

Problem 1: Estimation of the transmissibility of different strains of MRSA

Methicillin resistant *Staphylococcus aureus* is a bacterium that can cause severe infections in immunocompromised individuals. In the Netherlands a stringent infection prevention protocol exists with regard to MRSA. Whenever there is an unexpected case of MRSA all patients and health care workers who might have had (indirect) contact with this patient will be screened for colonization. Hence, once colonization is detected in one patient, we know the outbreak size at the moment of detection of the first case.

A questionnaire was sent to many hospitals in the Netherlands with the question to report all the outbreak sizes of MRSA during the last 6 months for two strains of MRSA: The hospital-associated strain and the pig-MRSA strain.

Question: Use a birth-death like model with as additional parameter a detection rate to estimate the transmission capacity of both strains using maximum-likelihood methods. Is this information sufficient to calculate the R_0 -value or is more information needed. If so, what type of information. Start with a birth death model in a population of infinite size. When this problem is solved, consider what changes when the population (ward) size is finite and depletion of susceptibles becomes important.

Requirements: Basic probability theory, linear algebra, first year analysis.

Problem 2: Network structure

The spread of a disease depends critically on how individuals interact with each other. There are major differences in the contact structure for different diseases: e.g., sexual transmitted diseases, airborne diseases, plant diseases and so on. Consider how the network influences the dynamics of a disease and whether R_0 has a meaningful interpretation for different types of networks. Will there be exponential growth if there is a spatial structure, e.g., for a regular lattice? On the 1-dimensional lattice, consider the small world circle model, in which individuals have contact with their neighbours and, with some probability, with another, randomly chosen, individual. Try to determine the critical transmission parameter on such a model and analyze numerically how the characteristics of a SIR-epidemic differ for different values of the probability of a long-range interaction.

Problem 3: Factors that make disease outbreaks controllable. (Can be divided into two groups)

(See for instance Fraser et al, PNAS 2004). Many intervention measures to control diseases have been suggested, vaccination, contact tracing, isolation, social distancing measures. Consider these measures and how these measures can be implemented in mathematical models. One option is to look at contact tracing. How effective is this for different diseases. (See for instance Müller et al. Mathematical Biosciences 2000 for a more theoretical approach or Klinkenberg et al. PLoS One 2006 for a more accessible article). Another option is to go into more detail in vaccination strategies. Does it matter whether a vaccine reduces the susceptibility or the infectivity? Does it matter whether all individuals in the population are vaccinated which leads to a reduction in infectivity (in infected) of $(1 - e)$ or whether a fraction e of the population is vaccinated which excludes them from being at risk for infection. Also comment on whether vaccination can have negative effects (apart from possible side-effects of the vaccination itself).

Problem 4: Macroparasites and/or & Backward bifurcations

For microparasites (bacteria, viruses), a single infection is sufficient to start the within-host dynamics. For macroparasites, e.g., helminths and other worm-like parasites, re-infection occurs frequently and is essential for acquiring a high number of parasites. Consider how R_0 can be calculated for this case and investigate and look in the literature for an example of modeling. (See e.g., Chapter 9 of Diekmann & Heesterbeek and)

Problem 5: Heterogeneity

For almost any disease, there is huge variety in infectivity and susceptibility between individuals. This can be related to many factors, behaviour, chance, genetic factors and so on. First consider an individual with N neighbours. Suppose this individual is infected and all neighbours are susceptible. With regard to chance: What is the distribution for the number of offspring if the infectious period is a) constant and b) exponentially distributed?

Problem 6: R_0

Consider the concept of R_0 from a more theoretical point of view, i.e., as dominant eigenvalue of the next generation matrix. Do this mathematically formal, i.e., use the Perron Frobenius theorem. (See Chapter 5 of Diekmann & Heesterbeek).

Problem 7: Vector borne diseases

For many diseases, vectors are important for the spread of the disease, for instance for malaria, dengue, and the West-Nile virus mosquitos are important, for plague rodents like rats and gerbils, for Lyme disease ticks. Hence interventions can also be aimed at the vectors. Consider the Ross-McDonald model. Determine how R_0 can be defined for these vector-borne diseases. Suppose that the second infection leads to more severe symptoms than the first infection and that also the infectivity is higher in the second case. What would be the consequence of such a phenomenon for the interpretation of R_0 . Does R_0 to be larger than 1 for disease persistence. If not, what are the consequences for control?

Problem 8: Study a particular disease

If people are interested in a specific disease, you can try to analyze this also, e.g., AIDS (demographics & network structure are important), Campylobacter infections among chicken (I don't no the answers yet), dengue (there are several types of dengue and the order in which you are infected is important for the consequences),.....