no small closed structures.

Reduced models suggested in similar settings (House and Keeling, 2008; Volz et al., 2011)  $\rightarrow$  epidemic at the level of **structures** characterised by a **type**  $x$ :

$$x = (n, s, \tau)$$

structure size      number of susceptibles      remaining infectious periods ( $\tau \in \mathbb{R}^n$ )

The diagram shows the equation  $x = (n, s, \tau)$  with three arrows pointing from descriptive text below to the variables  $n$ ,  $s$ , and  $\tau$ . A black arrow points from "structure size" to  $n$ . A black arrow points from "number of susceptibles" to  $s$ . A red arrow points from "remaining infectious periods ( $\tau \in \mathbb{R}^n$ )" to  $\tau$ .

**Solution:** keep track of each infected's remaining infectious period (similar in spirit to Ball et al., 2014).

# General idea

⇒ Measure-valued Markov process  $\zeta^K$  describing the epidemic process in a population of size  $K \rightarrow$  model reduction in two steps:

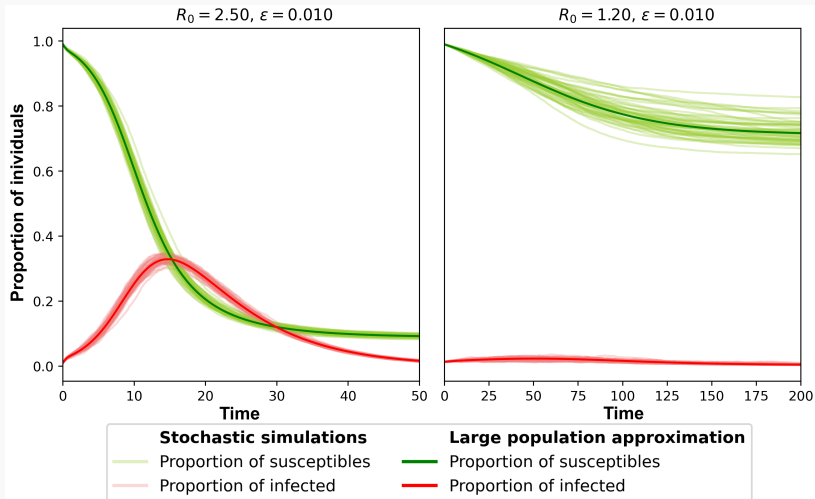
1. Tightness-identification-uniqueness strategy inspired by Tran, 2006  $\rightsquigarrow$  convergence in distribution when  $K \rightarrow \infty$  to the unique **deterministic solution**  $\eta$  of :

$$\begin{aligned} \langle \eta_T^X, f_T \rangle &= \langle \eta_0^X, f_0 \rangle + \int_0^T \langle \eta_t^X, \mathcal{A}f_t \rangle dt + \lambda_X \int_0^T \langle \eta_t^X, \mathbf{si}(f_t^I - f_t) \rangle dt \\ &+ \lambda_{\bar{X}} \int_0^T \frac{\langle \eta_t^{\bar{X}}, \mathbf{si} \rangle}{\langle \eta_t^{\bar{X}}, \mathbf{s} \rangle} \langle \eta_t^X, \mathbf{s}(f_t^I - f_t) \rangle dt + \beta_G \int_0^T \frac{\langle \eta_t^H, \mathbf{i} \rangle}{\langle \eta_0^H, \mathbf{n} \rangle} \langle \eta_t^X, \mathbf{s}(f_t^I - f_t) \rangle dt. \end{aligned}$$

2. Extract from  $\eta$  a **finite-dimensional closed dynamical system**.

# Simulations

**Examples:** Stochastic simulations (SSA) in a population of size  $K = 10000$  compared to the reduced model.



## **Conclusion and perspectives**

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# Key messages

- Proxy for the epidemic impact of the workplace size distribution: size distribution variance, exponential growth rate.
- Two **reduced models**:
  - Homogeneous mixing *SIR* model calibrated using the growth rate → key characteristics of the epidemic;
  - Large population approximation → asymptotically exact trajectories.
- Perspective: Closer study of the exponential growth phase?

**Thank you for your attention!**

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# References

- Ball, Frank G., David J. Sirl, and Pieter Trapman (June 2014). "Epidemics on Random Intersection Graphs". *The Annals of Applied Probability* 24.3, pp. 1081–1128.
- Bansaye, Vincent, François Deslandes, Madeleine Kubasch, and Elisabeta Vergu (Mar. 2023). *The Epidemiological Footprint of Contact Structures in Models with Two Levels of Mixing*.
- Decreusefond, Laurent, Jean-Stéphane Dhersin, Pascal Moyal, and Viet Chi Tran (Apr. 2012). "Large Graph Limit for an SIR Process in Random Network with Heterogeneous Connectivity". *The Annals of Applied Probability* 22.2.
- House, Thomas and Matt J. Keeling (May 2008). "Deterministic Epidemic Models with Explicit Household Structure". *Mathematical Biosciences* 213.1, pp. 29–39.
- Kubasch, Madeleine (May 2023). *Large Population Limit for a Multilayer SIR Model Including Households and Workplaces*.
- Luca, Giancarlo De, Kim Van Kerckhove, Pietro Coletti, Chiara Poletto, Nathalie Bossuyt, Niel Hens, and Vittoria Colizza (Jan. 2018). "The Impact of Regular School Closure on Seasonal Influenza Epidemics: A Data-Driven Spatial Transmission Model for Belgium". *BMC Infectious Diseases* 18.1, p. 29.
- Mendez-Brito, Alba, Charbel El Bcheraoui, and Francisco Pozo-Martin (Sept. 2021). "Systematic Review of Empirical Studies Comparing the Effectiveness of Non-Pharmaceutical Interventions against COVID-19". *Journal of Infection* 83.3, pp. 281–293.
- Pellis, Lorenzo, Neil M. Ferguson, and Christophe Fraser (Nov. 2009). "Threshold Parameters for a Model of Epidemic Spread among Households and Workplaces". *Journal of The Royal Society Interface* 6.40, pp. 979–987.
- Pellis, Lorenzo, Neil M. Ferguson, and Christophe Fraser (Oct. 2011). "Epidemic Growth Rate and Household Reproduction Number in Communities of Households, Schools and Workplaces". *Journal of Mathematical Biology* 63.4, pp. 691–734.
- Tran, Viet Chi (Dec. 2006). "Modèles particuliers stochastiques pour des problèmes d'évolution adaptative et pour l'approximation de solutions statistiques". PhD thesis. Université de Nanterre - Paris X.
- Volz, Erik M. (Mar. 2008). "SIR Dynamics in Random Networks with Heterogeneous Connectivity". *Journal of Mathematical Biology* 56.3, pp. 293–310.
- Volz, Erik M., Joel C. Miller, Alison Galvani, and Lauren Ancel Meyers (June 2011). "Effects of Heterogeneous and Clustered Contact Patterns on Infectious Disease Dynamics". *PLoS Computational Biology* 7.6. Ed. by Mark M. Tanaka, e1002042.