Density dependent transmission from process algebra models of disease spread

Chris McCaig, Rachel Norman, and Carron Shankland

Department of Computing Science and Mathematics, University of Stirling, {cmc,ran,ces}@cs.stir.ac.uk

Mathematical models for the spread of infectious diseases have been developed for centuries. As early as 1760 Bernoulli [Ber60] developed an ordinary differential equation (ODE) model for the spread of smallpox which considers the effect of inoculation on the spread of the disease. In the first half of the twentieth century Kermack and McKendrick [KM27] developed the classical epidemic model,

$$\begin{aligned} \frac{dS}{dt} &= -\beta SI, \\ \frac{dI}{dt} &= \beta SI - \alpha I, \\ \frac{dR}{dt} &= \alpha I, \end{aligned} \tag{1}$$

where S, I and R are respectively the numbers (or densities) of susceptible, infectious and recovered individuals in the population, β is the rate of infection and α is the rate of recovery. This model is still useful in many situations and the ideas behind this model have formed the basis of many epidemic models up to the present day. More recently there has been great interest in developing epidemic models building on the seminal work of Anderson and May [AM81].

One area that has been explored through the use of mathematical models is the biological mechanisms by which transmission of disease occurs. The Kermack-McKendrick model assumes that transmission can be described by a term of the form

$$\text{Transmission} = \beta SI, \tag{2}$$

which is referred to as density dependent transmission. Density dependent transmission assumes that the rate of contacts, which are suitable for transmission to occur, is proportional to the density of both susceptible and infectious individuals in the population. For some types of diseases, such as sexually transmitted diseases and vector-borne diseases, it is assumed that the contact rate remains constant when the density of the population changes. This is referred to as frequency dependent transmission and is commonly represented by a transmission term of the form

$$\text{Transmission} = \frac{\beta^* SI}{N}, \tag{3}$$

where N is the overall size of the population and β^* is a constant, different to β in (2). Begon et al. [BBB$^+$02] looked in detail at these transmission terms and presented a biological derivation of them.

Other studies have suggested that alternative transmission terms could lead to models which more closely match data than either density dependent or frequency dependent transmission, although the biological justifications for such terms are less well understood. Hochberg [Hoc91] proposed the transmission term

$$\text{Transmission} = \beta(S^p I^q) SI, \tag{4}$$

where p and q are constants which can be chosen to produce a variety of non-linear responses. Briggs and Godfray [BG95] proposed another alternative transmission term,

$$\text{Transmission} = \left[k \ln\left(1 + \frac{\beta I}{k}\right)\right] S, \tag{5}$$

where k is a scaling constant. Knell, Begon and Thompson [KBT98] tested the transmission term proposed by Hochberg and the term proposed by Briggs and Godfray, and found both of these could be more accurately fitted to their experimental data than the traditional βSI term.

All these ODE models seek to describe population level behaviours without taking into account the individual interactions which lead to transmission, and the variations inherent in them. This assumes that these population level behaviours are well understood, but this is not necessarily so. In general it is the behaviour of individuals which can be most easily measured and quantified. One way to investigate transmission terms more closely is to look at individual based models.

Our approach is to use process algebra to describe such models. The advantage of process algebras is that they can be used to bridge the gap between traditional ODE models and individual based simulation models. The process algebra *Weighted Synchronous Calculus of Communicating Systems* (WSCCS) [Tof90] was used by Tofts [Tof93] and Sumpter, Blanchard and Broomhead [SBB01] to model social insect colonies. Sumpter [Sum00] also introduced a simple model for the spread of an epidemic. This method of developing individual based models has the advantage that algebraic analysis is possible by deriving a system of mean field equations (MFE), which offers a population level description. Sumpter [Sum00] developed a heuristic method for deriving a system of MFE for WSCCS models and we have developed an algorithm to formalise this process for certain types of model. These systems of MFE are the discrete time equivalent of the traditional ODE models and as such well established techniques exist for analysing their behaviour. The existing WSCCS models [NS03] naturally feature frequency dependent transmission. For example the following system of difference equations for the numbers of susceptible, infectious and recovered individuals at time $t+1$:

$$\begin{aligned} S_{t+1} &= S_t - \frac{p_a S_t I_t}{S_t + I_t + R_t}, \\ I_{t+1} &= (1 - p_r) I_t + \frac{p_a S_t I_t}{S_t + I_t + R_t}, \\ R_{t+1} &= R_t + p_r I_t. \end{aligned} \tag{6}$$

In (6) S_t, I_t and R_t are respectively the numbers of susceptible, infectious and recovered individuals at time t, p_a is the probability that an infectious individual will attempt to pass on the infection and p_r is the probability that an infectious individual will recover.

The starting point for our current work is the model above and the system of MFE in (6) as well as the following questions regarding transmission terms:

- Can an individual based model be developed which leads to a transmission term of the form βSI?
- Are the rules of behaviour needed to obtain βSI as the transmission term biologically realistic, and do they describe what is meant by density dependent transmission?
- Do the MFE developed from biologically realistic rules of behaviour closely fit to models which have βSI as the transmission term?
- Do the MFE developed from biologically realistic rules of behaviour more closely fit other suggested transmission terms [Hoc91][BG95]?

Answering these questions will give us a clearer idea of the validity of the βSI transmission term and potentially indicate that other terms more accurately describe biologically realistic behaviours.

Achieving density dependent transmission in WSCCS models requires each infectious individual to be able to make contact with more than one individual at a time. There are several ways of achieving this, some more successful than others in matching the usual population level transmission terms. We have considered

- Parallel infectious agent made up of several agents which independently attempt to pass on the infection;

- Infectious agents attempt to pass on the infection on several consecutive timesteps, with the behaviour of the system being averaged over all these timesteps.

A parallel infectious agent, with the contact rate proportional to the size of the population, leads to the transmission term

$$\text{Transmission} = \text{Round}[kN_t]\frac{p_a S_t I_t}{N_t},$$

where k is some scaling constant. The Round function is required since the contact rate must always take an integer value. For cases where kN_t is an integer this becomes

$$\text{Transmission} = \beta S_t I_t,$$

with $\beta = kp_a$. In the general case where kN_t is non-integer this transmission term still provides a good fit to βSI. This establishes that it is possible to develop an individual based model which closely fits the traditional βSI transmission term.

Setting the contact rate over several timesteps leads to a more complex transmission term,

$$\text{Transmission} = \sum_{j=1}^{\text{Round}[kN_t]} (-1)^{j+1} \binom{\text{Round}[kN_t]}{j} \frac{p_a S_t I_t^j}{N_t^j},$$

which provides a much poorer fit to the traditional term. This methods of setting the contact rate can be seen as being more biologically realistic, since it does not involve infectious individuals having to split into several agents. This would suggest that the traditional transmission term may not be biologically realistic. The transmission terms derived from this method is too complex to be practical for use in mathematical models, but if it can be found to provide a good fit to other transmission terms (e.g. (4), (5)) it would suggest that the alternative terms are more appropriate.

References

[AM81] R.M. Anderson and R.M. May. The population-dynamics of micro-parasites and their invertebrate hosts. *Philosophical transactions of the Royal Society of London Series B*, 291:451–524, 1981.

[BBB+02] M. Begon, M. Bennet, R.G. Bowers, N.P. French, S.M. Hazel, and J. Turner. A clarification of transmission terms in host-microparasite models: numbers, densities and areas. *Epidemiology and infection*, 129:147–153, 2002.

[Ber60] D. Bernoulli. Essai d'une nouvelle analyse de la mortalité causée par la petite vérole, et des avantages de l'inoculation pour la prevenir. *Histoire de l'Acad. Roy. Sci. (Paris) avec Mém. des Math. et Phys. and Mém*, pages 1–45, 1760.

[BG95] C.J. Briggs and H.C.J. Godfray. The dynamics of insect-pathogen interactions in stage-structured environments. *American Naturalist*, 145:855–887, 1995.

[Hoc91] M.E. Hochberg. Non-linear transmission rates and the dynamics of infectious disease. *Journal of Theoretical Biology*, 153:301–321, 1991.

[KBT98] R.J. Knell, M. Begon, and D.J. Thompson. Transmission of *Plodia interpunctella* granulosis virus does not conform to the mass action model. *Journal of Animal Ecology*, 67:592–599, 1998.

[KM27] W.O. Kermack and A.G. McKendrick. Contributions to the mathematical theory of epidemics. *Proceedings of the Royal Society of London A*, 115:700–721, 1927.

[NS03] R. Norman and C. Shankland. Developing the use of process algebra in the derivation and analysis of mathematical models of infectious disease. In *Computer Aided Systems Theory - EUROCAST 2003*, volume 2809 of *Lecture Notes in Computer Science*, pages 404–414. Springer-Verlag, 2003.

[SBB01] D.J.T. Sumpter, G.B. Blanchard, and D.S. Broomhead. Ants and agents: a process algebra approach to modelling ant colony behaviour. *Bulletin of Mathematical Biology*, 63:951–980, 2001.

[Sum00] D. Sumpter. *From Bee to Society: an agent based investigation of honeybee colonies*. PhD thesis, UMIST, 2000.

[Tof90] C. Tofts. A synchronous calculus of relative frequency. In *Proceedings of CONCUR '90*, volume 458 of *Lecture Notes in Computer Science*, pages 467–480. Springer-Verlag, 1990.

[Tof93] C. Tofts. Using process algebra to describing social insect behaviour. *Transactions of the Society for Computer Simulation*, 9:227–283, 1993.