Worksheet 2: Stochastic models

Due in noon Wednesday Week 5

This example sheet is for credit. Example sheets 3 and 4 can help you. Please make sure code is well commented and shows your working for these answers. Code must be uploaded alongside your pdf solutions.

20 marks will be awarded for presentation (including LaTeXed solutions and clarity of answers). Your write up (including figures) should be no more than 8 pages using size 12 font and 2.5cm margins. You do not have to copy out the questions asked, but the solutions must make sense as a stand alone document. 15 marks will be given for appropriate use of code with comments.

In this worksheet we will consider the dynamics of measles outbreaks and elimination. Before starting this worksheet please read this webpage:
`https://www.who.int/news-room/fact-sheets/detail/measles`
and watch this video:
`https://youtu.be/PlGDYlMjtn8`

We will use the following model to describe the short-term transmission dynamics of an outbreak of measles virus in one region:

$$\begin{aligned}
\frac{\mathrm{d}S}{\mathrm{d}t} &= -\beta IS/N \\
\frac{\mathrm{d}E}{\mathrm{d}t} &= \beta IS/N - \sigma E \\
\frac{\mathrm{d}I}{\mathrm{d}t} &= \sigma E - \gamma I \\
\frac{\mathrm{d}R}{\mathrm{d}t} &= (1 - p_D)\gamma I \\
\frac{\mathrm{d}D}{\mathrm{d}t} &= p_D\gamma I
\end{aligned}$$

with $\beta = 5$ days^{-1}, a mean latency period of 10 days, and a mean duration in the I compartment of 3 days. We will assume the population size is 100,000 and at the start of the outbreak, 90% of the population have immunity. S, E, I and R have the standard interpretation, and additionally, D is the class representing deaths that occur due to measles. p_D denotes the probability of dying of measles for an infected person, and is assumed to be 0.01. Note that we will keep the frequency-dependent infection term to have N (a constant) as a denominator despite deaths from measles.

1. (a) Compute R_0 for measles in this region if there had been no immunity (completely susceptible population). Compute $R_e(0)$ – the instantaneous reproduction number – at the start of the outbreak when 90% of the population are immune. Show your working. [3 marks]

(b) Simulate the deterministic version of this model by numerically solving the ODEs. Start by assuming there is a single infectious individual (in I) and there are no deaths. Run your simulation for 2 years. Plot the I class for your outbreak showing the whole 2-year time period. How many deaths are there during that time? [5 marks]

2. Now we would like to see how the analogous stochastic model behaves, first by using Gillispie's direct method:

   (a) Write down the table of events (including their rates and associated change in model state). [3 marks]

   (b) Code the Gillespie algorithm for the measles model and simulate a single realisation, starting at the same initial conditions used in Q1(b). Plot the I class from this realisation against the ODE solution. [8 marks]

   (c) After how many days did your single Gillespie outbreak finish? What was the final size of the epidemic? [2 marks]

   (d) Run your model a sufficient number of times to be able to draw a histogram of the final sizes of the outbreaks. Add a line for the final size of the ODE model outbreak on the same plot. [3 marks]

   (e) Analytically compute the number of "outbreaks" that have only 0–3 additional infections after the index/initial case (i.e. the final size of the outbreak is between 1 and 4). How does this answer compare to your model simulations? What about the probability that the outbreak will go extinct before creating a large epidemic? [5 marks]

3. Next we will consider the long-term infection dynamics and elimination of measles by introducing demography into our model. We will consider a larger region with a population of 1 million people.

   (a) Write down the new ODE model equations assuming the natural per capita death rate is $\mu = \frac{1}{60}$ years^{-1}, a proportion v of infants are vaccinated at birth and this vaccine has a probability $p_e = 0.95$ of successfully immunising them. You may assume unsuccessful vaccinations result in those individuals remaining fully susceptible. Use a new class V to represent previously successfully vaccinated individuals. What is the new table of events associated with the stochastic version of the ODE model? [5 marks]

   (b) Use a tau-leap algorithm with time step $\tau = 1$ day to simulate this new model with demography and vaccination. Initially we will assume that $v = 0$ (i.e. there is no current vaccination). Run your simulations from the initial conditions $(S, E, I, R, D, V) = (66700, 430, 130, 751270, 0, 181470)$ for 20 years. Run sufficient realisations to allow you to describe key features of the dynamics including how infections might to change over time, the distribution of total measles deaths, and whether and/or when we see local elimination of measles. [12 marks]

   (c) Why is tau leap preferable to Gillespie for simulation of this new stochastic model? [5 marks]

(d) Now use your tau leap model to simulate the same thing again, but with vaccination starting from time 0 with 60% coverage ($v = 0.6$). Use the same initial conditions as in Q3b. How do the dynamics change compared to before? What is the probability that this vaccination coverage would lead to local elimination of infection within 5 years? To the nearest 1% coverage, what value of v would be needed to have more than 95% probability of elimination within 5 years? [8 marks]

(e) Discuss the feasibility and challenges of trying to conduct a measles vaccination campaign in rural Democratic Republic of Congo based on your answers to Q3d, the World Health Organization webpage, and the Médecins Sans Frontières video (links at the beginning of the worksheet). *[Hint: you should aim to write 150–250 words]* [6 marks]