Stochastic Multistrain Dengue Modeling

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Abstract

We proposed and analize a full multistrain Stochastic model for studying Dengue Dynamics. The model is presented both as a Continuous-time markov process and as a set of It stochastic differential equations. Sugestions of how to explore the dynamics numerically is also provided, along with source code examples.

Introduction

Multi-strain dynamics

In this paper we propose a stochastic 4-serotype SIR model with cross-immunity to describe multi-strain Dengue dynamics. The model permits up to 4 dengue infections with reduced susceptibility after the first Dengue episode due to cross immunity. Immunity to each serotype is considered complete and permanent. Figure 1 depicts all 48 possible states and 64 state-transitions included in the model.

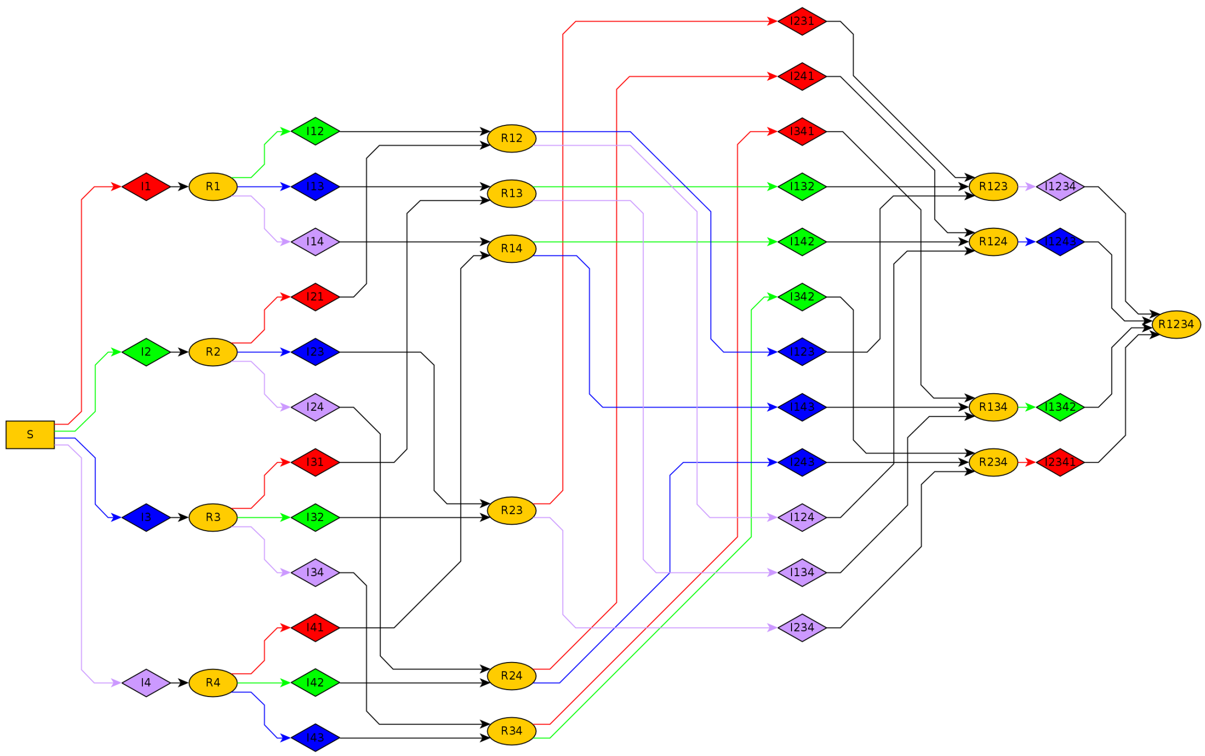

Figure 1: Block diagram detailing the stochastic model. Infected individuals with different Dengue viruses are represented by different colors. Infections are also represented by colored arrows matching the virus type.

Deterministic Model

The derivation of the stochastic model is based on the deterministic ordinary differential equations below

$$\begin{cases} \dfrac{dS}{dt} = -\beta S I_{*i} - \mu S + \mu N & (1) \\ \dfrac{dI_i}{dt} = \beta S I_{*i} - (\sigma + \mu) I_i & (2) \\ \dfrac{dI_{[i]j}}{dt} = \beta \delta R_i I_{*j} - (\sigma + \mu) I_{[i]j} & (3) \\ \dfrac{dI_{[ij]k}}{dt} = \beta \delta R_i j I_{*k} - (\sigma + \mu) I_{[ij]k} & (4) \\ \dfrac{dI_{[ijk]l}}{dt} = \beta \delta R_i jk I_{*l} - (\sigma + \mu) I_{[ijk]l} & (5) \\ \dfrac{dR_i}{dt} = \sigma I_i - \delta R_i (I_{*j} + I_{*k} + I_{*l}) - \mu R_i & (6) \\ \dfrac{dR_{ij}}{dt} = \sigma I_{ij} - \delta R_{ij} (I_{*k} + I_{*l}) - \mu R_{ij} & (7) \\ \dfrac{dR_{ijk}}{dt} = \sigma I_{ijk} - \delta R_{ijk} I_{*l} - \mu R_{ijk} & (8) \\ \dfrac{dR_{ijkl}}{dt} = \sigma I_{ijkl} - \mu R_{ijkl} & (9) \end{cases}$$

Table 1: **State-transitions and probabilities:** $P(\Delta X(t)|X(t))$. The transitions are summarized below. Fully expanded, the system contemplates 64 possible state transitions, as can be verified in figure 1. †: Non-zero elements of $(\Delta X)_i$.

i	Transition	Probability, p_i	State Change†	Description
1..4	$S \rightarrow I_i$	$\beta S I_{*i} \Delta t$	$\Delta S(t) = -1$, $\Delta I_i(t) = 1$	Primary infection
5..8	$I_i \rightarrow R_i$	$\sigma I_i \Delta t$	$\Delta I_i(t) = -1$, $\Delta R_i(t) = 1$	Primary recovery
9..20	$R_i \rightarrow I_{[i]j}$	$\beta\delta R_i I_{*j} \Delta t$	$\Delta R_i(t) = -1$, $\Delta I_{[i]j}(t) = 1$	Secondary infection
21..32	$I_{[i]j} \rightarrow R_{ij}$	$\sigma I_{[i]j} \Delta t$	$\Delta I_{[i]j}(t) = -1$, $\Delta R_{ij}(t) = 1$	Secondary recovery
33..44	$R_{ij} \rightarrow I_{[ij]k}$	$\beta\delta R_{ij} I_{*k} \Delta t$	$\Delta R_{ij}(t) = -1$, $\Delta I_{[ij]k}(t) = 1$	Tertiary infection
45..56	$I_{[ij]k} \rightarrow R_{ijk}$	$\sigma I_{[ij]k} \Delta t$	$\Delta I_{[ij]k}(t) = -1$, $\Delta R_{ijk}(t) = 1$	Tertiary recovery
57..60	$R_{ijk} \rightarrow I_{[ijk]l}$	$\beta\delta R_{ijk} I_{*l} \Delta t$	$\Delta R_{ijk}(t) = -1$, $\Delta I_{[ijk]l}(t) = 1$	Quaternary infection
61..64	$I_{[ijk]l} \rightarrow R_{ijkl}$	$\sigma I_{[ijk]l} \Delta t$	$\Delta I_{[ijk]l}(t) = -1$, $\Delta R_{ijkl}(t) = 1$	Quaternary recovery
65	$\rightarrow S$	$\mu N \Delta t$	$\Delta S = 1$	Birth
66..113	$All \rightarrow$	$\mu N \Delta t$	$\Delta S = \Delta I_* = \Delta R_* = -1$	Death
114	No transition	$1 - \sum_i p_i$	No change	—

Where S are individuals susceptible to all 4 types of dengue, I_i infectious with Dengue type i, R_i individuals recovered from Dengue type i and $N(t) = S(t) + I_*(t) + R_*(t)$ is the total population size at time t. Infectious individuals already on their secondary and later Dengue infections are represented by indices $\{i, j, k, l\}$ which can take values in the close interval $(1, 4)$. For example, $I_{[23]1}$ is an individual which has had Dengues type 2 and 3 in the past – and therefore is immune to them – and is currently transmitting Dengue 1. The index outside the bracket denotes current infection. Recovered individuals indices denote their immunity, so for instance R_{123} is an individual which is immune to Dengue types 1, 2 and 3, but not to 4. Let $I_{*i} = \sum I_{[\ldots]i}$ with $[\ldots]$ representing exposure history of the infected individual which can vary from 0 to 3 in length. All individuals are born to the S state and birth and death rates are equal.

Stochastic Model

Let's now assume that $S(t)$, $I_*(t)$ and $R_*(t)$ are random variables representing the state of a stochastic process. The possible state-transitions and their probabilities are listed in table 1.

The stochastic model can be described as a continuous time Markov jump process. Let

$$\overrightarrow{X}(t) = [S(t), I_1(t), I_2(t), \ldots, R_{1234}(t)]$$

be the state of the system at the time t. $\sum X(t) = N, \forall t$ with N being the population size. The system is written as a forward Kolmogorov differential equation, which in matrix form looks like

$$\frac{dP_X(t)}{dt} = QP_X(t) \tag{10}$$

Where $P_X(t)$ is the matrix of transition probabilities (given in table 1) and Q is the generator matrix, whose non-zero values are also given in table 1 (in the state change column). The full formula and matrices are ommited due to their large sizes.

Expected Change and Covariance Matrix

It is useful to calculate the expected change and the covariance matrix for the changes $\Delta X = [\Delta S, \Delta I_1, \Delta I_2, \Delta I_3, \Delta I_4, \Delta R_1, \Delta R_2, \Delta R_3, \Delta R_4, \Delta I_{12}, \Delta I_{13}, \Delta I_{12}, \Delta I_{13}, \Delta I_{14}, \Delta I_{21}, \Delta I_{23}, \Delta I_{24}, \Delta I_{31}, \Delta I_{32}, \Delta I_{34}, \Delta I_{41}, \Delta I_{42}, \Delta I_{43}, \Delta R_{12}, \Delta R_{13}, \Delta R_{14}, \Delta R_{23}, \Delta R_{24}, \Delta R_{34}, \Delta I_{231}, \Delta I_{241}, \Delta I_{341}, \Delta I_{132}, \Delta I_{142}, \Delta I_{342}, \Delta I_{123}, \Delta I_{143}, \Delta I_{243}, \Delta I_{124}, \Delta I_{134}, \Delta I_{234}, \Delta R_{123}, \Delta R_{124}, \Delta R_{134}, \Delta R_{234}, \Delta I_{1234}, \Delta I_{1243}, \Delta I_{1342}, \Delta I_{2341}, \Delta R_{1234}]^T$.

Thus from the probabilities of table 1,

$$E(\Delta X) = \sum_{i=1}^{114} p_i(\Delta X)_i = \begin{pmatrix} -\beta S I_{*1} + \mu N - \mu S \\ \vdots \\ \beta S I_{*4} + \mu N - \mu S \\ \beta S I_{*1} - \sigma I_1 - \mu I_1 \\ \vdots \\ \beta S I_{*4} - \sigma I_4 - \mu I_4 \\ \sigma I_1 - \beta\delta R_1 I_{*j} - \mu R_1 \\ \vdots \\ \sigma I_4 - \beta\delta R_4 I_{*j} - \mu R_4 \\ \beta\delta R_i I_{[i]j} - \sigma I_{[i]j} - \mu I_{[i]j} \\ \sigma I_{[i]j} - \beta\delta R_{ij} I_{*k} - \mu R_{ij} \\ \beta\delta R_{ij} I_{*k} - \sigma I_{[ij]k} - \mu I_{[ij]k} \\ \sigma I_{[ij]k} - \beta\delta R_{ijk} I_{*l} - \mu R_{ijk} \\ \beta\delta R_{ijk} I_{*l} - \sigma I_{[ijk]l} - \mu I_{[ijk]l} \\ \sigma I_{[ijk]l} - \mu R_{1234} \end{pmatrix} \Delta t \tag{11}$$

The expected change, $E(\Delta X)$, is a 48×1 vector. The covariance matrix is a 48×48 matrix, $\Sigma(\Delta X) = \sum_{i=1}^{114} p_i(\Delta X)_i(\Delta X)_i^T$