Stochastic Modelling of Measles in a Disease-Eliminated Setting in Europe

Student

10 September, 2017

Abstract

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Contents

1 Introduction

Measles is one of 25 vaccine preventable illnesses identified by the WHO as a global eradication target in their Global Vaccine Action Plan. While elimination efforts in some areas of the globe have seen great success, Europe still bears a disproportionate burden of the disease. This is due, at least in part, to low vaccination coverage in several nations[1].
While data on effective vaccination rates vary based on national surveillance capacity, regional efforts, like the European Sero-Epidemiology Network (ESEN), have provided more robust measurements ranging over a decade. Their findings reveal that all nations with an endemic spread of the disease fall short of the herd immunity threshold (around 96%)[2]. This shortfall reflects the recent trend of hesitancy on the part of parents to immunize their child with both doses of the MMR vaccine required for full coverage.
Beyond the immediate effects of endemic measles transmission within a country, it is reasonable to question whether these nations also put the elimination efforts of their neighbors at risk. It is this question that this project seeks to answer, particularly as more nations start to reach their elimination targets and are declared "measles eliminated" by the European divsion of the WHO[3].

2 Aims and Objectives

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3 Materials and Methods

3.1 Coding

All model functions were coded in R[4] with C++ suplement. The utilized packages were as follows:

- adaptivetau[5]
- ggplot2[6]
- data.table[7]
- Rcpp[8]
- Foreach[9]
- microbenchmark[10]
- profvis[11]

To increase modelling performance, the Foreach package parallelized the modelling function to utilize all availible processor threads. The data.table package provided the "data.table" R object that is capable of much faster data sorting and subsetting methods than the standard packages. Rcpp served as a linker package between R and C++, allowing for computationally intensive portions of the R code to be offloaded to C++ and called within the R environment. Finally, the microbenchmark and profvis packages were essential for code optimization and profiling.
In addition to the model functional code, this document was created in LaTeX and compiled to PDF using the XeLaTeX compiler.

3.2 SEIR Compartmental Model

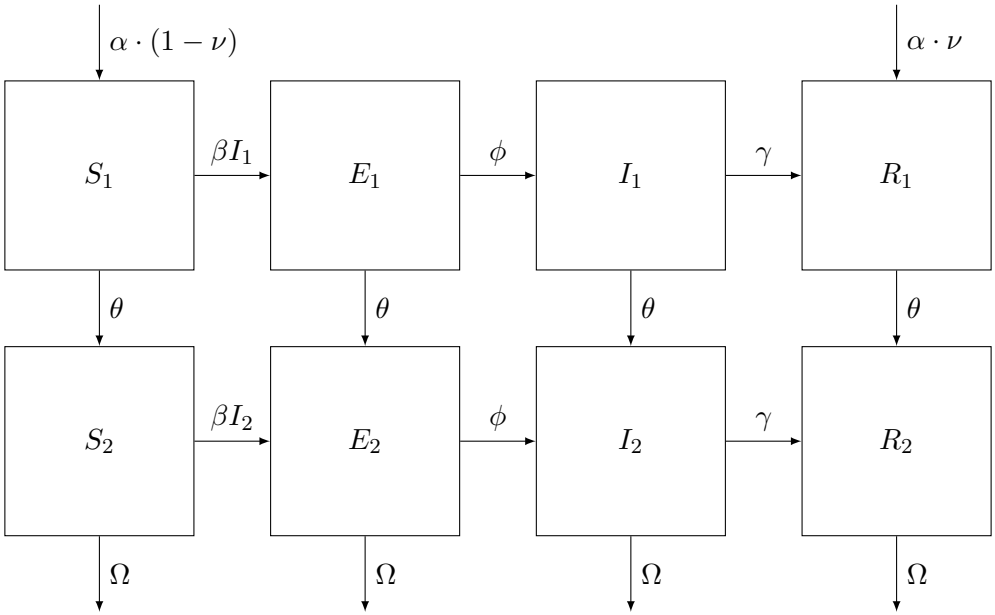

Figure 1: Age stratified SEIR Model with vital dyanmics

Where:
β_n = Rate of contact between infectious and susceptible persons
ϕ = Rate of onset of infectiousness subsequent to being infected
γ = Rate of recovery from measles from infectious period
α = Crude birth rate
ν = Effective vaccination rate at birth
Ω = Crude death rate
θ = Rate of aging from young to old compartments

To explore the infection dynamics of measles, a SEIR model was selected with two age compartments, subdividing younger and older populations. This was chosen for a few reasons. Firstly, it allows for the modelling of heterogeneous mixing within these age groups. Additionally, it allows for the model to more closely align with the age strata reported in seroprevalence data, thereby reducing the number of assumptions which would need to be made to fit incoming data. Finally, the selection of two compartments over some higher dimension limits the mathematical complexity of both modeling the data as well as mapping the parameter space while also allowing for some variation in age demographics.

3.3 Model Dynamics as Deterministic ODEs

The dynamics which describe the compartmental model can be written deterministically as ordinary differential equations :

$$\frac{\mathrm{d}S_1}{\mathrm{d}t} = N\alpha\,(1-\nu) - S_1\,(\beta I_1 + \theta) \tag{1}$$

As detailed in equation 1, this is a test of model 1.

3.4 The Model as a Stochastic System

Model stochasticity was accomplished through the R package, adaptivetau. The deterministic differential equations are supplied as a rate function and evaluated by adaptivetau. Transistions are supplied as a vector and their rates defined by a rate function. The model is then stepped using a process called "explicit tau-leaping"[12].
This process provides an approximation of the output expected from Gillespie algorithm by maximizing the time step (called τ) between data points while minimizing the rate of change of the transition. The resulting output supplies many data points where the rate of change in a transition is high and sparse data points where the rate of change is low. This serves a dual purpose:

- To provide vastly superior performance to the Gillespie algorithm
- To introduce model stochasticity by using a random walk variable to define transition advancement

In making the model stochastic, we can now represent the standard compartmental model as a markov chain process.

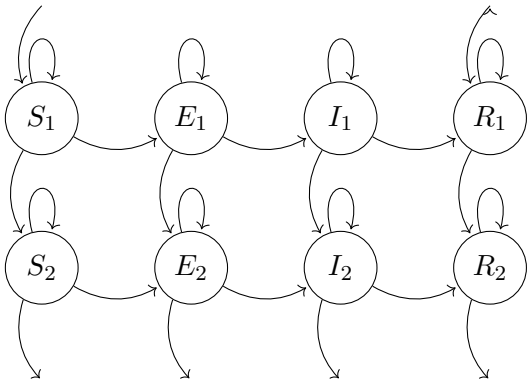

Figure 2: Markov-chain representation of the SEIR Model

This serves to highlight the possible transitions between each state per time step. The "force" of the transitions can stil be described in the same way as the comparmental SEIR Model in Figure 1. However, the probability of any transition per time step is now a function of a poisson-distributed random walk variable defined in the adaptivetau modelling function.

$$P\left(transition\right) \sim Poisson\left(R_{trans} \cdot \tau\right) \tag{2}$$

As a consequence, for sufficiently large transition rates (R_{trans}) or time steps (τ), Equation 2 can be simplified using the normal distribution:

$$P\left(transition\right) \sim N\left(R_{trans} \cdot \tau, \sqrt{R_{trans} \cdot \tau}\right) \tag{3}$$

3.5 Calculating R0

We can calculate R0 by taking the leading eigenvalue of the Next Generation Matrix. Probably not important

3.6 Defining Model Steady-State Conditions

This section may not need to exist

3.7 Visualizing Parameter Space

In order to determine the smallest inputs into the model which would result in an epidemic, it is necessary to visualize the hyperparameter space via grid search.
Let our two parameter inputs be defined as:

$$x \in \{1, 2, \cdots, n\} \tag{4}$$

and,

$$y \in \{1, 2, \cdots, n\} \tag{5}$$

where: x = number of new cases of measles being added to the model, and y = number of "insertion events" which occur during one model simulation.

The cost function, $f(x, y)$, provides scalar output of the maximum outbreak length when the model is evaluated with x and y as inputs.

The three dimensional surface of the hyperparameter space can be found by evaluating $f(x, y)$ with all reasonable combinations of x and y. The three values can then be expressed as cartesian coordinates and plotted. Importantly, this will help to reveal local maxima, minimizing for the input values. A random search or genetic algorithm methods could also have been used to this end, but due to the suspected spread of local maxima and minima, a whole grid search of the hyperparameter space provides more robust results, depite the time penalty.

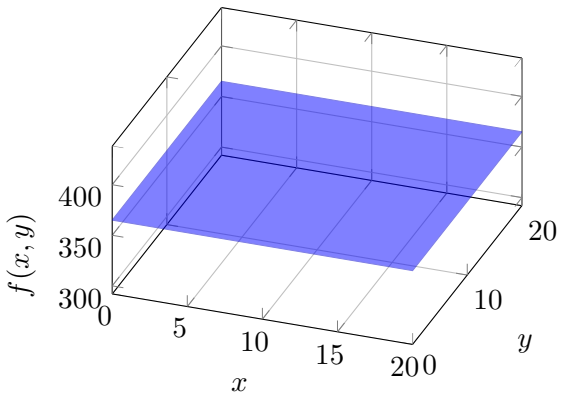

Figure 3: Example surface plot; only maxima above $f(x, y) = 365$ will be considered

4 Results

There will be some results here

5 Recommendations

There will be some conclusions drawn here from the data. Hopefully they will be useful.

References

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