

# Stochastic Multistrain Dengue model

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## 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.

Let  $S$  be individuals susceptible to all 4 types of dengue,  $I_i$  infectious with Dengue type  $i$  and  $R_i$  individuals recovered from Dengue type  $i$ . Infectious individuals already on their secondary and later Dengue infections are represented by multiple indices. 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  $I_{*i} = \sum I_{[...]}i$  with  $[...]$  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.

The possible state-transitions and their propensities are listed in table 1.

The model is implemented as a continuous time Markov jump process. Let

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

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

$$\frac{dP_X(t)}{dt} = QP_X(t) \quad (1)$$

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 omitted 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  $\Delta X = [\Delta S, \Delta I_1, \Delta I_2, \Delta I_3, \Delta I_4, \Delta R_1, \Delta R_2, \Delta R_3, \Delta R_4, \Delta I_{12}, \Delta I_{13}, \Delta I_{14}, \Delta I_{21}, \Delta I_{23}, \Delta I_{24}, \Delta I_{31},$

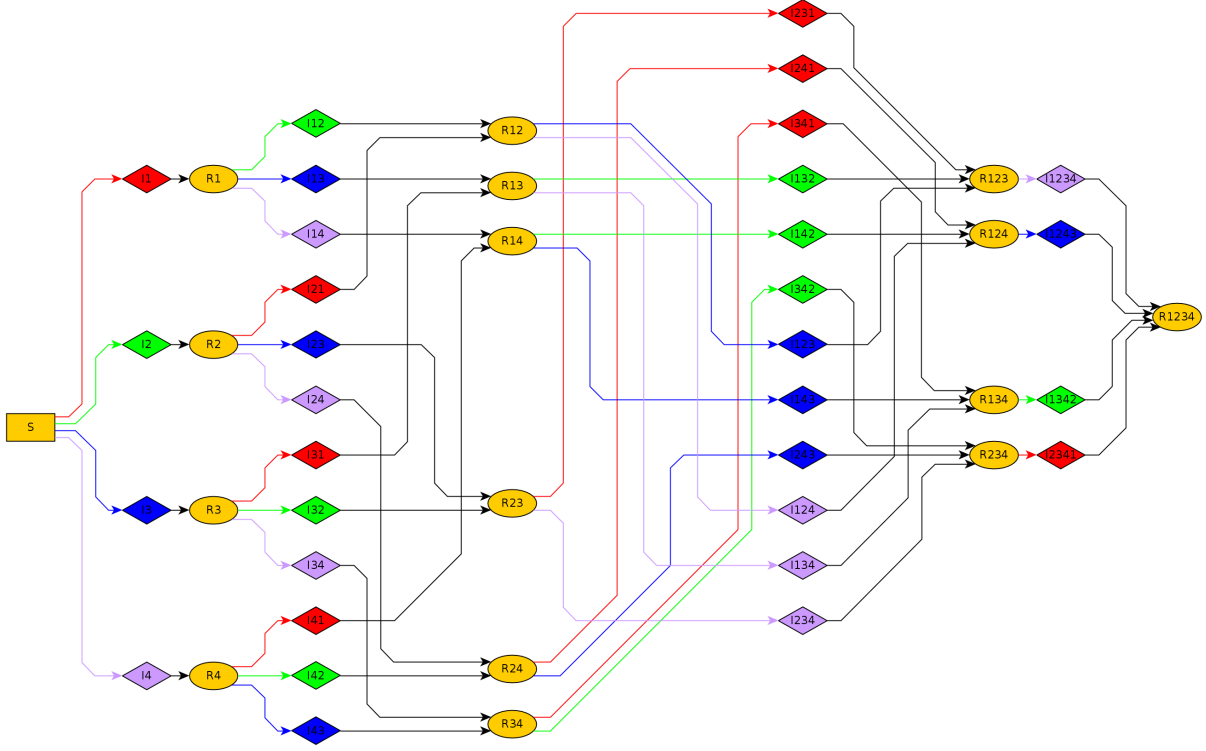


Figure 1: Block diagram detailing the stochastic model. Infected individuals with different Dengue viruses are represented by different colors. Infections are also represented by colored arrows matching the virus type.

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.**  $^\dagger$ :  $P(\cdot)$  is the sum of the probabilities of all possible state changing transitions.

Transition	Probability	State Change	Description
$S \rightarrow I_i$	$\beta S I_{*i} \Delta t$	$\Delta S(t) = -1, \Delta I_i(t) = 1$	Primary infection
$I_i \rightarrow R_i$	$\sigma I_i \Delta t$	$\Delta I_i(t) = -1, \Delta R_i(t) = 1$	Primary recovery
$R_i \rightarrow I_{[i]j}$	$\beta \delta R_i I_{*j} \Delta t$	$\Delta R_i(t) = -1, \Delta I_{[i]j}(t) = 1$	Secondary infection
$I_{[i]j} \rightarrow R_{ij}$	$\sigma I_{[i]j} \Delta t$	$\Delta I_{[i]j}(t) = -1, \Delta R_{ij}(t) = 1$	Secondary recovery
$R_{ij} \rightarrow I_{[ij]k}$	$\beta \delta R_{ij} I_{*k} \Delta t$	$\Delta R_{ij}(t) = -1, \Delta I_{[ij]k}(t) = 1$	Tertiary infection
$I_{[ij]k} \rightarrow R_{ijk}$	$\sigma I_{[ij]k} \Delta t$	$\Delta I_{[ij]k}(t) = -1, \Delta R_{ijk}(t) = 1$	Tertiary recovery
$R_{ijk} \rightarrow I_{[ijk]l}$	$\beta \delta R_{ijk} I_{*l} \Delta t$	$\Delta R_{ijk}(t) = -1, \Delta I_{[ijk]l}(t) = 1$	Quaternary infection
$I_{[ijk]l} \rightarrow R_{ijkl}$	$\sigma I_{[ijk]l} \Delta t$	$\Delta I_{[ijk]l}(t) = -1, \Delta R_{ijkl}(t) = 1$	Quaternary recovery
$\rightarrow S$	$\mu N \Delta t$	$\Delta S = 1$	Birth
$All \rightarrow$	$\mu N \Delta t$	$\Delta S = \Delta I_* = \Delta R_* = -1$	Death
No transition	$1 - P(\cdot)^\dagger$	No change	—

$\Delta I_{32}, \Delta I_{34}, \Delta I_{41}, \Delta I_{42}, \Delta I_{43}, \Delta R_{12}, \Delta R_{13}, \Delta R_{14}, \Delta R_{23}, \Delta R_{24}, \Delta R_{34}, \Delta I_{231}, \Delta I_{241}, \Delta I_{341}, \Delta I_{132}, \Delta I_{142},$   
 $\Delta I_{342}, \Delta I_{123}, \Delta I_{143}, \Delta I_{243}, \Delta I_{124}, \Delta I_{134}, \Delta I_{234}, \Delta R_{123}, \Delta R_{124}, \Delta R_{134}, \Delta R_{234}, \Delta I_{1234}, \Delta I_{1243}, \Delta I_{1342},$   
 $\Delta I_{2341}, \Delta R_{1234}]^T$ .

Thus from the probabilities of table 1,

$$E(\Delta X) = \sum_X p_i \Delta X_i = \begin{pmatrix} -\beta S I_{*1} + \mu N - \mu S \\ \vdots \\ \beta S I_{*4} + \mu N - \mu S \\ \beta S I_{*1} - \sigma I_1 - \mu I_1 \\ \vdots \\ \beta S I_{*4} - \sigma I_4 - \mu I_4 \\ \sigma I_1 - \beta \delta R_1 I_{*j} - \mu R_1 \\ \vdots \\ \sigma I_4 - \beta \delta R_4 I_{*j} - \mu R_4 \\ \beta \delta R_i I_{[i]j} - \sigma I_{[i]j} - \mu I_{[i]j} \\ \sigma I_{[i]j} - \beta \delta R_{ij} I_{*k} - \mu R_{ij} \\ \beta \delta R_{ij} I_{*k} - \sigma I_{[ij]k} - \mu I_{[ij]k} \end{pmatrix} \Delta t \quad (2)$$

The expected change,  $E(\Delta X)$ , is a  $48 \times 1$  vector.