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A unified stochastic modelling framework for the spread of nosocomial infections

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Outline I

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Nosocomial infections: a short overview

- Hospital-acquired infections (HAI, or nosocomial infections), are infections that are acquired in healthcare facilities.
- These infections can be viral or bacterial, and can be spread in many different ways:
  1. By means of the contaminated hands of healthcare workers (vectors)
  2. Airborne transmission,
  3. Contaminated clinical equipment,
  4. Contaminated surfaces (hand-to-surface and surface-to-hand contacts)
- They can be specially problematic due to many reasons:
  1. Opportunities for bacteria to infect open wounds,
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- Particularly problematic are multi-drug resistant bacteria (MDRB). In Europe, MDRB cause around 33,000 deaths per year, where around 75% of this burden of disease is due to hospital-acquired infections.[1]
- Control strategies usually implemented:
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Nosocomial infections: a short overview

- Mathematical models have recently shown the potential to analyse these outbreaks.
- To assess the efficacy of each control strategy
- To identify the most probable routes of spread for these infections
- But we need to note:
  1. Very small populations ($5 - 100$ patients & HCWs in a hospital ward)
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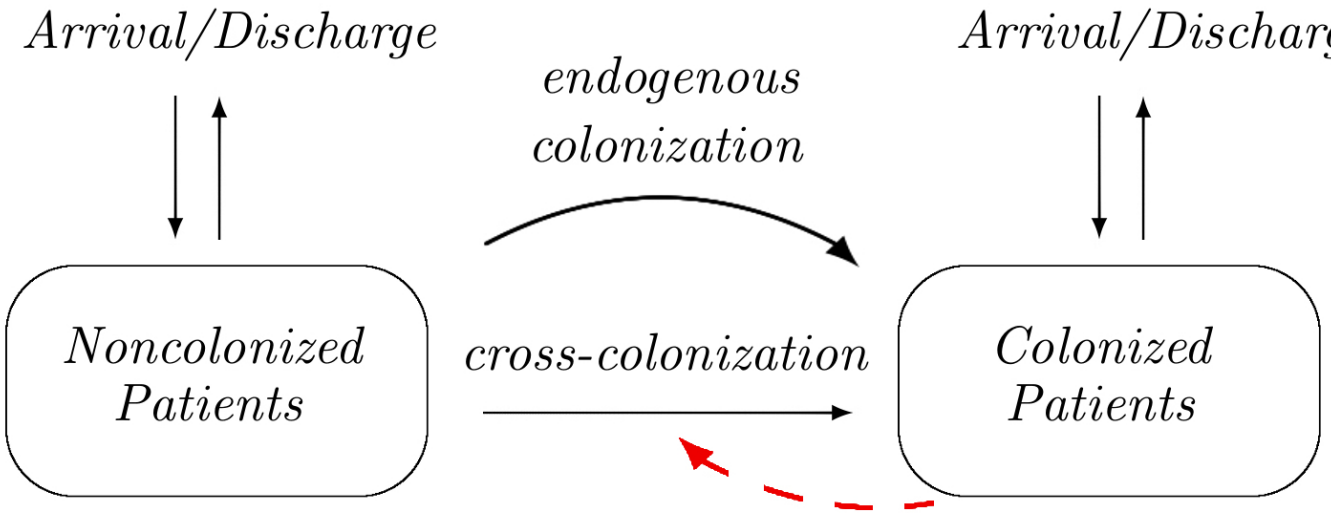
Simple models only with patients

Pelupessy et al. (2002)

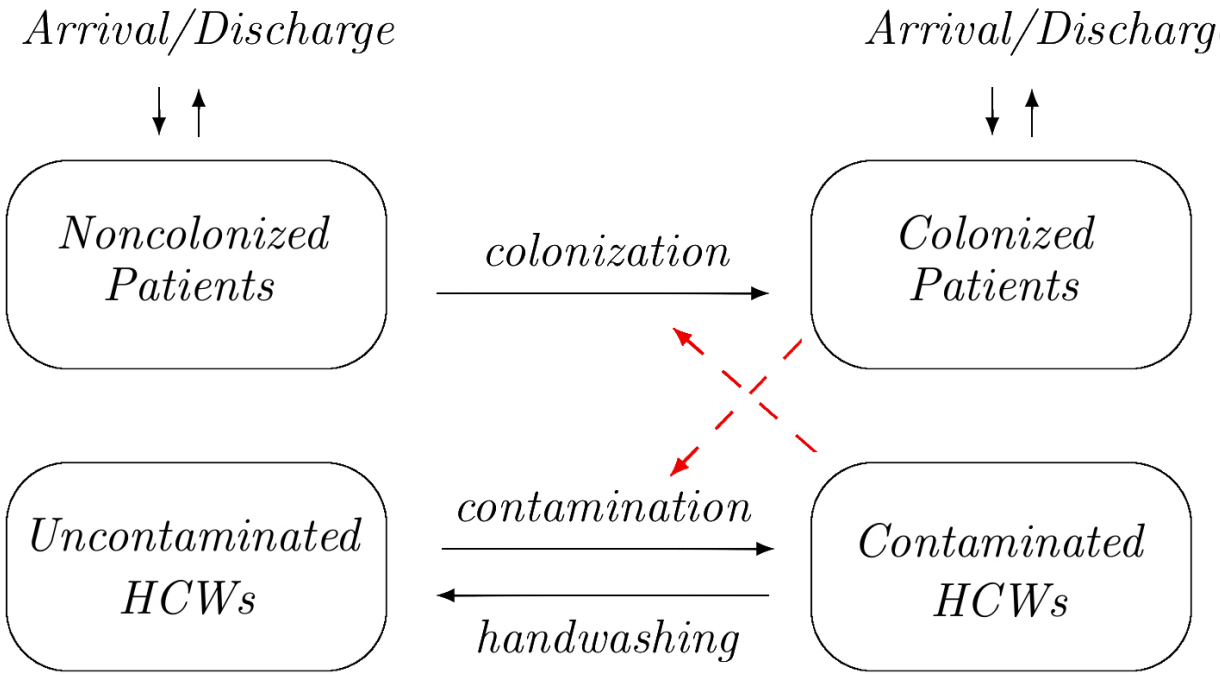


$I(t) \quad = \quad$ *Number of colonized patients at time t*

- Spontaneous colonization: α
- Cross-colonization: $\frac{\theta I(t)}{N}$
- Discharge of colonized patients: $\frac{1}{d'}$
- Discharge of non-colonized: $\frac{1}{d}$
- Probability of colonized admitted patient: q

Models that explicitly incorporate HCWs

Austin et al., Cooper et al. (1999), Chamchod & Ruan (2012), Artalejo (2014)



- N patients
- N' healthcare workers (HCWs)
- Discharge of patients: rate μ
- Colonization probability of admitted patients: σ
- Patient-to-HCW contamination: β'
- HCW-to-patient colonization: β
- Handwashing: rate μ'
- Detection of each patient: γ

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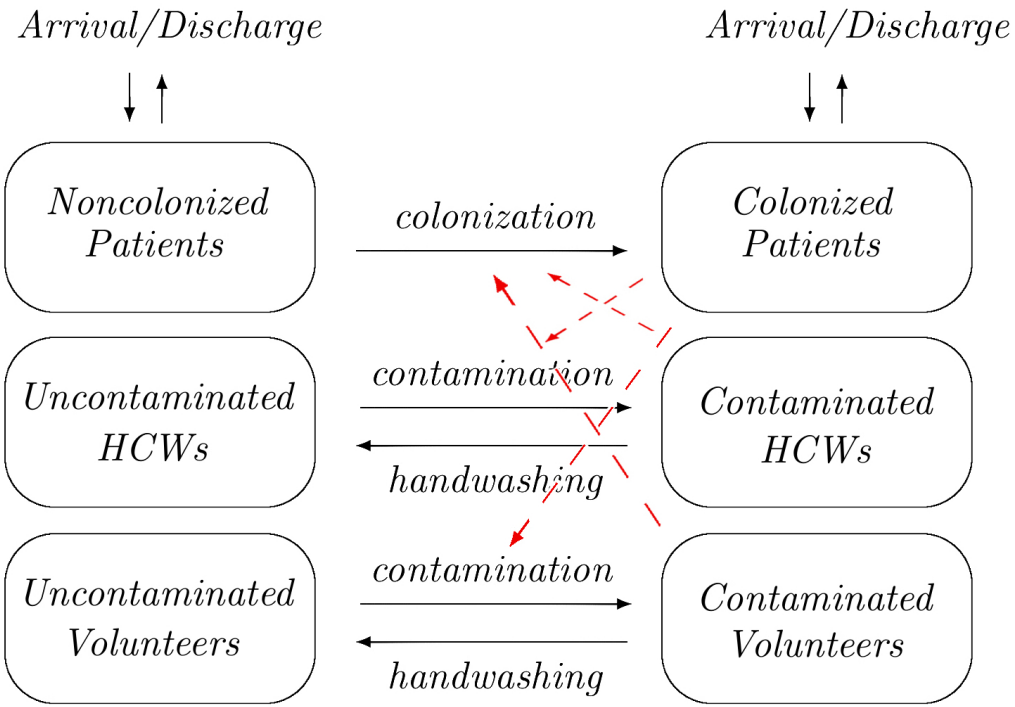
Models that include additional agents. E.g., volunteers

Wang et al. (2011)



- N_p patients
- N_{HCW} HCWs
- N_V volunteers
- Patients admission: λ
- Admitted patients colonized with probability φ
- HCW-patient contact: β_{PH}
- Volunteer-patient contact: β_{PV}
- Hygienic level during contacts for HCWs: $\eta \in (0, 1)$
- Hygienic level during contacts for volunteers: $\xi \in (0, 1)$

- HCWs hand-washing: γ_H
- Volunteers hand-washing: γ_V
- Discharge of colonized pat.: δ_C
- Discharge of non-colonized pat.: δ_U

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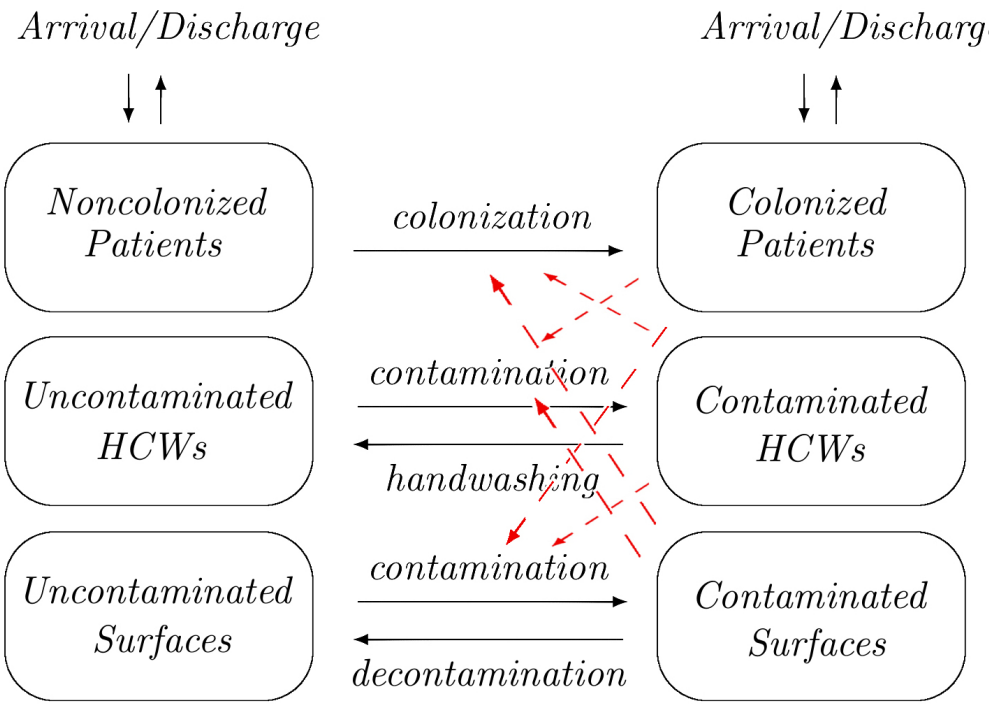
Addressing other factors: environmental contamination

Wolkewitz et al. (2008)



- N_p patients
- N_s HCWs
- N_e surfaces
- Discharge of colonized patients: γ'
- Discharge of non-colonized pat.: γ
- Colonization probability of admitted pat.: ϕ
- HCW decontamination: μ
- Surface decontamination: κ

- Staff-to-patient transmission: β_{sp}
- Patient-to-staff transmission: β_{ps}
- Surface-to-patient transmission: β_{ep}
- Patient-to-surface transmission: β_{pe}
- Staff-to-surface transmission: β_{se}
- Surface-to-patient transmission: β_{es}

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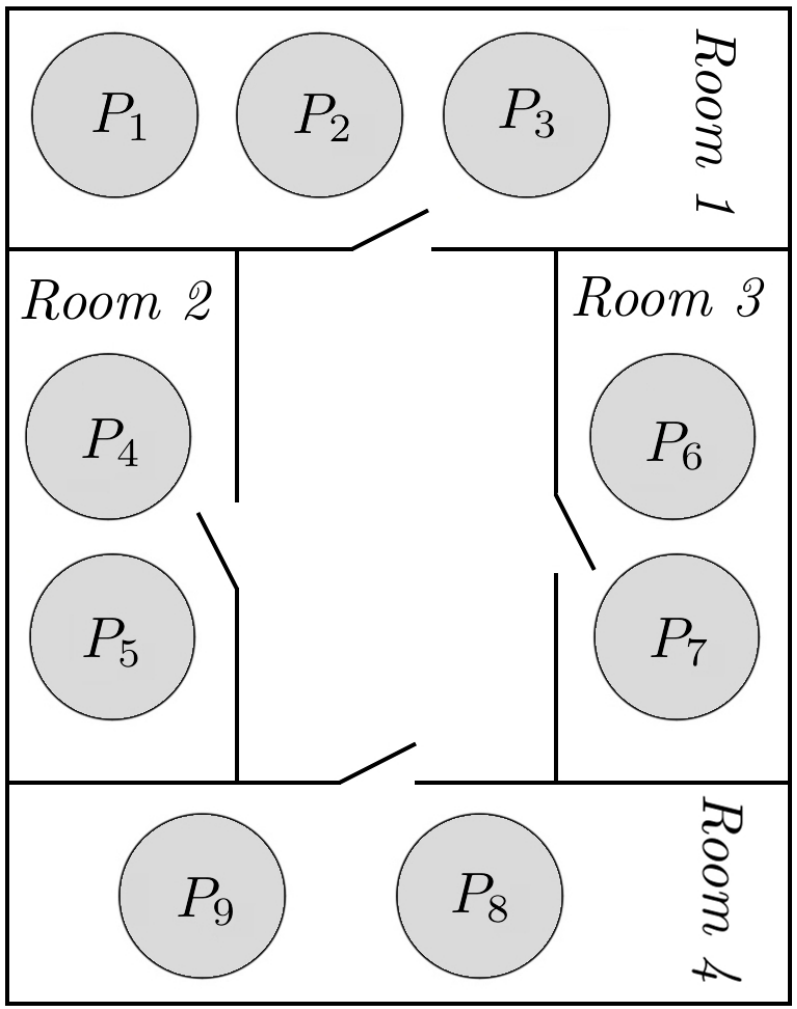
Incorporating room configuration

López-García (2016)



- 9 patients located among 4 different rooms
- Patients in the same room have transmission rate β
- Patients in different rooms have transmission rate β'
- Patients are discharged with rate γ, and immediately replaced by new ones

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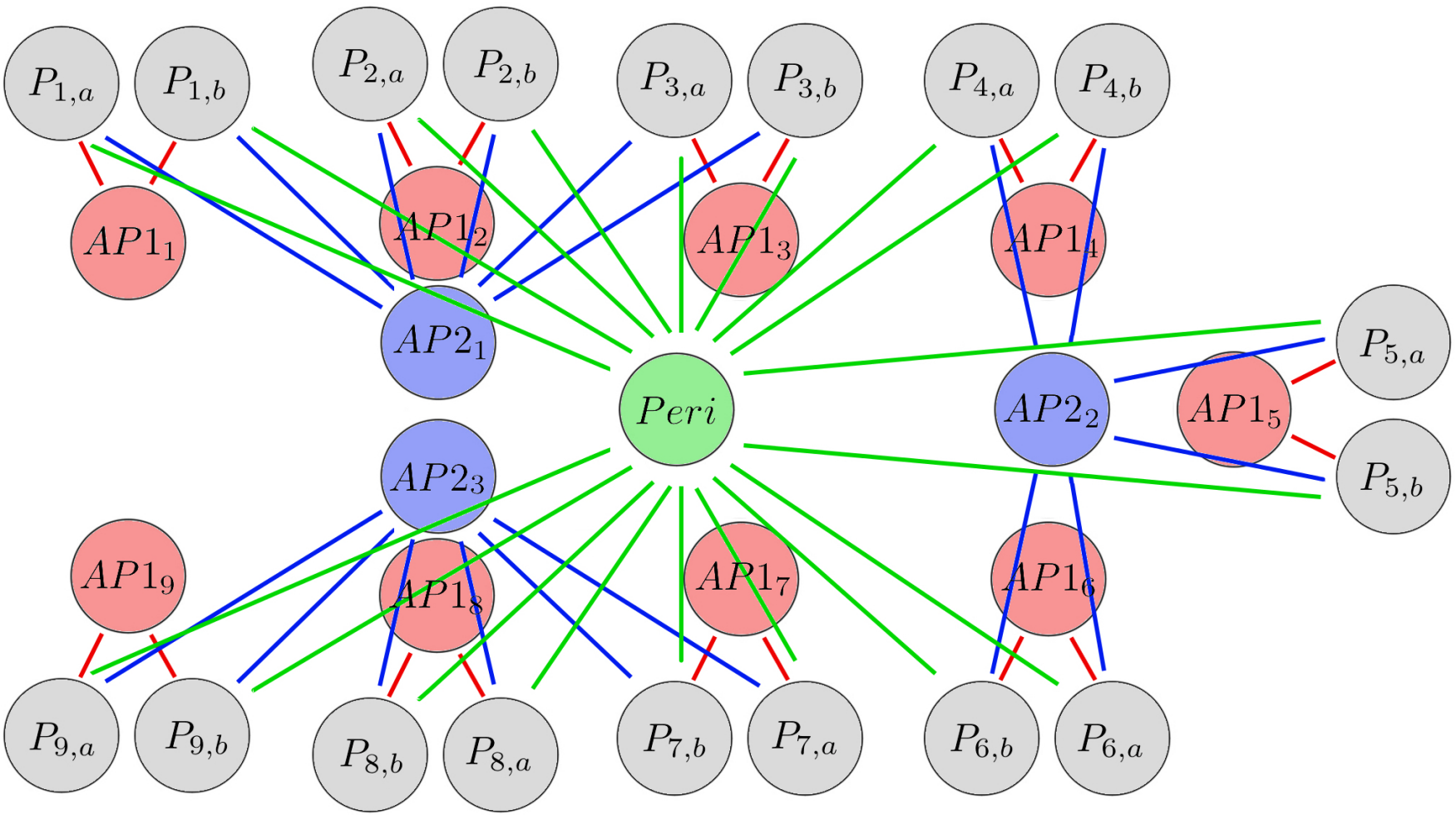
Patient cohorting

Temime et al. (2009)



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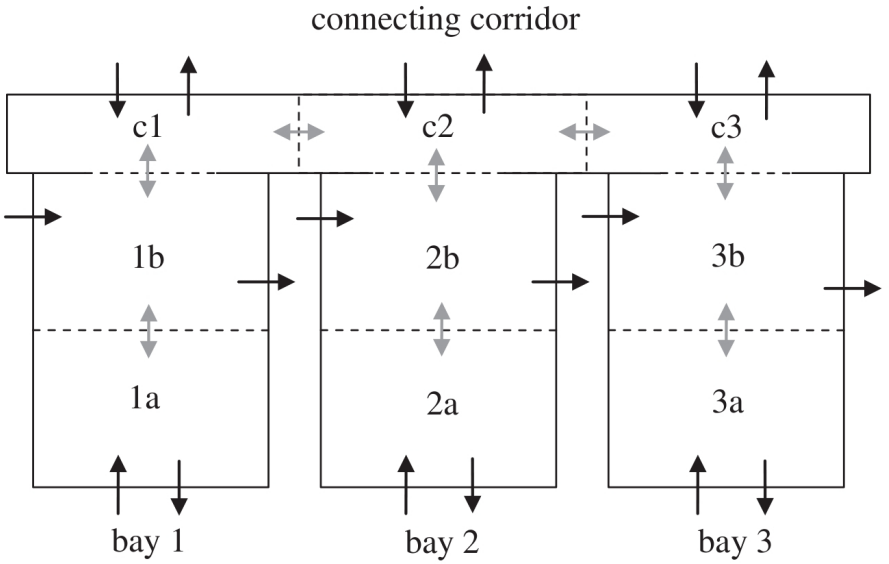
Airborne transmission: incorporating airflow dynamics



Noakes & Sleigh (2009)

$$\begin{pmatrix} \frac{\beta_1}{p_1} \\ \frac{\beta_2}{p_2} \\ \vdots \\ \frac{\beta_M}{p_M} \end{pmatrix} = \mathbf{V}^{-1} \begin{pmatrix} q_1 I_1 \\ q_2 I_2 \\ \vdots \\ q_M I_M \end{pmatrix},$$

- Patients are distributed among M different rooms, and pathogen spreads through air. For $1 \leq i \leq M$,

$$C_i = \text{“Pathogen concentration at ventilation zone } i\text{”},$$

$$V_i \frac{dC_i}{dt} = q_i I_i - Q_i C_i - \sum_{k=1}^{M} \beta_{ik} C_i + \sum_{k=1}^{M} \beta_{ki} C_k,$$

- Each time $(i_1, \ldots, i_M)$ changes $\Rightarrow$ Compute steady-state concentration of pathogen at each room
- Infection rate of an individual at room j: $\beta_j = f_j(i_1, \ldots, i_M)$

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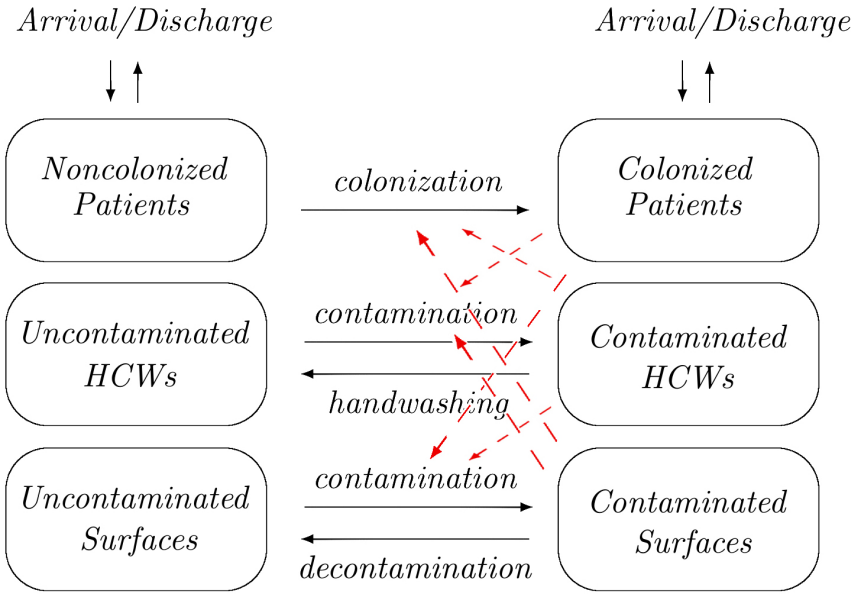
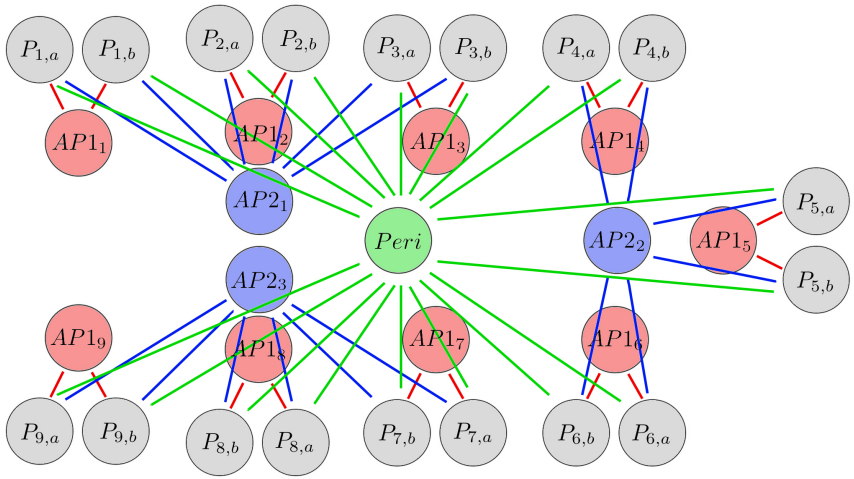
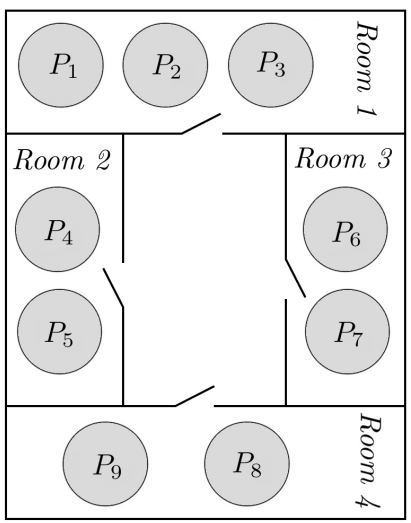
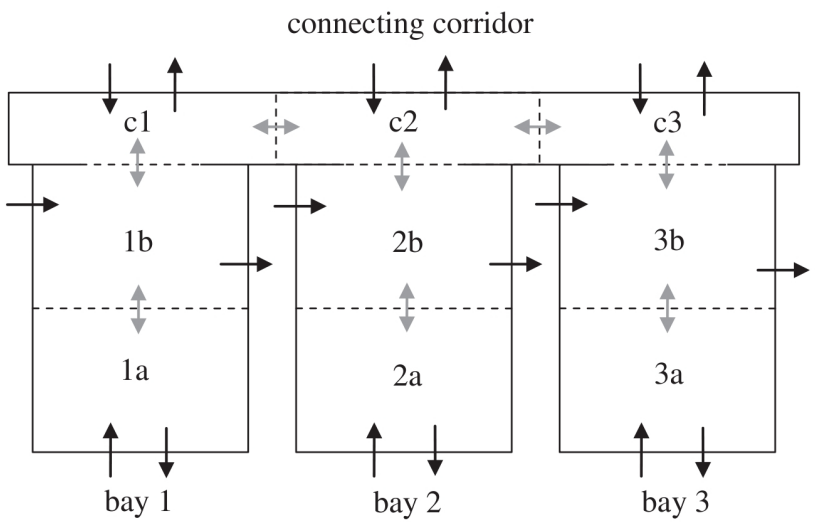


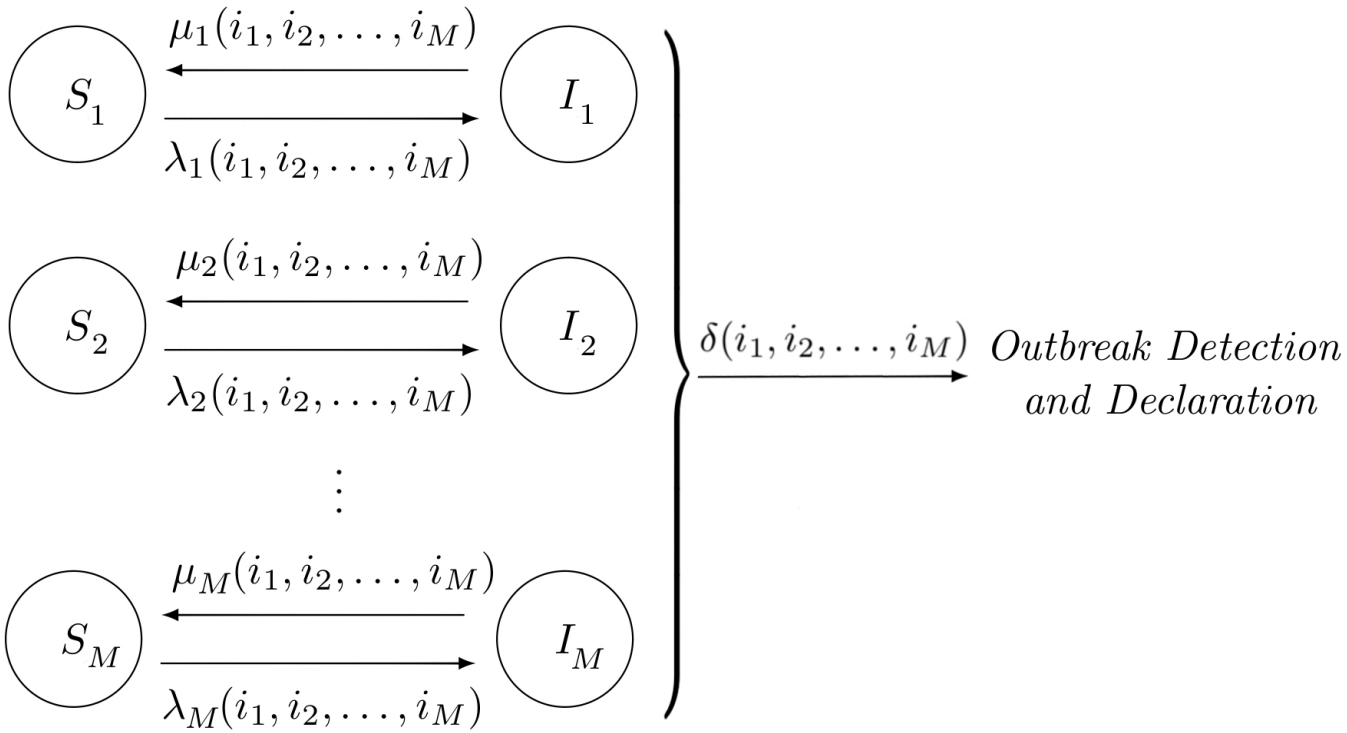






Outline I

A general stochastic framework



- Individuals are distributed among M different compartments
- At each compartment j, the number of individuals is constant, N_j
- Infection/Contamination of an individual at compartment i: $\lambda_i(i_1, i_2, \ldots, i_M)$
- Removal of an individual at compartment i: $\mu_i(i_1, i_2, \ldots, i_M)$
- Detection of the outbreak: $\delta(i_1, \ldots, i_M)$

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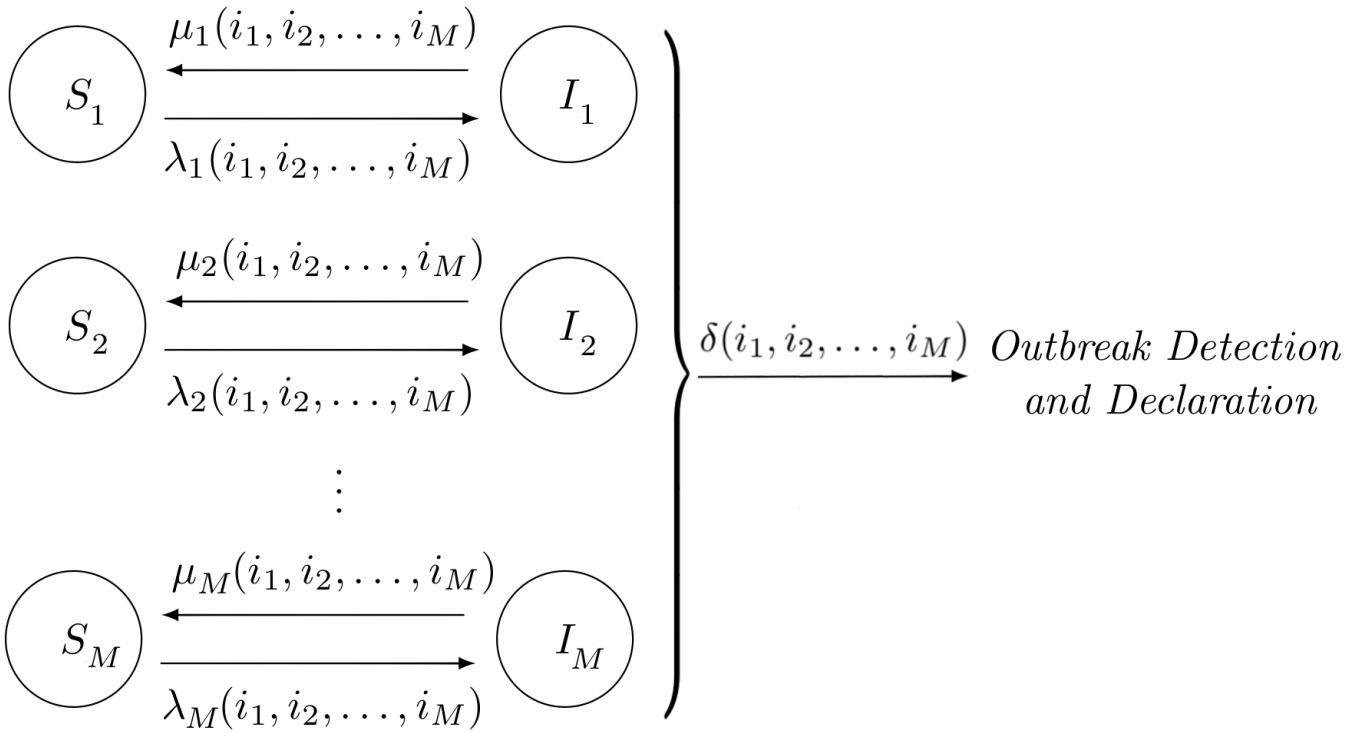

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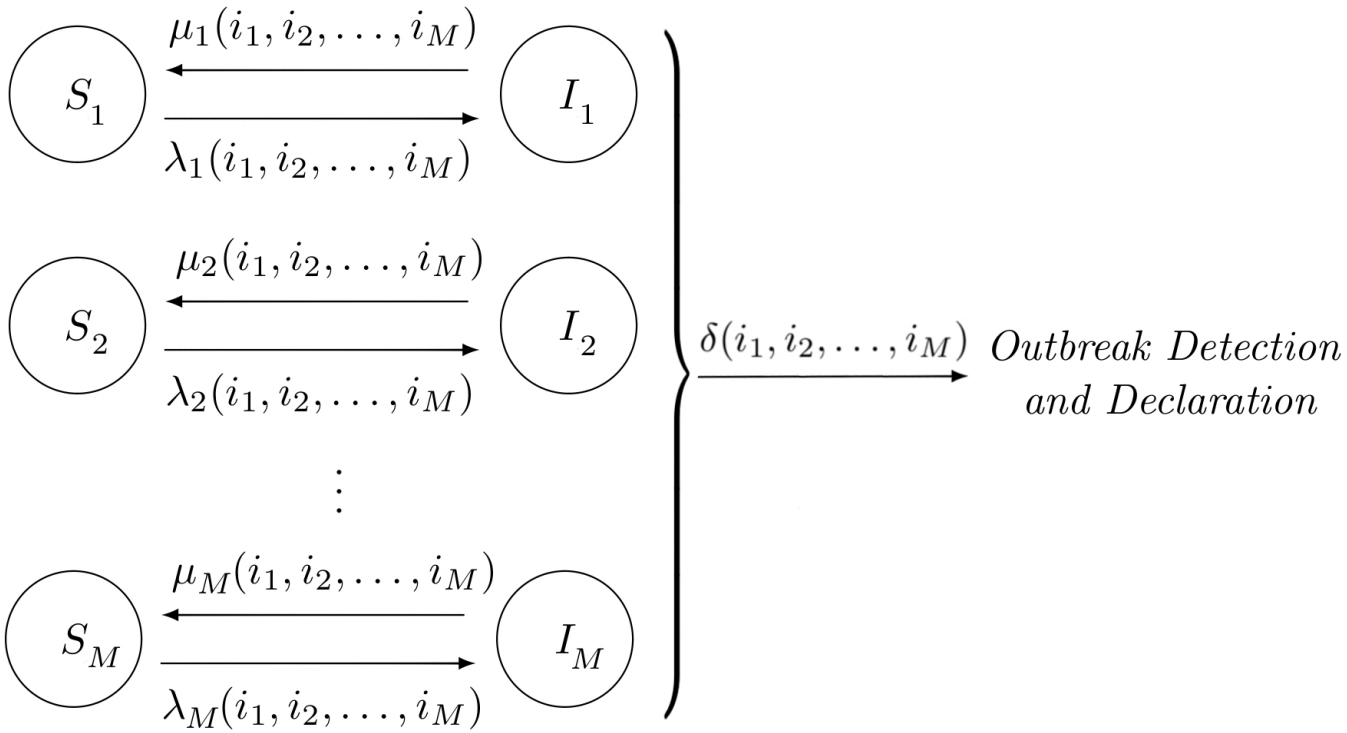

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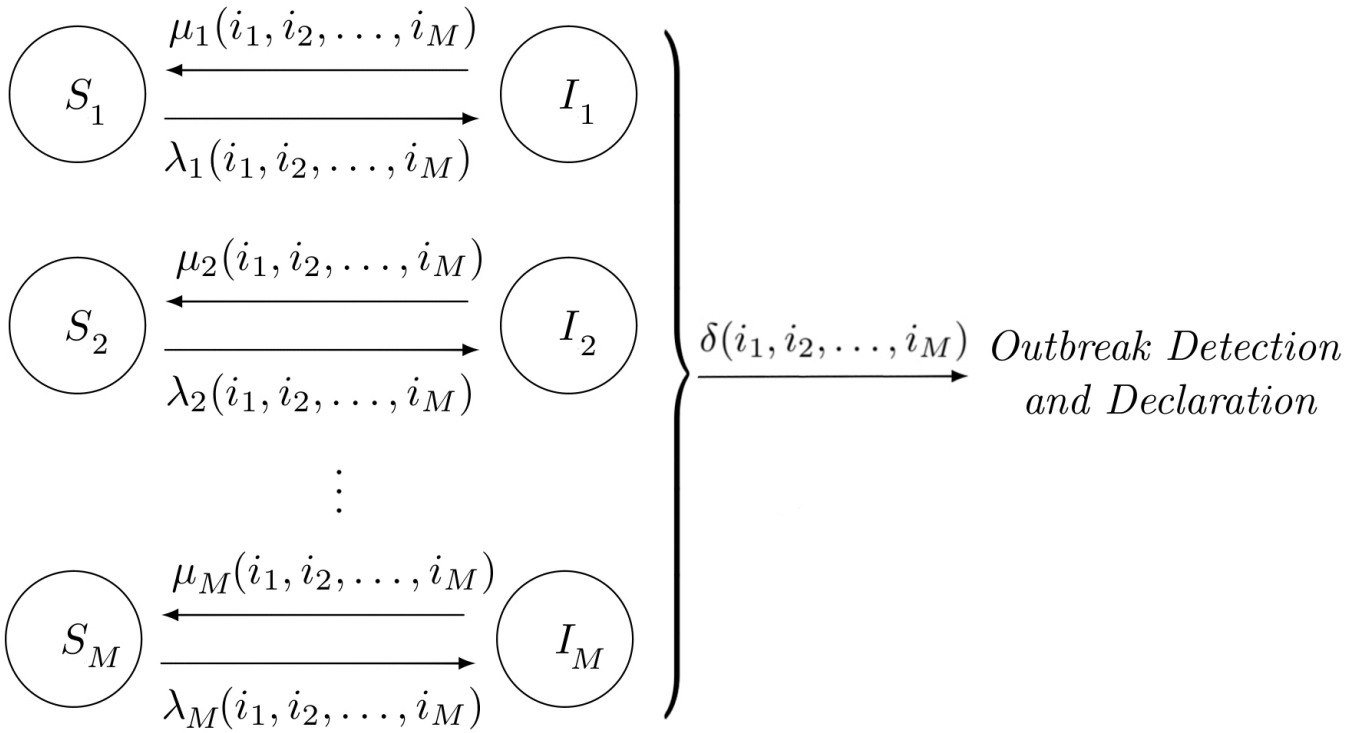

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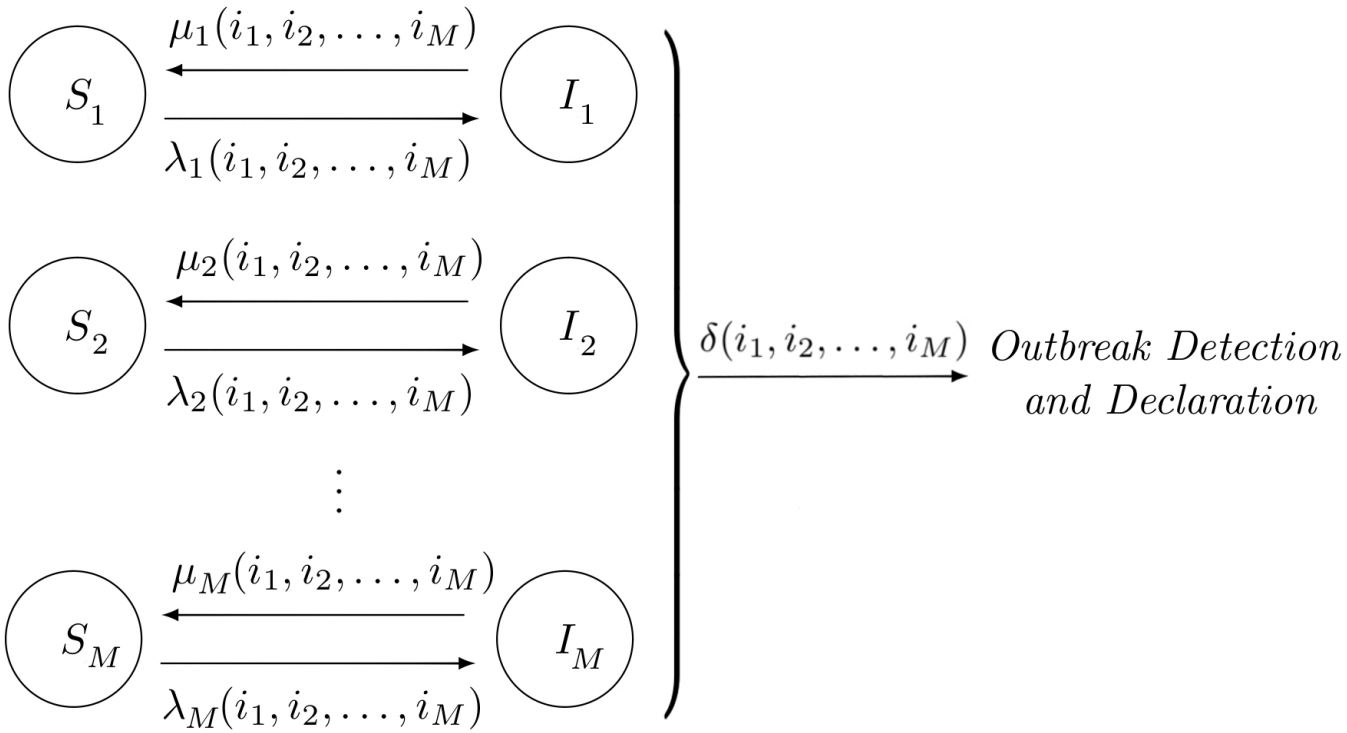

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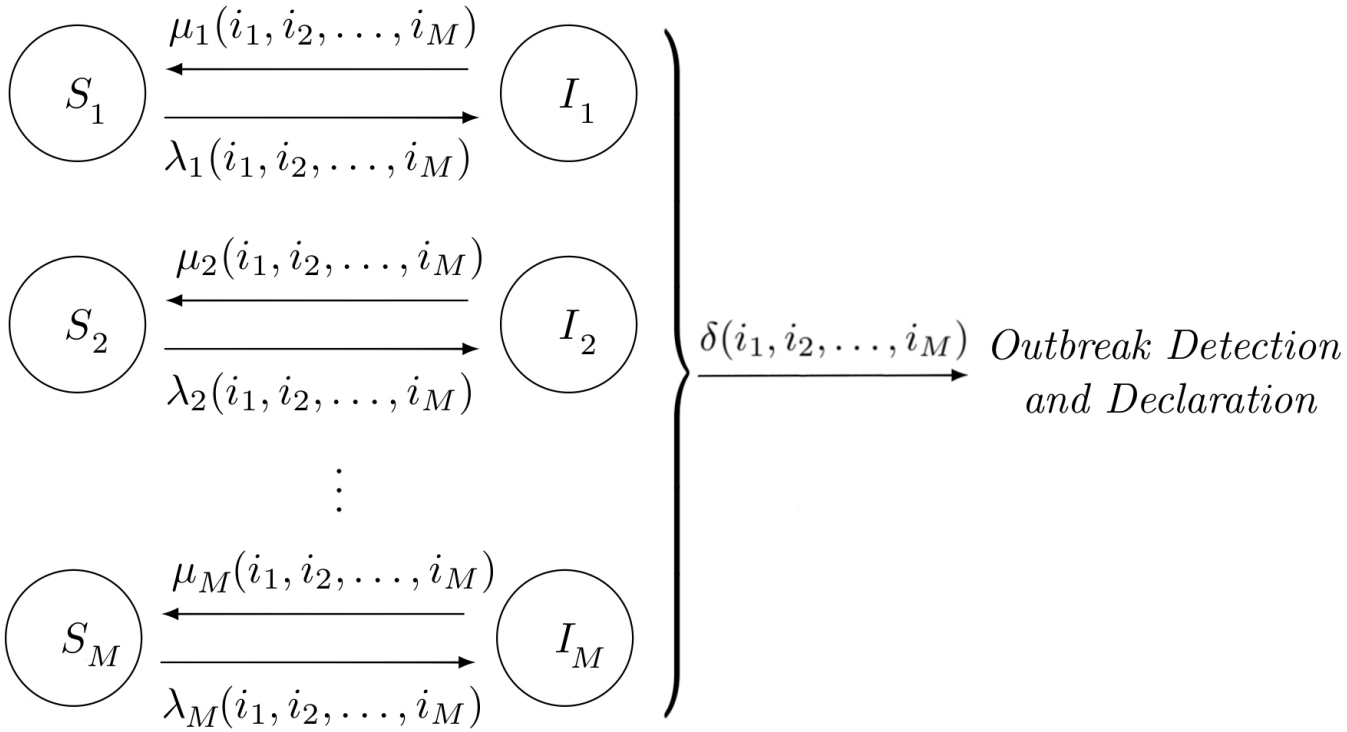

Continuous-time stochastic process: $\mathcal{X} = \{(I_1(t), I_2(t), \ldots, I_M(t)) : \ t \geq 0\}$

- $(i_1, i_2, \ldots, i_j, \ldots, i_M) \rightarrow (i_1, i_2, \ldots, i_j + 1, \ldots, i_M)$, with rate $\lambda_j(i_1, i_2, \ldots, i_M)$
- $(i_1, i_2, \ldots, i_j, \ldots, i_M) \rightarrow (i_1, i_2, \ldots, i_j - 1, \ldots, i_M)$, with rate $\mu_j(i_1, i_2, \ldots, i_M)$
- $(i_1, i_2, \ldots, i_j, \ldots, i_M) \rightarrow$ *Detection*, with rate $\delta(i_1, i_2, \ldots, i_M)$

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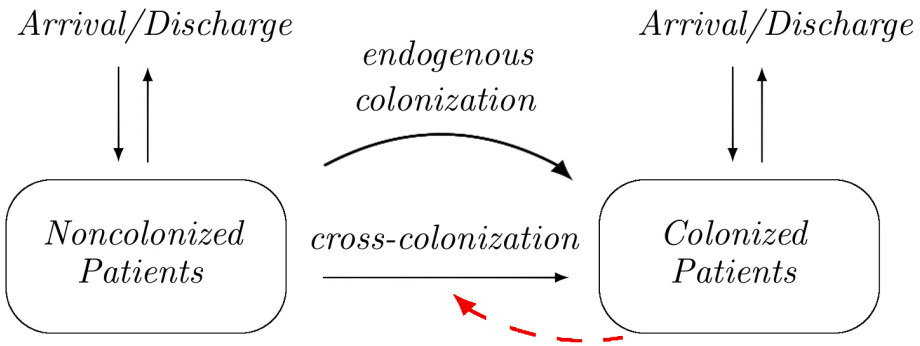
Model as in Pelupessy et al. (2002)

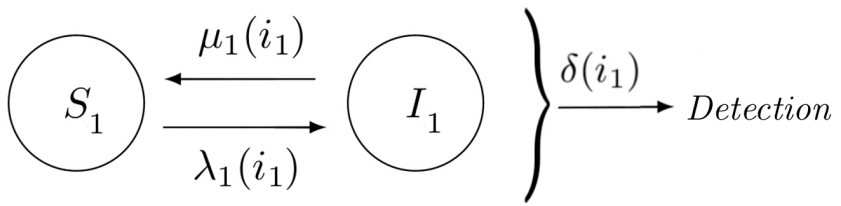


$I(t)$ = *Number of colonized patients at time t*

- Each patient can be spontaneously colonized at rate α
- Cross-colonization occurs at rate $\frac{\theta I(t)}{N}$
- Colonized patients are discharged at rate $\frac{1}{d'}$
- Noncolonized patients are discharged at rate $\frac{1}{d}$
- New patient immediately arrives after discharge, being colonized with probability q

Equivalent representation in our framework

$M = 1,\ N_1 = N$



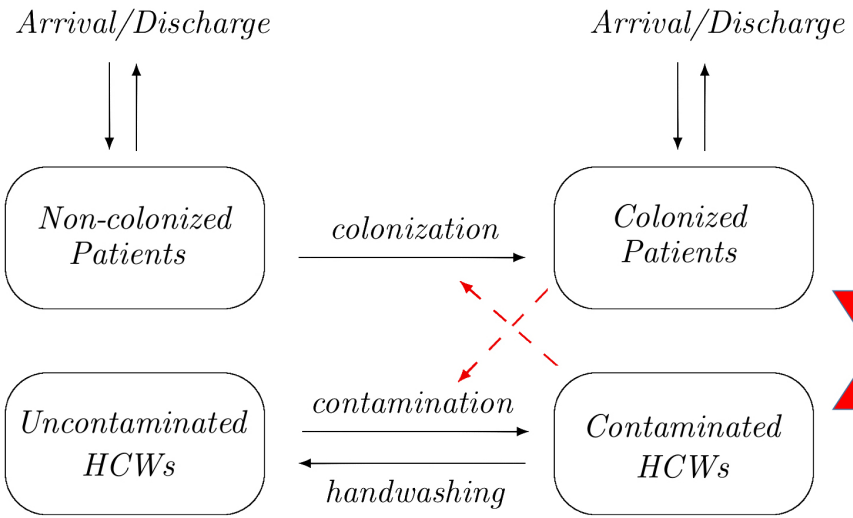
$I_1(t)$ = *Number of colonized patients at time t*

$$\lambda_1(i_1) = \left(\tfrac{q}{d} + \alpha + \tfrac{\theta i_1}{N}\right)(N_1 - i_1)$$

$$\mu_1(i_1) = \tfrac{1-q}{d'} i_1$$

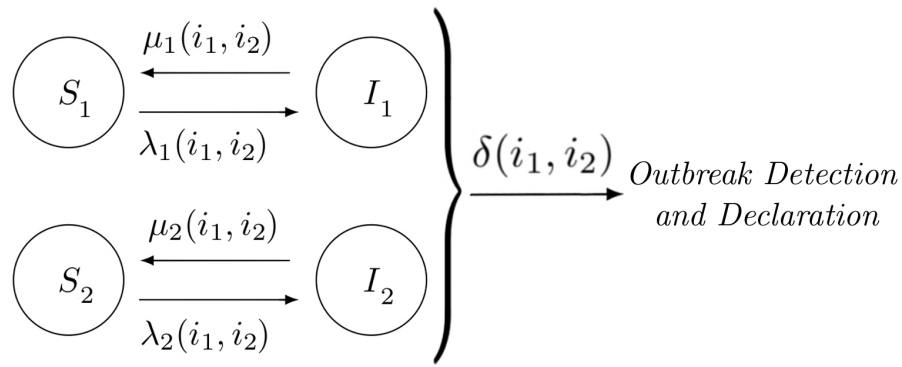
$$\delta(i_1) = \delta$$

Model as in Artalejo (2014)



Representation in our framework

$M = 2,\ N_1 = N_p,\ N_2 = N_{HCW}$



$I_1(t)$ = *Number of colonized patients at time t*

$I_2(t)$ = *Number of contaminated HCWs at time t*

$\lambda_1(i_1, i_2) = (\sigma\mu + \beta i_2)(N_1 - i_1)$ $\quad \mu_1(i_1, i_2) = (1-\sigma)\mu i_1$

$\lambda_2(i_1, i_2) = \beta' i_1 (N_2 - i_2)$ $\quad \mu_2(i_1, i_2) = \mu' i_2$

$\delta(i_1, i_2) = \gamma i_1$

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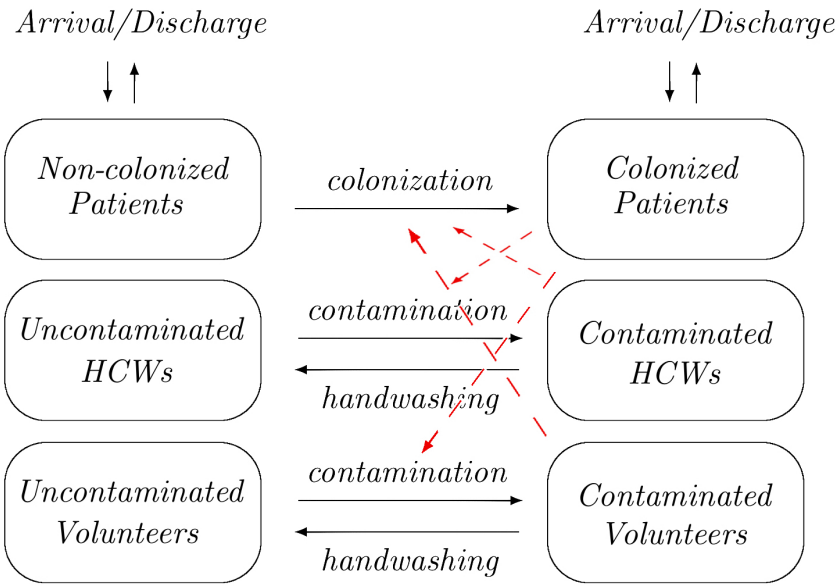
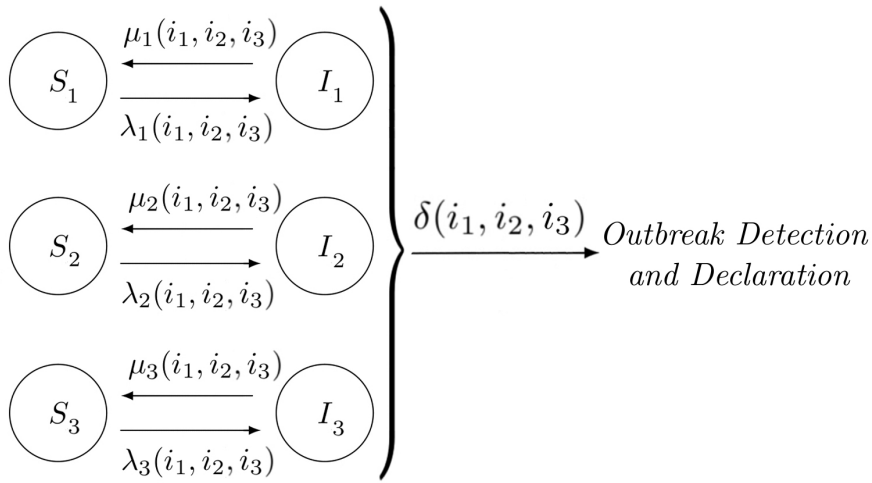
Model as in Wang et al. (2011)



*Representation in our framework**

$M = 3,\ N_1 = N_P,\ N_2 = N_{HCW},\ N_3 = N_V$



$I_1(t)$ = *Number of colonized patients at time t*

$I_2(t)$ = *Number of contaminated HCWs at time t*

$I_3(t)$ = *Number of contaminated volunteers at time t*

$$\lambda_1(i_1,i_2,i_3) = \left(\tfrac{1-\eta}{N_P}\beta_{PH} i_2 + \tfrac{1-\xi}{N_P}\beta_{PV} i_3 + \delta_U \varphi\right)(N_1 - i_1)$$

$$\lambda_2(i_1,i_2,i_3) = \tfrac{1-\eta}{N_P}\beta_{PH} i_1 (N_2 - i_2) \qquad \mu_1(i_1,i_2,i_3) = \delta_C i_1 (1-\varphi)$$

$$\lambda_3(i_1,i_2,i_3) = \tfrac{1-\xi}{N_P}\beta_{PV} i_1 (N_3 - i_3) \qquad \mu_2(i_1,i_2,i_3) = \gamma_H i_2$$

$$\mu_3(i_1,i_2,i_3) = \gamma_V i_3 \qquad \delta(i_1,i_2,i_3) = 0$$

**Immediate arrival assumed* ($\lambda \to \infty$)

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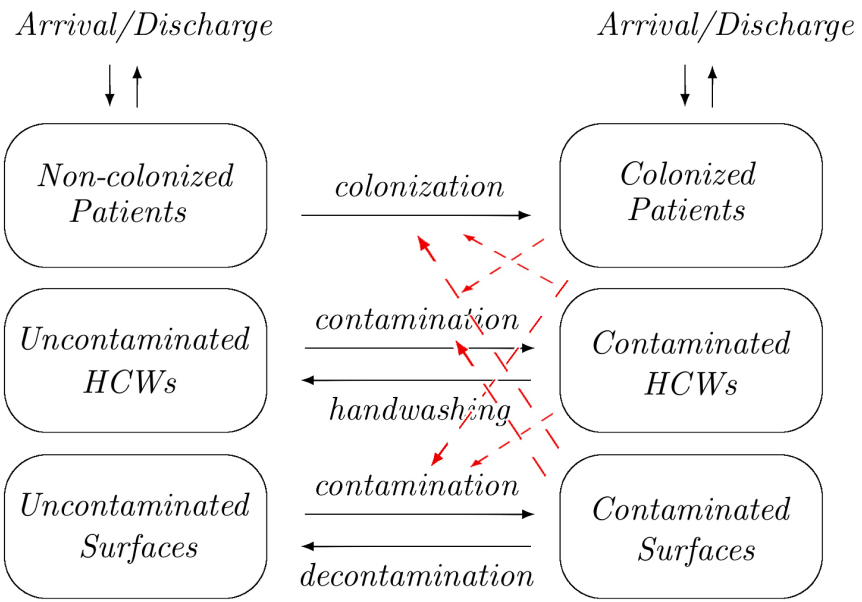
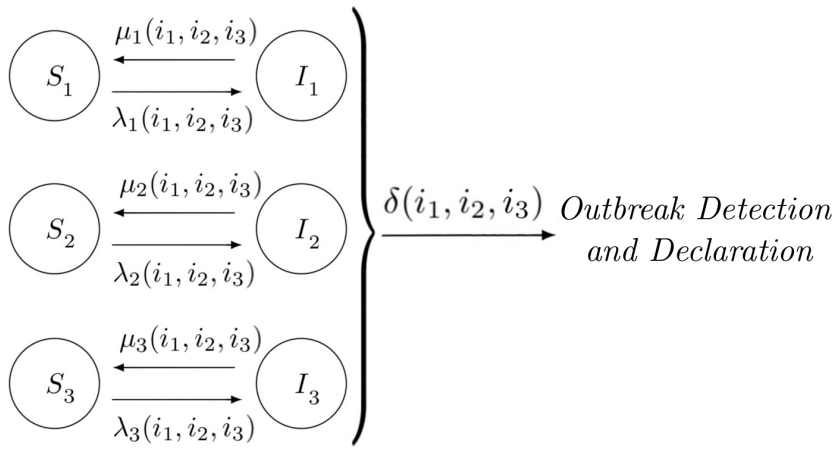
Model as in Wolkewitz et al. (2008)



Representation in our framework

$M = 3,\ N_1 = N_p,\ N_2 = N_s,\ N_3 = N_e$



$I_1(t)$ = *Number of colonized patients at time t*

$I_2(t)$ = *Number of contaminated HCWs at time t*

$I_3(t)$ = *Number of contaminated surfaces at time t*

$$\lambda_1(i_1,i_2,i_3) = \left(\gamma\phi + \frac{i_2\beta_{sp}}{N_s} + \frac{i_3\beta_{ep}}{N_e}\right)(N_1 - i_1)$$

$$\lambda_2(i_1,i_2,i_3) = \left(\frac{i_1\beta_{ps}}{N_p} + \frac{i_3\beta_{es}}{N_e}\right)(N_2 - i_2) \qquad \mu_1(i_1,i_2,i_3) = \gamma' i_1(1-\phi)$$

$$\lambda_3(i_1,i_2,i_3) = \left(\frac{i_2\beta_{se}}{N_s} + \frac{i_1\beta_{pe}}{N_p}\right)(N_3 - i_3) \qquad \mu_2(i_1,i_2,i_3) = \mu i_2$$

$$\mu_3(i_1,i_2,i_3) = \kappa i_3 \qquad \delta(i_1,i_2,i_3) = 0$$

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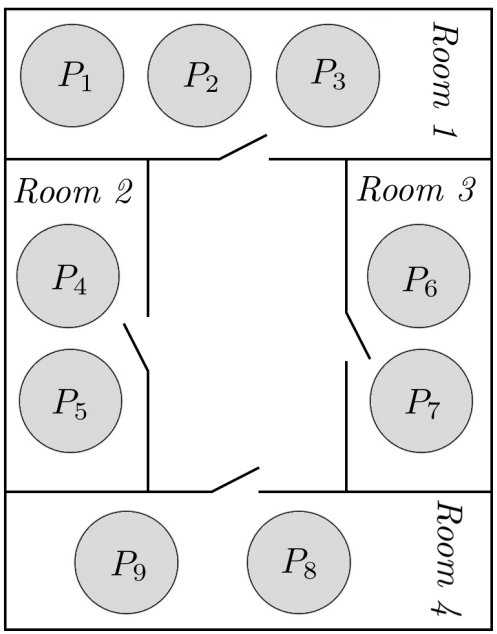
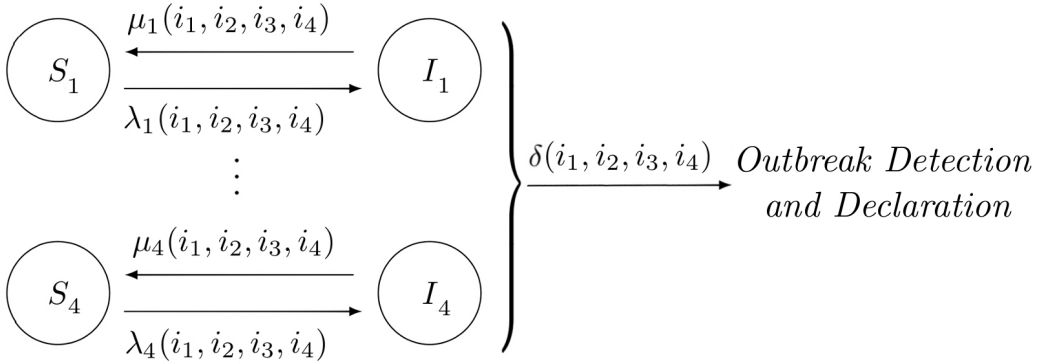
Hospital ward room configuration from López-García (2016)



*Representation in our framework**

$M = 4,\ N_1 = 3,\ N_i = 2\ 2 \le i \le 4$



$I_j(t)$ = *Number of colonized patients at room* j *at time* t, $1 \le j \le 4$

ν = *discharge rate* p_C = *probability of admission of colonized patient*

$\mu_j(i_1, i_2, i_3, i_4) = \nu(1 - p_C)\, i_j,\ 1 \le j \le 4 \qquad \delta(i_1, i_2, i_3, i_4) = 0$

$$\lambda_j(i_1, i_2, i_3, i_4) = \left(\nu p_C + \beta_{DR} \sum_{k \neq j} i_k + \beta_{SR} i_j + \lambda\right)(N_j - i_j),\ 1 \le j \le 4$$

*Discharge and arrival of patients considered, instead of recovery

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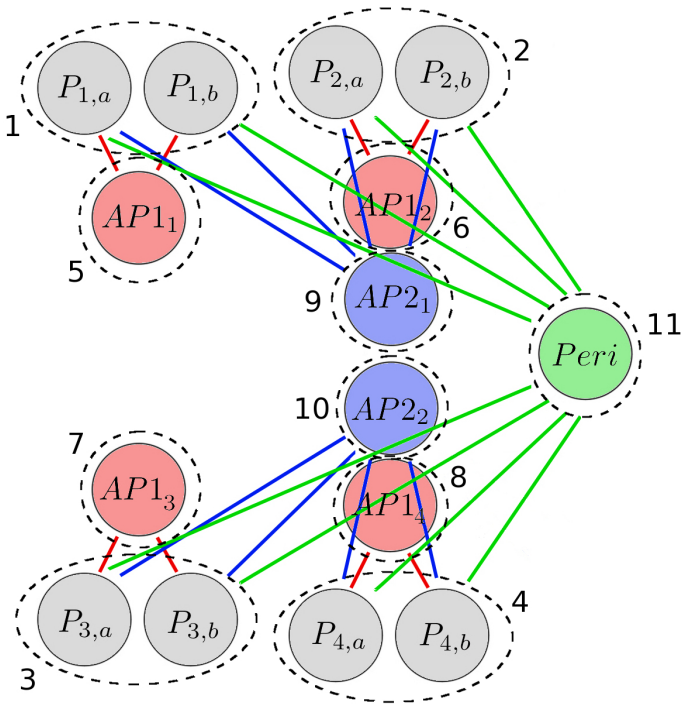
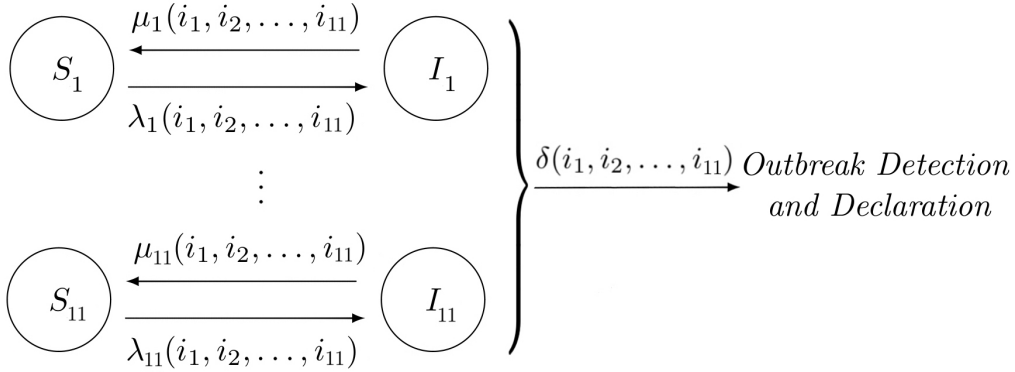
Hospital ward contact network from Temime et al. (2009)



Representation in our framework

$M = 11,\ N_i = 2\ 1 \le i \le 4,\ N_j = 1\ 5 \le j \le 11$



$I_i(t)$ = *Number (0, 1 or 2) of colonized patients treated by* $AP1_i$ *at time* t, $1 \le i \le 4$

$I_{4+j}(t)$ = *Number (0 or 1) of contaminated* $AP1_j$ *at time* t, $1 \le j \le 4$

$I_{8+k}(t)$ = *Number (0 or 1) of contaminated* $AP2_k$ *at time* t, $1 \le k \le 2$

$I_{11}(t)$ = *Number (0 or 1) of contaminated Peri at time* t

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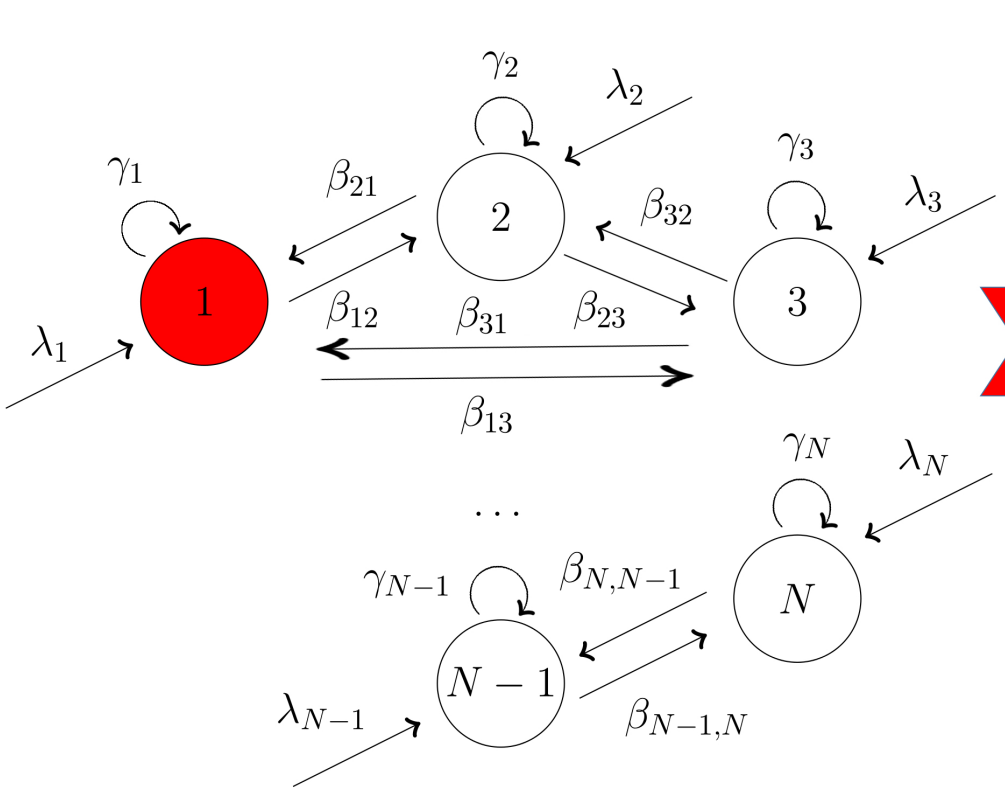
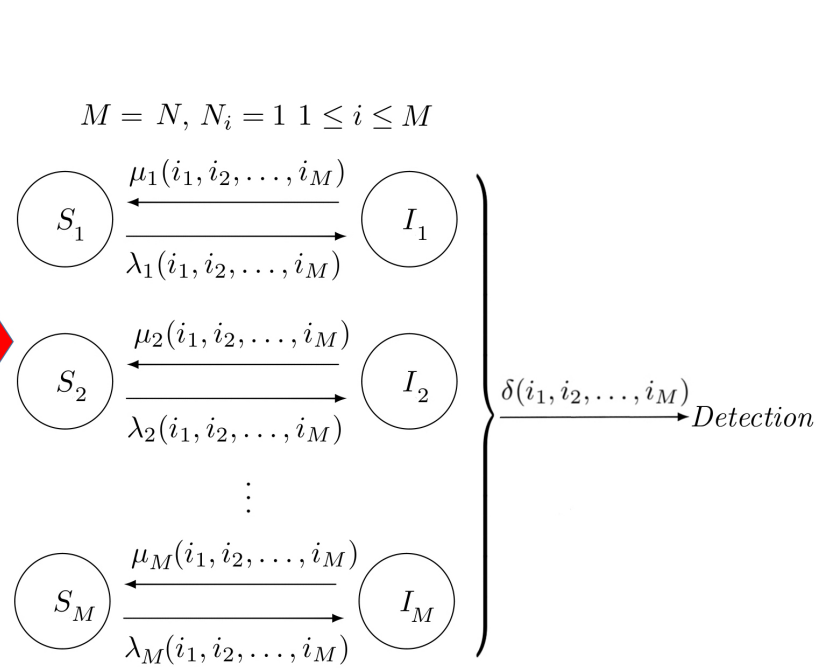
Epidemics on networks





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Stochastic descriptors in an SIR epidemic model for heterogeneous individuals in small networks

M. López-García*

Department of Applied Mathematics, School of Mathematics, University of Leeds, Leeds LS2 9JT, United Kingdom

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Physica A

journal homepage: www.elsevier.com/locate/physa

A stochastic SIS epidemic model with heterogeneous contacts

A. Economou[a,*], A. Gómez-Corral[b,c], M. López-García[d]

[a] *Section of Statistics and Operations Research, Department of Mathematics, University of Athens, Panepistemiopolis, Athens 15784, Greece*
[b] *ICMAT – Institute of Mathematical Sciences, Calle Nicolás Cabrera, 13-15, Madrid 28049, Spain*
[c] *Department of Statistics and Operations Research, Faculty of Mathematics, Complutense University of Madrid, Madrid 28040, Spain*

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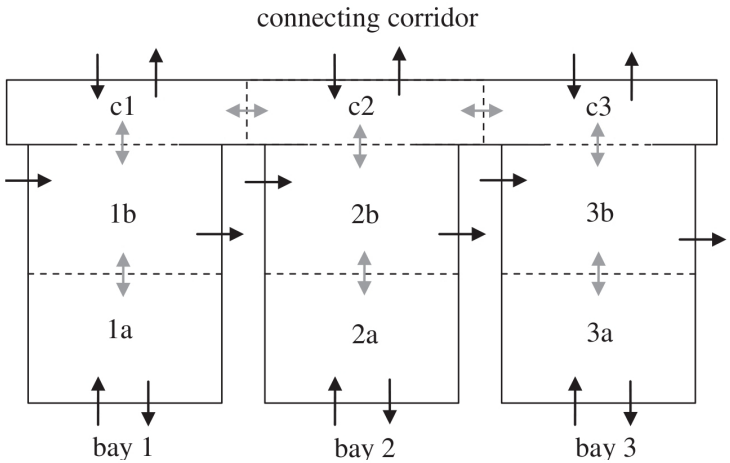
Model as in Noakes & Sleigh (2009)

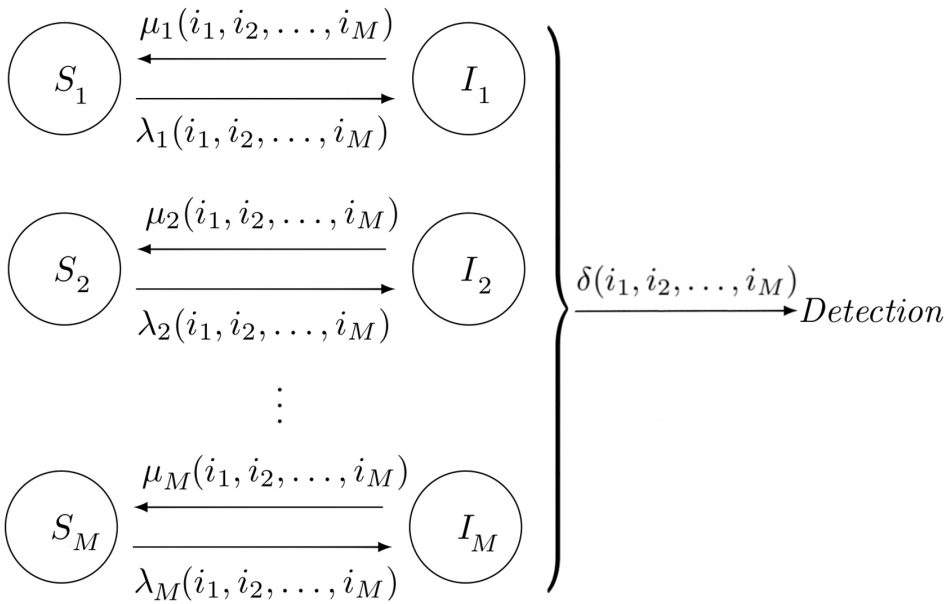


$$C_i = \text{“Pathogen concentration at ventilation zone } i\text{”},$$

$$V_i \frac{dC_i}{dt} = qI_i - Q_i C_i - \sum_{k=1}^{M} \beta_{ik} C_i + \sum_{k=1}^{M} \beta_{ki} C_k,$$

$$\begin{pmatrix} \beta_1 \\ \beta_2 \\ \vdots \\ \beta_M \end{pmatrix} = {}_p\mathbf{V}^{-1} \begin{pmatrix} qI_1 \\ qI_2 \\ \vdots \\ qI_M \end{pmatrix}$$

Equivalent representation in our framework



$$\begin{pmatrix} \lambda_1(i_1,\ldots,i_M) \\ \lambda_2(i_1,\ldots,i_M) \\ \vdots \\ \lambda_M(i_1,\ldots,i_M) \end{pmatrix} = {}_p\mathbf{V}^{-1} \begin{pmatrix} qi_1 \\ qi_2 \\ \vdots \\ qi_M \end{pmatrix}$$

Outline I

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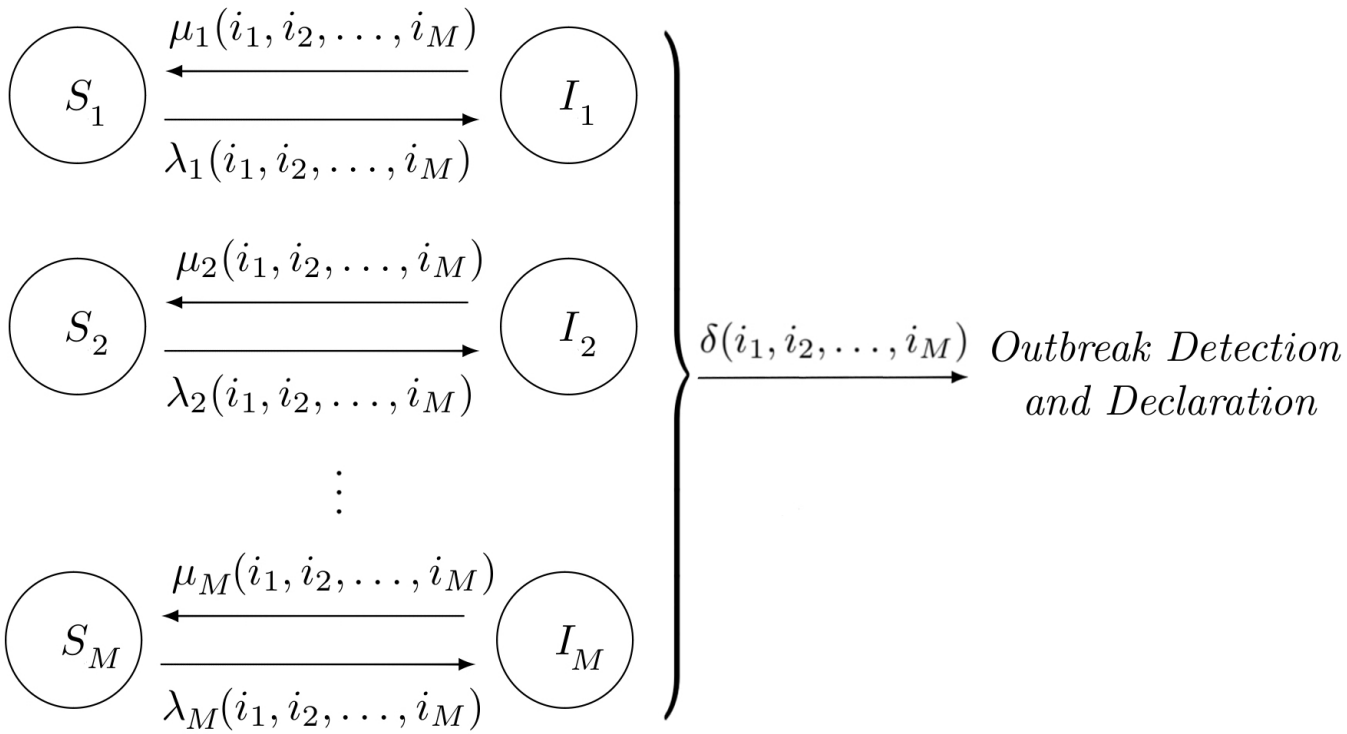
A general stochastic framework



Continuous-time stochastic process: $\mathcal{X} = \{(I_1(t), I_2(t), \ldots, I_M(t)) : \ t \geq 0\}$

- $(i_1, i_2, \ldots, i_j, \ldots, i_M) \to (i_1, i_2, \ldots, i_j + 1, \ldots, i_M)$, with rate $\lambda_j(i_1, i_2, \ldots, i_M)$
- $(i_1, i_2, \ldots, i_j, \ldots, i_M) \to (i_1, i_2, \ldots, i_j - 1, \ldots, i_M)$, with rate $\mu_j(i_1, i_2, \ldots, i_M)$
- $(i_1, i_2, \ldots, i_j, \ldots, i_M) \to$ *Detection*, with rate $\delta(i_1, i_2, \ldots, i_M)$

Summary statistics

JOURNAL OF THE ROYAL SOCIETY Interface

J. R. Soc. Interface (2008) **5**, 171–181
doi:10.1098/rsif.2007.1106
Published online 17 July 2007

On methods for studying stochastic disease dynamics

M. J. Keeling[1,*] and J. V. Ross[2]

[1]*Department Biological Sciences and Mathematics Institute, and* [2]*Mathematics Institute, University of Warwick, Gibbet Hill Road, Coventry CV4 7AL, UK*

- Instead of stochastic simulations, one can explore the transient solutions from the Kolmogorov forward differential equations
- Even better, there are *exact* methods for analysing quantities of interest (*summary statistics*) of the epidemic:

1. Time until epidemic extinction
2. Costs functions related to the outbreak
3. Reproduction number
4. Size of the outbreak, peak of the outbreak,...

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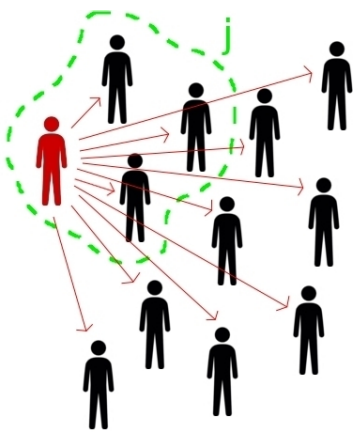
Quantities of interest

Reproductive number of an individual at compartment j:

$R^{(j)}$ = *Number of infections caused by an infective individual located at compartment j until detection of the outbreak or removal of this individual*

Reproductive number of an individual at compartment j among individuals at compartment k:

$$R^{(j)} = \sum_{k=1}^{M} R^{(j)}(k), \quad R^{(j)}(k) = \text{Number of infections caused by an infective individual located at compartment } j, \text{ among individuals at compartment } k, \text{ until detection of the outbreak or removal of this individual}$$



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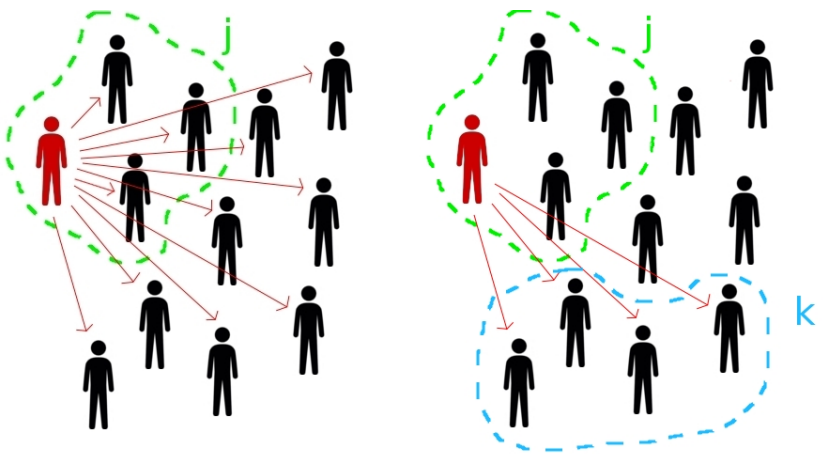

Quantities of interest: first-step argument

The analysis of these random variables is carried out in terms of a first-step argument:

$$\nu^{(j)}_{(i_1,\ldots,i_M)}(n) \quad = \quad \mathbb{P}(R^{(j)} = n \mid (I_1(0),\ldots,I_M(0)) = (i_1,\ldots,i_M)), \quad n \geq 0,$$

$$\theta_{(i_1,\ldots,i_M)}\nu^{(j)}_{(i_1,\ldots,i_M)}(n) \quad = \quad \sum_{k=1,\ k\neq j,\ i_k>0}^{M} \mu_k i_k \nu^{(j)}_{(i_1,\ldots,i_k-1,\ldots,i_M)}(n) + \mu_j(i_j-1)\nu^{(j)}_{(i_1,\ldots,i_j-1,\ldots,i_M)}(n)$$

$$+ \sum_{k=1,\ i_k<N_k}^{M} (N_k - i_k)\Big((\lambda_k + \sum_{l=1,\ l\neq j}^{M} \beta_{lk} i_l + \beta_{jk}(i_j-1))\nu^{(j)}_{(i_1,\ldots,i_k+1,\ldots,i_M)}(n)$$

$$+1_{n>0}\beta_{jk}\nu^{(j)}_{(i_1,\ldots,i_k+1,\ldots,i_M)}(n-1)\Big) + (\mu_j + \delta(i_1,\ldots,i_M))1_{n=0}, \quad n \geq 0,$$

$$\theta_{(i_1,\ldots,i_M)} = \delta(i_1,i_2,\ldots,i_M) + \sum_{j=1}^{M}(\mu_j(i_1,i_2,\ldots,i_M) + \lambda_j(i_1,i_2,\ldots,i_M))$$

System of linear equations: $\prod_{j=1}^{M}(N_j+1)$ *equations* per each value of $n \geq 0$

$$\mathbf{D}^{(j)}(n)\boldsymbol{\nu}^{(j)}(n) \quad = \quad \mathbf{e}^{(j)}(n),$$

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$$\begin{aligned}\theta_{(i_1,\ldots,i_M)}\nu^{(j)}_{(i_1,\ldots,i_M)}(n) \quad = \quad & \sum_{k=1,\ k\neq j,\ i_k>0}^{M} \mu_k i_k \nu^{(j)}_{(i_1,\ldots,i_k-1,\ldots,i_M)}(n) + \mu_j(i_j-1)\nu^{(j)}_{(i_1,\ldots,i_j-1,\ldots,i_M)}(n) \\ & + \sum_{k=1,\ i_k<N_k}^{M} (N_k - i_k)\Big((\lambda_k + \sum_{l=1,\ l\neq j}^{M} \beta_{lk} i_l + \beta_{jk}(i_j-1))\nu^{(j)}_{(i_1,\ldots,i_k+1,\ldots,i_M)}(n) \\ & + 1_{n>0}\beta_{jk}\nu^{(j)}_{(i_1,\ldots,i_k+1,\ldots,i_M)}(n-1)\Big) + (\mu_j + \delta(i_1,\ldots,i_M))1_{n=0}, \quad n \geq 0,\end{aligned}$$

$$\theta_{(i_1,\ldots,i_M)} = \delta(i_1,i_2,\ldots,i_M) + \sum_{j=1}^{M}(\mu_j(i_1,i_2,\ldots,i_M) + \lambda_j(i_1,i_2,\ldots,i_M))$$

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The analysis of these random variables is carried out in terms of a first-step argument:

$$\nu^{(j)}_{(i_1,\ldots,i_M)}(n) \quad = \quad \mathbb{P}(R^{(j)} = n \mid (I_1(0),\ldots,I_M(0)) = (i_1,\ldots,i_M)), \quad n \geq 0,$$

$$\begin{aligned}\theta_{(i_1,\ldots,i_M)}\nu^{(j)}_{(i_1,\ldots,i_M)}(n) \quad = \quad & \sum_{k=1,\ k\neq j,\ i_k>0}^{M} \mu_k i_k \nu^{(j)}_{(i_1,\ldots,i_k-1,\ldots,i_M)}(n) + \mu_j(i_j-1)\nu^{(j)}_{(i_1,\ldots,i_j-1,\ldots,i_M)}(n) \\ & + \sum_{k=1,\ i_k<N_k}^{M} (N_k - i_k)\Big((\lambda_k + \sum_{l=1,\ l\neq j}^{M} \beta_{lk} i_l + \beta_{jk}(i_j-1))\nu^{(j)}_{(i_1,\ldots,i_k+1,\ldots,i_M)}(n) \\ & + 1_{n>0}\beta_{jk}\nu^{(j)}_{(i_1,\ldots,i_k+1,\ldots,i_M)}(n-1)\Big) + (\mu_j + \delta(i_1,\ldots,i_M))1_{n=0}, \quad n \geq 0,\end{aligned}$$

$$\theta_{(i_1,\ldots,i_M)} = \delta(i_1,i_2,\ldots,i_M) + \sum_{j=1}^{M}(\mu_j(i_1,i_2,\ldots,i_M) + \lambda_j(i_1,i_2,\ldots,i_M))$$

System of linear equations: $\prod_{j=1}^{M}(N_j+1)$ *equations* per each value of $n \geq 0$

$$\mathbf{D}^{(j)}(n)\boldsymbol{\nu}^{(j)}(n) \quad = \quad \mathbf{e}^{(j)}(n),$$

Quantities of interest: first-step argument

The analysis of these random variables is carried out in terms of a first-step argument:

$$\nu^{(j)}_{(i_1,\ldots,i_M)}(n) \quad = \quad \mathbb{P}(R^{(j)} = n \mid (I_1(0),\ldots,I_M(0)) = (i_1,\ldots,i_M)), \quad n \geq 0,$$

$$\begin{aligned}\theta_{(i_1,\ldots,i_M)}\nu^{(j)}_{(i_1,\ldots,i_M)}(n) \quad = \quad & \sum_{k=1,\ k\neq j,\ i_k>0}^{M} \mu_k i_k \nu^{(j)}_{(i_1,\ldots,i_k-1,\ldots,i_M)}(n) + \mu_j(i_j-1)\nu^{(j)}_{(i_1,\ldots,i_j-1,\ldots,i_M)}(n) \\ & + \sum_{k=1,\ i_k<N_k}^{M} (N_k - i_k)\Big((\lambda_k + \sum_{l=1,\ l\neq j}^{M} \beta_{lk} i_l + \beta_{jk}(i_j-1))\nu^{(j)}_{(i_1,\ldots,i_k+1,\ldots,i_M)}(n) \\ & + 1_{n>0}\beta_{jk}\nu^{(j)}_{(i_1,\ldots,i_k+1,\ldots,i_M)}(n-1)\Big) + (\mu_j + \delta(i_1,\ldots,i_M))1_{n=0}, \quad n \geq 0,\end{aligned}$$

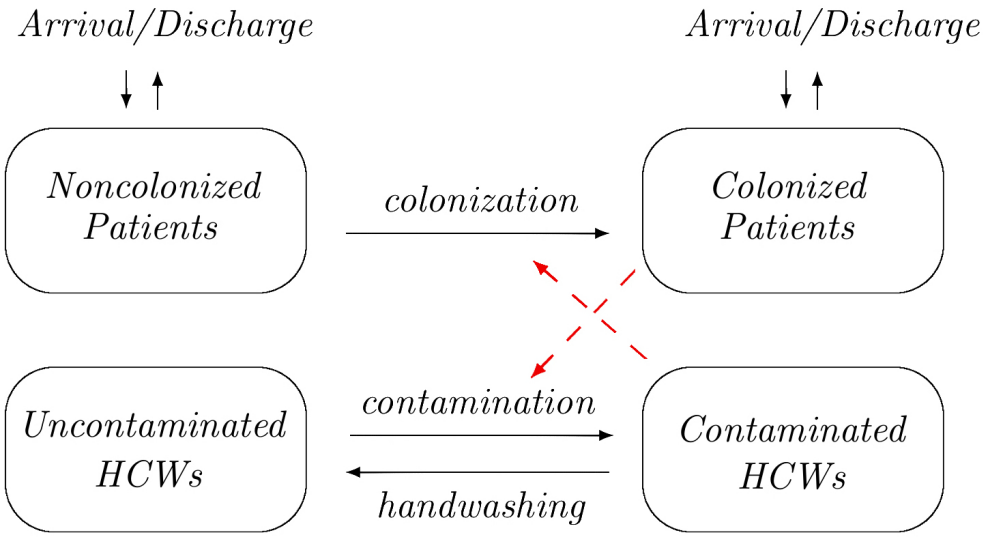
$$\theta_{(i_1,\ldots,i_M)} = \delta(i_1,i_2,\ldots,i_M) + \sum_{j=1}^{M}(\mu_j(i_1,i_2,\ldots,i_M) + \lambda_j(i_1,i_2,\ldots,i_M))$$

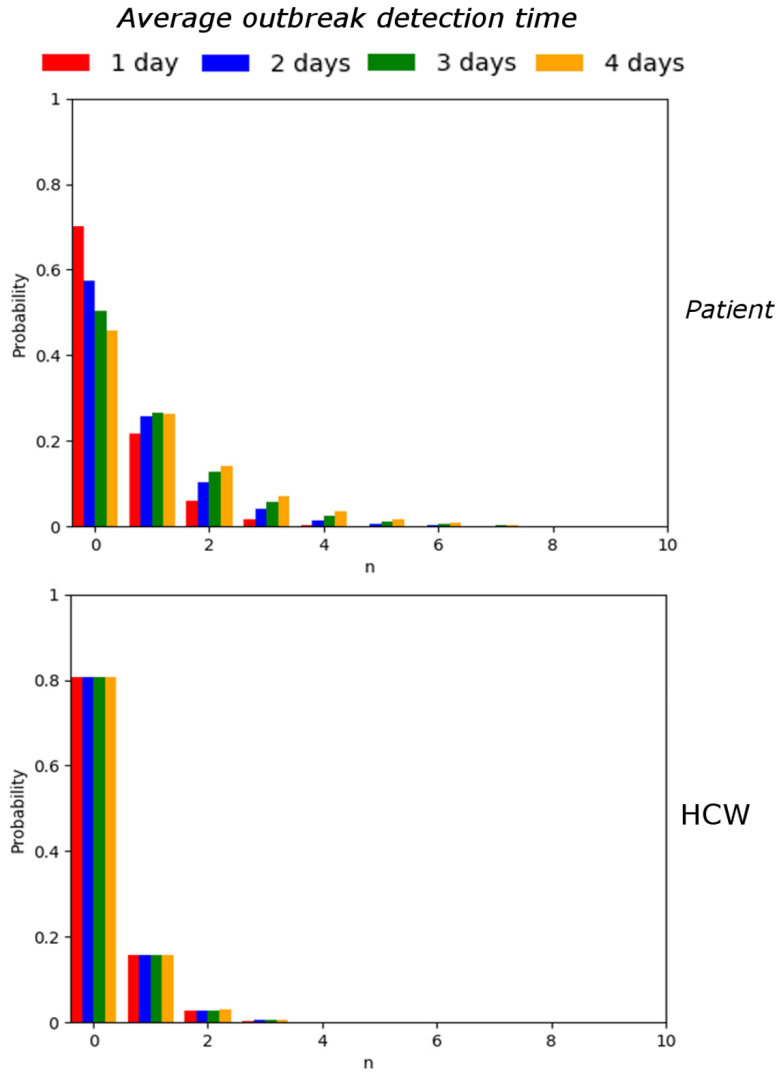
System of linear equations: $\prod_{j=1}^{M}(N_j+1)$ *equations* per each value of $n \geq 0$

$$\mathbf{D}^{(j)}(n)\boldsymbol{\nu}^{(j)}(n) \quad = \quad \mathbf{e}^{(j)}(n),$$

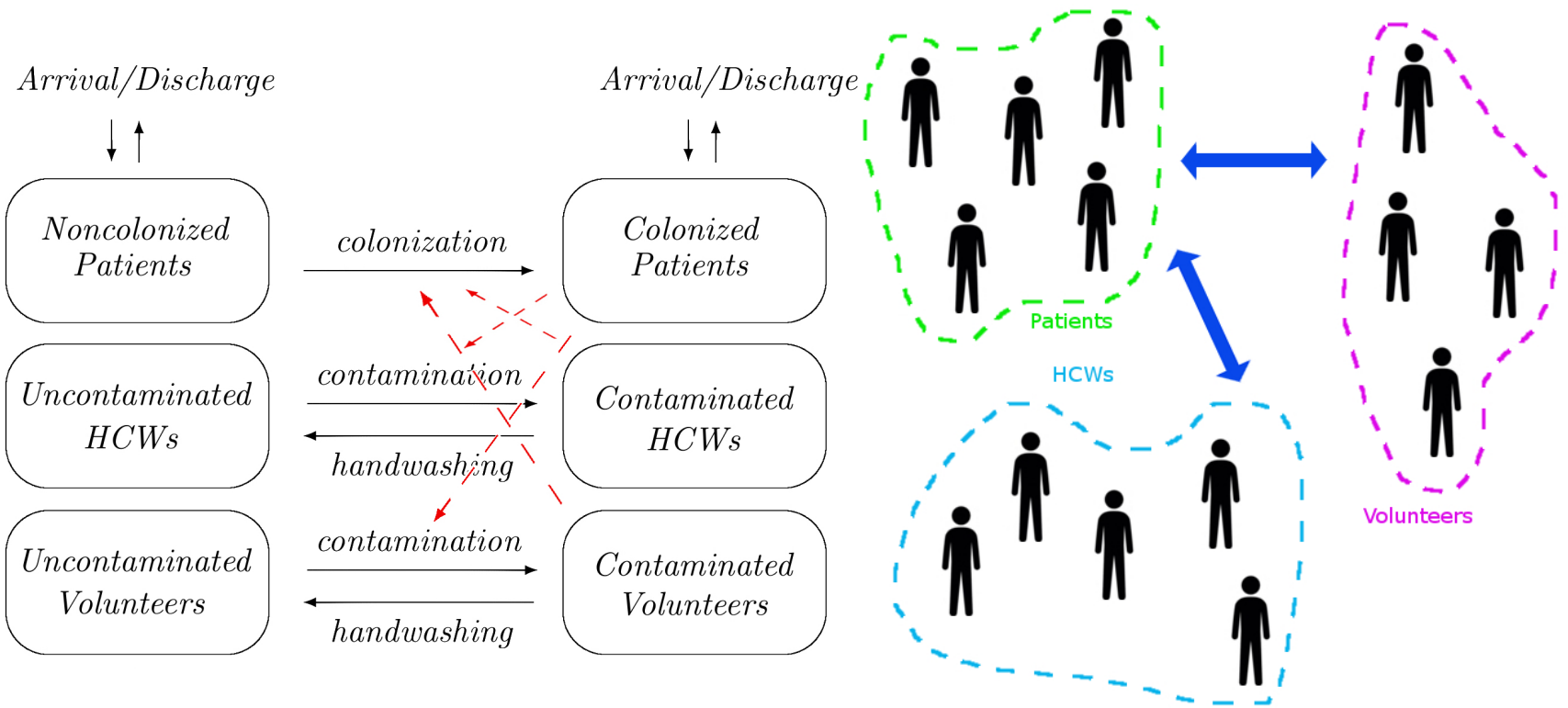
Outline I

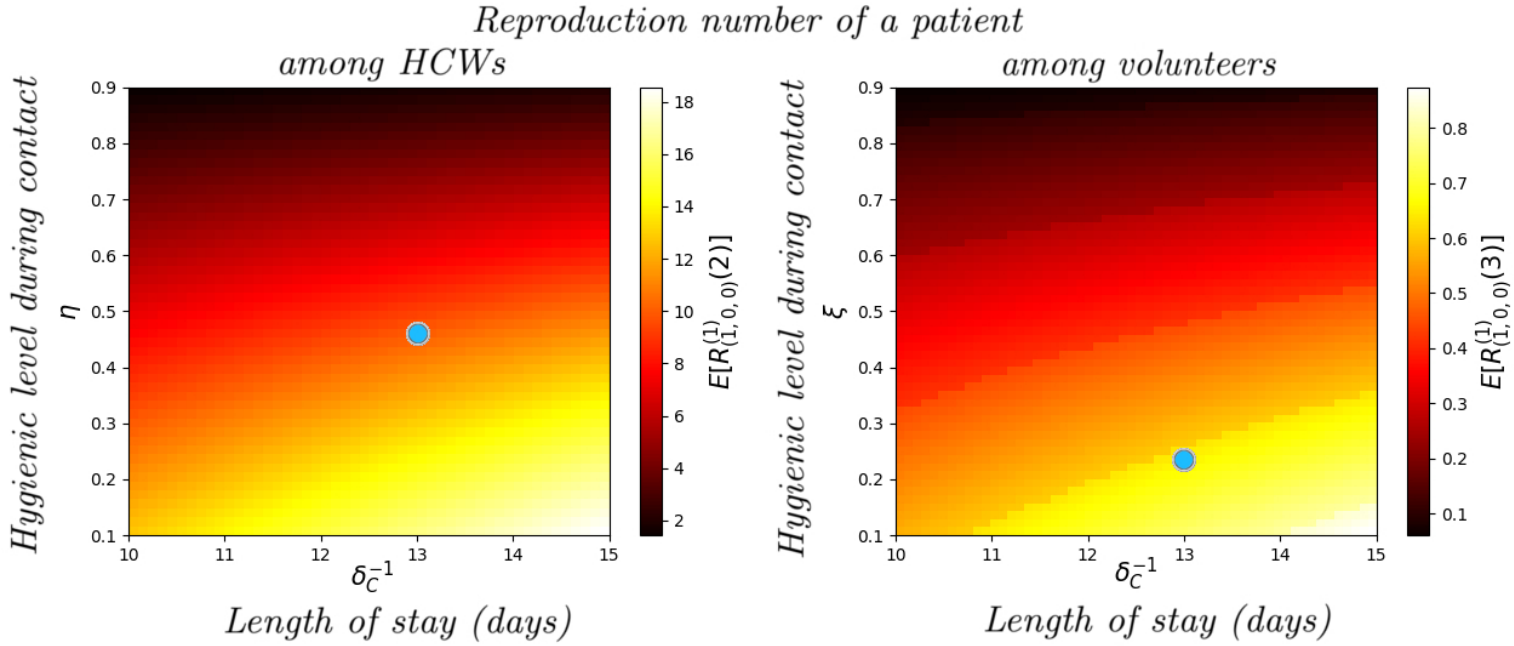
Model as in Artalejo (2014)

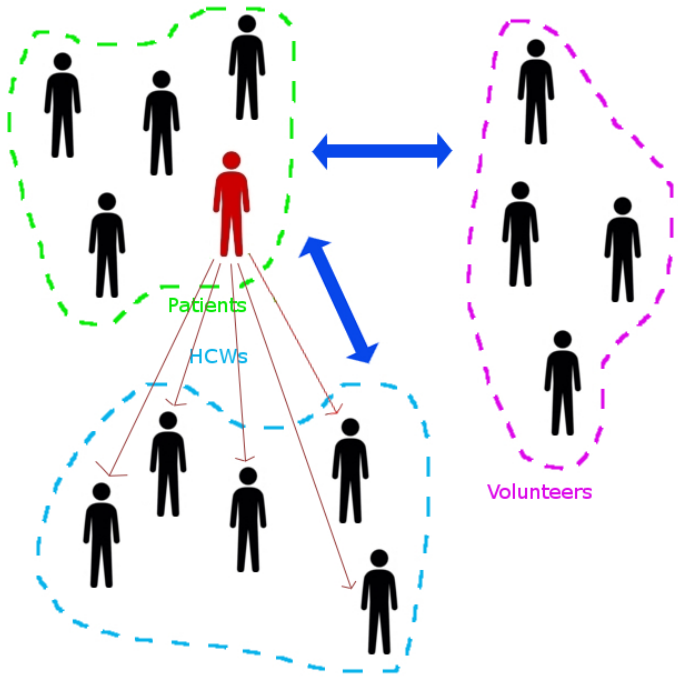


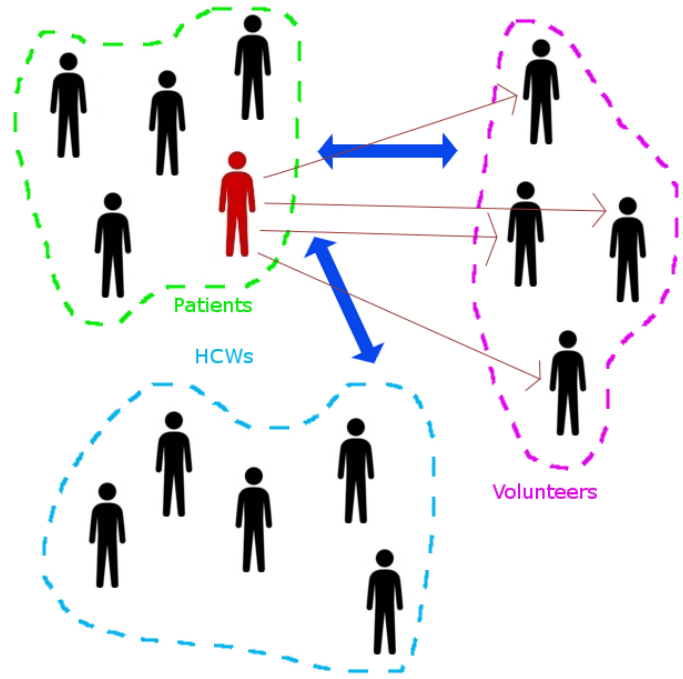


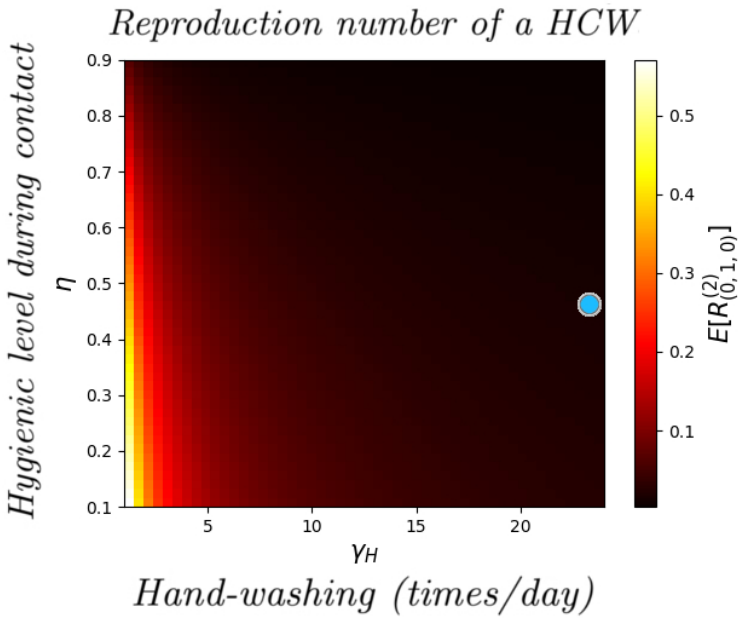
Respiratory Intensive Care Unit at Beijing Tongren Hospital

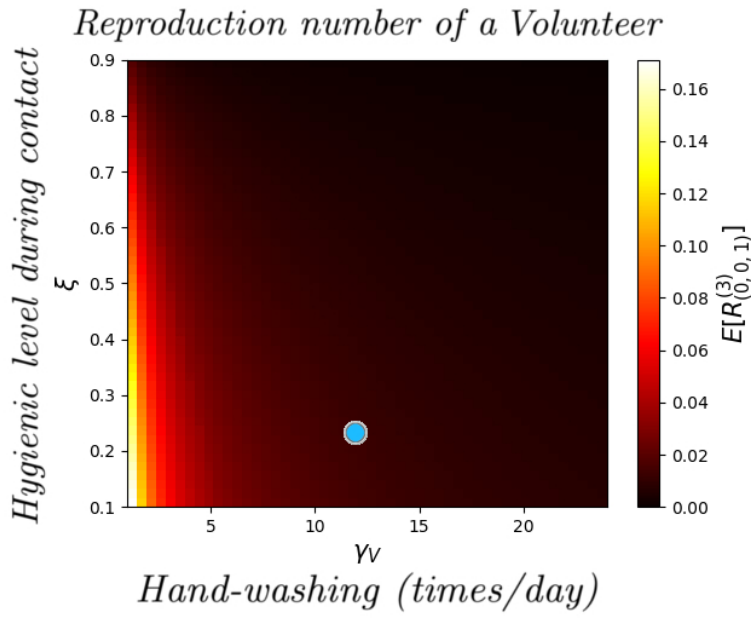


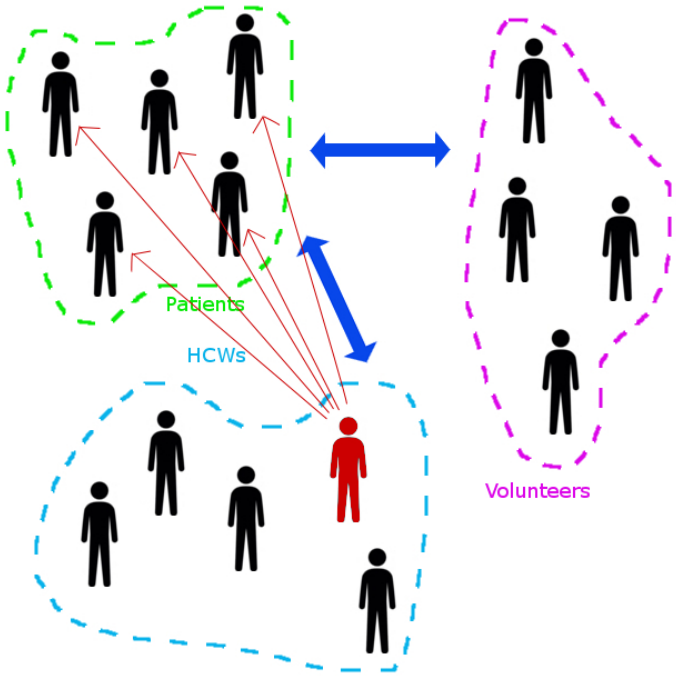

Reproduction number of a patient
among HCWs
among volunteers
Hygienic level during contact
η
ξ
Length of stay (days)
δ_C^{-1}
$E[R^{(1)}_{(I,0,0)}(2)]$
$E[R^{(1)}_{(I,0,0)}(3)]$

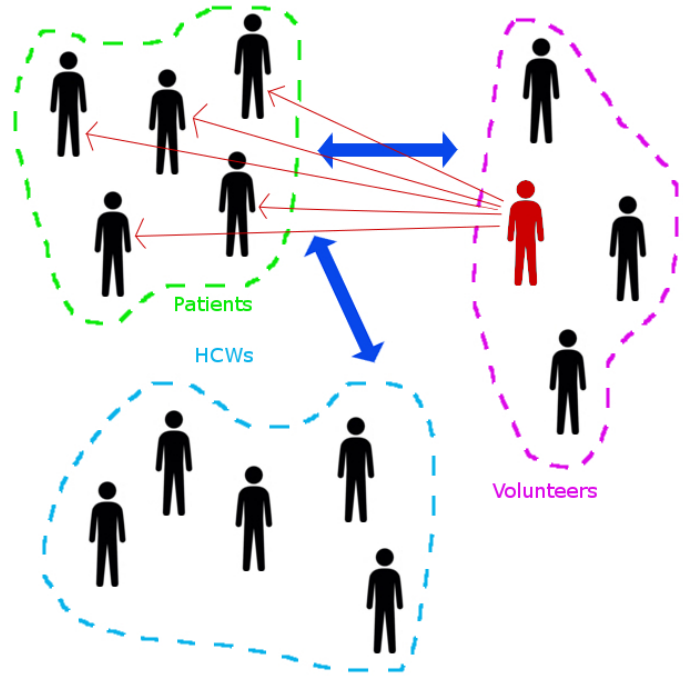

Patients
HCWs
Volunteers


Patients
HCWs
Volunteers

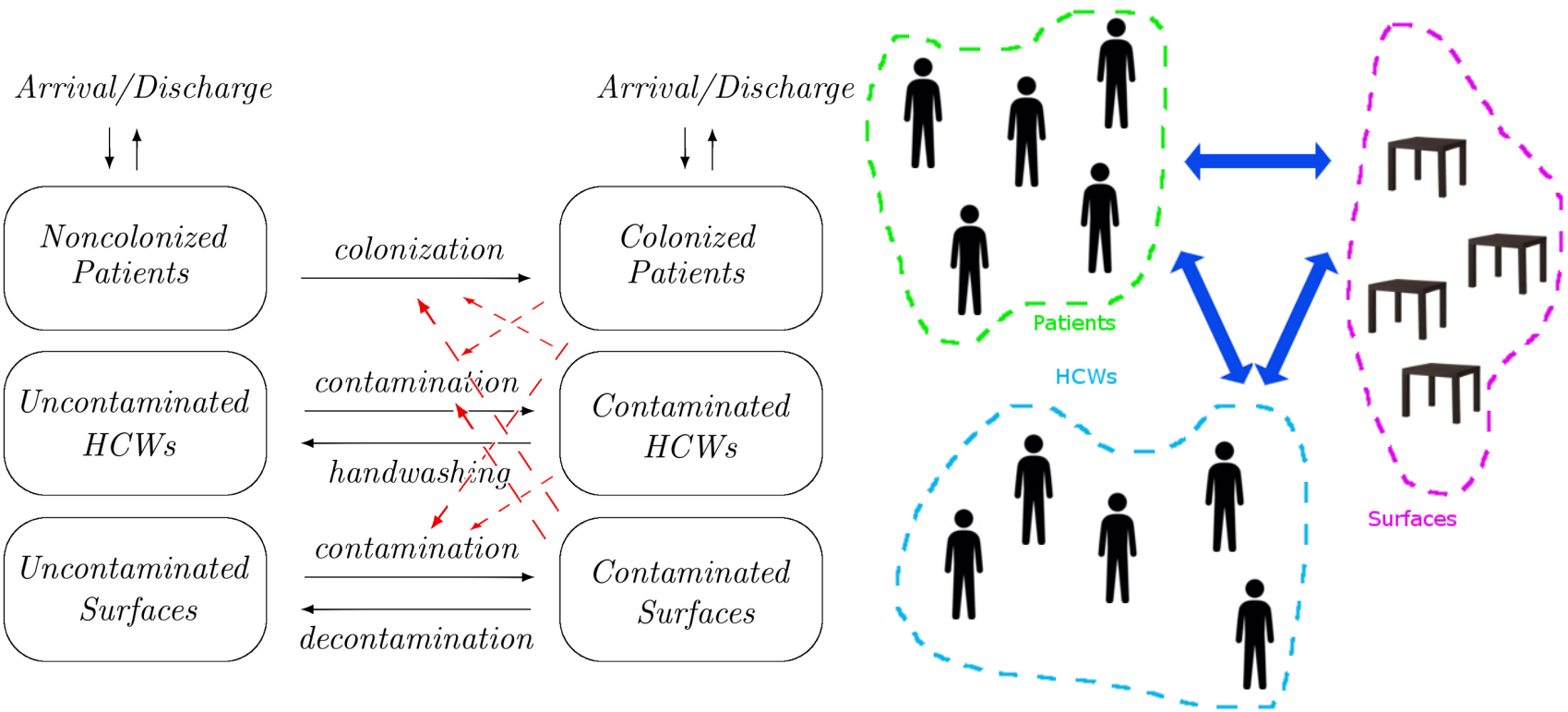

Reproduction number of a HCW
Hygienic level during contact
η
γH
Hand-washing (times/day)
E[R(2)(0,1,0)]

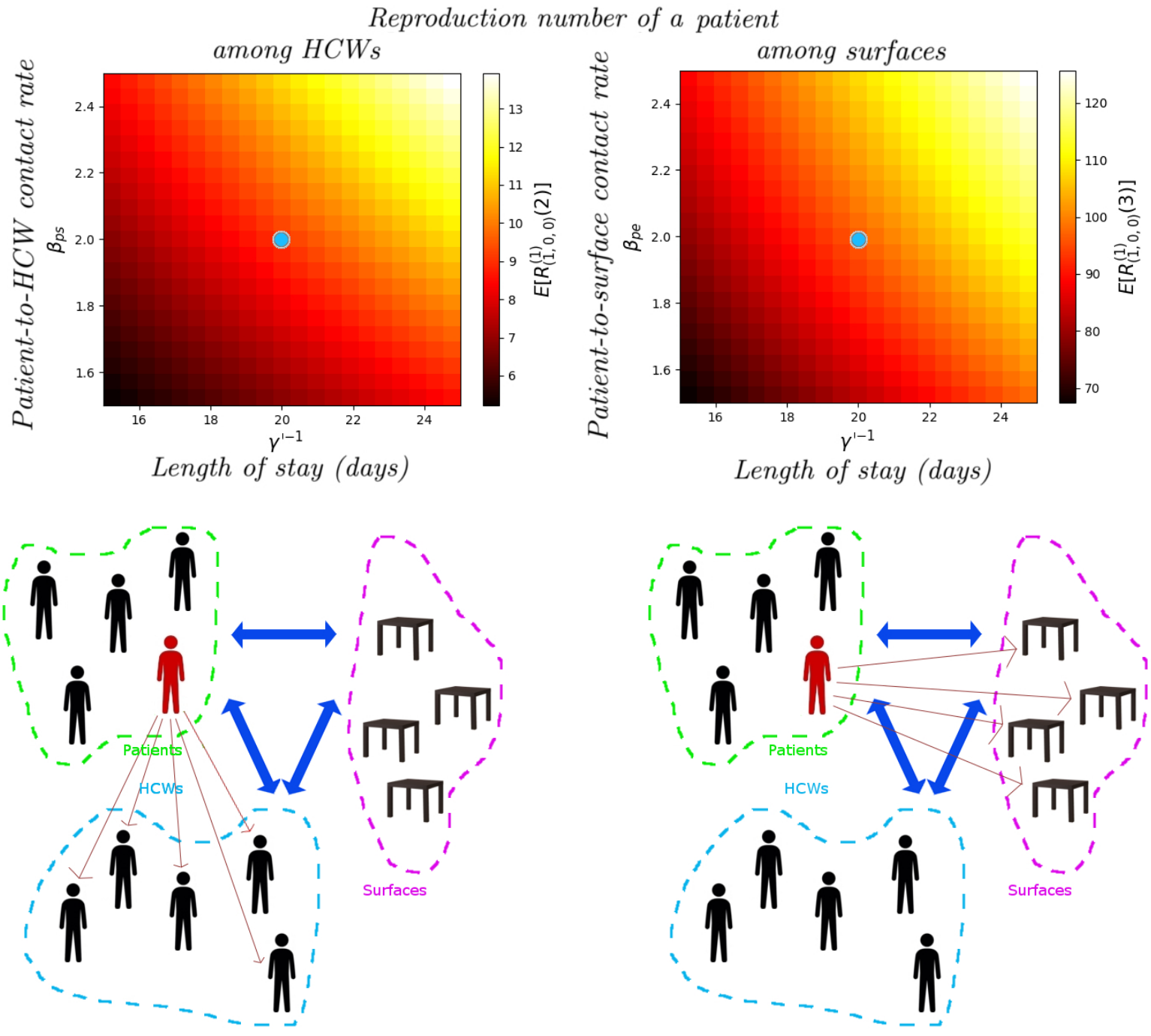

Reproduction number of a Volunteer
Hygienic level during contact
ξ
γV
Hand-washing (times/day)
E[R(3)(0,0,1)]

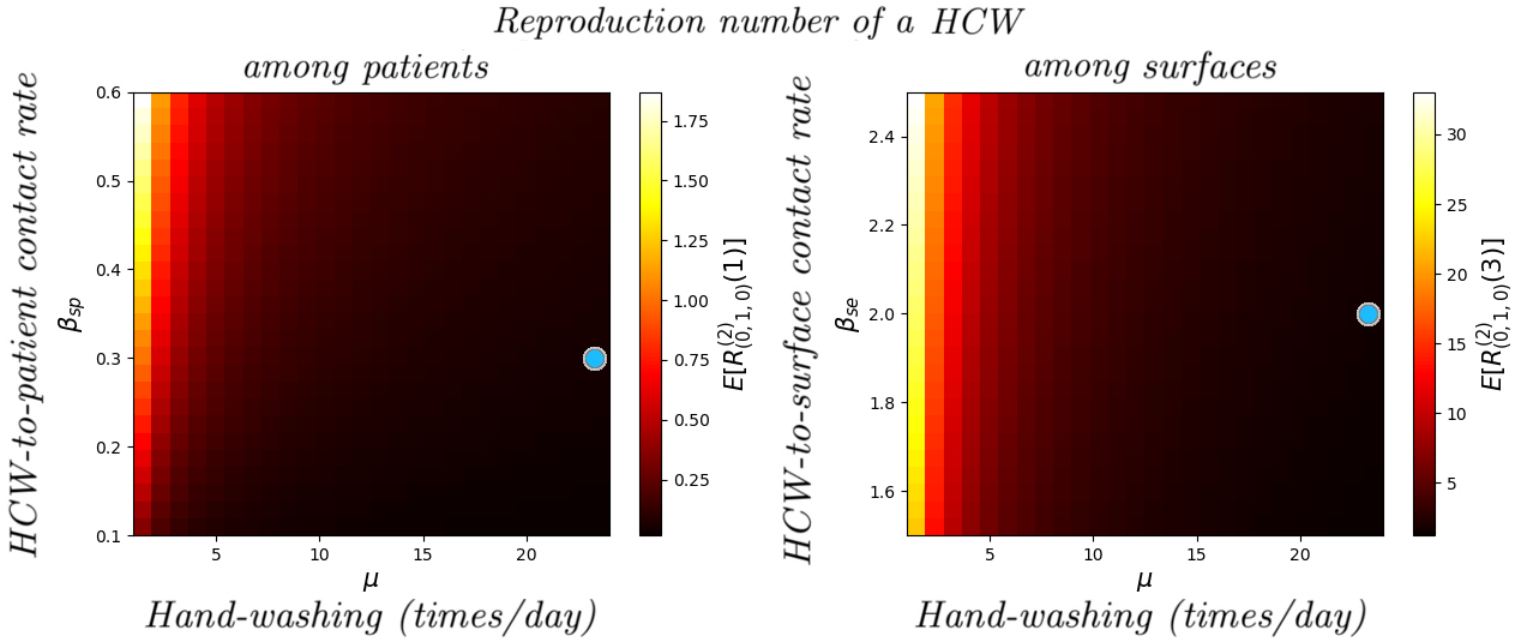

Patients
HCWs
Volunteers

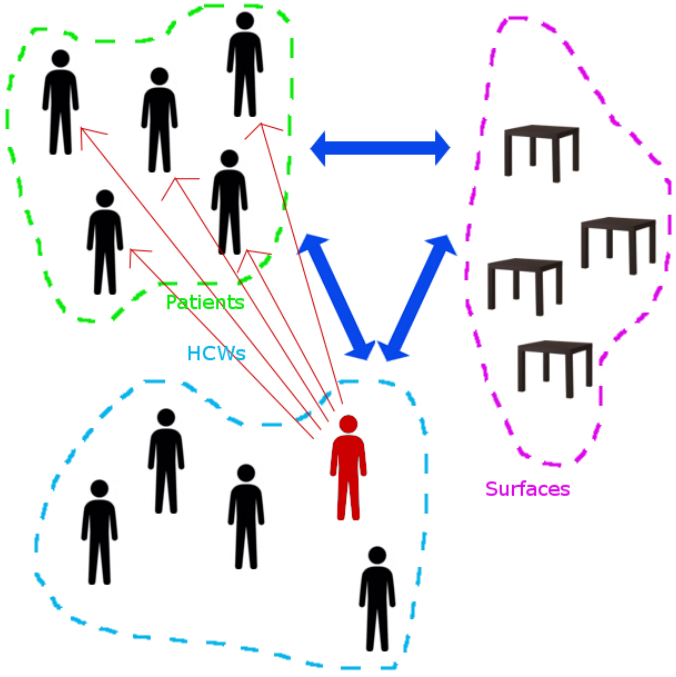

Patients
HCWs
Volunteers

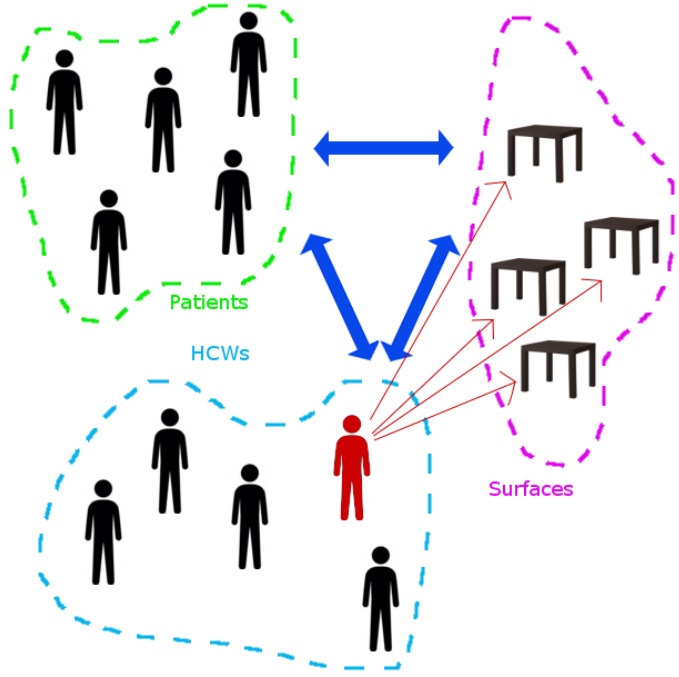
Onco-haematological unit at UMC in Germany

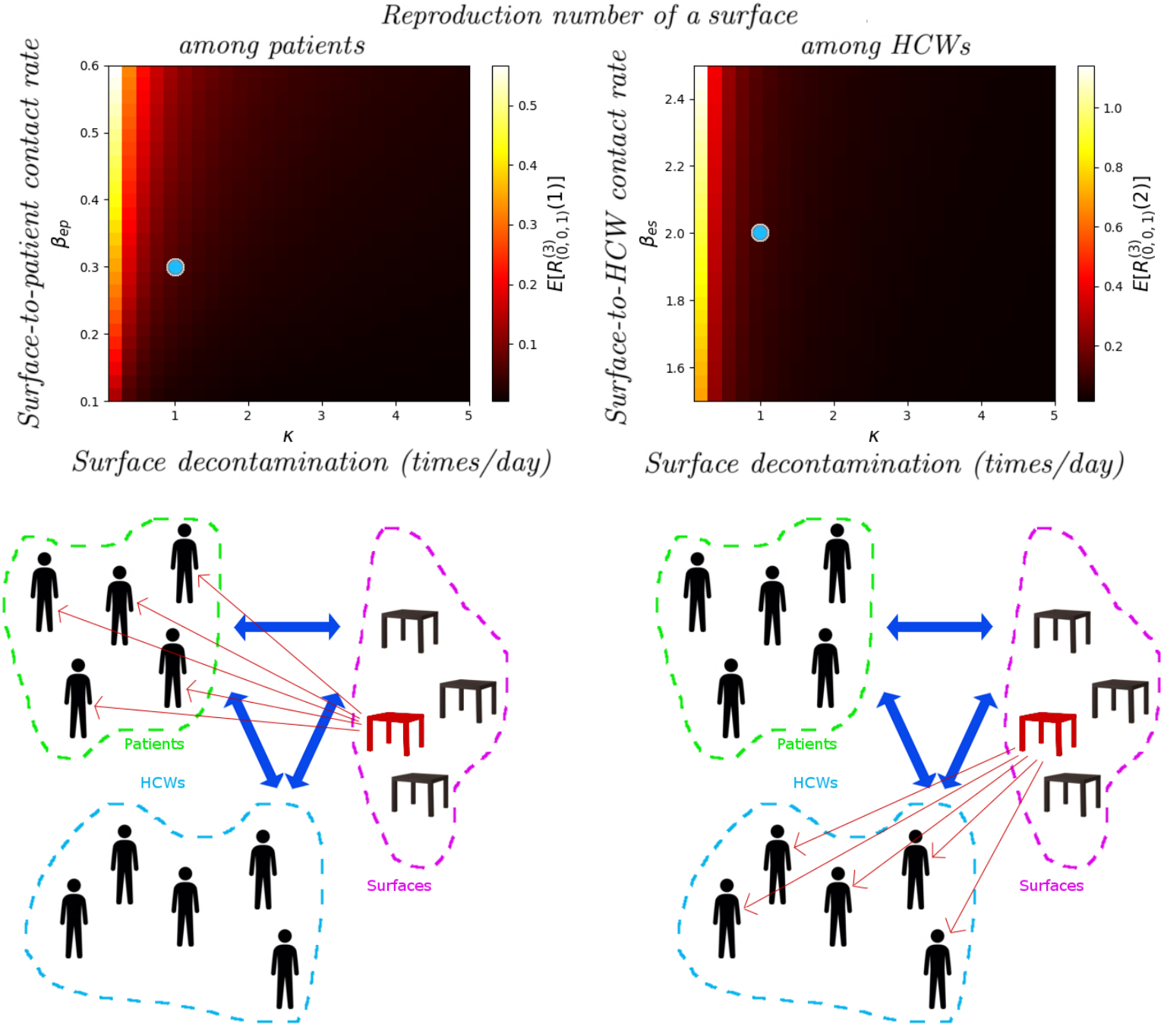



Reproduction number of a patient
among HCWs
Patient-to-HCW contact rate
β_{ps}
γ'^{-1}
Length of stay (days)
$E[R^{(1)}_{(1,0,0)}(2)]$
among surfaces
Patient-to-surface contact rate
β_{pe}
γ'^{-1}
Length of stay (days)
$E[R^{(1)}_{(1,0,0)}(3)]$
Patients
HCWs
Surfaces
Patients
HCWs
Surfaces


Reproduction number of a HCW
among patients
HCW-to-patient contact rate
β_{sp}
μ
Hand-washing (times/day)
$E[R^{(2)}_{(0,1,0)}(1)]$
among surfaces
HCW-to-surface contact rate
β_{se}
μ
Hand-washing (times/day)
$E[R^{(2)}_{(0,1,0)}(3)]$


Patients
HCWs
Surfaces


Patients
HCWs
Surfaces


Reproduction number of a surface
among patients
among HCWs
Surface-to-patient contact rate
Surface-to-HCW contact rate
β_{ep}
β_{es}
κ
$E[R^{(3)}_{(0,0,1)}(1)]$
$E[R^{(3)}_{(0,0,1)}(2)]$
Surface decontamination (times/day)
Surface decontamination (times/day)
Patients
HCWs
Surfaces
Patients
HCWs
Surfaces

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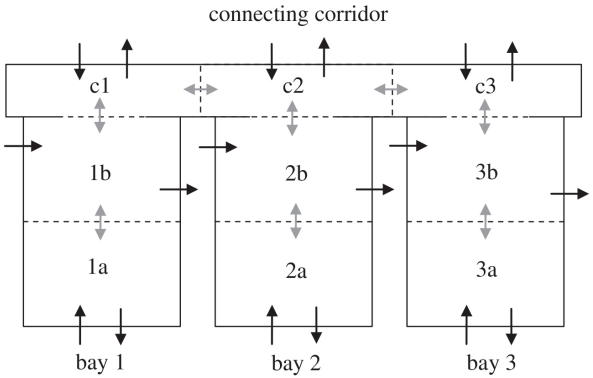
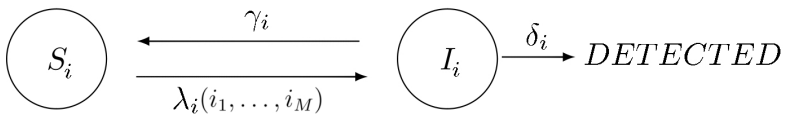
Airborne transmission: incorporating airflow dynamics

Noakes & Sleigh (2009), López-García & King & Noakes (2019)



Infection spread dynamics in each zone:



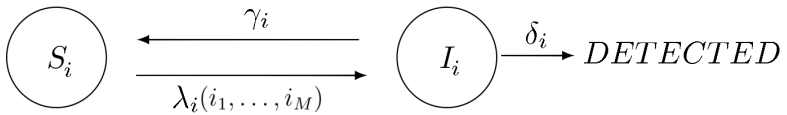
Patients are distributed among M different *zones*, and pathogen spreads through air. If one has $(I_1, I_2, \ldots, I_M)$ infective individuals in each zone at any time, the concentration of pathogen in the air among the different zones can be modelled as

$$V_i \frac{dC_i(t)}{dt} = qI_i - Q_i C_i(t) - \sum_{k=1}^{M} \beta_{ik} C_i(t) + \sum_{k=1}^{M} \beta_{ki} C_k(t), \quad 1 \leq i \leq M$$

$$\begin{aligned} C_i(t) &= \textit{Pathogen concentration at ventilation zone } i, \quad 1 \leq i \leq M \\ V_i &= \textit{Volume of zone } i, \quad 1 \leq i \leq M \\ q &= \textit{generation rate of infectious quanta per infected individual}, \\ Q_i &= \textit{extract ventilation rate in zone } i, \quad 1 \leq i \leq M, \end{aligned}$$

and $\sum_{k=1}^{M} \beta_{ik} C_i$ and $\sum_{k=1}^{M} \beta_{ki} C_k$ represent pathogen spread between zones k and i.

Infection spread dynamics in each zone:



By assuming steady-state conditions for the concentration of pathogen in the air between infection dynamics events, one gets

$$\begin{pmatrix} \lambda_1(i_1,\ldots,i_M) \\ \lambda_2(i_1,\ldots,i_M) \\ \vdots \\ \lambda_M(i_1,\ldots,i_M) \end{pmatrix} = p\mathbf{V}^{-1} \begin{pmatrix} qi_1 \\ qi_2 \\ \vdots \\ qi_M \end{pmatrix},$$

where p is the pulmonary rate of individuals in the ward, and $\mathbf{V}$ is the *ventilation matrix*

$$\mathbf{V} = \begin{pmatrix} Q_{o,1} + \sum_k \beta_{1k} & -\beta_{21} & \cdots & -\beta_{M-1,1} & -\beta_{M1} \\ -\beta_{12} & Q_{o,2} + \sum_k \beta_{2k} & \cdots & -\beta_{M-1,2} & -\beta_{M2} \\ -\beta_{13} & -\beta_{23} & \cdots & -\beta_{M-1,3} & -\beta_{M3} \\ \vdots & \vdots & \ddots & \vdots & \vdots \\ -\beta_{1M} & -\beta_{2M} & \cdots & -\beta_{M-1,M} & Q_{o,M} + \sum_k \beta_{Mk} \end{pmatrix}$$

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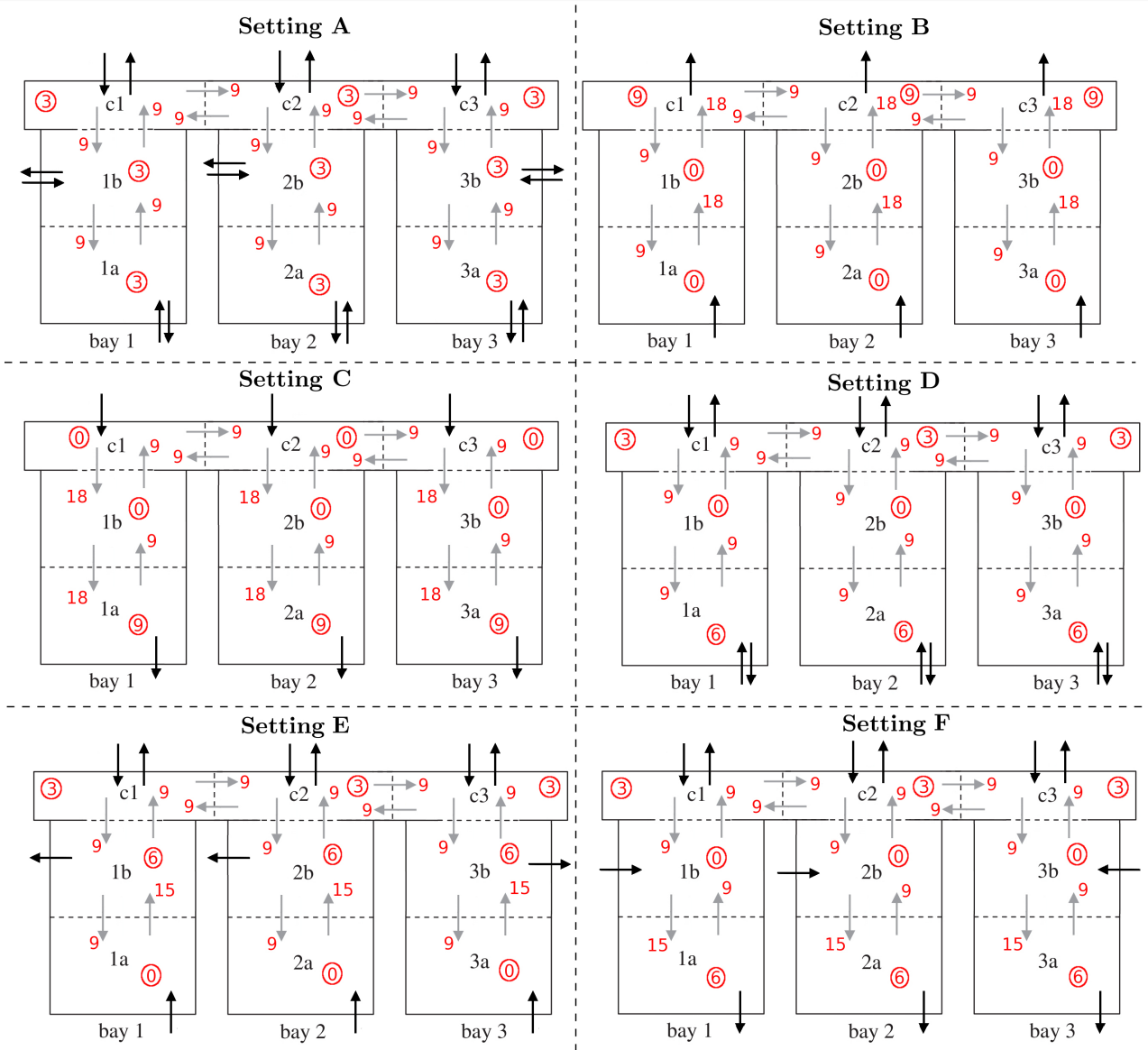
Comparing between ventilation regimes



Summary statistic: number of infections until detection

R = *Number of infections in the ward until detection of the outbreak*,

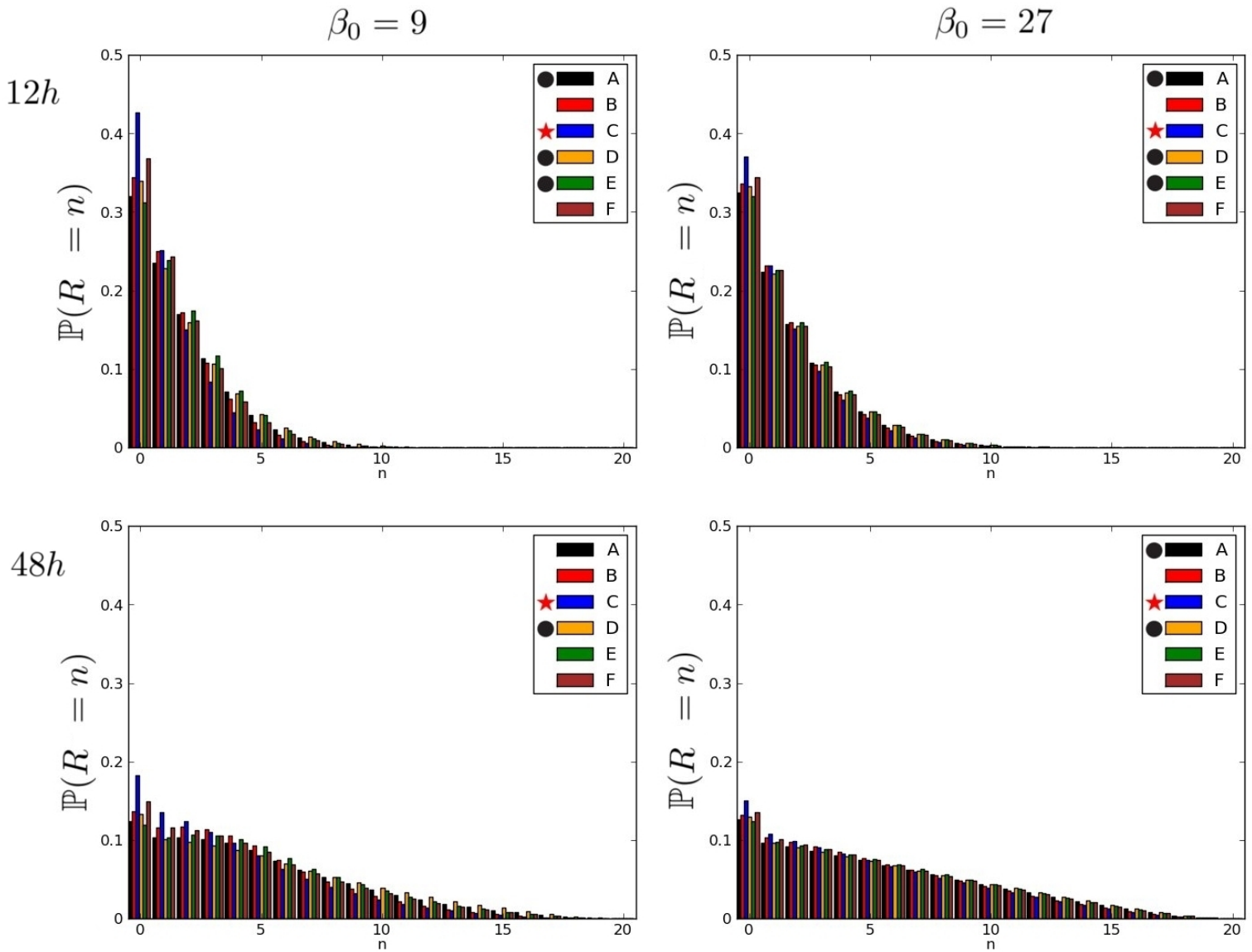
$$p_{(i_1,\ldots,i_M)}(n) = \mathbb{P}(R = n \mid (I_1(0),\ldots,I_M(0)) = (i_1,\ldots,i_M)), \quad n \geq 0, \quad \textit{any } (i_1,\ldots,i_M).$$

One can analytically (and exactly) compute this distribution by solving a (finite) system of linear equations

$$p_{\mathbf{i}}(n)\sum_{j=1}^{M}\left(\lambda_j(\mathbf{i})(N_j - i_j) + (\gamma_j + \delta_j)i_j\right) = \sum_{k=1}^{M}\Big(\gamma_k i_k p_{\mathbf{i}-(k)}(n) + \lambda_k(\mathbf{i})(N_k - i_k)p_{\mathbf{i}+(k)}(n-1)\Big),$$

for all $n \geq 0$, and any possible $\mathbf{i} = (i_1,\ldots,i_M)$.

Detection dominates ventilation



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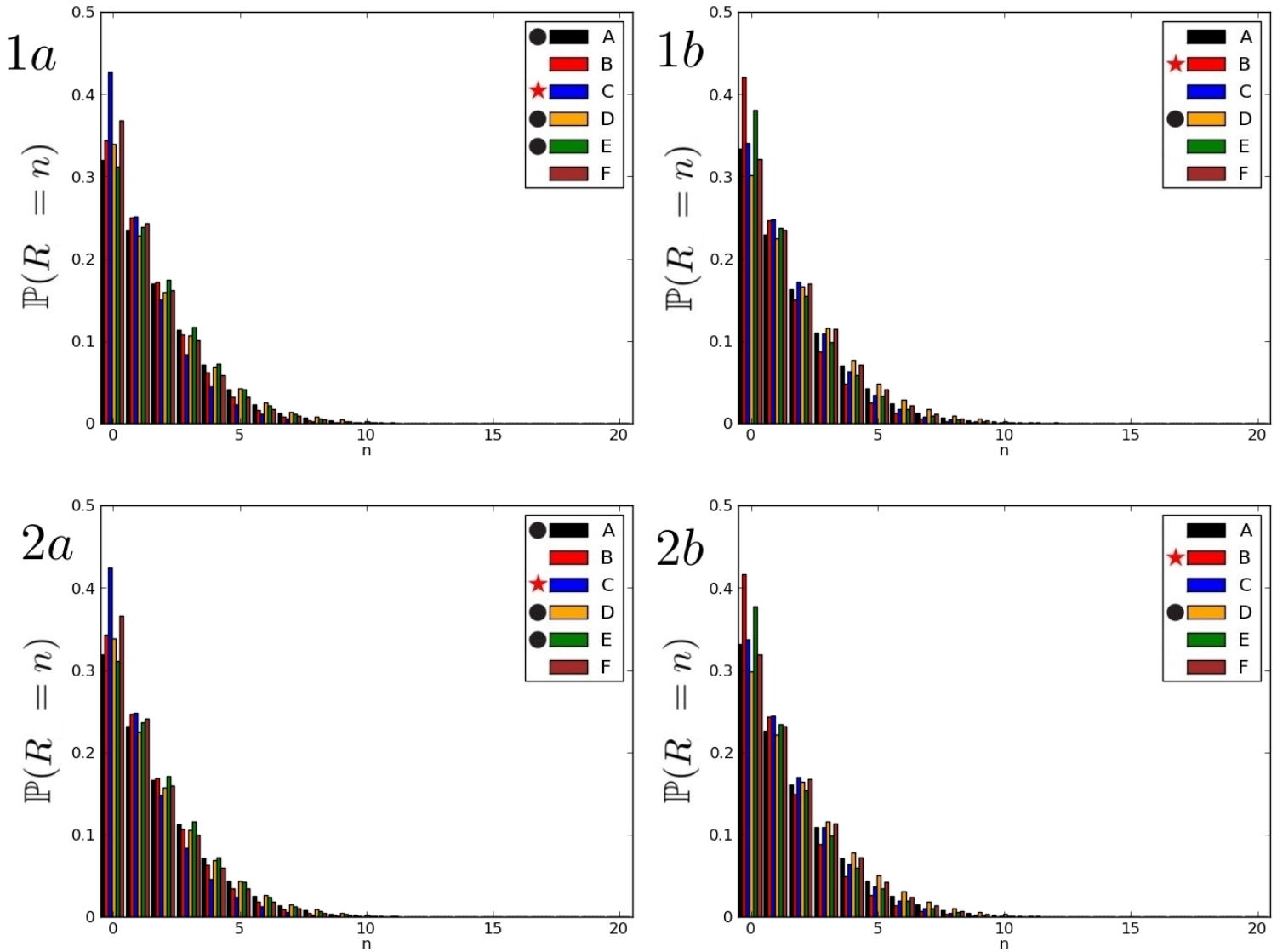
Interplay between ventilation and location of individual starting the outbreak



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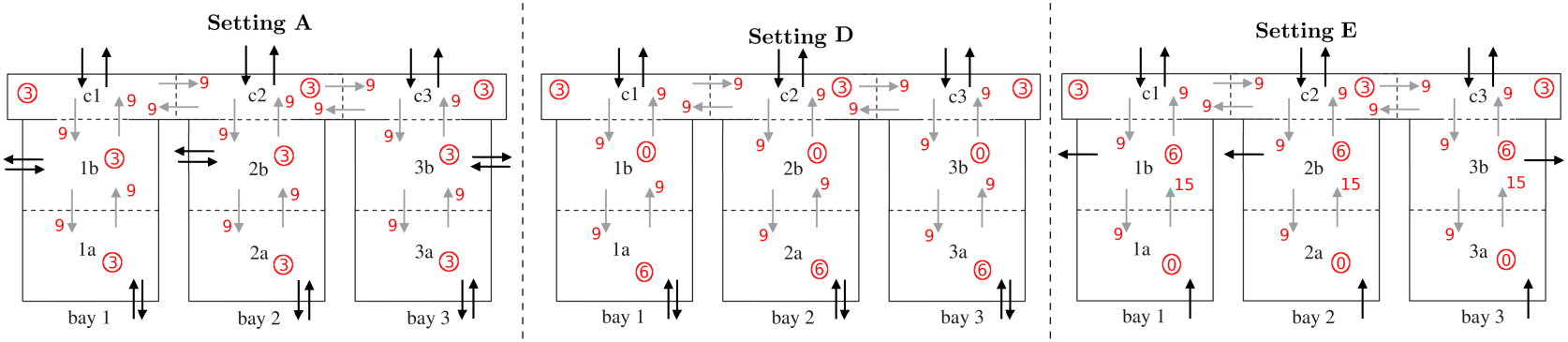
Decreasing hospital ward infection spread risk might increase risk at specific bays



$$R = R(1) + R(2) + R(3)$$

Regime	$E[R]$	$E[R(1)]$	$E[R(2)]$	$E[R(3)]$
A	5.01	2.65	1.34	1.02
D	5.20	2.56	1.47	1.17
E	4.86	2.69	1.25	0.92

Mean values of $E[R]$, $E[R(1)]$, $E[R(2)]$, *and* $E[R(3)]$, *for* $\delta^{-1} = 48h$ *and ventilation settings A, D, and E; initially infective individual in zone* 1*a*

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- Theodore Kypraios (University of Nottingham, UK)
- Catherine Noakes & Marco-Felipe King (Institute for Public Health and Environmental Engineering, University of Leeds, UK)
- Antonio Gómez-Corral (Complutense University of Madrid, Spain)
- Carmen Molina-París, Grant Lythe & Jonty Carruthers (University of Leeds, UK)
- Nagasuma Chandra (Indian Institute of Science, Bangalore, India)

"Mathematical modelling of the emergence and spread of antibiotic resistant bacteria in healthcare settings: a stochastic approach"
MR/N014855/1, **2016-2019**

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References

INTERFACE

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A unified stochastic modelling framework for the spread of nosocomial infections

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[2]School of Mathematical Sciences, University of Nottingham, NG7 2RD Nottingham, UK

Research

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Original Research Article

A Multicompartment SIS Stochastic Model with Zonal Ventilation for the Spread of Nosocomial Infections: Detection, Outbreak Management, and Infection Control

Martín López-García, Marco-Felipe King, Catherine J. Noakes

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