

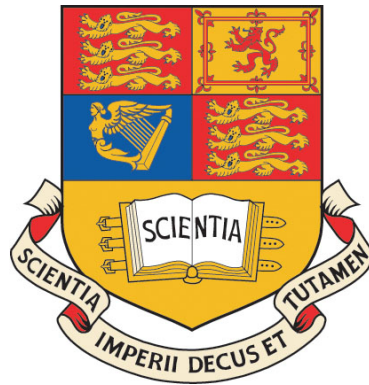
IMPERIAL COLLEGE LONDON

DEPARTMENT OF COMPUTING

On-the-fly Modelling and Prediction of Epidemic Phenomena

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Abstract

Acknowledgements

I would like to thank all my mates who without my mates I would not be able to do my project, like at all.

1 Introduction

1.1 Overview

This project provides a framework with which the dynamics of an epidemic event composed of multiple, overlapping sub-epidemics may be modelled and forecasted in real time. We aim to provide an optimised model fit to a given set of epidemic data where all model parameters are assumed to be unknown. The challenge of considering various candidate model types is also considered. Unlike previous approaches, the presented framework is implemented in object oriented style using a general purpose programming language, allowing improved customisability and speed. Furthermore, we attempt to implement a maximum likelihood based fitting procedure, which has previously only been considered for single epidemic models.

1.2 Motivation

Epidemic spreading processes can be observed in a wide range of fields. Any type of interaction between individuals will allow the propagation of ideas or parasites through a population, with some spreading processes arising unexpectedly in excess of background levels. In the case of infectious diseases, such outbreaks are termed epidemics. Indeed, many significant historical events have been heavily influenced by epidemics, and the WHO estimates that infectious diseases account for more than 13 million deaths per year.[1] It is therefore no wonder that epidemiology, the study of the mechanisms and population dynamics of infectious diseases, has become a central field of research. With the advancement of computing technology and methodology, new opportunities to develop complex mathematical and computational models of real-time epidemics have emerged.

Although the study of infectious disease spread continues to be an area of particular research focus, globalisation and advances in communication technologies have led to a new and rapidly developing type of internet based epidemic. With the entire world connected online, new ideas, trends and information can disseminate through the world wide web almost instantaneously, and as these spreading processes become increasingly central to modern day life, interest from academic, commercial and social fields continues to increase. One highly relevant theory is that of ‘memes’ as proposed by Richard Dawkins, who suggests that ideas, behaviours and styles spread like “mind viruses” between individuals within a culture.[2] The adaptation of this term to describe the spread of fads on the internet demonstrates the relevance of studying the dynamics of epidemic processes over the internet. [6]

Research into the dynamics of internet-based phenomena are largely at an early stage, and have mostly focused on Online Social Networks (OSNs) such as Facebook and Twitter, and content sharing websites such as YouTube.[3, 4] The analogy between infectious diseases and the spread of content online is easy to consider: the social networks formed on OSNs simulate physical interactions in real life as users interact and share content on their profiles, whilst viewing and subsequently sharing a YouTube video may be compared to contracting and spreading an infectious disease. There is a growing body of research that aims to use ideas from epidemiology to better understand the spread of internet-based phenomena. [5, 6, 7] Taking inspiration from epidemiology, the study of internet-based epidemic phenomena has investigated the applicability of both locally and globally driven models. For example, some studies have investigated the use of diffusion models to describe the dissemination of influence, whilst others have investigated the use of global mathematical models.[5, 6, 7, 8]

Whilst these studies have shown generally promising results, a recent study highlighted the limitations of the single epidemic based approach.[5] The co-occurrence and interaction between diseases and with environmental factors is increasingly realised as important, and the authors suggest that the corresponding field of *synepidemiology* can be applied to internet-based epidemics.[48, 10] The authors go on to coin the term *synthedemics* to describe the co-occurrence of a set of infections that may or may not be dependent on each other.[11] Taking inspiration from Fourier analysis, the study goes on to investigate how an incoming epidemic signal can be broken down and described in terms of multiple epidemic components (Figure 1). Furthermore, the authors build on a previous study to allow models to be fit in real time without making assumptions regarding the initial model parameters.

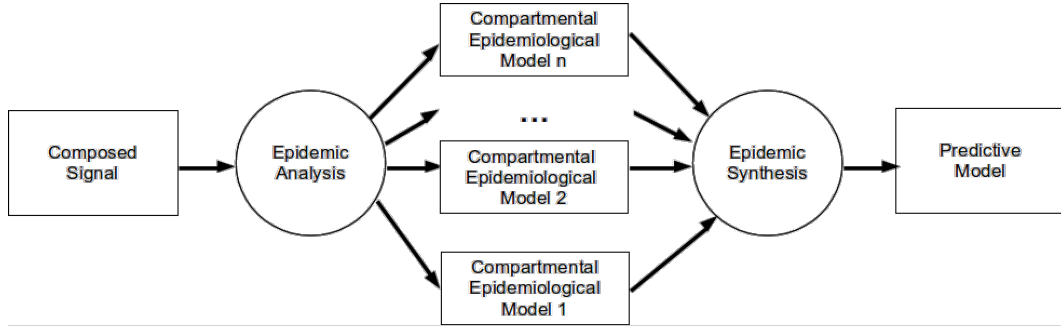


Figure 1: Model construction framework as proposed by Nika et al. 2014.[11]

1.3 Objectives

The aim of this project is to implement a real time model fitting framework with which epidemic phenomena might be characterised and forecasted. When provided with epidemic data up to an arbitrary time point, we attempt to fit an appropriate number of sub-epidemics of various types to best describe the current data, and to allow future time points to be predicted. The course of the project can be split up into the following sub goals:

1.3.1 Single Epidemics

The first objective of this project is to implement a single epidemic fitting framework, treating the growth and recovery rates of the epidemic as unknown parameters. This framework is then extended to additionally consider the initial number of susceptible individuals and the actual epidemic start time as unknown parameters. The model fitting procedure is undertaken using optimisation with both least squares and maximum likelihood estimations. The framework allows for ‘on the fly’ fitting, such that a model may be fit to the data as the epidemic unfolds and more data points are obtained.

The initial implementation of this framework is initially undertaken using the R statistics programming environment due to the availability of useful packages and functions. For example, the *deSolve* for solving first-order ordinary differential equations (ODEs), the *optim* function for optimising a set of model parameters, and the *bbmle* package for maximum likelihood based fitting.

An extension of this objective that arose during the course of the project is the implementation of the fitting framework in C++ ‘from scratch’.

1.3.2 Multiple Epidemics

Not all epidemic phenomena are constrained to a single population, and the single epidemic fitting methodology is therefore inadequate in characterising all epidemics. For example, the measure of *YouTube* video views over time might be composed of multiple spikes of interest as the video is shared in new online social groups. This limitation also affects to infectious disease dynamics, wherein the total number of infected individuals in a country might be affected by the penetration of the disease into different cities. The second objective of this project is therefore to implement a model fitting framework that can simultaneously fit and combine multiple sub epidemics into a single model.

As in the single epidemic fitting framework, the multiple epidemic fitting framework makes no assumptions regarding model parameters such as growth rate, recovery rate, start time and number of susceptibles. As above, an initial implementation will be attempted using R. However, as the computational difficulty of fitting multiple sets of parameters simultaneously increases as the number of sub epidemics increases. We therefore provide a final ‘from scratch’ implementation in C++.

A significant extension of this fitting methodology is to allow different epidemic models to be considered. That is, which one of a number of model equations can be used to best describe the data? An object-oriented C++ implementation is therefore provided to consider the addition and removal of various candidate models to describe a set of data.

1.3.3 Maximum Likelihood Estimation

A novel objective of this project is to use maximum likelihood rather than least squares to find an optimised model fit. A significant challenge of this is to implement an efficient likelihood function in C++ with which a set of parameters might be optimised in reasonable time. An advanced extension of this objective is to generate confidence intervals characterise uncertainty in the optimised parameters.

1.3.4 Evaluation

All of the above objectives must be validated, and we use a number of data sources to assess the model fitting framework. Synthetic data provides the core of the evaluation, as it allows for the retrieval of known parameters from artificially generated data. Finally, we consider the framework’s ability to provide model fits to historic infectious disease data and online epidemic phenomena.

1.4 Contributions

1.5 Report Structure

2 Background

2.1 Modelling Infectious Disease Dynamics

Throughout history, infectious diseases can consistently be cited as one of the leading causes of death across the world. Whilst many such diseases may be endemic in a population, a large proportion of diseases may outbreak as epidemics. That is, a disease may arise in a community, region or even worldwide in excess of normal levels following a particular outbreak. In an age of increasing urbanisation, global connectivity and a larger immuno-compromised population, monitoring and controlling the spread of epidemics is absolutely paramount.[12] Recent events such as the 2009 flu pandemic highlight the incredible need for a solid understanding of the underlying mechanisms of such diseases. This section will discuss the history and current standards in epidemiology.

A general understanding of infectious disease behaviour can be seen as early as the 8th century A.D., when the Indians and Chinese used a rudimentary form of vaccination known as variolation to control smallpox.[14] Even earlier than this, Hippocrates (c. 460-c. 370 BC) was amongst the first to propose that disease spread could be explained rationally through human behaviour and environmental factors.[15] Unfortunately, the understanding of infectious disease dynamics appeared to regress until the 17th century when the collection of the first public health statistics allowed for a more scientific approach.

One of the first predictive mathematical models was by Bernoulli in 1760, who used mathematical techniques to establish that variolation for smallpox could help increase the life expectancy in the French population.[16] Similarly, another systematic study of disease dynamics took place in 1854 by John Snow, who identified a single water pump in London as the likely source of a Cholera epidemic.[17] However, it was the early 1900s in which the most fundamental advances in mathematical epidemiology were made. Firstly by Ross in 1911, who used a spatial model to describe the spread of malaria due to mosquitoes.[17] This study was the first to demonstrate that infectious diseases could be controlled by reducing the population of infected individuals below a certain threshold. The next and arguably most central breakthrough was then made by Kermack and McKendrick in 1927, who proposed the use of ordinary differential equations (ODEs).[18] ODEs represented the first deterministic, general epidemic model to describe mass action. The general idea behind ODE models in the context of epidemiology is that individuals in a given population are members of various compartments depending on their relationship to the infection (eg. infected, recovered), and individuals switch between compartments as described by these ODEs.

The most basic form of the model proposed by Kermack and McKendrick's ODEs is the Susceptible-Infected-Recovered (SIR) model. Given a population of size N , individuals are divided into three states or compartments:

1. Individuals that are susceptible to the infection, denoted by $S(t)$
2. Individuals that are infected with the disease and are therefore capable of infecting others, denoted by $I(t)$
3. Individuals that have been removed from the population or recovered, denoted by $R(t)$.

Individuals move between compartments in the following order:

$$S \implies I \implies R$$

Simply, individuals start off as being free of the disease, but susceptible to infection. Individuals are then infected with the disease and begin to display symptoms, thereby becoming infectious themselves. After a certain period of time, individuals are no longer infectious as they recover and become immune to the disease. In this model, the population size is assumed to be fixed such that:

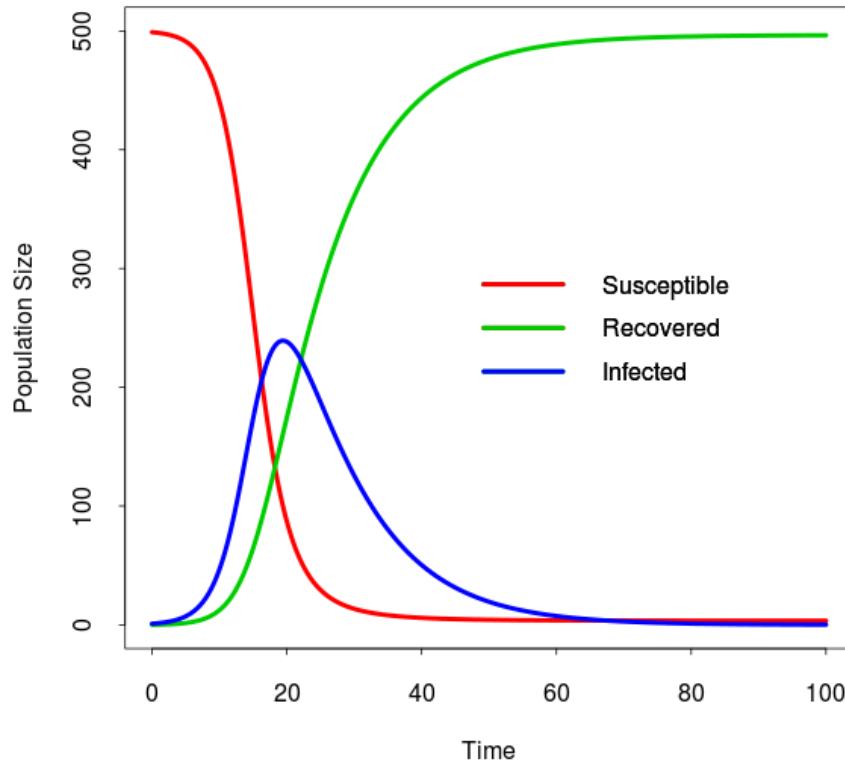


Figure 2: Generic example of the classic SIR model demonstrating the change in population size for each compartment as the epidemic unfolds

$$N = S(t) + I(t) + R(t)$$

The way in which individuals move between these compartments are described by the following set of ODEs:

$$\begin{aligned}\frac{dS}{dt} &= -\beta IS, \\ \frac{dI}{dt} &= \beta IS - \gamma I, \\ \frac{dR}{dt} &= \gamma I\end{aligned}$$

The dynamics of these ODEs are influenced by two key parameters: the contact rate, β , and the recovery rate, γ . β describes the probability of an infected person coming into contact with any

susceptible person per unit time, whereas γ describes the rate at which an individual recovers from the disease. When β is large, the contact rate between individuals is high, and the disease spreads rapidly. Similarly, when γ is large, then individuals recover rapidly and move to the recovered compartment quickly. Note that these parameters make global assumptions about the population, in that all individuals have an equal chance of interacting, and all individuals recover at the same rate. Infected individuals therefore come into contact with βN individuals per unit time. Only susceptible individuals may become infected, and the number of new infections per unit time is therefore $\beta N(S/N)$, resulting in a new infection rate of $\beta N(S/N)I = \beta SI$. Finally, as individuals recover with rate γ , they are removed from the infected compartment and enter the recovered department with rate γI .

Considering these parameters allow for useful insights into the dynamics of a given disease: a disease with a high β and lower γ will obviously spread more than one with a lower contact rate and higher recovery rate. With this in mind, we can make the intuitive leap to conclude that an infection will either: spread as an epidemic when each individual is causing more than one secondary infection; remain endemic in a population when each individual causes exactly one further infection before recovering; will die out when each individual causes less than one secondary infection before recovering. This idea is formalised by the concept of a *basic reproductive number*, R_0 (not to be confused with $R(0)$, which denotes the initial size of the recovered population!). R_0 denotes the number of secondary infections caused by a single infected individual when introduced into an initial susceptible population, $S(0)$. As this infected individual will come into contact with βN individuals per unit time over a period of $1/\gamma$ (the mean infectious period), the reproductive number will be given as the number of secondary infections per unit time multiplied by the amount of time that an individual can infect others:[20, 21]

$$R_0 = (\beta N)/\gamma$$

R_0 describes the number of secondary infections resulting from one individual in a completely susceptible population; however, this rate will obviously decrease as the proportion of susceptible individuals in the population decreases. Rather than considering the initial reproductive number, it is often more useful to consider the effective reproduction number, R_n . In simplest terms, $R_n = R_0 \times s$, where s is the proportion of the population that is susceptible ($S(t)/N$).

As an aside, it should be noted that calculating R_0 is a crucial stage in understanding how a disease will spread. A high R_0 (eg. malaria) means that the disease will spread rapidly, with each individual causing a high number of secondary infections, whereas a low R_0 (eg. monkeypox) means that a disease will spread slowly.[19] As discussed above, an R_0 greater than 1 is necessary for an epidemic to take hold. Even at an early stage of an epidemic, R_0 can be estimated based on the growth rate of an epidemic, as was the case during the 2003 SARS virus.[31] Therefore, decreasing the proportion of susceptible individuals below a certain level (ie. through vaccination) will result in an effective reproduction number of less than 1, preventing the epidemic from taking hold. This critical threshold is defined as the *herd immunity threshold*, and provides a crude but often effective target for immunization programmes:[30]

$$HIT = 1 - \frac{1}{R_0} = \frac{R_0 - 1}{R_0}$$

The model shown above describes three compartments, however there are a number of extensions to this model where different compartments and interactions might be appropriate. For example,

an "exposed" compartment might be added which encompasses individuals that have been exposed to the disease, but are not yet infectious. Such a model is known as the SEIR model. As well as additional compartments, the transitions between these compartments might be varied. For example, in cases where immunity is only transient, individuals might be able to re-enter the susceptible compartment following recovery (the SIRS model). Choosing the model structure is dependent on the nature of the disease and population under consideration. For example, using an SIS (infected individuals return to the susceptible state) to model HIV, or an MSIR model (initial maternal-derived immunity) in the case of measles.[19]

It should be noted that there are further considerations to take when modelling real epidemics. For example, the inclusion of birth and death rate, seasonal dynamics, stochasticity and age-dependent interactions.[19] However, the basic principles discussed above are sufficient to begin considering how we might model the spread of other epidemic processes.

With the solid theoretical basis described above, advanced mathematical and computational models are becoming increasingly central to making public health decisions. One recent application of mathematical models in epidemiology was to describe and predict the dynamics of an epidemic in real time.[32] A study by Tizzoni et al. used a Monte Carlo Maximum Likelihood (MCML)-based approach on historical data from the 2009 flu pandemic to develop a global stochastic simulation model, referred to as GLEAM, to obtain basic model parameters.[34, 35] (Note that this project will aim to similar methodologies to fit epidemic models in real time, and a brief overview of maximum-likelihood estimation and least squares estimation is provided in Box 1). Tizzoni et al. used GLEAM to estimate the seasonal transmission ability of the 2009 H1N1 pandemic, generating forecasts for the activity peaks in the northern hemisphere. The robustness of this stochastic forecast was also explored as a function of data completeness by fitting the model using only partial data.[33]

Tizzoni et al. showed that the GLEAM model was in good agreement with the actual 2009 epidemic data, even when only partial data was used (for example, pre-exposure immunity and adherence to vaccination campaigns. However, a key feature of the model is that it accounts for the way in which populations interact and connect, and it was shown that model accuracy was reduced considerably when using only a partial dataset for population mobility. The GLEAM model uses three layers: a population layer (a grid representing the population of the world); a mobility layer (using real flight data to represent travel between cells in the grid); and an epidemic model (consisting of susceptible, latent, symptomatic infectious able to travel, symptomatic infectious unable to travel, asymptomatic infectious and permanently covered compartments). Indeed, consideration of multiple networks layers in epidemic modelling is a growing area of consideration for real infectious diseases, as it allows for the consideration of more realistic population dynamics.[36]

Box 1

To fit model parameters in real time, we consider two methods to fit a continuous-time model to a given set of data: least squares and Maximum Likelihood Estimation (MLE).

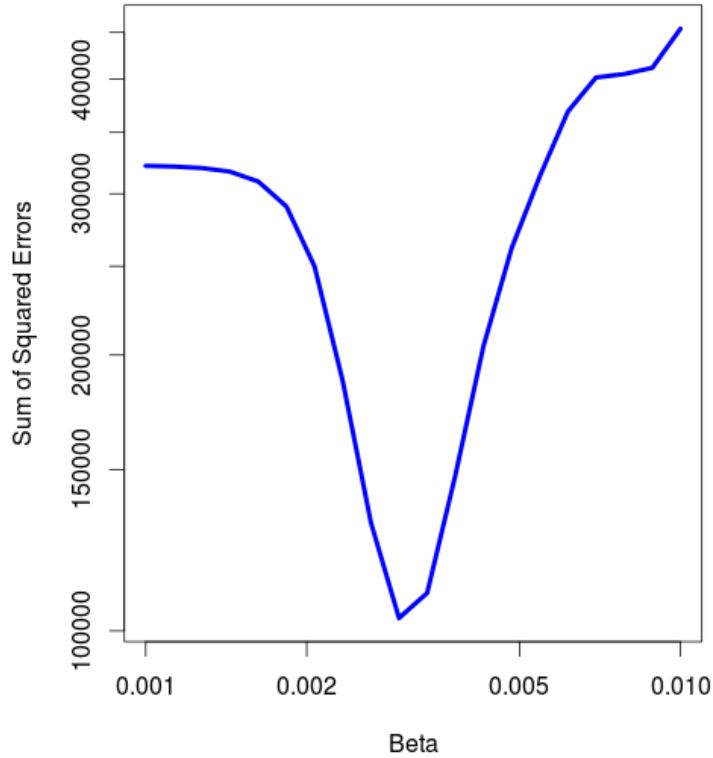
Least squares is the simpler of the two approaches, and assumes that the only source of variability in the data is measurement error (which is distributed symmetrically with a constant variance eg. Gaussian). By estimating the "least squares" for a set of parameters, we aim to find the set of parameters that minimises the sum of the squares of the errors (ie. the difference between an observed value and the fitted value).

More formally, given a simple data set of n points of the form (x_i, y_i) , we aim to minimise the following formula:

$$S = \sum_{i=1}^n r_i^2$$

Where r_i is the residual for each point, given by the difference between the actual value of the dependent variable and the variable fitted by the model: $r_i = y_i - f(x_i, \beta)$

In the context of our SIR model, we aim to find the β and γ values that provide the best fitting SIR model for a given epidemic dataset (we will use the Nelder-Mead algorithm with R).[5]

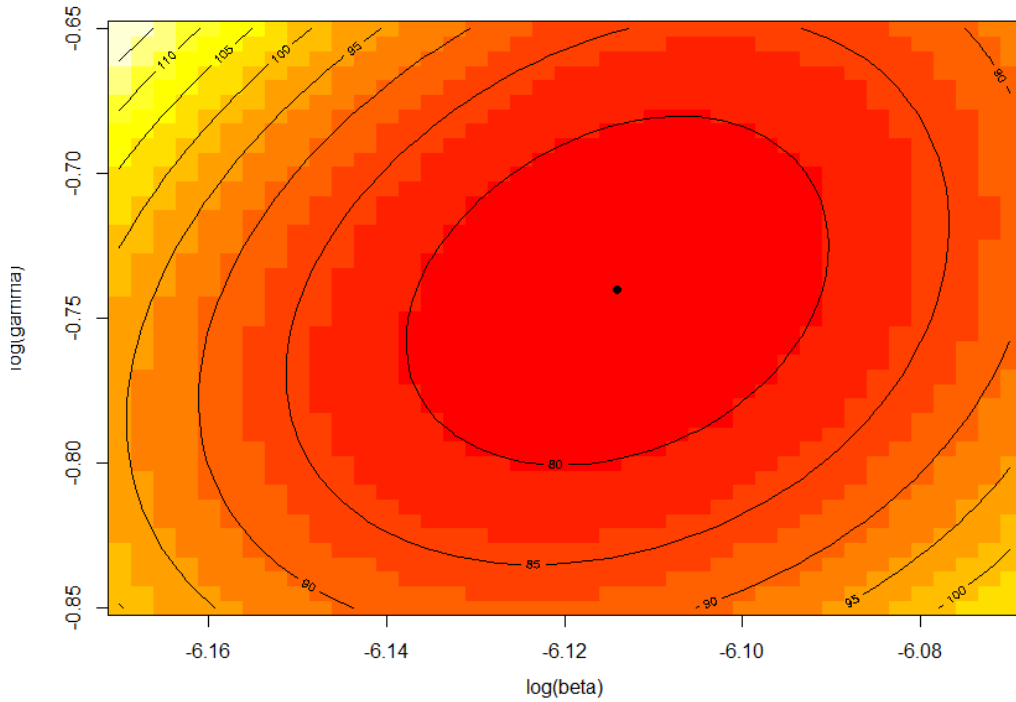


Shown above is an example sum of squared errors (SSE) plot demonstrating how a particular value for β minimises the SSE to a given dataset at around 0.003. This plot was created using a test flu dataset. Note that this plot assumes a γ value of 1, though multiple parameters may be optimised simultaneously using R's *optim* (Nelder-Mead) function.

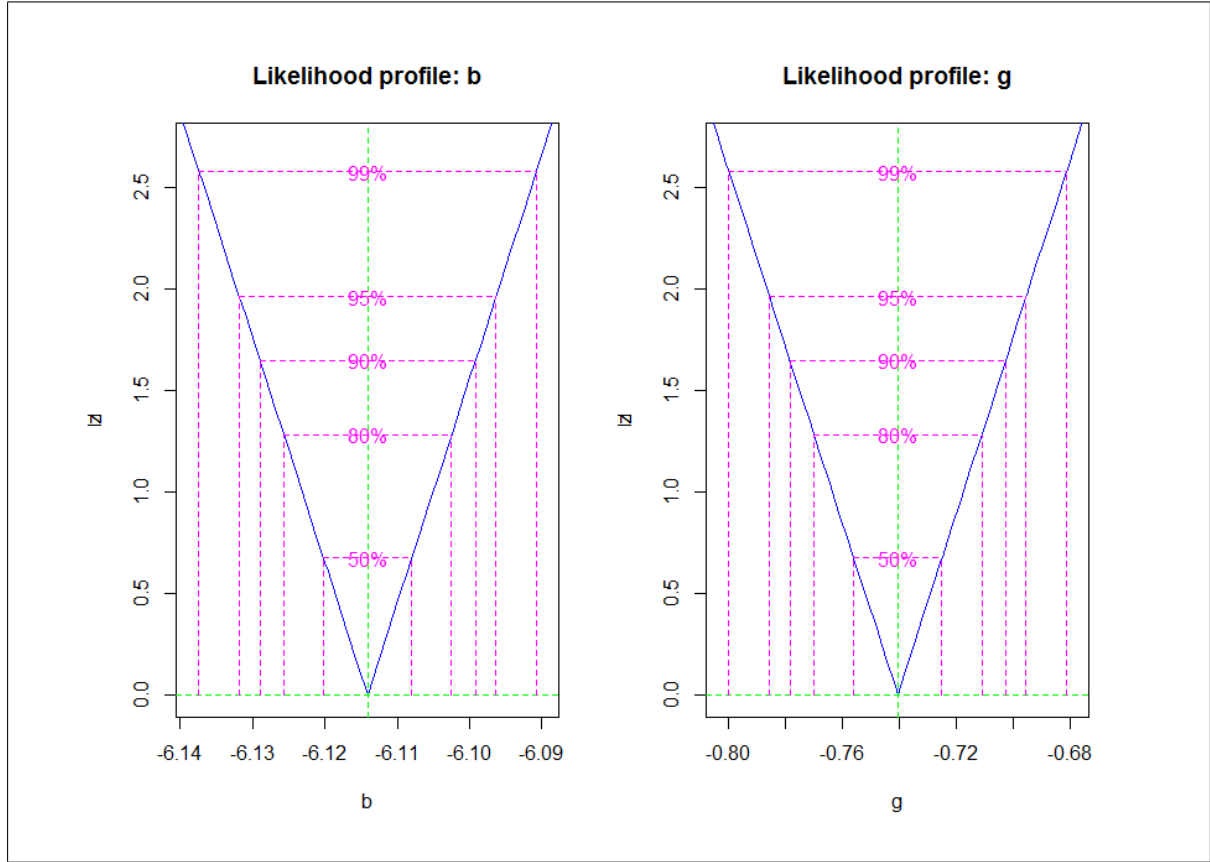
Maximum-likelihood estimation (MLE) is the method of estimating the parameters of a statistical model based on a given hypothesis and a set of data that has occurred. This method essentially selects the set of values for the model parameters that maximise the likelihood function:

$$\mathcal{L}(\theta|x) = P(x|\theta)$$

In other words, we aim to find the set of parameters that provide a model fit would be most likely to produce our given data. As above, we aim to find the set of parameters, β and γ that maximise this likelihood function. Specifically, we calculate the negative log-likelihood of the data given some combination of parameters. Methods using MLE are very common when fitting epidemic models in real time.[37, 38, 39]



The graph above depicts the two-dimensional parameter space (the likelihood surface) for beta and gamma when fit to a set of epidemic data. Note that we use log values to avoid underflow/overflow. Each point represents a separate fit to the data, and the height of the surface shows the negative log-likelihood of that parameter combination. In this particular example, we find that a $\log(\beta)$ value of -6.11 and a $\log(\gamma)$ value of -0.74 provide the best fit. We can also show the confidence intervals for each parameter in the form of a likelihood profile, as shown below.



Epidemic Phenomena on the Internet

A more recent application of epidemic modelling methods is to the spread of information and trends. In particular, the continual development of the internet has opened up a vast area of research into the dynamics of social networks, viral marketing and computer security. It is quite easy to see the analogy between the spread of an online trend to the spread of an infectious disease: individuals have either been exposed to the trend or not; may be actively spreading the trend; or may have lost interest in the trend. The relatively recent surge of interest in online social networks and rapidly rising occurrence of viral phenomena has brought with it an interest in understanding and modelling these trends. In this section, we will briefly discuss the history of epidemiology-based analyses of information dissemination and the resulting application of classical epidemiology to online phenomena.

The first application of epidemiology in a social context was made by Goffman and Newill in 1964 who directed attention to the analogy between the spreading of an infectious disease and the dissemination of information.[22] This was closely followed by Daley and Kendal, who examined the spreading of rumours using mathematical epidemiology.[22] As in Kermack and McKendrick's SIR model, Daley and Kendal used three compartments to describe their population: those individuals that had not heard the rumour, those that were actively spreading the rumour and those that were no longer spreading the rumour. The way in which these compartments interacted was described by parameters indicating those that heard the rumour and those that lost interest or 'forgot' the rumour, corresponding to β and γ . Daley and Kendal

found that the fit was somewhat limited by the difference in behaviours of a rumour and an infectious disease. Specifically, the way in which individuals "lost interest" in the rumour was not comparable to recovery from an infectious disease. Although not a perfect fit, Daley and Kendal's study did highlight the potential application of mathematical epidemiology in a social context.

More recently, the ever increasing relevance of the internet to modern day life has resulted in more studies being undertaken to model and predict the spread of trends and information on the internet. Bauckhage et al. present one such study, investigating the application of statistical models in describing the spread of internet memes.[6] That is, viral catch phrases, images or videos that spread through instant messaging, blogs, forums and social networking sites. Bauckhage et al. use *Google Trends* data as an indicator of search frequency and therefore interest in the internet population. Classifying these as 'fads', Bauckhage et al. go on to fit established statistical distributions to over 200 meme related time series compared to a fitted Log-Normal model. Using a multinomial maximum likelihood fit, the authors find that the Weibull, Gompertz and Frechet distributions all provided a better model of general trends for meme related search activity, suggesting that growth dynamics cannot be attributed to chance. The authors conclude that these dynamics can be described as a 'hype cycle', encompassing a period of rapid uptake followed by a gradual loss of appeal. Although Bauckhage et al. did not use epidemic modelling, they demonstrated that mathematical modelling could be effectively used to describe online trend dynamics.

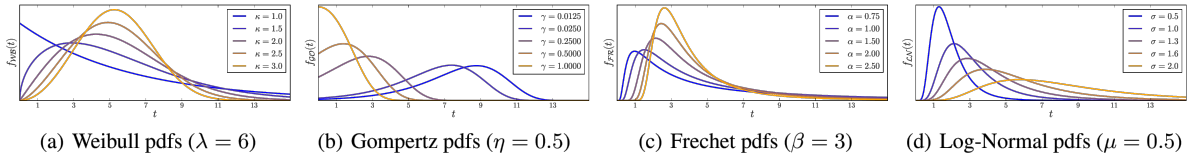


Figure 3: Examples of the statistical distributions considered in Bauckhage et al.[6]

The study by Bauckhage et al. demonstrates the applicability of mathematical modelling to the dynamics of internet memes, however research has also been undertaken to describe the spread of internet 'celebrities'. Tweedle and Smith undertook one such study, investigating the usefulness of SIR modelling in describing the spread of popularity of the music artist, Justin Bieber.[4] Tweedle and Smith demonstrated that an SIR model could be fit to *Google Trends* search data relatively well. Furthermore, the study investigated how 'media effects' might impact epidemic spread (for example, an album release or television appearance). It was found that the inclusion of media effects improved the usefulness of the model in describing the search trend data. Although a fairly 'tongue in cheek' study, Tweedle and Smith demonstrated that SIR modelling could be successfully used to describe the spread of online popularity, particularly when additional media effects are considered.

A recent study by Nika et al. showed the potential for epidemiology to explain and predict outbreaks of internet-based information spreading, with the novelty that the size of the initial susceptible population was assumed to be unknown.[5] The aim of this study was to fit SIR and SEIR models to celebrity outbreaks on the internet in real time, improving model fit as the epidemic progresses. Using the Nelder-Mead algorithm with a least-squares-based objective function to fit SIR and SEIR models in real time (see Box 1), Nika et al. were able to demonstrate real time model fitting with unknown initial parameters. The authors validate their approach on synthetic epidemic data, a historical influenza epidemic and BitTorrent and YouTube video views. Both the SIR and SEIR models fit the synthetic and historical data

well, and showed good predictive power. However, whilst the models were fit to the internet-based data with some success, the authors acknowledge limitations in their methodology, such as the generation of confidence intervals without due regard for parameter uncertainty. This study demonstrates a promising framework for fitting parameters to data in real time, though highlights the limitations of classic SIR modelling in its basic form.

One recent study using similar methodology that recently received public interest was by Cannarella and Spechler, who investigated the use of SIR modelling in describing public interest in OSNs, namely MySpace and Facebook.[23] Cannarella and Spechler used an adapted SIR model that modified the dynamics of the recovering population such that contact between recovered and infected individuals was required for recovery. That is, individuals would only stop using the OSN if they came into contact with someone who had already stopped using it. The authors named this adaptation the ‘irSIR’ model. As in the above studies, Cannarella and Spechler used *Google Trends* search data as a proxy for service usage. Similar to Nika et al., the authors used the Nelder-Mean algorithm to find a best fit curve based on sum of squared error, also assuming that all initial parameters, including population size are unknown. The study found that in the case of MySpace, whilst the basic SIR model did not fit particularly well, the modified irSIR model provided a good fit to the adoption and abandonment phases of the OSN. When applied to the ongoing OSN, Facebook, the authors found that Facebook had reached peak popularity in 2012 and was in the early stages of abandonment, predicting that the OSN would reach 20% of its maximum size by the end of 2014. The authors do concede that there exists an infinite range of possible slower declining solutions.

Facebook posted a rebuttal to the study, using similar methodology to show that Princeton would cease to exist by 2021 based on Google search results.[24] Although not a formal, peer reviewed study, Facebook’s rebuttal did highlight some shortcomings with the methodology employed by Cannarella and Spechler. Namely the assumption that Google searches were an indicator of usage, and also the flawed assumption that Facebook would not ‘evolve’ to keep users. These studies highlight the importance of making valid assumptions and using appropriate data when attempting to study a rapidly evolving area such as OSNs.

With huge implications for marketing and commercial success, Interest in viral phenomena has become an area of particular interest outside of the academic community. As a result, commercial circles have also taken an interest in attempting to understand the spread of online trends. A review posted by the global strategic insight agency, *Facegroup*, inadvertently touched upon the application of SIR modelling in explaining the spread of viral videos.[25] The main conclusion that *Facegroup* came to was that there is no single model of virality. Rather, different types of viral videos could be spread in different ways, proposing ‘spike’ and a ‘growth’ types depending on their spreading pattern. In the ‘spike’ case, videos tend to peak early and drastically drop in views within a week. In the latter case, videos achieve their peak views after a few days and decline slowly, interrupted by secondary peaks of interest.

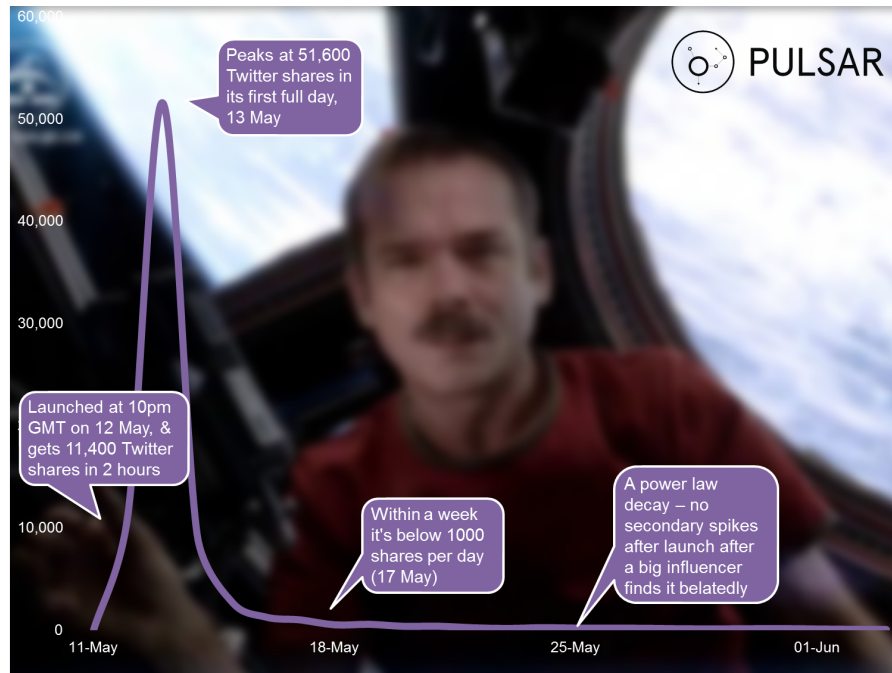


Figure 4: Graph *Facegroup* depicting the uptake of the "Commander Hadfield" YouTube video, demonstrating the "growth" model as proposed by *Facegroup*.^[25]

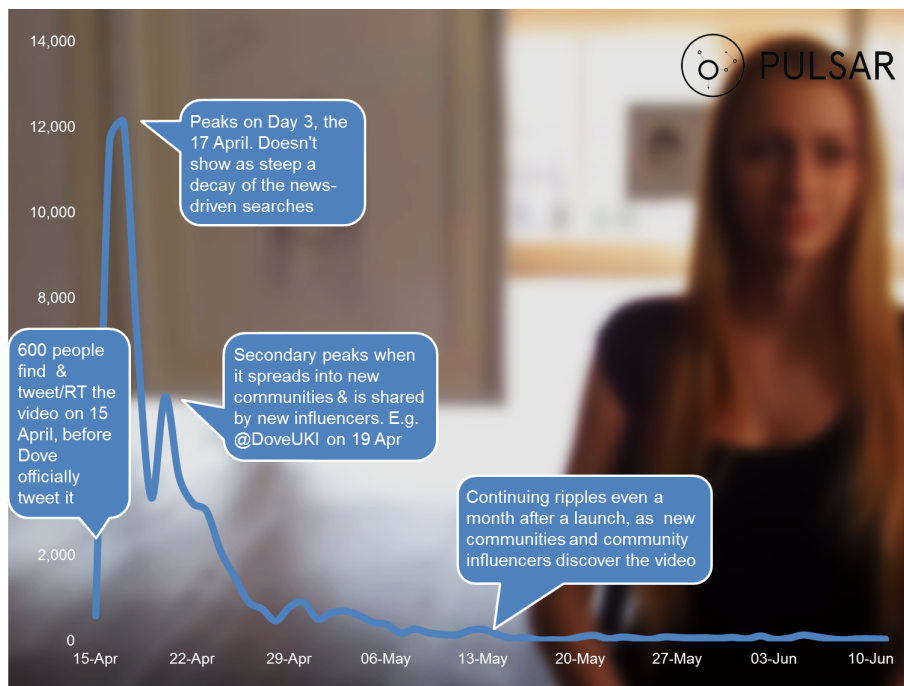


Figure 5: Graph from *Facegroup* depicting the uptake of the "Dove Real Beauty Sketches" YouTube video, demonstrating the "spike" model as proposed by *Facegroup*.^[25]

Returning to an academic setting, Nika et al. recently undertook another study to improve the fit of their real time fitting framework, stating that, based on their previous study, a single epidemic is inadequate to characterise a complex internet-based phenomena. This may be because internet based trends may be influenced by multiple underlying spreading mechanisms at different times, similar to the ‘media effects’ as described by Tweedle and Smith in their analysis of ‘Bieber Fever’. Nika et al. took inspiration from Fourier analysis, proposing that modelling and predicting internet-based phenomena could be better described by considering multiple compartmental epidemiological models. That is, an epidemic signal can be broken down into a number of sub-epidemic models which, when recombined, can be used as a predictive model (see Figure 1). Nika et al. go on to coin the term *synthedemic* from the field of syndemics - the idea that infections can co-occur and interact with each other as well as environmental factors.

The term *synthedemic* is used to describe the co-occurrence of a set of infections, whether they are dependent or not. The aim of the study was to account for the potential influence of multiple underlying spreading mechanisms which may begin at different times by breaking an incoming epidemic signal into component parts, and selecting the model that best explains each component. Using only a classical SIR model and exponential decay model as candidates, Nika et al. are able to adequately characterise the evolution of synthetic data and four real-world data sets from internet trends (BitTorrent downloads and daily Youtube views) well. Please refer to Box 2 for a detailed explanation of the theory used by Nika et al. Using synthetic double epidemic data, the model by Nika et al. successfully predicts two overlapping epidemics, predicting the peak of the second, spike epidemic with a high RSquare value. The model is also fit successfully to the BitTorrent downloads of two popular songs and a viral YouTube video; detecting the presence of multiple outbreaks and exponential decay of interest.

Box 2

Methodology:

The modelling procedure begins by considering a small, truncated dataset of an epidemic outbreak. At each time point, an additional data point is added until the end of the considered time frame is reached. This might be a synthetic epidemic dataset, a historical infectious disease epidemic, or some measure of interest in an online phenomena (Nika et al. use BitTorrent downloads and daily YouTube views). Nika et al. propose two candidate models that provide theoretical analogues to the *growth* and *spike* trends as proposed by *Facegroup*: an SIR model to represent gradual growth, and an exponential model to represent a rapid outbreak and decay of public interest.[25]

At every time point, the multiple epidemic is optimised by attempting to minimise the sum of squared error of the model against the data. At each stage of fitting, the latest residuals are checked at each additional time point for the presence of an additional epidemic outbreak. If detected, a new epidemic is temporarily added to the model from the list of candidate models. If the addition of this model improves the R^2 value, then this additional epidemic is included in all future model fittings. After the multiple epidemic model has been optimised, an autoregressive model is fitted to capture the remaining variability in the data. Finally, the fit of the multiple epidemic AR model is assessed against benchmarked fitting procedures, such as a single epidemic model, using a range of statistical tests, including rSquare comparison.

Candidate Models:

Let M be the class of sub epidemic models under consideration:

$$M = \{f_1^{(i)}, f_2^{(i)}\}$$

Where $f_1^{(i)}$ and $f_2^{(i)}$ are defined as follows:

A. $f_1^{(i)}$ denotes the SIR model $f_1^{(i)}(\theta^{(i)}, t)$ with parameter vector $\theta^{(i)} = [I_0^{(i)}, S_0^{(i)}, \beta^{(i)}, \gamma^{(i)}]$

$$\begin{aligned}\frac{dS}{dt} &= -\beta IS, \\ \frac{dI}{dt} &= \beta IS - \gamma I, \\ \frac{dR}{dt} &= \gamma I\end{aligned}$$

B. $f_2^{(i)}$ denotes the Exponential decay model $f_2^{(i)}(\theta^{(i)}, t)$ with parameter vector $\theta^{(i)} = [I_0^{(i)}, \gamma^{(i)}]$

$$\frac{dI}{dt} = -\gamma I$$

Parameter t denotes a particular time, where $S_0^{(i)}$ and $I_0^{(i)}$ denote the initial number of susceptible and infectious individuals at time t , whilst $\beta^{(i)}$ and $\gamma^{(i)}$ denote the infection and

recovery rate. Furthermore, the current number of sub epidemics within the overall model is given by k , where the combined value of the epidemic model at time t is given by the following formula:

$$\hat{y}(\theta, t) = \sum_{i=1}^k f^{(i)}(\theta^{(i)}, t)$$

Global mathematical models of epidemic processes provide a useful insight into infectious disease dynamics; however, they make a number of potentially unrealistic assumptions. Most notably, SIR models assume complete mixing of the population. That is, each individual in the population has an equal chance of coming into contact with every other individual in the population. Although this assumption may hold in certain scenarios (it is generally safe to assume that the internet population observes random mixing), it may not be applicable to many systems that are affected by local dynamics. Consider the population of a town comprising of schools, offices and homes. Obviously a student will mix much more frequently with other students and their family rather than office workers. In such cases, the approach of SIR based modelling may not be sufficient to capture the underlying dynamics of the population. Many researchers have therefore developed extended models to investigate stochasticity, multiple compartments representing different subpopulations, branching processes and chain-binomial models.[12]

One recent approach of particular relevance to the study of epidemic phenomena in a social context is that of networked epidemiology: an approach that encompasses individual behaviour, heterogenous multiscale networks and the dynamical processes on these networks. Although this particular project focuses on the application of classical SIR modelling, it is worth discussing networked epidemiology in brief to give a complete picture of the field.

Networked Epidemiology and Social Networks

We have briefly touched on the idea of networks in epidemiology with reference to multi-layered epidemic models, however it is worth discussing the basics behind network considerations.[33, 36] Networked epidemiology takes its inspiration from graph theory, using nodes to denote individuals and edges to denote interactions.

Let $G(V, E)$ denote a contact graph on a population of V individuals, where each edge, $e = (u, v) \in E$ denotes those individuals, $u, v \in V$ that come into contact. As in the SIR model, each node might be in the S , I or R state. However, the key difference is that the infection may only spread from u to v along an edge with a probability of $\beta(e, t)$ at time instant t after u has become infected. Similarly, a node only remains infected for a set amount of time denoted by $\tau(u)$. After this time, the node u switches to state R . By considering this network model over a given number of time steps, the dynamics of an epidemic taking place in a network can be modeled. With this basic idea, it is easy to see how real world networks structures and data can be used to vastly improve models of epidemic processes in reality, thereby improving approaches to vaccination and disease control programmes.[42] On the other hand, the reality of transmission networks is not quite so ideal, with information regarding population connectivity and interactions being limited. In this section, we will discuss a sample of studies that build

on the concept of local network approaches, and discuss some approaches that have been taken towards applying these to online trends.

With the basis for another approach to epidemic modelling, we can begin to consider general frameworks to describe local dynamical processes. One such approach is called the graphical discrete dynamical system (GDDS)[26], which is defined as a tuple (G, F, π) , where: $G = (V, E)$ represents the underlying contact network; $F = \{f_v | v \in V\}$ is a set of local functions for each node, v , to compute the state of v based on its neighbours; and π is a schedule that specifies the order in which the stages of the nodes are updated. It is possible to view the configuration space of a GDDS as a Markov chain, M , where each node in M is the state vector of the node states in the GDDS, G . For example, in the SIR model these three states correspond to the susceptible, infectious and recovered states.

A conceptually simpler approach to local network modelling is that of a cellular automata model. Cellular automata models take into consideration local behaviour and heterogeneity by ascribing each individual to a particular cell as part of a grid. Individual cells may have a certain state, such as infected or susceptible, and may interact with other cells depending on the assumptions made. Turner et al. provide one such example of this type of model, proposing two spatial host-pathogen models that are described as equivalent to a density and frequency dependent global model.[27] Another example is provided by Zanette and Risau-Gusman, who investigate the effect of evolving connections between individuals affects the spread of an infection. Zanette and Risau-Gusman use an SIS based model where susceptible agents are able to break their links with infected agents either temporarily or permanently, showing that a moderate contact reconnection frequency is sufficient to suppress infection.[28] It is possible to stretch the analogy of human networks to the internet, with towns and cities representing various internet communities. However, the drastically higher level of connectivity and transmission speed on the internet does limit the applicability of these locally driven models.

Global models may provide a more appropriate approach to global internet trends compared to locally driven models; however, research into using network based models to describe the dynamics of social networks has recently shown some success. The aim of such models are largely to predict future viral trends. One such example is a study by Altshuler et al., who investigated the use of social diffusion models in trend prediction in an online social trading community.[29] Altshuler et al. set out to answer the following question: given a snapshot of a social network with some behaviour occurrences, what is the probability that these occurrences will result in a viral diffusion and a wide-spread trend? The authors model the diffusion process using scale-free networks (ie. probability that v has d neighbours follows a power law); taking into account local fluctuations and heterogeneity. From this, Altshuler et al. develop a theoretical mathematical model to understand trend diffusion in social networks. However, as the authors points out, their framework needs to be tested in the field by conducting an active experiment in which the emergence of a trend is predicted in real time.

Conclusion

Research into the mathematical modelling of epidemic processes is now an established field, with the majority of work based on the original SIR model as proposed by Kermack and McKendrick.[18] Extensions of the SIR model take into account additional compartments and inter-compartment dynamics, such as the inclusion of an ‘exposed’ group or of births and deaths. By customising model parameters and structure, public health authorities and researchers can

improve their understanding of the way in which infectious diseases spread. For example, using an SIS (infected individuals return to the susceptible state) to model HIV, or an MSIR model (initial maternal-derived immunity) in the case of measles.[19] Understanding these population dynamics in combination with the critical vaccination threshold, given by the reproductive ratio of the virus, allows for effective vaccination and control strategies. Particular topics of note in recent years are the use of multi-layered epidemic models and the use of maximum-likelihood estimations to predict the spread of an epidemic in real time. [33, 36, 37, 38, 39]

Although infectious diseases are the focus of mathematical modelling of epidemic processes, a novel application is in the modelling of internet-based phenomena and trends. As online social networks and content sharing site become increasingly popular, the relevance of understanding the dissemination of information online becomes an increasingly important area of research both from an academic and commercial perspective.[23, 24] Studies in this area are still at an early stage, though a few recent studies have shown promising early results. [5, 11, 4] The study by Nika et al. shows promising results by considering the presence of multiple, overlapping epidemics to describe one epidemic phenomena in real time using a least-squares based fit. That is, the popularity of a single online trend may be described through considering its underlying sub-epidemic components. Nika et al. consider two types of sub epidemic model as proposed by the strategic insight agency, *Facegroup*, and is the first study to consider multiple overlapping epidemics to explain the spread of internet trends.

Although applying epidemic modelling techniques to the spread of internet trends has shown promising results, there are a number of limitations and flawed assumptions that must be considered. Firstly, the analogy between an internet trend and an infectious disease is limited. Nika et al. point out that whereas normal SIR modelling will be able to make realistic assumptions or measurements regarding the size of the initial susceptible population, this is not possible when considering online trends. This S_0 value must therefore be treated as an additional unknown parameter.[5] Furthermore, the spreading mechanisms and lifecycle of internet trends are different to those of infectious diseases. Whereas infectious diseases must be passed on through physical contact, internet trends can be spread instantaneously to any other user through a ‘tweet’ or ‘share’. Trends such as online videos or memes may also typically experience media spikes when a video or celebrity is shown on television or highly frequented web pages. The dangers of making such assumptions can be observed in the study by Cannarella et al. who attempted to show that Facebook would be abandoned by 2015, neglecting to consider that Facebook will continue to ‘evolve’ to keep users.[23, 24] Proxies for interest in internet trends such as *Google Trends* search results should therefore be used with caution.

Despite these limitations, promising early results encourage the pursuit of further research. There are a number of other techniques and models currently being investigated in infectious disease modelling that might be applicable to the spread of internet trends. For example, the use of maximum-likelihood estimations rather than least squares;[33] the use of multi-layered epidemic models that might account for underlying social network structure (for example, the spread of a viral video on or between social network sites);[29, 33] and the consideration of alternative compartmental models or statistical distributions.[6]

With so many potential routes to follow, this project will focus on furthering the work done by Nika et al. to fit a multiple epidemic model in real time to the spread of online phenomena.

2.2 Development Environment

2.2.1 Programming Languages

There were a number of candidate programming languages, each with their own strengths and weaknesses. In the end, R and C++ were chosen for initial and final implementations. Previous approaches to epidemic and synthedemic model fitting frameworks use R due to its readily available ODE solvers, optimisation functions and graph plotting functionality.[5, 11] R therefore provided an ideal means to implement the single and multiple epidemic fitting frameworks initially. Once this initial model fitting framework was implemented, we went on to provide a C++ implementation with the aim of providing a faster, more transparent ‘from scratch’ fitting methodology.

At the start of the project, it was desirable to begin exploring and understanding the theory behind epidemic modelling and optimised model fitting. As such, the first development consideration was to decide on a language that was well adapted for easy implementations with a large number of available packages and functions. R and Matlab were candidates for this initial approach. Whilst Matlab has an arguably better programming environment with better documentation, R has already been shown to be effective in epidemic model fitting. The R community provides a number of statistical analysis tools and is suited to dealing with non-typed data sets, making it an ideal choice. These packages can easily be obtained via the Comprehensive R Archive Network (CRAN).

The nature of parameter optimisation means that fitting a large number of parameters simultaneously can be extremely slow, and an approach to providing a faster implementation was to reimplement the model fitting procedure in C++. C++ has been shown to be considerably faster than both R and Matlab when solving stochastic neoclassical growth models, suggesting that an efficient C++ implementation might provide a much faster fitting framework than an R counterpart.[13] However, the trade off with run time speed is the fact that coding the same algorithms and functions in C++ is very time consuming. Whilst there are R packages readily available that allow parameter fit optimisation, maximum likelihood estimations and graph plotting in only a few lines of code, the equivalent functionality in C++ had to be implemented from scratch. A significant challenge of this project was therefore to find, adapt or create source code for the essential functions of the model fitting framework. For graph plotting, a Gnuplot iostream was called from C++ code.

Python and Java were also considered as potential languages for a faster implementation. However, the relatively lower speed of Python and unfamiliarity with Java meant that C++ remained the ideal choice.

It should be noted that whilst C++ provides an ideal way of speeding up computational bottlenecks in the model fitting procedure (namely the optimisation step), it may still be desirable to call R functions from within the C++ program. For example, the generation of a likelihood profile. This can be achieved using the Rcpp library if needed. Furthermore, the quick generation of synthetic data with which to evaluate and develop the fitting framework is clearly not a limiting factor. R therefore remained the ideal language for synthetic data generation using *GillespieSSA* package, exporting the data as a .csv file to be imported in the C++ implementation.

3 Single Epidemic Fitting

In this section we explore the theory and implementation behind a model fitting framework for single SIR models with unknown parameters. To provide a simulation of real time model fitting, we iteratively fit a new optimised model at each data point. Firstly, a least-squares fitting procedure is implemented in R for a single SIR epidemic where beta, gamma and S0 are assumed to be entirely unknown. We then extend the implementation to include the start time of the epidemic, t0 as a fourth unknown parameter. This also raises the issue of epidemic outbreak detection and model selection, which we will revisit in section SECTIONNNN!. We go on to use a maximum likelihood based approach which allows for the generation of confidence intervals. Finally, we reimplement the above approaches in C++ to provide a much faster implementation.

3.1 Parameter Optimisation

The ultimate aim of the optimisation procedure is to find the set of parameters for a set of ODEs that, when solved, best fit the given data. As discussed in section BACKGROUND, we

3.2 Data Management

The data that we wish to characterise is the change in number of infected individuals over time, whether infected individuals is defined as individuals infected with a disease or individuals that have viewed a particular *YouTube* video or ‘liked’ a particular *Facebook* post. An example of this type of data is shown in Figure XX. It is very easy to deal with data in R, as the use of ‘data frames’ allows for .csv files of epidemic data to be easily imported and manipulated. In C++, we also import data as .csv files, but as data must be stored in vectors, initial data formatting is more crucial.

3.3 Candidate Models

As we aim to find a model that best describes our data, the next consideration is the creation of data that best fits our epidemic data through candidate model equations. With a candidate model in mind, namely the *SIR* model, and a set of candidate parameters (beta, gamma and S0), we find the data described by the model and parameters and compare this to the epidemic data. When implementing the model fitting framework in R, we utilise the *ode* function from the *deSolve* package to return a matrix of values calculated from a given set of parameters, a set of ODEs and a desired time frame. A simple R implementation of the *SIR* is shown in Figure XX.

With a model solving framework and a set of data that we wish to fit, one can begin to visualise how the model fitting process might take place. Even with completely unknown parameters, candidate models can be generating by choosing parameters that might fit the data. Figure XX depicts how using various model parameters can give different shaped curves.

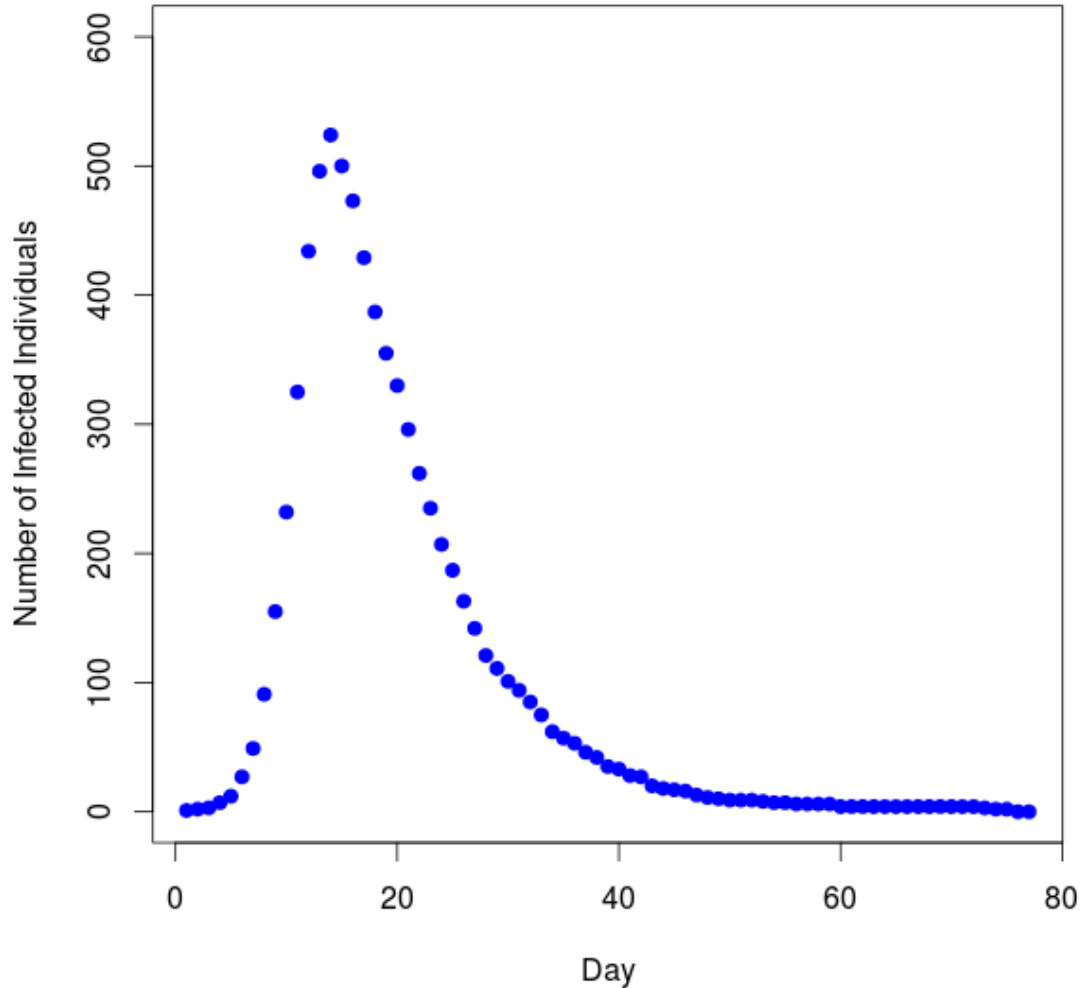


Figure 6: Example synthetic epidemic data generated using the *GillespieSSA* algorithm in *R*. In this model: $\beta = 0.0015$, $\gamma = 0.1$, $S_0 = 800$, $I_0 = 1$.

As a theoretical aside, it should be highlighted that the *ode* function uses the LSODA integration method by default, based on FORTRAN code. The benefit of the LSODA method is that it automatically switches between stiff and non-stiff systems, and is very robust. However, in our C++ implementation, we provide a ‘from scratch’ ODE solver using the Runge-Kutta method in an attempt to speed up the model fitting process. A theoretical introduction to ODE solving is provided in Box 4.

Box 4

Solving Ordinary Differential Equations:


```

function(time, data, parameters) {
  S <- data[1]
  I <- data[2]
  R <- data[3]

  beta <- parameters[1]
  gamma <- parameters[2]

  dS <- -beta*S*I
  dI <- beta*S*I - gamma*I
  dR <- gamma*I

  list(c(dS, dI, dR))
}

```

The epidemic models take the form of ordinary differential equations (ODEs), wherein the dynamics of the population are described by the transition of individuals between different compartments. In the case of the the *SIR* model, individuals transition from susceptible, to infected and finally to recovered. As discussed in Box 1, the rate of transition between these states depends on the model parameters (namely beta and gamma), as well as the number of individuals currently in each compartment.

For the purpose of model fitting, it is necessary to calculate the number of individuals in each compartment at each time point. This requires the set of ODEs to be solved. Given a set of parameters and initial compartment sizes, we wish to find the number of individuals over the course of the epidemic at each time point. For a simple differential equation, it is possible to find the closed form solutions. Given a function, g , we wish to find the solution such that:

$$\begin{aligned}
 Y'(t) &= g(t) \\
 Y(t) &= \int g(s)ds + c
 \end{aligned} \tag{1}$$

where c is an arbitrary constant, and the value of $Y(t)$ can be obtained at a given time point:

$$Y(t_0) = Y_0 \tag{2}$$

In the case of first-order differential equations (as is our case), we take the above equation as the initial value condition and are presented with an initial value problem of the form:[46]

$$\begin{aligned}
 y'(t) &= f(t, y(t)), \\
 y(t_0) &= y_0
 \end{aligned} \tag{3}$$

It is often impractical to derive analytical solutions to differential equations. In the case of models in epidemiology, the first-order different equations are often non-integrable.[43] In

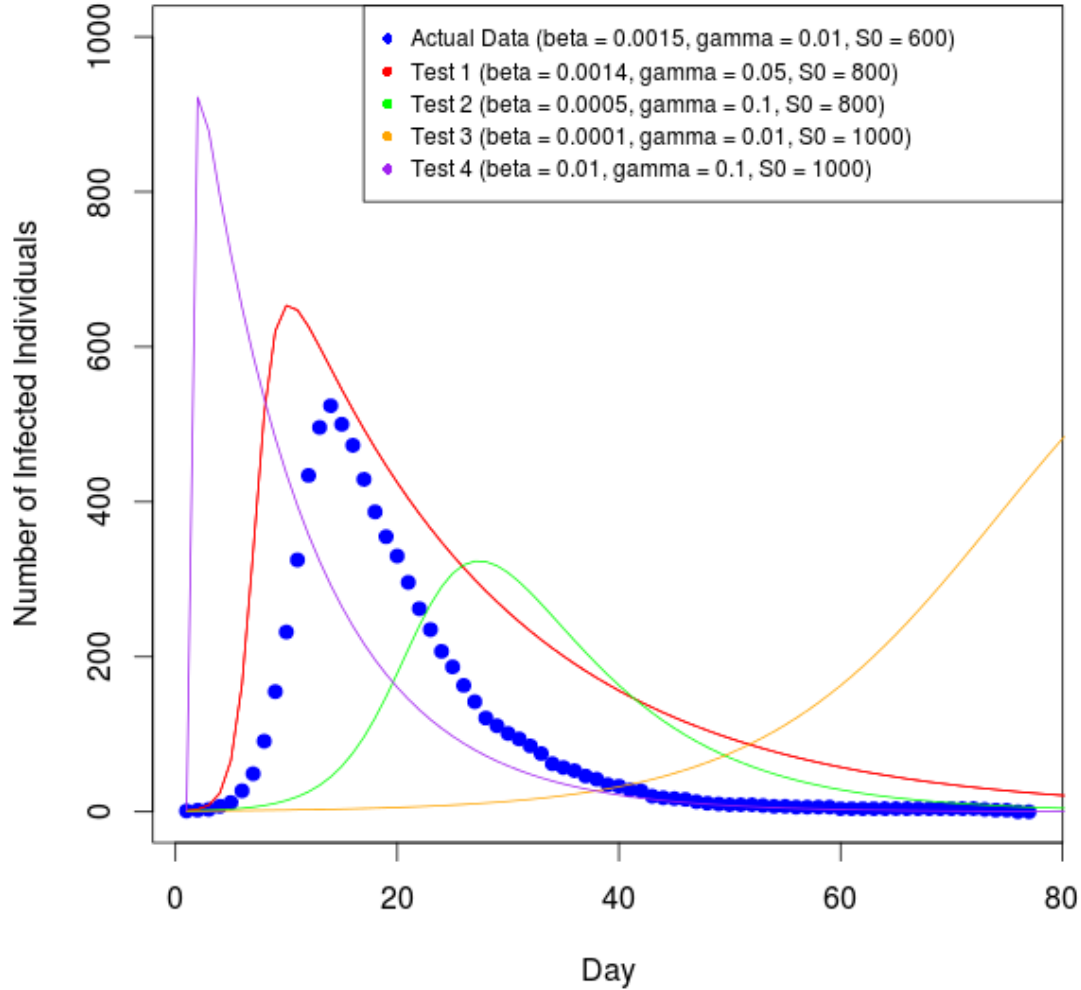


Figure 7: Depiction of how various candidate model parameters give varying levels of fit for a given dataset

the case of *SIR* modelling and similar sub types, considerable work has been undertaken to attempt to solve *SIR* models analytically using Lie analysis and homotopy analysis.[44, 45] Such approaches are difficult to implement and are not fit for the purpose quickly solving ODEs in a generalisable way. We therefore turn to numerical analysis.

Numerical methods are used to find numerical approximations to the solutions of ODEs rather than solving them analytically. For the purpose of obtaining population values that can be used in model fit assessment, such numeric approximations are sufficient. The simplest numerical method for solving the initial value problem is *Euler's method*, which involves finding an approximate nearby point on the curve by moving along a line tangent. Euler's method forms the basis for a highly popular group of methods for solving initial

value problems known as Runge-Kutta methods, which are relatively easy to implement.

The most basic member of the Runge-Kutta methods is simply known as the “classical Runge-Kutta method”, and is the method that we chose to implement in C++. Given the above initial value problem and an initial condition, we can attempt to find later values of $y(t)$ with the following definitions:

$$\begin{aligned} y_{n+1} &= y_n + \frac{h}{6}(k_1 + 2k_2 + 2k_3 + k_4) \\ t_{n+1} &= t_n + h \end{aligned} \quad (4)$$

for $n = 0, 1, 2, 3, \dots$, using

$$\begin{aligned} k_1 &= f(t_n, y_n), \\ k_2 &= f\left(t_n + \frac{h}{2}, y_n + \frac{h}{2}k_1\right), \\ k_3 &= f\left(t_n + \frac{h}{2}, y_n + \frac{h}{2}k_1\right), \\ k_4 &= f(t_n + h, y_n + hk_3) \end{aligned} \quad (5)$$

Note that y_{n+1} is the Runge-Kutta approximation of $y(t_{n+1})$, where y_{n+1} is determined by the weighted average of four increments of y_n at interval size, h , with the estimated slope specified by the right hand side of the differential equations. Note that greater weighting is given to the increments at the midpoint of the chosen interval.

Box 4

The Nelder-Mead Algorithm:

The Nelder-Mead algorithm, or simplex search algorithm, is one of the best known and commonly used algorithms for multidimensional unconstrained optimisation without derivatives. The algorithm is relatively simple to understand and implement, which makes it an ideal candidate for solving parameter estimation problems. The method ultimately approximates a local optimum of a problem with N variables when provided with an objective function to be minimised.

Given a nonlinear function, $f : \mathbb{R}^n \rightarrow \mathbb{R}$, the Nelder-Mead algorithm uses a simplex-based search method to minimise the f , where a simplex, S in \mathbb{R}^n is defined as the convex hull of $n + 1$ vertices, $x_0, \dots, x_n \in \mathbb{R}^n$. In the case of \mathbb{R}^2 , the simplex is a triangle, whereas in the case of \mathbb{R}^3 , the simplex is a tetrahedron. In the case of epidemic model fitting, each vertex of the simplex corresponds to a set of model parameters.

Starting with a set of $n + 1$ points (the initial ‘seed’ parameters) and a corresponding set of function values at the vertices, $f_i := f(x_i)$, for $j = 0, \dots, n$, the Nelder-Mead method performs a sequence of transformations on the working simplex S with the aim of decreasing the function values at its vertices. Once the method has satisfied some minimisation condition,

whether it be a number of steps or a desired minimisation range, the final simplex can be used to return the optimised parameters.

To summarise, the Nelder-Mead algorithm follows the following set of steps:

1. Construction of the initial working simplex, S , around an initial point based on initial parameters
2. Repeat the following steps until maximum number of iterations reached or minimisation condition satisfied:
 - (a) Calculate the function value for the current working simplex
 - (b) Check if termination criteria met
 - (c) If not met, transform towards the best vertex of the working simplex to give new vertex values with the following sub steps:
 - i. Determine the order of vertices in terms of function values (from best to worst)
 - ii. Calculate the centroid, c of the side opposite the worst vertex
 - iii. Compute a new working simplex from the current simplex using a series of transformations
3. Return the best vertex of the current simplex, S , along with its associated function value.

In the transformation step, replacing the worst vertex is attempted using reflection, expansion or contraction with respect to the best side. Firstly, the worst vertex is replaced with a reflection of the best vertex. If this point provides an improvement on the current best value, then the simplex is expanded towards the new point. Otherwise, the simplex is contracted towards the current best point. If successful, then the new point replaces the worst vertex of the working simplex. If not, then the simplex is shrunk towards the best vertex. A later addition of the algorithm is to shrink the entire simplex in the event of failed contractions, though this is a rare and slow step.

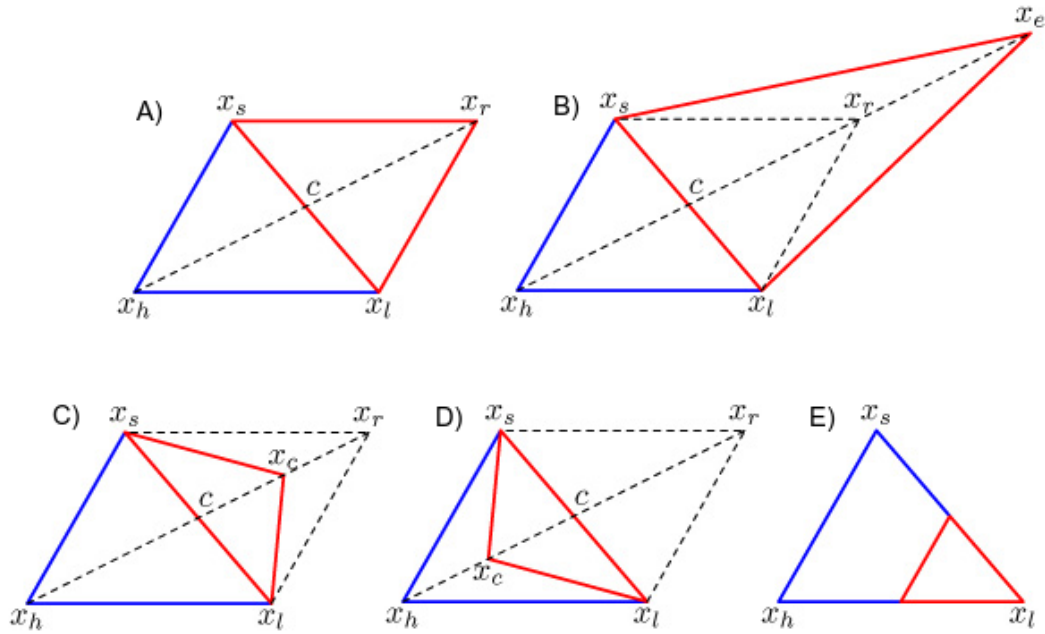


Figure 8: A) Reflection. B) Exansion. C) Outside contraction. D) Inside contraction. E) Shrink transformation

Ultimately, the Nelder-Mead method is a fast and relatively simple algorithm for obtaining a good reduction in function value in a relatively small number of function evaluations. For optimisation problems where a precise optimum (eg. parameters are subject to noise) is not necessarily required, the Nelder-Mead method is ideal. However, it is possible for the Nelder-Mead algorithm to undertake an extremely high number of iterations with little to no function value improvement at a region far from the actual minimum. A heuristic solution to this problem is to restart the algorithm at multiple start points and to only allow a small number of iterations during each run.[47, 48]

3.4

4 Multiple Epidemic Fitting

5 Evaluation

6 Conclusions and Future Work

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Appendix