SOME MATHEMATICAL MODELS FOR BACTERIAL HOSPITAL INFECTIONS

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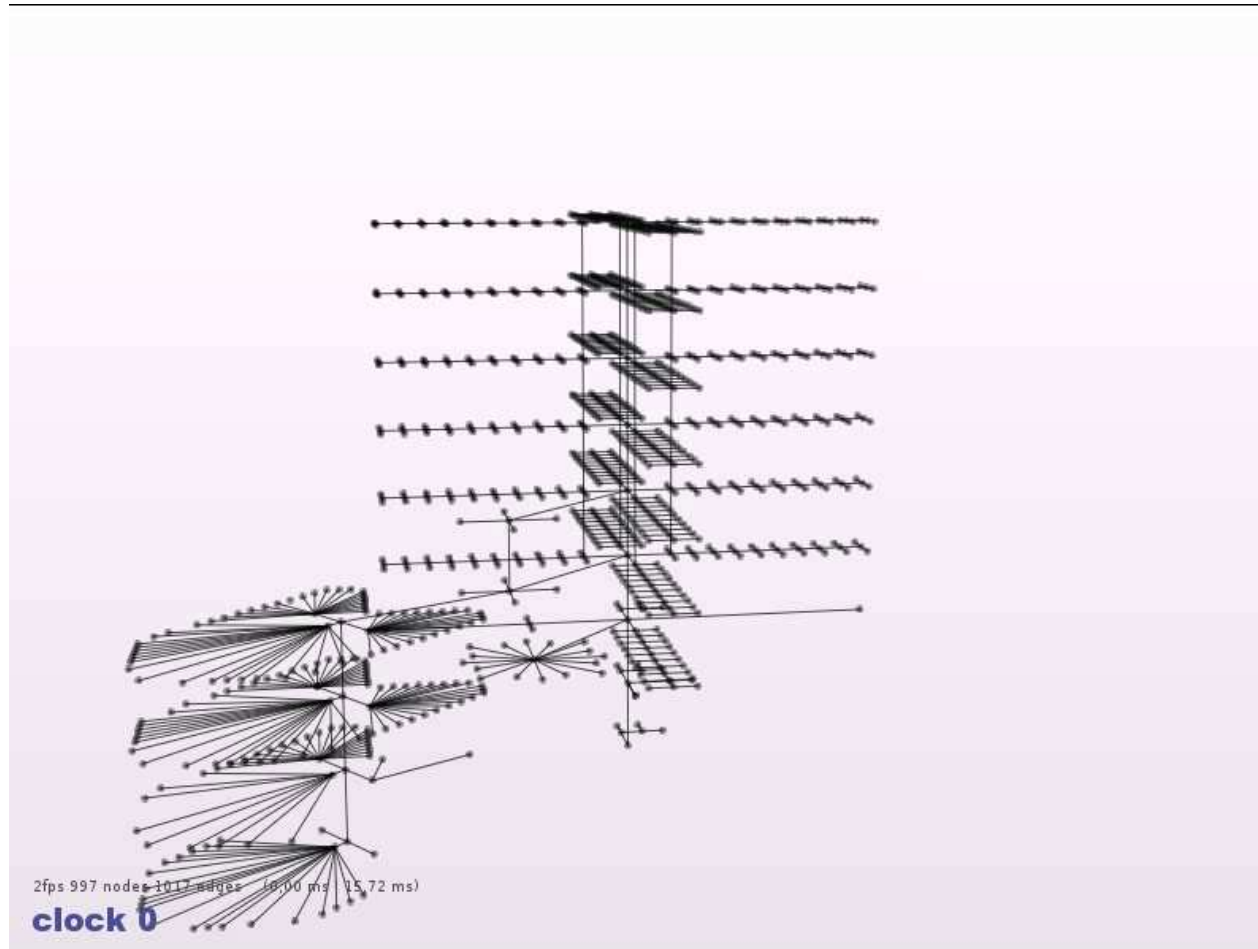
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Everything Disperse to Miami

University of Miami, December 2012

INFECTION OF P*seudomonas-Aeruginosa* iN LE HAVRE'S HOSPITAL

A. Dutot, PM, D. Olivier, and G. Savin, In Eurosis, (2006)

Contact network for one Intensive Care Unit

L. Temime, L. Opatowski, Y. Pannet, C. Brun-Buisson, PY Boëlle, D. Guillemot, *PNAS*, (2009)
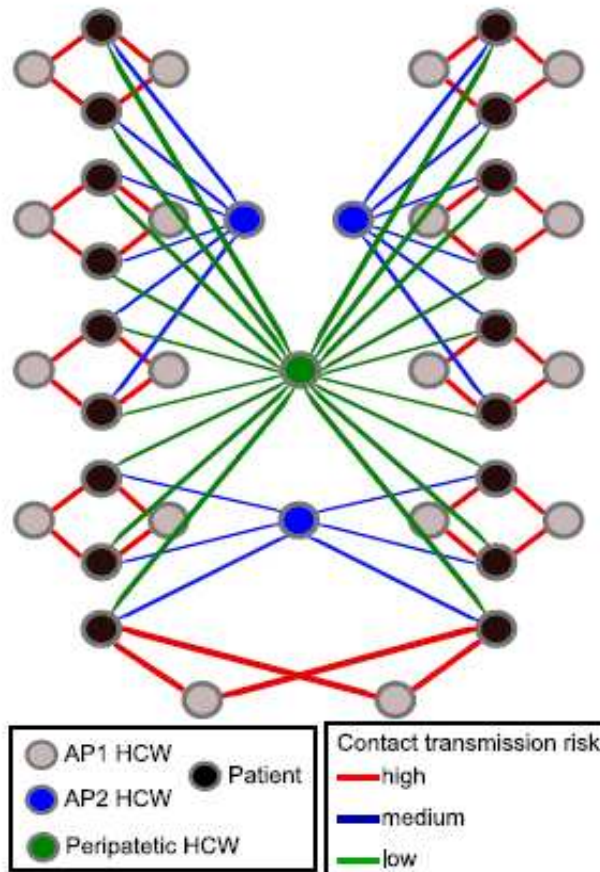

Fig. 1. Network of contacts in the modeled ICU. There are 18 patients (black circles) and 3 types of HCWs: 2 profiles of HCWs assigned to subgroups of patients (assigned profiles 1 and 2, beige and blue circles) and peripatetic-type HCWs (green circles). Per contact transmission risks may be high (investigated range: from 8.5% to 25%, red edges), medium (investigated range: from 5.5% to 17%, blue edges) or low (investigated range: from 3% to 10%, green edges). All contacts are undirected, meaning that transmission may occur in both directions. Patient-AP1 HCWs contacts occur 3 times a day, while other contacts occur once a day.

$$\begin{cases} \dfrac{dS(t)}{dt} = \Lambda - DS(t) - diag(S(t))\int_0^{+\infty} B(a)i(t,a)da \\[3mm] \left(\partial_t + \partial_a\right)i(t,a) = -\left[M(a) + D\right]i(t,a) \\[3mm] i(t,0) = diag(S(t))\int_0^{+\infty} B(a)i(t,a)da \\[3mm] \dfrac{dR(t)}{dt} = \int_0^{+\infty} M(a)i(t,a)da - DR(t) \end{cases}$$

SIR models revisited: from individual level to population level

PM and Shigui Ruan *In preparation* **(2012)**

$$
\begin{cases}
\dfrac{dS(t)}{dt} = -\beta S(t)I(t) \\[2em]
\dfrac{dI(t)}{dt} = \beta S(t)I(t) - \eta_R I(t) \\[2em]
\dfrac{dR(t)}{dt} = \eta_R I(t)
\end{cases}
$$

S Susceptible, **I** Infectious, **R** Recovered

When one neglects the demography, an epidemic becomes a combination of the following aspects:

(a) a rule of contacts between individuals;

(b) a rule of transmission per contact;

(c) a rule of development of the infection at the level of individuals.

Some references

- **Monte-Carlo:** Gillespie's algorithm (see Doob's book)
- **Epidemic on Networks**
  - Durrett and Levin (1994)
  - Newman (2003) (2010)
  - Meyers (2006)
  - Durrett (2007) and (2010)

  - Barrat Bathélemy and Vespignani (2008)
- **Epidemics and IBMs:**
  - Levin and Durrett (1996)
  - Keeling and Grenfell (2000)
  - DeAngelis and Mooij (2005)
  - Grimm and Railsback (2005)
- **Epidemics and comparison between IMBs:**
  - Smieszek, Fiebig and Scholz (2009)
  - Ajelli et al. (2010)
- **Comparison between IMB and DEM:**
  - Pascual and Levin (1999) (in the context of predator-prey)
  - D'Agata et al. (2007) (in the context of epidemics and nosocomial infections)
  - Hinow et al. (2009) (in the context of cell population dynamics)
  - Sharkey (2008) (in the context of epidemics in networks)

Rules of Contacts

Assumption 2.1
(a) At any time each individual has initiated exactly one contact with an individual in the population (possibly himself).

(b) The duration of a contact follows an exponential law and the average duration of a contact is $T_C > 0$.

(c) At the end of a given contact the initiating individual randomly chooses a new individual within the population and the duration for this contact is determined.

Diagram of the contact network at a given time t>=0.
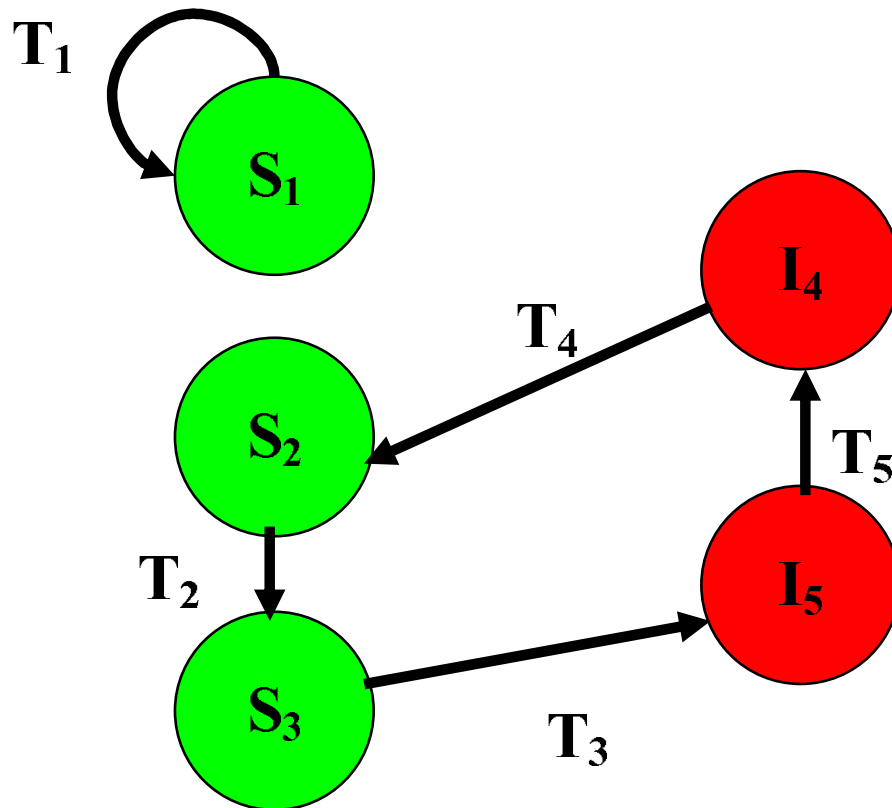
The first *S*-individual (S_1) only contacts with himself.

The second *S*-individual (S_2) chooses to contact with a third *S*-individual (S_3) who in turn contacts with an *I*-individual (I_5).

I_5 contacts another *I*-individual (I_4) who chooses S_2 for contact.

Contacts between S and I individuals

Define
- S_C is the number of S-individual in Contact with a I-individual
- S_F is the number of S-individual in contact Free with a I-individual
- I_C is the number of I-individual in Contact with a S-individual
- I_F is the number of I-individual in contact Free with a S-individual

Under Assumption 2.1, we obtain the following model

$$
\begin{cases}
S'_C = \nu_C \frac{I}{S+I} (S_C + S_F) - \nu_C S_C \\
S'_F = \nu_C \frac{S}{S+I} (S_C + S_F) - \nu_C S_F \\
I'_C = \nu_C \frac{S}{S+I} (I_C + I_F) - \nu_C I_C \\
I'_F = \nu_C \frac{I}{S+I} (I_C + I_F) - \nu_C I_F
\end{cases}
\tag{2.1}
$$

with

$$ S = S_C + S_F \text{ and } I = I_C + I_F. $$
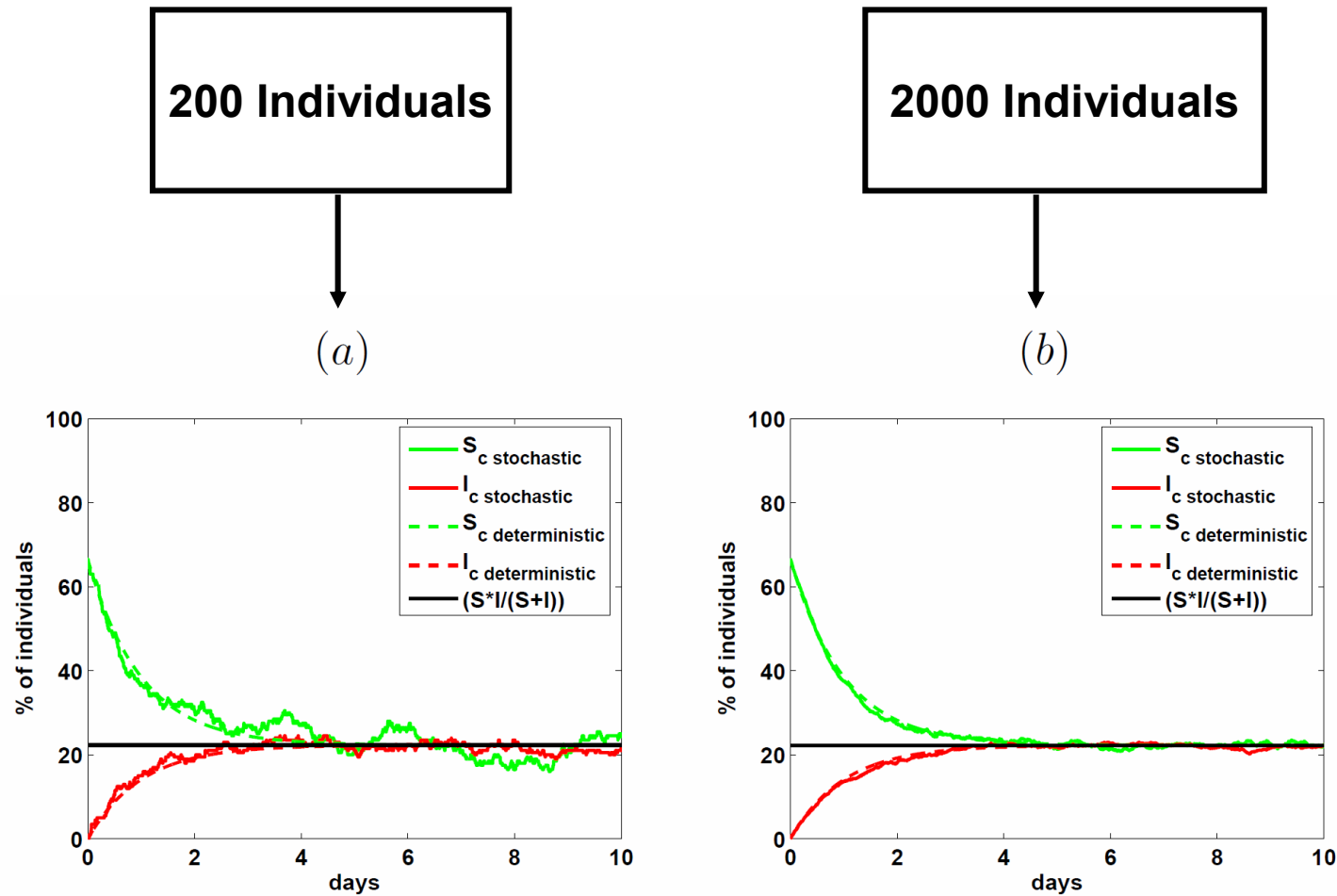
Game theory like model!

Figure 2: The comparison between solutions of the ordinary differential equation model and a Monte Carlo simulation of the model. The solutions of the stochastic model converge to the equilibrium solutions of the ODE model (2.1).

Rules of transmission

Assumption 2.3
During a given contact between an S-individual and an I-individual the probability of transmission is

(a) p_S if the contact was initiated by an S-individual

(b) p_I if the contact was initiated by an I-individual

Definition : We will say that

(i) the **transmission is driven only by S-individuals** if $p_S>0$ and $p_I=0$

(ii) the **transmission is driven only by I-individuals** if $p_S=0$ and $p_I>0$

Assumption 2.4 (Time of Transmission) For a given contact between a susceptible individual and an infective individual, the transmission of the disease occurs (with a probability p_S or p_I) only at one of the following two moments:

(c) the beginning of the contact;
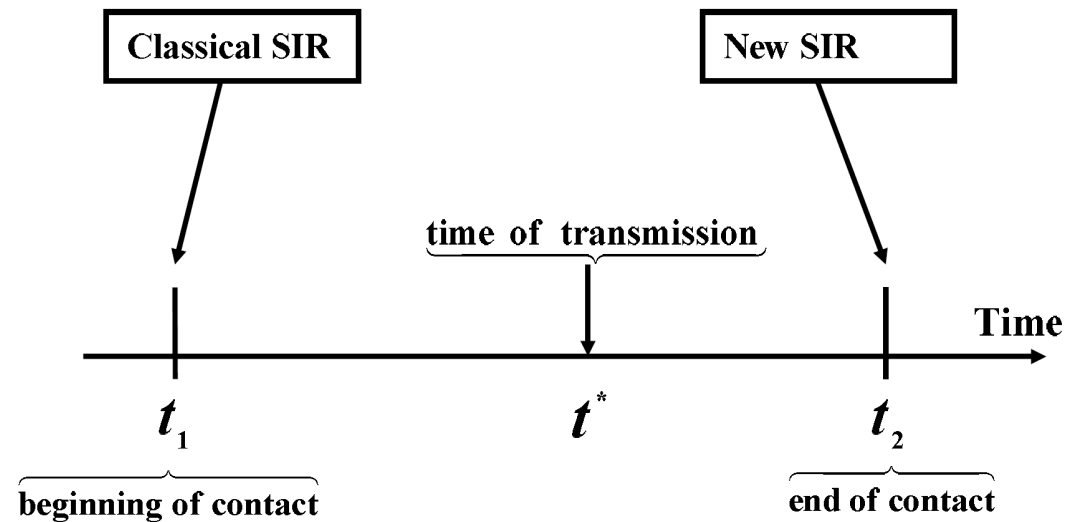
(d) the end of the contact.

Figure 3: Time of transmission. (a) Transmission occurs at the beginning of a contact as assumed in the classical SIR model and (b) transmission occurs at the end of a contact as assumed in the new SIR model. In general, transmission can occur at any moment in between.

Individual Based Models (IMB)

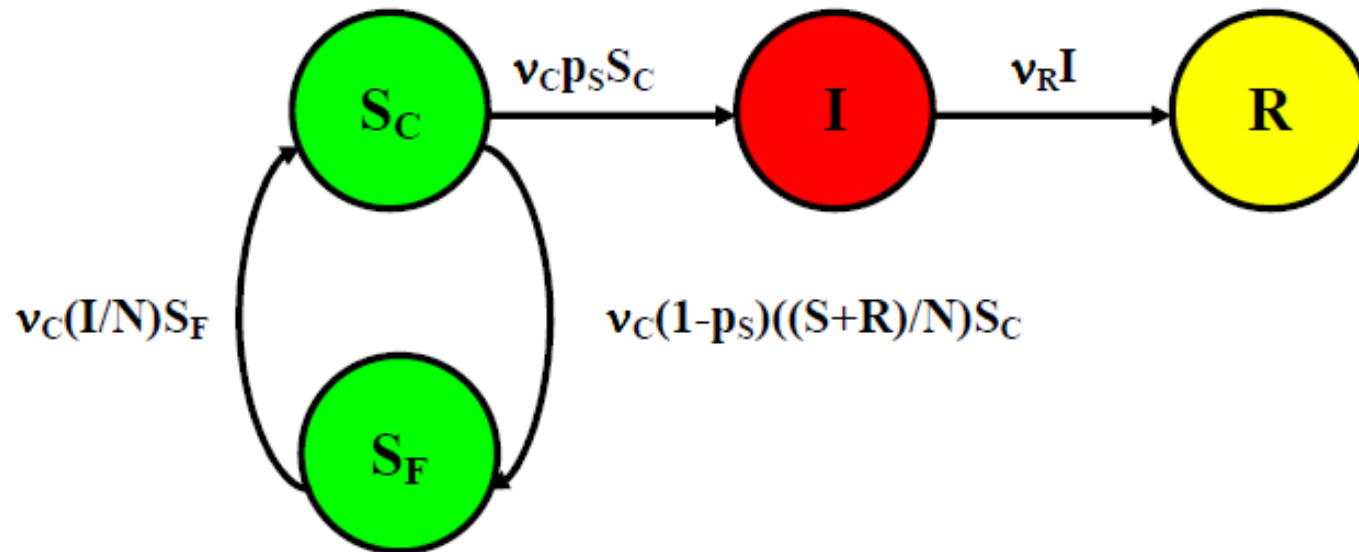|	Transmission driven by S	Transmission driven by I
Begging of contact	**IBM$_{11}$** Classical SIR	**IBM$_{12}$** Classical SIR
End of contact	**IBM$_{21}$** First new SIR	**IBM$_{22}$** Second new SIR

Transmission Driven only by S-Individuals

Let Assumptions 2.1 (Rules of contacts) and 2.3 (Rules of transmission) be satisfied. Assume in addition that

$$p_S > 0 \text{ and } p_I = 0.$$

Assumption 3.1 The duration of an infection follows an exponential law and the average duration of an infection is $T_R > 0$.

$$
\begin{cases}
S_c{}' = \nu_c \left\{ \dfrac{I}{N} \left[S_F + (1 - p_s) S_c \right] - S_c \right\} \\[2ex]
S_F{}' = \nu_c \left\{ \dfrac{S + R}{N} \left[S_F + (1 - p_s) S_c \right] - S_F \right\} \\[2ex]
I' = \nu_c p_s S_c - \eta_R I \\[1ex]
R' = \eta_R I
\end{cases}
$$

Asymptotic behavior

Setting

$$s = \frac{S}{N}, i = \frac{I}{N}, s_C = \frac{S_C}{N}, s_f = \frac{S_f}{N}, \text{ and } r = \frac{R}{N}$$

we obtain

$$
\begin{cases}
s_C' = \nu_c \left\{ i(s - p_s s_c) - s_c \right\} \\
s_f' = \nu_c \left\{ (s + r)(s - p_s s_c) - s_f \right\} \\
i' = \nu_c p_s s_c - \eta_R i \\
r' = \eta_R i
\end{cases}
$$

Define $\bar{s}_C = \dfrac{s_C}{s}$ one obtain

$$\begin{cases} s' = -\nu_c p_s \bar{s}_C s \\[2mm] i' = \nu_c p_s \bar{s}_C s - \eta_R i \\[2mm] r' = \eta_R i \\[2mm] \bar{s}'_C = \nu_c (i - \bar{s}_C)(1 - p_s \bar{s}_C) \end{cases}$$

Conservation law property

$$\frac{d}{dt}\left\{ s + i - \frac{\eta_R}{\nu_c p_s}\left[\ln\left(1 - p_s \bar{s}_C\right) + \ln(s) \right] \right\} = 0$$

Proposition 3.3 *Assume that $p_S \in (0,1)$, $\nu_c > 0$, $\eta_R > 0$, and further suppose that*

$$s_0 > 0 \text{ and } i_0 > 0.$$

Then all solutions of model (3.7) and their limits satisfy the following property for initial values with $i_0 > 0$

$$\lim_{t \to +\infty} \begin{pmatrix} s(t) \\ i(t) \\ r(t) \\ \bar{s}_c(t) \end{pmatrix} = \begin{pmatrix} s^* \\ 0 \\ r^* \\ 0 \end{pmatrix}$$

with the equilibrium satisfying

$$s^* + r^* = 1$$

and s^* being the unique solution in $\left(0, \frac{\eta_R}{p_S \nu_c}\right]$ of the equation

$$s^* - \frac{\eta_R}{p_S \nu_c} \ln(s^*) = \{s_0 + i_0 - \frac{\eta_R}{p_S \nu_c}[\ln(1 - p_S \bar{s}_{c0}) + \ln(s_0)]\}. \qquad (3.11)$$

Comparison with the classical SIR model

Set $v_c = \dfrac{1}{\varepsilon} \Leftrightarrow T_c = \text{time of contact} = \varepsilon$, and $p_s = \beta_s \varepsilon$ then we obtain

(New SIR)
$$\begin{cases} s'_\varepsilon = -\beta_s \bar{s}_{C\varepsilon} s_\varepsilon \\ i'_\varepsilon = \beta_s \bar{s}_{C\varepsilon} s_\varepsilon - \eta_R i_\varepsilon \\ r'_\varepsilon = \eta_R i_\varepsilon \\ \bar{s}'_{C\varepsilon} = \dfrac{1}{\varepsilon}(i_\varepsilon - \bar{s}_{C\varepsilon})(1 - \beta_s \varepsilon \bar{s}_{C\varepsilon}) \end{cases}$$

(Classical SIR)
$$\begin{cases} s' = -\beta_s s i \\ i' = \beta_s s i - \eta_R i \\ r' = \eta_R i \end{cases}$$

Theorem : (Uniform convergence in time)

$$\begin{pmatrix} s_\varepsilon \\ i_\varepsilon \\ r_\varepsilon \end{pmatrix} \rightarrow \begin{pmatrix} s \\ i \\ r \end{pmatrix} \text{ as } \varepsilon \rightarrow 0 \text{ uniformly in time for } t \geq 0.$$
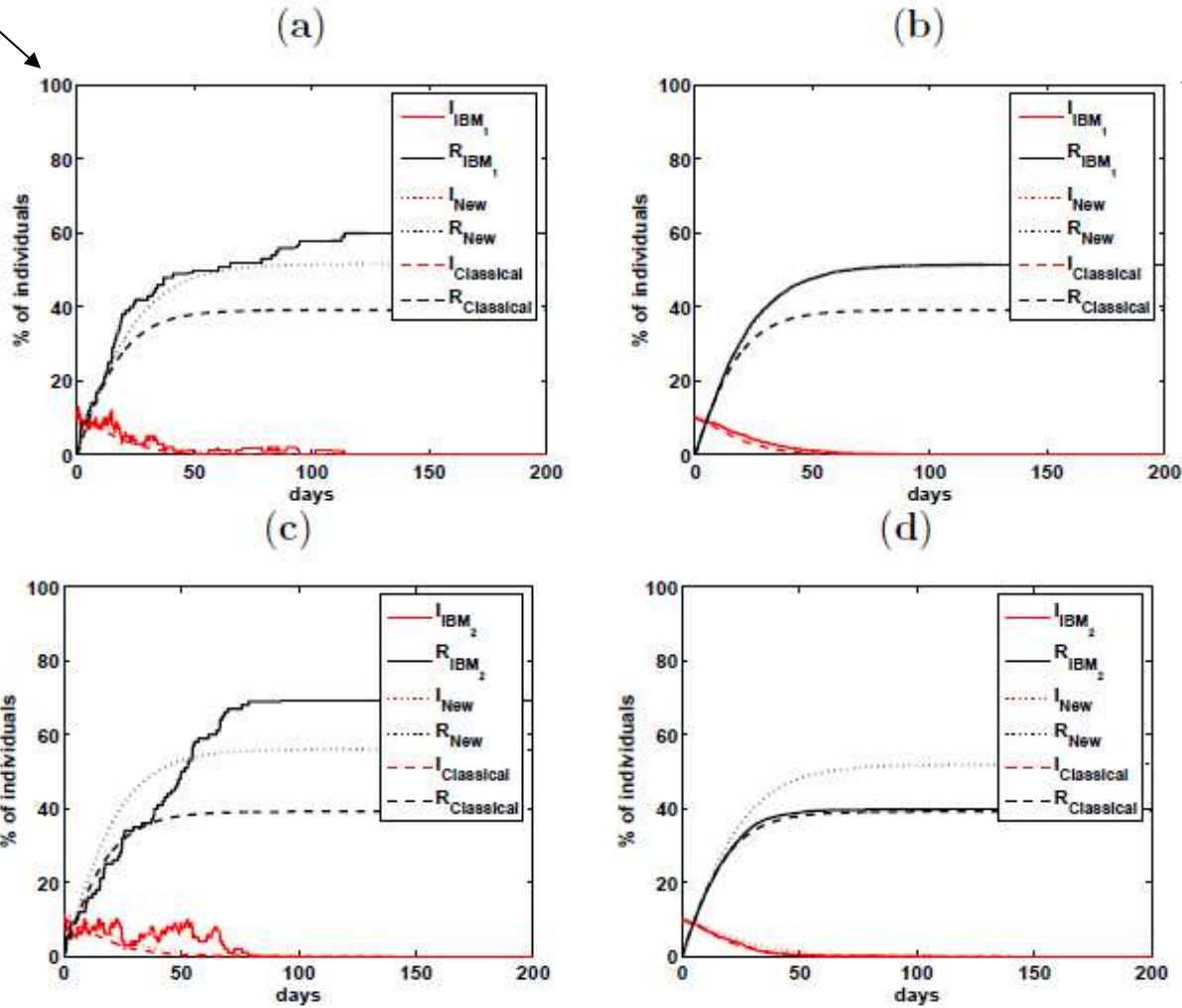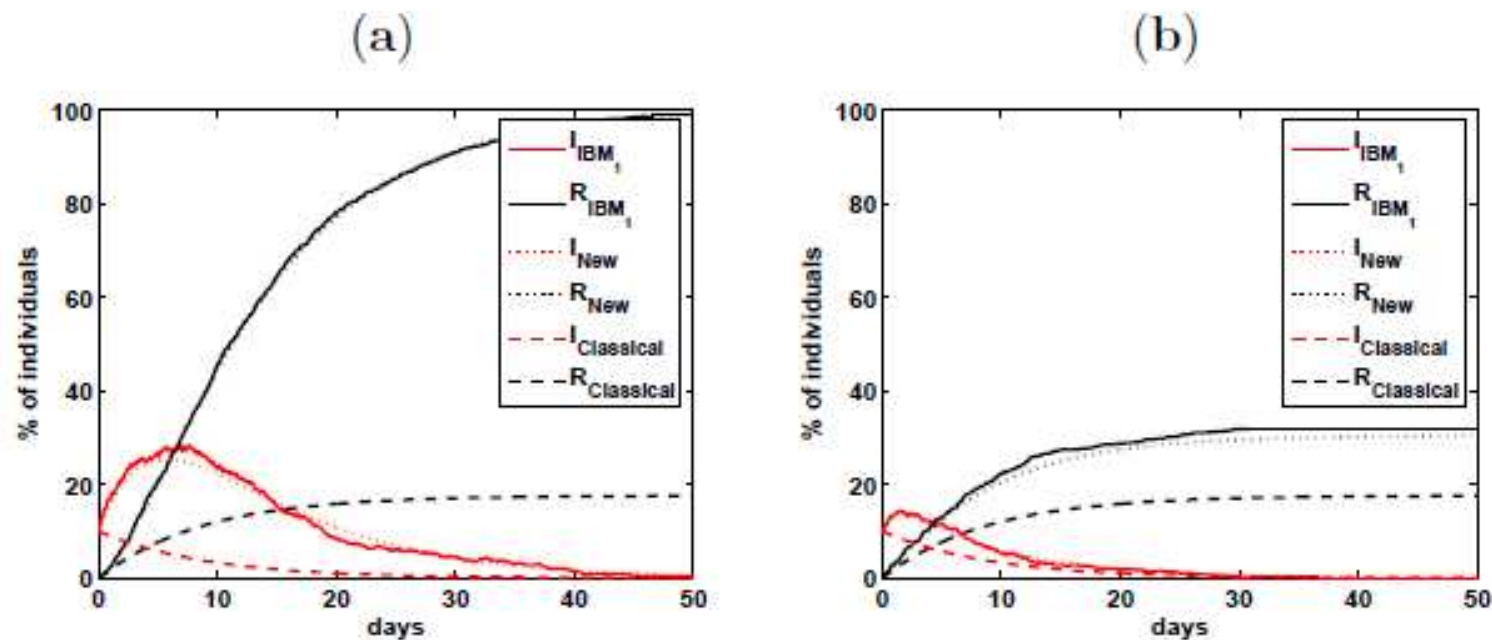
Figure 6: Comparison of simulations of the IBM (solid curves), the classical SIR model (1.1) (dashed curves) and the new SIR model (3.2) (dotted curves) with $\beta = \beta_S$.

In this subsection we run some simulations assuming that $S_C = S$ at time $t = 0$. This means that all S-individuals choose randomly a contact with an I-individual at $t = 0$, and for $t > 0$ all individuals choose randomly a contact within the all population (i.e. including the S, I and R individuals). This also means that the contacts are not yet stabilized at time $t = 0$.

Figure 7: Comparison of simulations of the IBM_1 (solid curves), the classical SIR model (1.1) (dashed curves) and the new SIR model (3.2) (dotted curves) with $\beta = \beta_S$ and a non-fully random graph of connection at time $t = 0$.

Transmission driven only by I-individuals

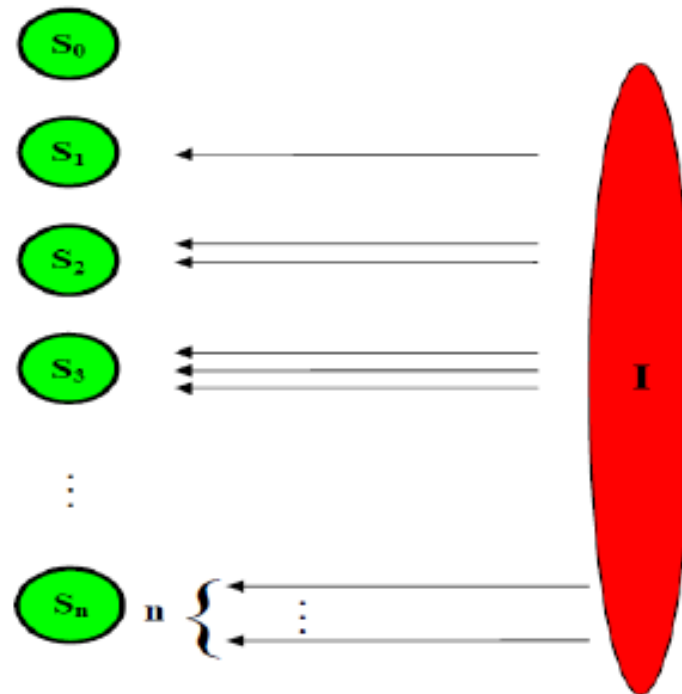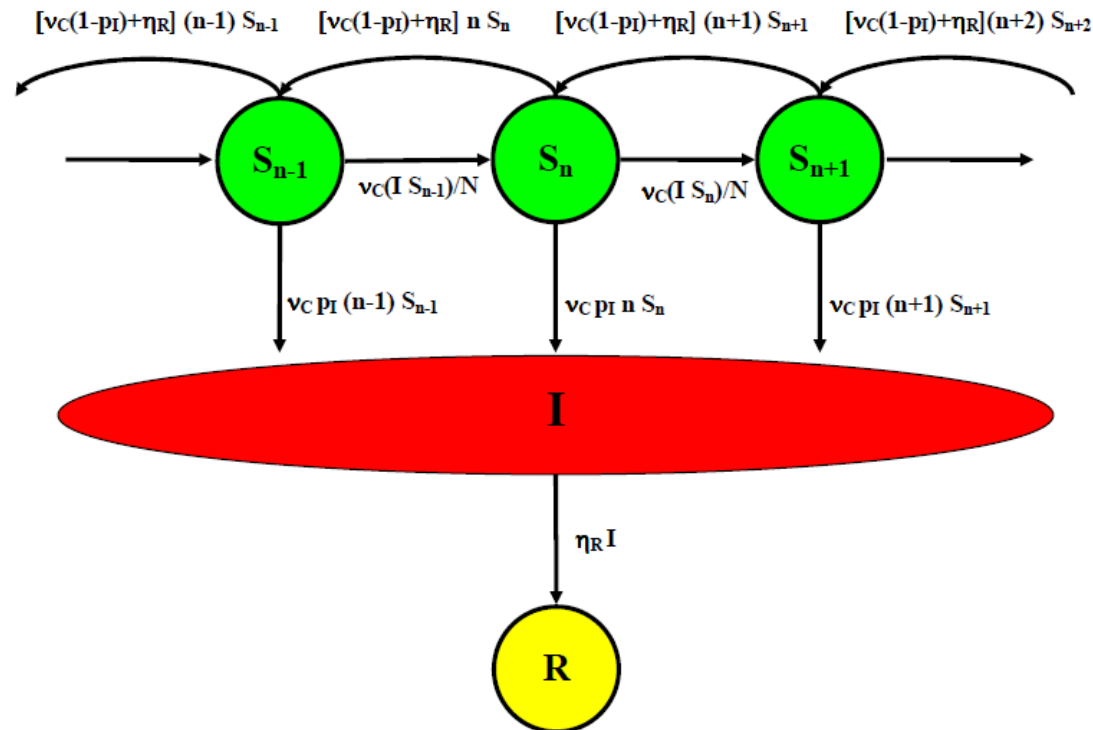Define $S_n(t)$ the number of susceptible which have been chosen n-times for a contact by an infectious (at time t)

Figure 8: Structured diagram of the population in term of contacts.

$$
\begin{cases}
S_0' = \nu_c \left[(1 - p_I)\, S_1(t) - \dfrac{I(t)}{N} S_0(t) \right] + \eta_R S_1(t) \\[2mm]
S_1' = \nu_c \left[\dfrac{I(t)}{N} S_0(t) + (1 - p_I)\, 2 S_2(t) - S_1(t) - \dfrac{I(t)}{N} S_1(t) \right] + \eta_R [2 S_2(t) - S_1(t)] \\[2mm]
\cdots \\[1mm]
S_n' = \nu_c \left[\dfrac{I(t)}{N} S_{n-1}(t) + (1 - p_I)\, (n+1) S_{n+1}(t) - n S_n(t) - \dfrac{I(t)}{N} S_n(t) \right] \\[2mm]
\qquad + \eta_R [(n+1) S_{n+1}(t) - n S_n(t)] \\[1mm]
\cdots \\[1mm]
I' = \nu_c p_I \displaystyle\sum_{n=1}^{+\infty} n S_n(t) - \eta_R I(t) \\[2mm]
R' = \eta_R I(t).
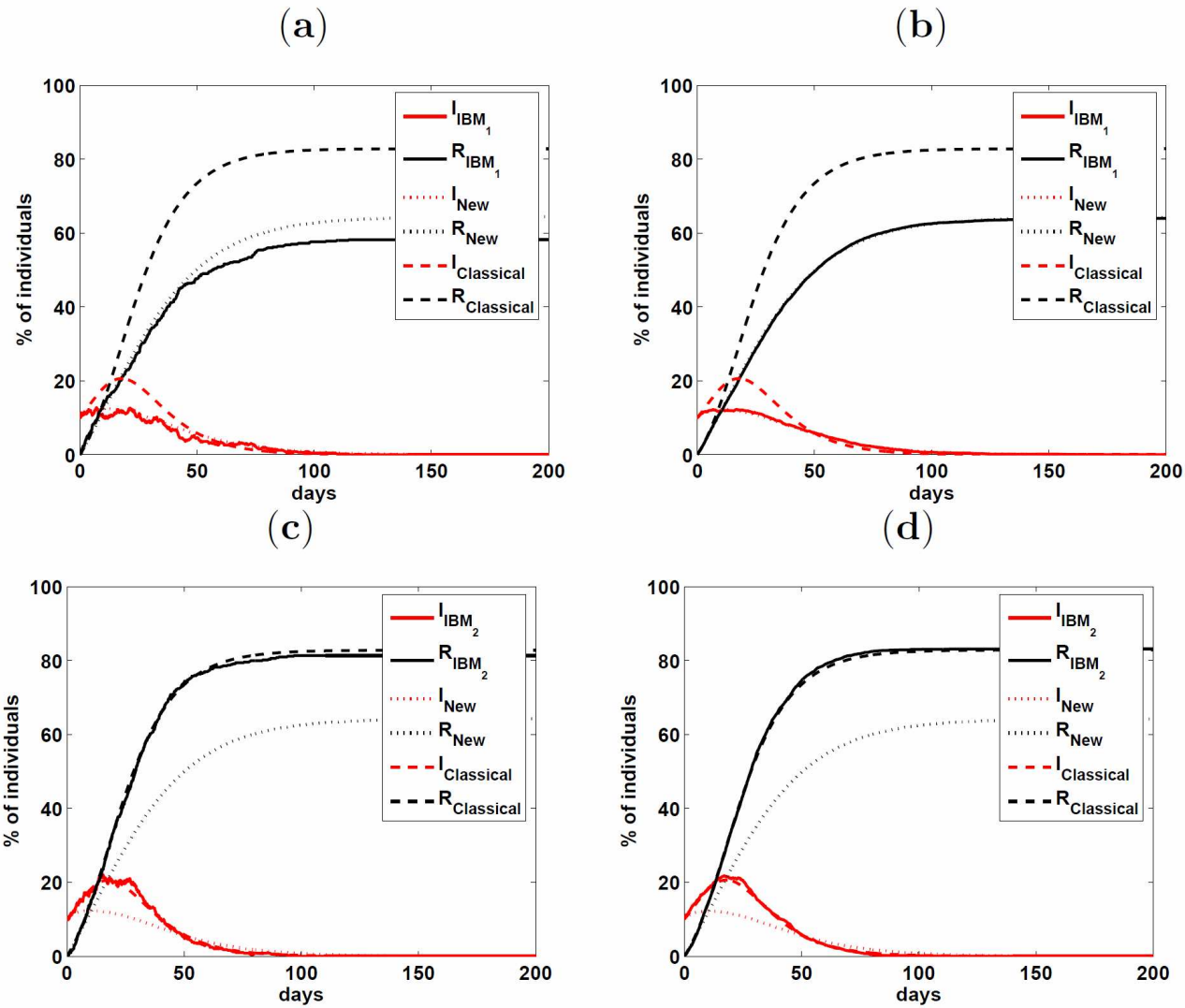\end{cases}
\tag{4.4}
$$

Figure 11: Comparison of the IBM (solid curves), the new SIR model (4.10) (dotted curves), and the classical SIR model (1.1) (dashed curves) with $\beta = \beta_S$.

Happy birthday Chris!