

A Method for Modelling and Calibrating Disaggregated Diffusion Models

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Abstract

Complex dynamic problems, such as infectious disease spread, have at their core diffusion processes that are driven by reinforcing feedback loops. System dynamics approaches tend to view such diffusion problems at an aggregate level, based on the assumption of random mixing within the population. However, in the public health area, assortative (within-type) mixing is a recognised empirical phenomenon, and therefore simulation models must disaggregate across key cohorts in order to maximize engagement with policy makers, and provide more robust and accurate models of disease spread. This paper integrates key ideas from modern infectious disease modeling approaches into a system dynamics context, and presents robust formulations to allow for the disaggregation of SD diffusion models. It also shows how case data can be aligned with SD models, thereby allowing the model to be calibrated and fit to historical data. The approach is validated using an SEIR model, and based on a case study of the 1957 flu outbreak.

Introduction

This paper aligns key ideas from the literature of infectious disease modeling to the system dynamics method, and in doing so, provides an approach to construct disaggregate models of diffusion processes. The model provides a robust formulation, and also facilitates accurate calibration against available data sources. This can be particularly useful during the early stage of an infectious disease outbreak, where data from previously similar strains can be used to inform diffusion dynamics. The approach is illustrated using a two-cohort model, and results are demonstrated against empirical data from the 1957 influenza outbreak. The approach can also be viewed as an alternative approach to agent-based models, as it can capture non-random mixing dynamics.

Diffusion Models

Diffusion is a fundamental process in physical, biological, social and economic settings (Rahmandad and Sterman 2008). In system dynamics modeling, the conventional approach (Sterman 2000) to modeling (chronic) epidemic processes using the Susceptible (S) – Infected (I) model is via the formulation of the infection rate (IR) as follows:

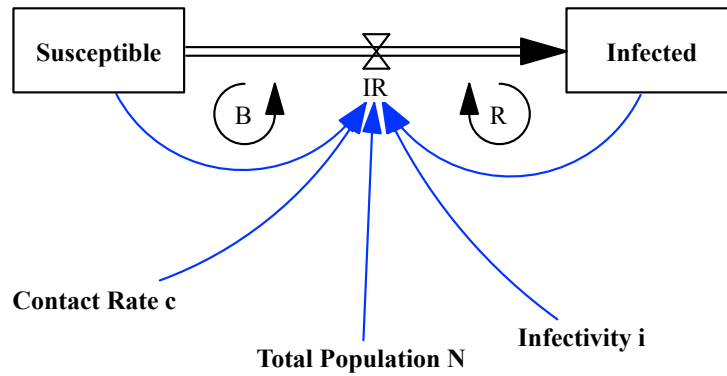


Figure 1: Structure of a simple model of an epidemic - (SD Literature)

$$IR = c * S * i * (I/N) \quad (1)$$

Where

- c is the contact rate (person/person/time)
- (I/N) is the chance of meeting an infected person in a population of size N
- i is a measure of infectivity, which is the chance that a contact between an infectious person and a susceptible person will lead to an infection.

This formulation is robust and intuitive, as an infection will not spread under the following conditions: (1) there are no contacts, (2) the probability of transfer is zero, and (3) there are no infectious people in the population. However, a challenge for modellers is to find good approximations for the contact rate and infectivity, as these estimates are crucial in order to present decision makers with realistic models to support policy analysis. In the epidemiology literature (Vynnycky and White 2010), a different approach (see Figure 2) is used to express the infection rate of a population. Key to this are the following definitions:

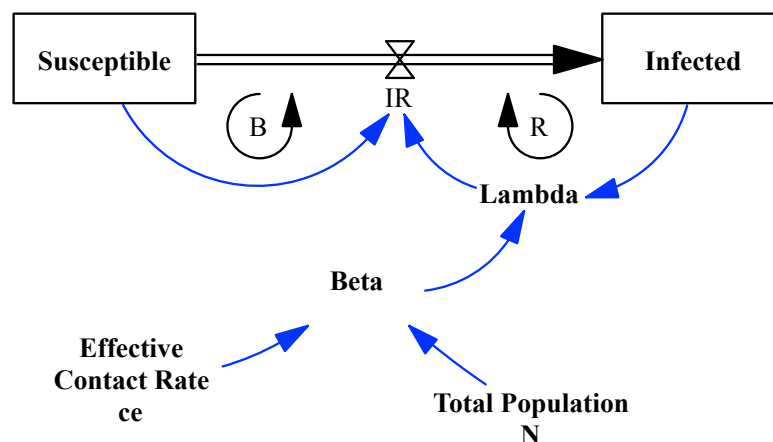


Figure 2: Structure of a simple model of an epidemic - (Epidemiology Literature)

Effective contact (c_E). A contact that is sufficient to lead to transmission if it occurs between an infectious and susceptible person, and this is simply the product of the contact rate, and the probability of infection (2).

$$c_E = c * i \quad (2)$$

Beta (β). The per capita rate at which two specific individuals come into effective contact per unit time. Beta is defined as:

$$\beta = c_E / N \quad (3)$$

Force of Infection (λ). The rate at which susceptible individuals become infected per unit time.

$$\lambda = \beta * I \quad (4)$$

Finally, the infection rate – using this terminology and formulation - is simply the force of infection times the number of susceptible people in the population.

$$IR = \lambda * S = \beta * I * S \quad (5)$$

By a process of substitution, it can be seen that equations (5) and (1) are the same, and therefore both models capture the transmission dynamics of contagion.

The strength of equations (2-5) is that they allow for the separation of the constant β (assuming that the population size remains constant), and therefore facilitates modeling building and parameterization based on historical outbreak data. The estimation of β provides a focal point for the model calibration process, and its role in equation (4) also supports the development of disaggregated models of infection transmission.

The case for disaggregate system dynamics models of disease infection is compelling, given the strong evidence for age-dependent mixing. While aggregate models have value in terms of elegance and ease of explanation, in reality their disadvantage is their assumption that contact between individuals is random. A number of key studies have confirmed non-random mixing in populations (Vynnycky and White 2010), including data on the transmission of tuberculosis (Borgdorff, Nagelkerke, and Broekmans 1999), and the recent extensive study of contact patterns across Europe, which confirmed that contact patterns are highly assortative (i.e. with-like) with age (Mossong *et al.* 2008).

A Non-Random Mixing System Dynamics Model

In order to illustrate the method, we present a disaggregation of the SI model to include two cohorts¹: young and adult (Figure 3). The force of infection is also disaggregated, with one for each cohort, and the beta contact parameters now cover the four contact pairs in the population, namely young-young, young-adult, adult-young and adult-adult.

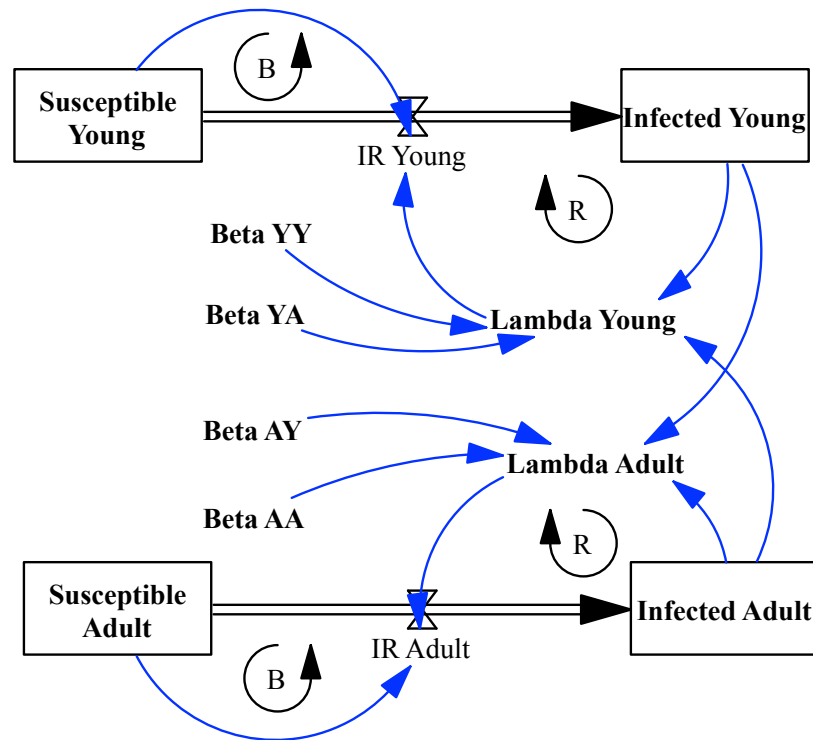


Figure 3: Disaggregated model of the diffusion process

An important aspect of this disaggregated model are the cohort-interaction beta values, β_{ij} , which capture the effective per capita contact rate between a specific susceptible cohort i and a specific infectious cohort j . Therefore, in our two-cohort model, the constant β_{ya} models the per capita effective contact rate between *infectious adults* and *susceptible young*. Building on the earlier equations for the force of infection as shown in equation (4) results in a force of infection value for each cohort (young and adult), and the corresponding equations for λ_y (6) and λ_a (7). Therefore, the overall force of infection (Vynnycky and White 2010) for young people (λ_y) is expressed as the sum of the force of infection attributable to contact with other young people (λ_{yy}) and that attributable to contact with adults (λ_{ya}). Similarly, the overall force of infection for adults (λ_a) is

¹ The approach can accommodate any number of cohorts, in our case, just two have been selected to simplify the model.

the sum of the force of infection attributable to contact with infectious young people (λ_{ay}), and infectious adults (λ_{aa}).

$$\lambda_y = \lambda_{yy} + \lambda_{ya} \quad (6)$$

$$\lambda_a = \lambda_{ay} + \lambda_{aa} \quad (7)$$

The cohort lambda equations from (6,7) can also be expressed in terms of their beta values (8,9). Interestingly, these equations be rearranged algebraically in matrix form, and this isolates the beta terms into a distinct matrix 2x2 structure that has a special significance in epidemiological modeling.

$$\lambda_y = \beta_{yy} * I_y + * I_a \quad (8)$$

$$\lambda_a = \beta_{ay} * I_y + \beta_{aa} * I_a \quad (9)$$

The 2x2 matrix, is termed the who acquires infection from whom (WAIFW) matrix, and this matrix captures the effective per capita rates between (and within) each model cohort.

$$\begin{bmatrix} \lambda_y \\ \lambda_a \end{bmatrix} = \begin{bmatrix} \beta_{yy} & \beta_{ya} \\ \beta_{ay} & \beta_{aa} \end{bmatrix} \begin{bmatrix} I_y \\ I_a \end{bmatrix}$$

Figure 4: Matrix format for force of infection, and the WAIFW Matrix

From a model building perspective, a key challenge is to estimate these beta parameters, and therefore approximate the rate at which two specific individuals come into effective contact for each time unit. The general approach used in Epidemiology is to constrain the WAIFW matrix to N distinct values, where N is the number of cohorts being modeled (in our case, this would be 2, so we would identify new parameters β_1 and β_2). Matrices tend to be symmetric, therefore the chance of transmission from adult to young would be the same as young to adult. The range of possible mappings are shown in Figure 5.

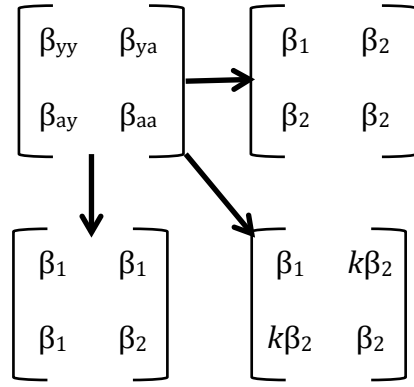


Figure 5: Possible symmetric matrix structures to estimate the contact parameters

In the illustrated example that follows, we will use the WAIFW matrix (with β_1 and β_2) to estimate contact parameters via a data fitting algorithm. However, before showing that example in detail, we summarise an additional use of the contact parameters to estimate the basic reproduction number (R_0) of an infection in the population.

R_0 is defined as the “average number of secondary infectious persons resulting from one infectious person following their introduction into a totally susceptible population” (Vynnycky and White 2010), and its formulation is described in equation (10). It is a key concept for public health officials as they coordinate action following an outbreak, as it provides the basis for calculating vaccination proportions in the population and herd immunity values.

$$R_0 = \beta * N * D = c_E * D \quad (10)$$

In a non-randomly mixing population, such as the example we explore in this paper, the cohort-to-cohort R_0 values are expressed in the *Next Generation Matrix* (NGM), which is a matrix of the number of secondary infectious persons generated by an infectious person in each cohort of the model.

$$\begin{bmatrix} \beta_{yy} * N_y * D & \beta_{ya} * N_y * D \\ \beta_{ay} * N_a * D & \beta_{aa} * N_y * D \end{bmatrix} \quad \begin{bmatrix} 4 & 1 \\ 1 & 1 \end{bmatrix}$$

Figure 6: The Next Generation Matrix (Equations) and Illustrative Values

Figure 6 (left hand side) shows the general equations for the NGM, where N_y and N_a are the population cohort sizes. On the right, we see sample values for an NGM, and these can be interpreted the following way:

- A young infectious person would infect 4 young susceptible people and 1 susceptible adult (reading down the column of the matrix)
- An adult infectious person would infect 1 susceptible young person and 1 susceptible adult.

The remaining question for policy makers would be what the overall value of R_0 is for the population. The formal definition of the overall R_0 value is that it is *the dominant eigenvalue of the NGM* (Diekmann, Heesterbeek, and Metz 1990), and we will use this method in the example that follows.

SEIR Example - 1957 Influenza Outbreak

In order to demonstrate the utility of this approach, a model based on the 1957 Asian Flu outbreak is built (Vynnycky and Edmunds 2008). The data is disaggregated across two cohorts (although the original model has seven cohorts), and the outbreak data is shown in Figure 7, with infection rate values shown on the left, and cumulative infection values captured on the right.

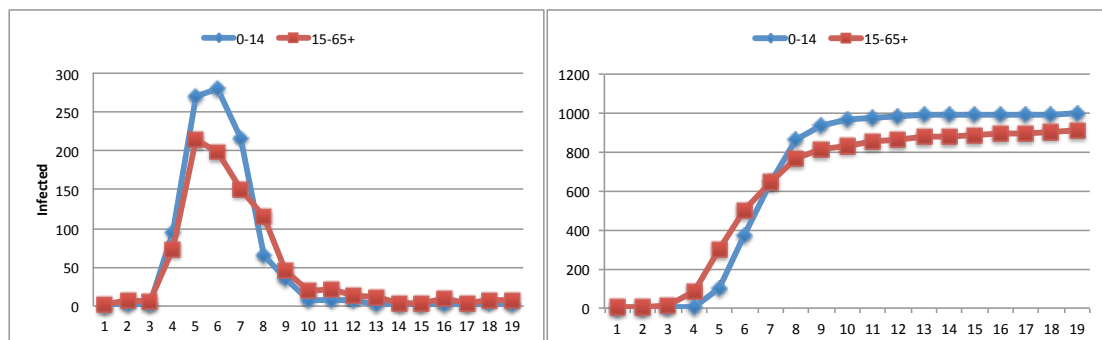


Figure 7: Sample cohort data for 1957 flu outbreak (UK)

Given the dynamics of the influenza pathogen, with a recognised incubation time estimated at 2 days, followed by an infectious period which is also estimated at 2 days), the SEIR model is the most suitable structure to capture the core virus dynamics. The disaggregated model is shown in Figure 8, whereby the infection rate equations are identical to those summarized in the previous section (8, 9).

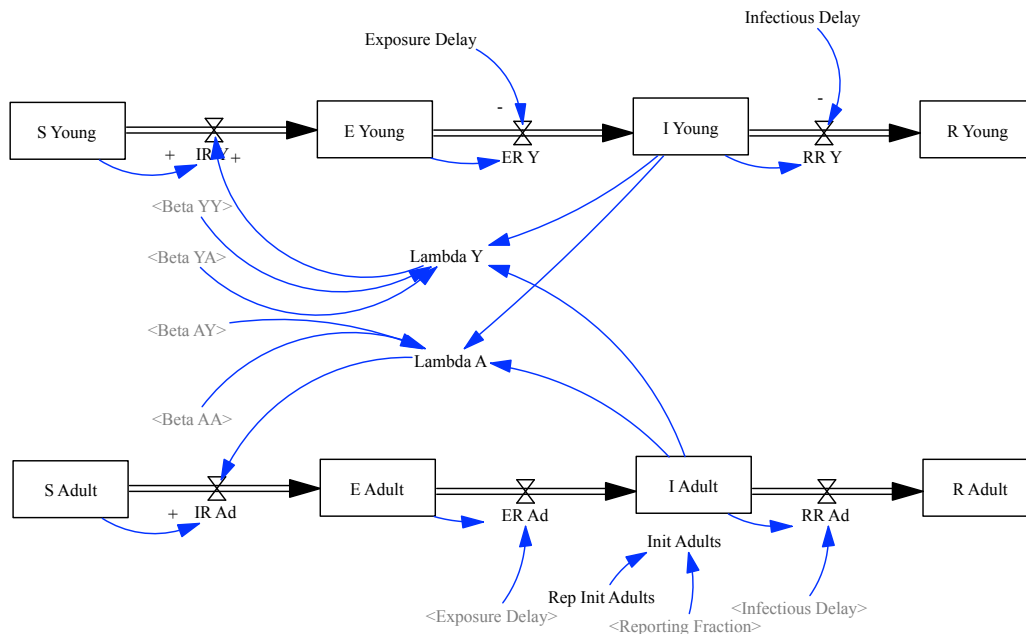


Figure 8: SEIR Model Structure for 1957 Influenza Case Data²

In comparison to the model in Figure 3, the addition flow equations are simply first order delay processes, and these model the exposure delay and the recovered delay. The SEIR model was subsequently calibrated using Vensim's optimizer, and these results show (Figure 9) close alignment when compared to the original data set, where the blue line shows the actual data, and the red line captures the model output for the fitted β parameters.

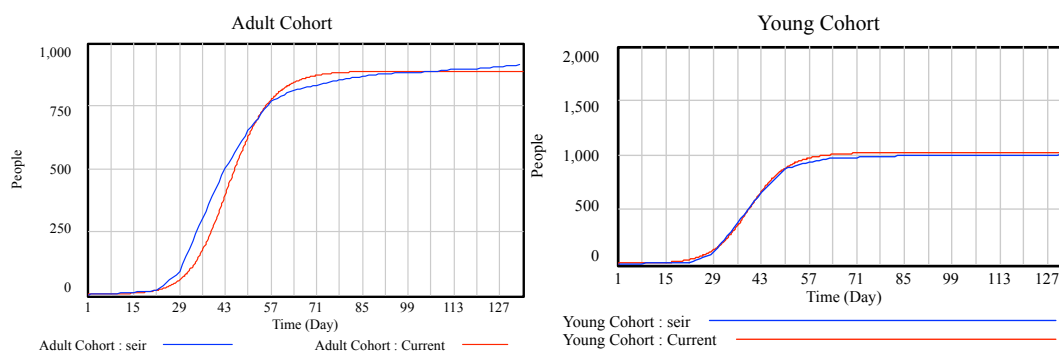
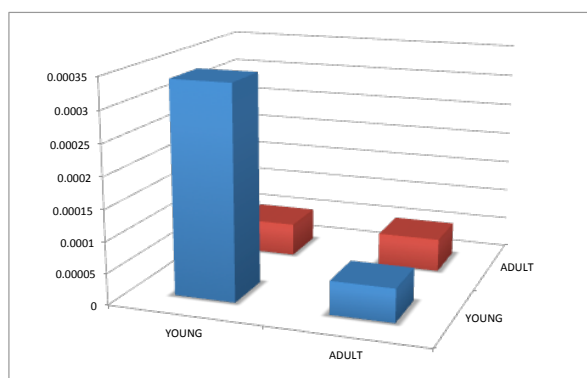


Figure 9: Visualisation of calibration using Vensim's Optimizer algorithm

² The full VENSIM model is included in the conference paper submission

The model fitting results are explored in more detail in

Figure 10, where the results of the optimization process in VENSIM are also shown. The contact parameters are highest in the young-young cohort, and given our initial WAIFW matrix assumption, the contact parameter for the other cohort contacts are the same. It would be recommended to explore all matrix structures (as presented in Figure 5), in order to provide a sensitivity analysis across the contact patterns, and also to maximize the confidence of end-users in the model.



Maximum payoff found at:

Beta 1 = 0.000338636

Beta 2 = 5.31474e-05

Simulations = 172

Pass = 3

Payoff = -321834

The final payoff is -321834

Figure 10: Values for contact parameters and WAIFW Matrix Visualisation

$$\begin{bmatrix} 1.787 & 0.2805 \\ 0.5703 & 0.5703 \end{bmatrix}$$

```
import numpy as NP
from scipy import linalg as LA

a = NP.zeros((2,2))
a[0,0] = 1.787 a[0,1] = 0.2805 a[1,0] = 0.5703
a[1,1] = 0.5703

e_vals, e_vecs = LA.eig(a)
```

```
>>> e_vals
array([ 1.90670142+0.j, 0.45059858+0.j])
```

Figure 11: Based on contact rates, calculation of NGM and resulting eigenvalue analysis (Numpy, Scipy - Python)

Finally, as the model has now calculated estimates for values β_{yy} , β_{ya} , β_{ay} , β_{aa} , these can now be used to estimate the overall reproduction number (R_0) of the virus in the population. This value is the dominant eigenvalue of the NGM (Figure 11), and using a solver such as `scipy` (python), this is calculated at 1.906. Subsequently, this value can be used to inform vaccination policies, and also which cohorts to target in order to maximize the efficiency of the vaccination process.

Of course it is also important to remind ourselves of a fundamental of systems thinking, which requires understanding that all models are wrong (Sterman 2002), therefore model fitting and calibration can yield parameters values that effectively explain past behaviour, but they will not necessarily project future outcomes. However, despite these realities, there are situations where model calibration across different cohorts can enhance the engagement of users in the modeling process, and therefore this approach has value, when used in that context.

Conclusion

This paper has aligned key ideas from the literature of infectious disease modeling to system dynamics, and demonstrates, through an empirically-based example, how to formulate and calibrate disaggregate (non random mixing) diffusion models. The approach is scalable in that it can model a high number of cohorts, and also provides a mechanism to calibrate models and data, and so improve end-user confidence in models. The approach can be used diverse areas of diffusion, including infectious disease modeling, market dynamics and modeling wider contagion effects in an economy.

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