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Nadine Enright

AUTEUR DE LA THÈSE / AUTHOR OF THESIS

M.Sc. (Epidemiology)

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Department of Epidemiology and Community Medicine

FACULTÉ, ÉCOLE, DÉPARTEMENT / FACULTY, SCHOOL, DEPARTMENT

**Testing the Pair-Wise Network Model: Does it Accurately Predict the Dynamics of STIs on a
Network?**

TITRE DE LA THÈSE / TITLE OF THESIS

A. Jolly

DIRECTEUR (DIRECTRICE) DE LA THÈSE / THESIS SUPERVISOR

R. Smith

CO-DIRECTEUR (CO-DIRECTRICE) DE LA THÈSE / THESIS CO-SUPERVISOR

EXAMINATEURS (EXAMINATRICES) DE LA THÈSE / THESIS EXAMINERS

D. Kohen

J. Little

Gary W. Slater

Le Doyen de la Faculté des études supérieures et postdoctorales / Dean of the Faculty of Graduate and Postdoctoral Studies

**TESTING THE PAIR-WISE NETWORK MODEL: DOES IT ACCURATELY
PREDICT THE DYNAMICS OF STIs ON A NETWORK?**

Nadine Enright

Thesis submitted to the
Faculty of Graduate and Postdoctoral Studies
in partial fulfillment of the requirements
for the MSc in Epidemiology and Community Medicine

Epidemiology and Community Medicine
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University of Ottawa

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Abstract

Background: Mathematical models are an essential tool in infectious disease epidemiology. The most fundamental, and still widely used mathematical model for looking at infectious diseases, is the simple SIS (susceptible-infected-susceptible) compartmental model. However, this type of model does not integrate the local contact network of individuals making them inappropriate for studying sexually transmitted infections (STIs).

Goal: To evaluate the accuracy of the pair-wise network model, proposed by Eames & Keeling (2002), which incorporates the sexual contact network.

Results: Compared to observed data, the predictions of the pair-wise model were a much better fit to the prevalence of chlamydia than those of the traditional simple SIS model.

Conclusions: The results demonstrate the critical role of the network structure in the spread of chlamydia and other STIs. If decision-makers continue to rely on the simple SIS model, they could underestimate the effectiveness of prevention and control strategies, actually hindering our efforts to eliminate chlamydia. Also, good quality data on the sexual network structure of the target population is necessary in order to make accurate and useful predictions.

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Table Of Contents

Abstract	ii
Acknowledgements	iii
Table of Contents	iv
List of Tables	vi
List of Figures	vii
Introduction and Overview.....	1
Sexually transmitted infections (STIs).....	1
Chlamydia.....	2
Mathematical models in epidemiology	4
The compartmental model	5
Assumptions	7
Limitations	8
Network theory in epidemiology.....	10
Integrating networks into the compartmental model.....	11
The pair-wise model	12
Assumptions	18
Purpose of the research	18
Significance	19
Methodology	21
The data	21
The simulations	24
Building the pair-wise model for Chlamydia.....	26
Initial conditions	27
Assumptions	30
Comparing the models.....	33
Results	35
Simple SIS model.....	35
Pair-wise model.....	36
Accuracy of predictions.....	43
Discussion	45
Summary of the findings.....	45
Strengths and limitations.....	48
Implications of the findings	51
Conclusions	53
Looking ahead.....	53

Appendices	55
Appendix A	55
Appendix B.....	57
Appendix C.....	58
Appendix D	60
Appendix E.....	93
Appendix F	116
Appendix G	122
References	126

List of Tables

- Table 1: Notation used for the pair-wise model.
- Table 2: Infection and recovery events of pairs and the corresponding ordinary differential equation terms.
- Table 3: Description of the four initial condition scenarios explored for the pair-wise model.
- Table 4: Number of pairs between an individual with 'm' sexual partners and one with 'n' sexual partners for each possible combination of $m=1$ to 12 and $n=1$ to 12.

List of Figures

- Figure 1: All reported cases of notifiable diseases across Canada for 2006
- Figure 2: Rates of chlamydia in Canada from 1991 to 2004 (PHAC, 2006)
- Figure 3: Flow diagram of the SIS compartmental model
- Figure 4: A sexual network graph (Bearman et al., 2004)
- Figure 5: Visual representation of a pair, a triple and a quad
- Figure 6: Solutions of the simple SIS model
- Figure 7: Solutions of the pair-wise model; case 1
- Figure 8: Solutions of the pair-wise model; case 2
- Figure 9: Solutions of all five simulations together
- Figure 10: Solutions of all simulations along with the prevalence from the Manitoba data for 24 months time

Introduction and Overview

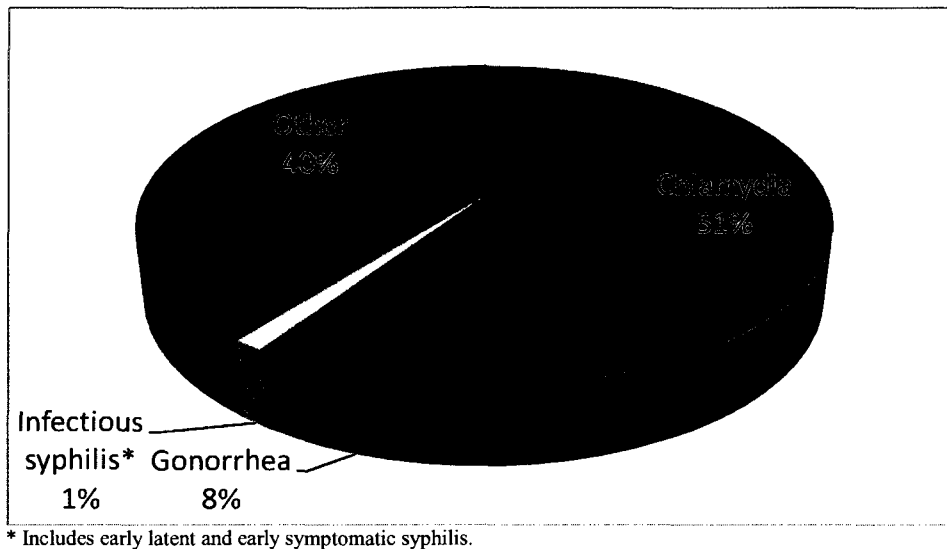
Sexually Transmitted Infections (STIs)

Sexually transmitted infections (STIs) are a major health concern throughout the world. It is estimated that there are 340 million new cases of curable STIs and many million incurable viral infections every year (World Health Organization [WHO], 2008). In addition to the impact of the infections in their own right, STIs increase the risk of acquiring or transmitting the human immunodeficiency virus (HIV) by a factor of up to 10, and they can lead to complications with severe consequences such as ectopic pregnancy, pelvic inflammatory disease and infertility (WHO, 2001).

STIs refer to a broad category of infections caused by more than 35 different pathogens including bacteria, viruses, fungi and protozoa. All of them have one thing in common; they spread through human sexual relations. Although control measures and prevention programs have been in place, the number of STIs has been on the rise since 1997 and is still rising (WHO, 2001). Furthermore, with new variants of various STIs emerging and bacteria developing resistance to existing treatments, the need for new prevention programs and control measures is important now more than ever.

In Canada, genital chlamydia, gonorrhea and infectious syphilis are notifiable (i.e. every case must be reported by law). In 2006, chlamydia alone accounted for more than 50% of all notifiable diseases (sexually transmitted or not) reported in Canada (Fig 1, Public Health Agency of Canada [PHAC], 2007). Most important, this disease is entirely preventable, and is easy to diagnose and treat.

Figure 1: All reported cases of notifiable diseases across Canada for 2006.



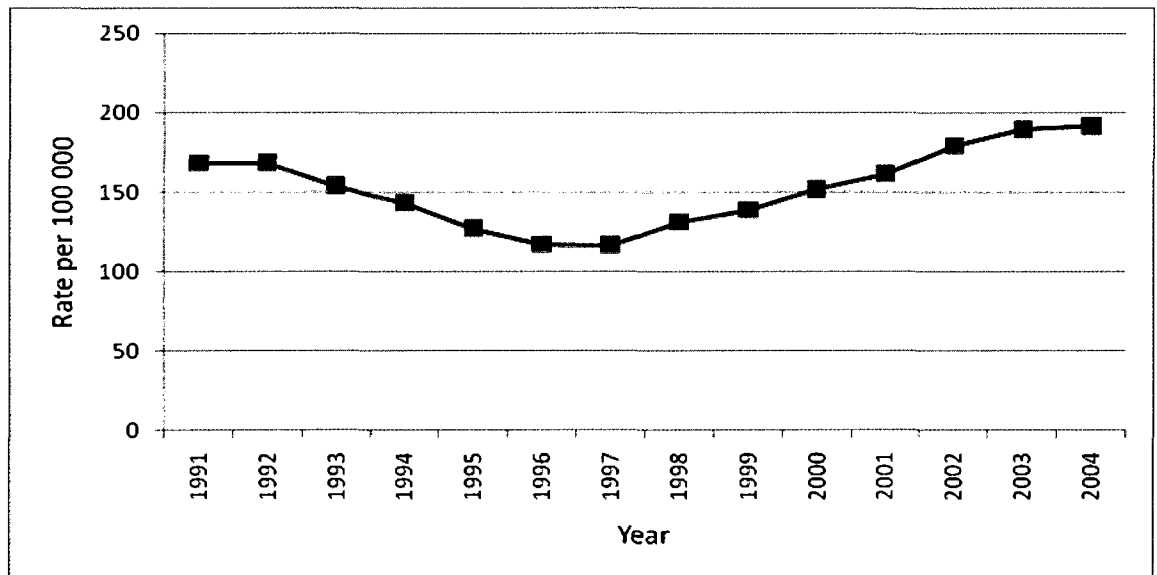
Chlamydia: Chlamydia infections are caused by *Chlamydia trachomatis* which is an obligate intracellular pathogen and one of several bacterial species in the genus *Chlamydia*. The organism is mainly transmitted through sexual contact but it can also be transmitted from mother to infant during birth.

One major challenge in controlling chlamydia is that many infections are asymptomatic. Women are more often asymptomatic than men, with almost 70% of sexually active infected women being asymptomatic (Holmes et al., 2008). The danger of asymptomatic infections is that the people affected do not seek medical attention, the infections remain untreated and not only continue to spread but can lead to some serious long-term medical consequences. In Britain, it was estimated that less than 10% of prevalent cases are in fact diagnosed or treated (Moens, Baruch & Fearon, 2003).

Canada recommended national screening programs in the late 1980s. This was followed by a decrease in reported cases, but since 1997, incidence rates have been steadily

increasing (Fig 2, PHAC, 2006). Preliminary data shows chlamydia incidence at 211.4/100 000 for 2006 and 219.5/100 000 for 2007 (PHAC, 2008), based on all reported cases for 2006 and the 2006 updated postcensal population estimates, while 2007 estimates are based on all reported/extrapolated cases for 2007 and the 2007 preliminary postcensal population estimates. These rates are subject to change but they show a continuing increasing incidence trend for chlamydia. Clearly, current efforts are not effective and more must be done to control this disease.

Figure 2: Rates of chlamydia in Canada from 1991 to 2004 (PHAC, 2006).



Mathematical Models in Epidemiology

Mathematical models are an essential tool in infectious disease epidemiology. First, they are valuable heuristic devices as they encourage thinking about the basic epidemiology of infections and how it affects populations. Models can help understand the underlying mechanisms of transmission and the effect of varying parameters values, thereby indicating effective control strategies.

Second, they are used to evaluate the potential impact of control strategies by allowing the comparison of different strategies without having to implement them, thus saving both time and money. For example, Vickerman et al. (2006) used mathematical models to compare the number of averted HIV infections with and without periodic presumptive treatment (PPT) for bacterial sexually transmitted infection (STI). The model predicted that, with the use of PPT, 53 HIV infections would be averted over a one year period in Hillbrow, Johannesburg. This number was then used in the economic analysis of PPT.

Third, simulations can be run using the models and predictions made which enable public health officials to anticipate the future course of a disease and prepare accordingly. They can support and guide decision-making and development of programs aimed at increasing the health of the general population.

Fourth, it is also possible to observe the outcome of experiments which are otherwise impossible. For example, it would be unethical to introduce an infection into a human population in order to study the effects, but introducing it into a simulated population and using mathematical models to study it is feasible and potentially of great interest and usefulness.

It is important to note that mathematical models are a mathematical description of the simplified dynamics of disease. Because of the complexity of the actual dynamics, a mathematical model is never exactly “correct” in absolute terms, but it nonetheless produces useful relative comparisons.

The compartmental model

The most fundamental mathematical model for looking at infectious disease transmission is the compartmental model (Kermack & McKendrick 1927, Anderson & May 1979), which is described as a system of ordinary differential equations (ODEs). A derivative, written as dY/dt , denotes an instantaneous rate of change. For example, dY/dt , means the change in variable of interest Y per (small) unit of time, t . The solution to the ODE, denoted $Y(t)$, is a function of time t and it gives the value of variable Y at time t . Once the ODE is defined and solved, one can use the solution $Y(t)$ to obtain the value of the variable Y for any given point in time.

In the model, the population is conceptually divided into compartments, or classes, depending on disease status. The ODEs describe the rate of change from one class to another. The most basic model has two classes, the susceptible and the infected classes. In other words, individuals can be in one of two possible states: they can be susceptible, where they are not yet infected and are at risk of infection, or they can be infected, where they are assumed to be immediately infectious and capable of passing on infection (Fig 3). The variables in this model are the proportion of susceptible and infected individuals in the population and will be denoted $[S]$ and $[I]$ respectively. Infected individuals are assumed to recover and return to the susceptible class and so the model is commonly referred to as

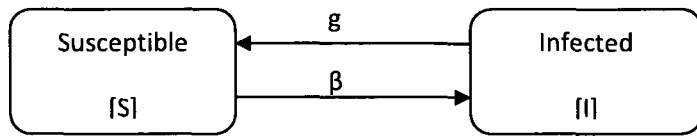
the SIS model; this reflects the passage of individuals from the susceptible class to the infectious class and then back to the susceptible class again. For a susceptible to become infected, one must come into contact with an infected individual (the definition of contact depends on the disease being modeled). Assuming this to be random, the rate at which this happens depends on the number of infected and susceptible individuals. It is directly proportional to $[S][I]$ (the product of both proportions). Given contact between an infected and a susceptible individual, there is a transmission probability β that the infection will in fact be transmitted. Therefore, the rate of infection (transition from the susceptible class to the infected class) is the product of all three values, $\beta[S][I]$. The recovery of infected individuals back into the susceptible class is assumed to happen at a constant rate. Thus, if the duration of the disease is ' δ ' units of time, then the recovery rate (number of individuals who recover per unit of time) is ' g ' where $g = 1/\delta$. The movement of individuals between classes can then be described by the following set of ODEs:

$$\frac{d[S]}{dt} = g[I] - \beta[S][I]$$

$$\frac{d[I]}{dt} = \beta[S][I] - g[I]$$

where $[S]$ and $[I]$ are the dynamic variables (i.e. their values change over time) and $\frac{d[S]}{dt}$ and $\frac{d[I]}{dt}$ are the rates at which they change in time. The solutions of the differential equations, $S(t)$ and $I(t)$, are the proportions of individuals who are susceptible and infected at time ' t '.

Figure 3: Flow diagram of the SIS compartmental model.



Assumptions: Underlying the compartmental model are some basic assumptions. One of the main assumptions is that individuals mix randomly or homogeneously so that each individual comes into contact with other individuals at random. In other words, an individual has the same probability of coming into contact with any other individual in the population regardless of demographics, physical proximity or disease status. More formally, this means that individuals mix according to mass-action kinetics. Mass-action kinetics states that the rate of contacts between susceptible and infected individuals (number of such contacts per unit of time) is directly proportional to the density of the two populations. As a result, we get the term $\beta[S][I]$ for the rate of change from class S to class I (Diekmann & Heesterbeek, 2000).

It is also assumed that each compartment acts like a distinct, homogeneous, well-mixed population, meaning that, within a class, all individuals have similar characteristics relevant to transmission and risk of disease.

The system is generally assumed to be closed, and the total population is assumed to remain constant. The model doesn't account for births, deaths, emigration or immigration which is a reasonable assumption, based on the time scale of most disease progressions relative to the human lifespan. The change in the total population during a

cycle of the disease is usually negligible, except for HIV, in which case these population fluctuations must be taken into consideration.

Finally, the basic SIS model presented above assumes that when individuals become infected, they immediately become infectious (i.e. there is no latent period). An extra class can be added to reflect the latent period; in this case, we would have an SEIS model, where the E class consists of individuals who are exposed and infected, but not yet infectious. The name of the model, SEIS, represents the movement of individuals from being susceptible, becoming infected and latent, then infectious, and finally becoming susceptible again once recovered. Similarly, immunity can be added to the model. In the SIS model, infected individuals recover and return directly to the susceptible class. To include immunity, an extra class can be added to reflect either temporary immunity (individuals eventually return to the susceptible class) or lifelong immunity (individuals remain in the immune class). These models are referred to as SIRS or SIR models, where the R class represents individuals who have been infected and have recovered with immunity.

Limitations: The quality of mathematical models for complex phenomena such as the spread of STIs depends on the accuracy of the underlying assumptions. Violations of these assumptions can reduce the validity of the model and make its predictions less accurate.

For example, the assumption of homogeneity within classes doesn't hold when it comes to modelling STIs; individuals within either the susceptible or infected class do not all have the same risk of contracting an STI. The number of partners an individual has

varies greatly from person to person, even within the same class (either S or I). It is known that, in the presence of infection, having a high number of sexual partners increases a person's risk of contracting an STI (Richert et al., 1993). Therefore, individuals in a given disease-status class are not homogeneous (i.e. their different risk of contracting an STI can be very different). There have been some modified SIS models that attempt to make this homogeneity assumption hold by further sub-classifying individuals based on their level of sexual activity or some demographic factors (Hethcote & Yorke, 1984). This can address the issue of homogeneity but the assumption of random mixing and the dependence of one individual's disease status on their neighbours' status remain problematic.

The assumption of random mixing is also violated when modelling STIs where a contact must be a sexual contact in order to transmit infection. Generally, each individual only has a finite number of sexual partners whom they can infect and be infected by. Consequently, an individual no longer has the same probability of coming into contact (i.e. contact that is capable of directly transmitting infection) with any other individual in the population. The probability is in fact 0 for all those individuals who aren't a sexual partner and greater than 0 if they are.

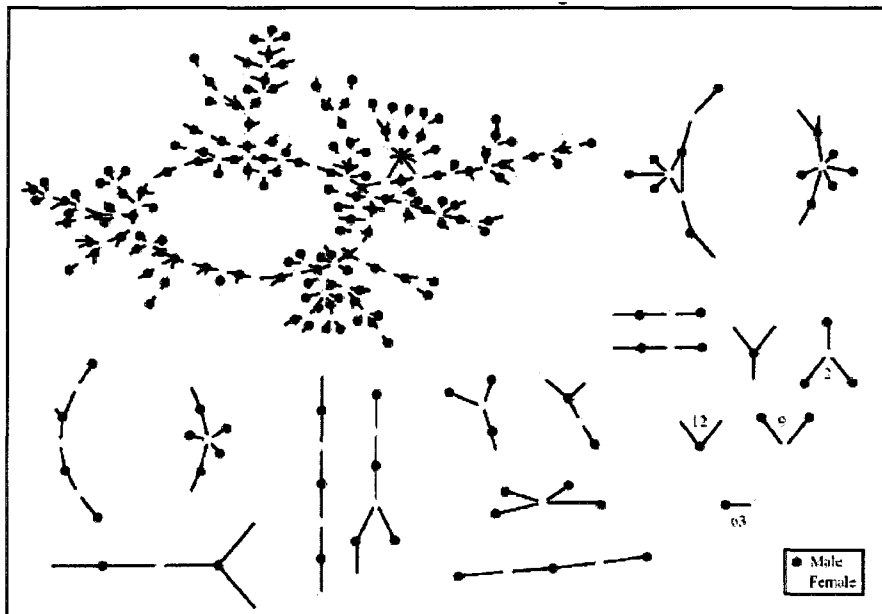
Finally, the model presented above is not appropriate in the study of STIs because it does not take into account the dependence between infected individuals infecting their sexual partners, and the corresponding decrease in their number of susceptible partners which reduces the overall probability of infection being transmitted (Eames 2002; Newman, 2002; Rothenberg et al., 1994; Rothenberg & Narramore, 1996). Consequently, the simple SIS model tends to overestimate the spread of STIs (Keeling, 1999).

Network theory in epidemiology

Social network theory, based on graph theory, has been used extensively in social sciences (Wasserman & Faust, 1994) and is now a powerful tool in the study of infectious diseases, particularly STIs (Rothenberg et al., 1994; Rothenberg, & Narramore, 1996).

Like social networks, sexual networks can be represented as graphs (Fig 4), where individuals are represented by nodes, and sexual contacts or relationships by edges or links connecting nodes which denote sexual contact. Principles of graph theory can then be applied to study the characteristics, structure and the flow of contents across the nodes. In the context of sexual networks, the flow corresponds to the study of disease transmission through individuals and the graph theory measures can be used to determine risk characteristics.

Figure 4: A sexual network graph (Bearman et al., 2004). Each circle represents an individual, either male or female (node). Each line represents a sexual contact (edge) between individuals.



Obviously, sexual networks change over time, but, when modelling dynamics involving a network, it is extremely difficult and computationally demanding to also model the changing network. Consequently, networks are often assumed to be static (i.e. they do not change over time) and partnerships are considered concurrent (i.e. all contacts are active at the same time). The validity of these assumptions depends on the time period represented by the network. For example, if the network represents sexual contacts over a ten year period, the assumptions that the network is static and that contacts are concurrent is much less valid than if the network represents sexual contacts over a one year period.

Integrating Networks into the Compartmental Model

Because of the limitations of the compartmental model, integrating the information from sexual networks into the mathematical model of transmission is crucial for the model to be valid and accurate (Newman, 2002). As mentioned above, an important effect of networks on a model is the presence of correlations between the infection statuses of connected individuals. An infected individual will have infected neighbours (that he/she infects or is infected by), reducing the proportion of susceptible contacts this individual has. The compartmental model, however, doesn't take this correlation into account and assumes all infected individuals have the same proportion of susceptible individuals [S] to whom they can transmit the infection.

A concrete example of the importance of this correlation is that if an infected individual has infected all their sexual partners, then they can no longer contribute to

disease transmission, regardless of how many susceptible individuals there may be in the total population.

Some models have incorporated information on partnerships in order to capture the local sexual network structure (Dietz & Hadel, 1988; Waldstatter, 1989). The problem with these is that they don't account for concurrency (i.e. when one or both individuals have multiple partners with overlapping dates of intercourse). Since transmission occurs only when there is a partnership between an infected individual and a susceptible individual, a partnership consisting of two susceptible individuals is protective. However one or both susceptible partners may have another infected partner outside of this susceptible-susceptible relationship introducing infection into this protective dyad.

The Pair-Wise Model: Eames and Keeling (2002) propose a pair-wise model that predicts the spread of infection through a network, accounting for both the network structure and concurrency. It uses the same approach as the compartmental model described previously, but the variables being modeled are now the sexual partnerships, as opposed to strictly the individuals. In addition, it subdivides these partnerships by the number of sexual partners and allows the existence "triples" (i.e. two partnerships that have a common individual). This way, it accounts for the great variance in the number of sexual partners and concurrency. Consequently, the model incorporates the effects of the entire sexual network and the resulting dependencies into the ODEs.

The compartments or classes are no longer the proportion of susceptible and infectious individuals ($[S]$ and $[I]$ respectively), but are now all possible partnerships or pairs. As before, individuals can either be susceptible or infectious resulting in three

different types of partnerships: both partners can be susceptible ([SS] class), both partners can be infectious ([II] class) or one partner can be infectious and the other susceptible ([IS] or [SI] class). Since partnerships are undirected, [IS] is equivalent to [SI]. These three classes are further broken down according to the total number of sexual partners each individual has denoted by superscript. For example, $[S^n]$ is the proportion of susceptible individuals with 'n' different sexual partners and $[S^n I^m]$ is the proportion of partnerships between a susceptible individual with 'n' sexual partners and an infectious individual with 'm' sexual partners (see Table 1 for detailed notation).

Table 1: Notation used for the pair wise model.

$[S^n]$	number of susceptible individuals with 'n' partners
$[I^n]$	number of infected individuals with 'n' partners
$[S^n I^m]$	number of pairs made up of a susceptible individual with 'n' partners and an infectious individual with 'm' partners
$[S^n S^m I^q]$	number of triples made up of a susceptible individual with 'm' partners paired with both a susceptible individual with 'n' partners and an infected individual with 'q' partners
$\sum_q [I^n S^m I^q]$	number of $[I^n S^m I^q]$ triples summed over all possible values of q
'g'	recovery rate
' β '	transmission probability

As before, one of two things can happen. Susceptible individuals can be infected by an infectious partner and infected individuals can recover. Therefore, the ODE for the change in number of infected individuals with 'n' sexual partners for example, is the following:

$$\begin{aligned}\frac{d[I^n]}{dt} &= \beta [S^n I^1] + \beta [S^n I^2] + \dots + \beta [S^n I^m] - g[I^n] \\ &= \beta \sum_q [S^n I^q] - g[I^n]\end{aligned}$$

where \sum_q refers to the sum of the terms that immediately follow, for all possible values of 'q'.

Each term in the ODE represents the different ways in which an $[I^n]$ can arise (come into the $[I^n]$ class) and be lost (leave the $[I^n]$ class). An $[I^n]$ arises when an $[S^n]$ becomes infected and a susceptible individual must have at least one infected partner for him or her to become infected. Therefore, given that he or she has sexual contact with an infected partner (that he or she is part of an $[SI]$ pair), newly infected individuals arise with probability ' β '. Any given infection occurs at the same rate, regardless of the total number of sexual partners that the infected individual has. This is why the infection term is the sum of all partnerships between an $[S^n]$ and an infected individual with any number of sexual partners ($[S^n I^1]$, $[S^n I^2]$, $[S^n I^3]$, ..., $[S^n I^k]$), where 'k' is the maximum number of sexual partners observed. An $[I^n]$ can be lost when they recover at a rate 'g'.

Similarly, the ODE for change in the number of pairs, say $[S^a I^b]$ for example, is the following:

$$\frac{d[S^a I^b]}{dt} = \beta \sum_q [S^a S^b I^q] + g[I^a I^b] - \beta [S^a I^b] - \beta \sum_q [I^q S^a I^b] - g[S^a I^b]$$

An $[S^a I^b]$ pair can arise one of two ways. One is when the $[S^b]$ individual from an $[S^a S^b]$ pair becomes infected by another (infected) partner. Again, since the number of sexual partners of the infected individual doesn't affect the rate at which they infect the $[S^b]$ individual, the infection term is the sum of all partnerships between the $[S^b]$ individual from a $[S^a S^b]$ pair and an infected individual with any number of partners ($[S^a S^b I^1]$, $[S^a S^b I^2]$, ..., $[S^a S^b I^c]$), where 'c' is the maximum number of sexual partners observed. The second way an $[S^a I^b]$ pair can arise is when the $[I^a]$ individual from a $[I^a I^b]$ pair recovers (at rate 'g'). An $[S^a I^b]$ pair can be lost one of three ways. Two are when the $[S^a]$ individual from a $[S^a I^b]$ pair becomes infected by either the $[I^b]$ or a second infected partner, regardless of the number of sexual partners of that second infected partner ($[I^1 S^a I^b]$, $[I^2 S^a I^b]$, ...). The third is when the $[I^a]$ individual from a $[I^a I^b]$ pair recovers (at rate 'g'). Table 2 summarizes all the transitions, or events, that can occur and the corresponding ODE terms.

Table 2: Infection and recovery events of pairs and the corresponding ordinary differential equation terms.

Starting pair	End pair	Event	Corresponding ODE terms (subtracted from the ODE of the starting pair and added to the ODE of the end pair)
$[S^n S^m]$	$[S^n I^m]$	Infection of S^m by an infected partner outside of the $S^n S^m$ partnership (at rate β)	$\beta \sum_q [S^n S^m I^q]$
$[S^n S^m]$	$[I^n S^m]$	Infection of S^n by an infected partner outside of the $S^n S^m$ partnership (at rate β)	$\beta \sum_q [I^q S^n S^m]$
$[S^n I^m]$	$[I^n I^m]$	Infection of S^n within the partnership (at rate β)	$\beta [S^n I^m]$
$[I^n S^m]$	$[I^n I^m]$	Infection of S^m within the partnership (at rate β)	$\beta [I^n S^m]$
$[S^n I^m]$	$[I^n I^m]$	Infection of S^n by an infected partner outside of the $S^n I^m$ partnership (at rate β)	$\beta \sum_q [I^q S^n I^m]$
$[I^n S^m]$	$[I^n I^m]$	Infection of S^m by an infected partner outside of the $I^n S^m$ partnership (at rate β)	$\beta \sum_q [I^n S^m I^q]$
$[S^n I^m]$	$[S^n S^m]$	Recovery of I^m (at rate g)	$g [S^n I^m]$
$[I^n S^m]$	$[S^n S^m]$	Recovery of I^n (at rate g)	$g [I^n S^m]$
$[I^n I^m]$	$[S^n I^m]$	Recovery of I^n (at rate g)	$g [I^n I^m]$
$[I^n I^m]$	$[I^n S^m]$	Recovery of I^m (at rate g)	$g [I^n I^m]$

The dependency between variables in the model means that the number of individuals in each class, infected or susceptible, depends on the number of pairs in that class. Similarly, the number of pairs depends on the number of “triples” involving that pair. A “triple” consists of an individual who has two different sexual partners (see figure 5). These “triples” are necessary to allow for infection from outside the particular pair being modeled. The number of “triples” in turn depends on the number of “quads” where

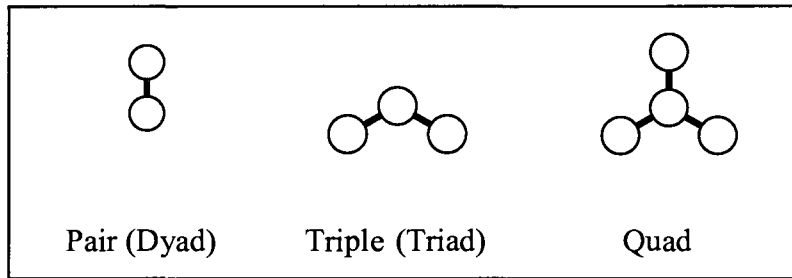
a “quad” consists of an individual with three different sexual partners (see figure 5) and so on. In a closed population, every term in any of the ODEs must have a corresponding ODE to define its own rate of change over time.

Therefore, each “triple” must have corresponding ODE, $\frac{d[\text{no. of “triples”}]}{dt}$. But the rate of change of any “triple” is a function of the number of “quads” involving that “triple” and therefore the rates of change of these “quads” must also be defined in additional ODEs. In order to end this cycle and close the population, an approximation needs to be made at some level. Therefore, even if the number of “triples” is known, an approximation in terms of pairs must be made (Ferguson & Garnett, 2000). Eames and Keeling (2002) use the following approximation to obtain the number of “triples” (made an individual in class B with ‘n’ partners and an individual in class D with ‘p’ partners in a partnership with a common individual in class C with ‘m’ partners) in terms of the number of pairs:

$$[B^n C^m D^p] \approx \frac{(m-1)}{m} \frac{[B^n C^m] \times [C^m D^p]}{[C^m]}$$

where ‘m’ is the number of partners of the common individual, C. This approximation supposes that all “triples” are formed by two pairs who share a common individual but are otherwise independent (Ferguson & Garnett, 2000; Keeling, Rand & Morris, 1997). This approximation doesn’t capture triangular connections but this isn’t a concern since we are only using the data for heterosexual partnerships. A complete list of the differential equations of the pair-wise model can be found in Appendix A.

Figure 5: Visual representation of a pair, a triple and a quad.



Assumptions: The pair-wise model uses the same approach as the SIS compartmental model and the same assumptions apply: homogeneity within classes, random mixing, closed population, no latent period and no immunity. The main concern in the simple SIS model was that the number of sexual partners (a major risk factor for STI infection) was not homogeneous within classes but the pair-wise model further breaks down the classes by number of sexual partners and assuming that the classes are homogeneous in other characteristics relevant to STI transmission is acceptable.

Purpose of the research

The main objective of this project is to evaluate the accuracy of the pair-wise network model proposed by Eames & Keeling (2002), by examining how well it predicts the dynamics of chlamydia spreading through a network, compared to the simple SIS model, using actual data from Manitoba. First, the chlamydia pair-wise and simple SIS models will be built, then used to make predictions of how the disease will spread, based on actual initial conditions. Finally, these predictions will be compared to each other and to data collected two years later.

The research questions are: 1) How do the predictions of the pair-wise network model for STI transmission in a network compare to those of simple SIS model's? 2) Are the predictions significantly different when compared with actual data collected for the same time period?

Significance: Models are often used to make predictions on the effectiveness of infectious disease control strategies. Funding the most effective control strategies is more important now than ever. The numbers of STIs both in the developed and the developing world are on the rise together with an increase in bacterial STIs in the developed world (WHO, 2001). A new variant of chlamydia which evades two of the three most widely used test technologies in the developed world has emerged (Herrmann, 2007), and the CDC in Atlanta has been forced to recommend only one drug for the treatment of uncomplicated gonorrhea, due to high levels of resistance. Finally, new strategies, such as network-enhanced contact tracing (Rothenberg & Narramore, 1996), need to be evaluated in order to determine their effectiveness. With the shrinking resources that we face today, maximizing the impact of our efforts is especially important. It is therefore crucial that the predictions used to make these decisions be accurate.

Simple compartmental models are still widely used, although we know they can be inappropriate. We will test the pair-wise network model which has been presented as a robust and reliable model that takes the network structure into consideration, thus making up for the major shortcomings of SIS compartmental models (Eames & Keeling, 2002). The pair-wise network model has been built using real data, but its predictive ability has

yet to be evaluated. The proposed study will be the first attempt to our knowledge of applying the pair-wise network model to empirical data.

Methodology

The data

In Manitoba, chlamydia is a notifiable disease, and Manitoba Health maintains an STI registry containing information on each laboratory confirmed case of *C. trachomatis* in the province, as well as on their contacts. This is done in accordance with The Public Health Act (1987), and Diseases and Dead Bodies Regulation (1988). As part of the provincial STD control strategy (2001), these data record cases and co-ordinate contact tracing, which is the standard public health prevention strategy for sexually transmitted disease since at least 1948, if not earlier (Iskrant & Kahn, 1948).

This database has been the subject of other research and is well described in Jolly et al. (2005). When a laboratory identifies a positive result for chlamydia, the report is forwarded to the Communicable Disease Control (CDC) Unit of Manitoba Health. For the 1990-1992 time period, completeness of reporting was very high, about 95% of all chlamydia cases, as the overwhelming majority of specimens were tested at Cadham Public Health lab which had computerized the reporting of all notifiable isolations and detections to Manitoba Health CDC (MCDC) nightly. For each report of a positive result for chlamydia, an identification number, followed by a letter, was assigned. If the individual who tested positive (known as an index case or simply a case), had been diagnosed with a reportable STI in the previous three years, then a record already existed for that case. The new report was then assigned the same identification number, but the letter following it was now the next letter in the alphabet to indicate repeated diagnoses (i.e. 'A' for first diagnosis, 'B' for the second, 'C' for the third, etc). If the case did not

have a previous record then a new, unique identification number was created followed by the letter 'A' (for first diagnosis).

Next, the corresponding public health unit was notified and a public health nurse or the responsible physician would follow up with the case to complete a Notification of STD form (see Appendix B). The form was forwarded to the MCDC, where the report's identification number, along with the case's laboratory result, demographic information, symptoms, treatment and sexual contact information, was entered or updated in the Manitoba Health STI Registry database.

Next, sexual partners (i.e. contacts) of the case were notified. Notification was carried out one of three ways. First, the contacts' information could have been entered on the form and a public health nurse or primary caregiver would have followed up with them directly. Second, the health professional could have taken the contacts' information but allowed the case to inform his or her own contacts, knowing that if the contacts did not come in for testing and treatment within 24 hours, the provider would intervene. Finally, if the case was judged to be capable of locating and notifying his or her own contacts, it is possible the provider did not note the contacts' information, in which case the MCDC would not have records for those contacts. As a result, the contact database is not as complete or as accurate as the case database, but it is nonetheless the best data of its kind in Canada.

The information obtained on the contacts of cases was entered into a second database. The contact's name and demographic information as well as the identification number of the case who named them were entered into this contact database. Additional information, such as whether or not the contact was reached, tested or treated was also

recorded. If a contact tested positive for chlamydia and this was reported to the lab, then he or she became a case, was followed up with, and added to the first database (the STI Registry).

Information in the databases was regularly validated against the Manitoba Health Insurance Registry, which includes nearly the entire Manitoba population because of its access to government-funded healthcare.

To avoid duplicate entries in the data as much as possible, the following guidelines were used to determine if two records referred to the same individual:

- If the first name and surnames matched exactly AND:
 - i. at least two of the three birth date entries were the same or,
 - ii. the month and day of the birth date were the same but reversed or,
 - iii. the addresses were the same (including apartment and house numbers),then the reports were deemed to belong to the same individual.
- If the first name was shortened or if the surname was the same but spelled differently AND:
 - i. one of the three birth date/address conditions mentioned above was met.then they were deemed to belong to the same individual.
- If contacts (named by confirmed cases) have the first name shortened and/or same surname but spelled differently AND:
 - i. one of the three birth date/address conditions mentioned above was met.
 - ii. the confirmed case who named the contact matched or,
 - iii. the ages matched (allowing for the year of reporting) and the addresses matched exactly.

Ethics approval was obtained from The Ottawa Hospital Research Ethics Board (OHREB) on July 28, 2008 (see Appendix C).

The simulations

In order to use the model to make predictions concerning the spread of chlamydia through the network, simulations were run using MatLab® software (TheMathWorks, 2007). The differential equations were programmed into MatLab, along with the initial conditions and parameter values g and β .

The data from both Manitoba STI databases was available for this research to build the model and define initial conditions for the simulations. It was obtained in the form of two tables; one for the cases and the other for the contacts. In order to link both tables, each individual was assigned a new unique indicator such that when a contact is also an index case (or vice versa) they are recognized as the same person. The entire network, using three years of data collection, consisted of 20,223 nodes (i.e. individuals). Because of the timescale of the pair-wise model and the assumption that the network does not change, only data from 1990 was used to determine initial conditions. This smaller network, using one year of data collection, consisted of 6,838 nodes and was constructed with relationships between all pairs using the network software Pajek (Batagelj & Mrvar, 2007). The software was then used to determine the degree of each node (i.e. the number of contacts or sexual partners for each individual) and the degree frequency distribution. Same-sex couples, cases diagnosed based on clinical symptoms alone or with missing laboratory test information (32 records or 0.019% in all) were excluded. The initial values

required for the simulations were obtained from the Manitoba data using SAS® (SAS Institute Inc. ©2002) along with Pajek (Batagelj & Mrvar, 2007).

The model parameter values for g and β were based on the literature. In recent work, the duration of infection has been determined as 10 months for chlamydia, giving a value of 0.1 for g (Jolly et al., 2005). As for β , the transmission probability of chlamydia, the value 0.327 was used. This parameter value is very hard to quantify because it depends on many factors. Given a sexual partnership, the value depends on the probability per sexual act, the number of sexual acts in a given relationship, the use of condoms, the presence of other STIs amongst others factors. Often in the literature, the parameter is not adequately defined in regards to these factors, resulting in a wide range of published values (Katz, Caine & Jones, 1990; Turner et al., 2006). Katz (1992) presents a table with the probability estimates for a single exposure depending on the average number of contacts and whether it is male-to-female transmission or vice versa. These estimates were derived from a deterministic model and using contact tracing data from Indianapolis, Indiana. Because of the wide range of values in the table itself, a weighted average was calculated. Assuming that the population is 50% male and 50% female, the weighted average was calculated based on the proportion of individuals in the Manitoba data with 1, 2, 3, 4, 5 or 6-12 contacts. The result, 0.327, was used for value of β in the model simulations.

The MatLab® code for each simulation can be found in appendix D. The first m-files ('simple.m' and 'thesis.m') are the function files. They express the differential equations of the model in vector form. The other m-files ('Ssolver.m' and 'Tsolver1_1.m'/'Tsolver1_2.m'/'Tsolver2_1.m'/'Tsolver2_2.m') are used to solve the system of differential equations listed in the corresponding function file and plot the

solutions over time. These include the parameter values and initial conditions in vector form.

A slight adjustment had to be made when coding the differential equations to avoid dividing by zero. The value 0.0001 was added to all denominators such that even if the $[S^n]$ variable in the denominators had value of zero, the denominator would not be zero. Since the only terms in the model with division are the “triples” approximation, the number of individuals central to that triple ($[S^n]$ for different values of ‘n’) is always in the denominator. If $[S^n]$ has a value, then the addition of 0.0001 is insignificant. On the other hand, if $[S^n]$ is zero, then the numerator would also be zero, since the number of pairs involving $[S^n]$ (the central individual in the triple) is necessarily in the numerator (see the approximation formula on p.16) and if there are no susceptible individuals with ‘n’ partners ($[S^n]$) then there are no pairs (or triples) involving such an individual. Therefore, the numerator is equal to zero, making the entire term equal to zero.

Building the pair-wise model for chlamydia

Based on the data, in 1990, the number of sexual contacts ranged from 1 to 12 partners. The pair-wise model was built from the six basic equations in Appendix A for every observed n/m combination (n=1 to 12, m=1 to 12). The resulting model has 178 variables representing the proportion of susceptible ($[S^n]$) and infected individuals ($[I^n]$) for all values of ‘n’, as well as the proportion of pairs ($[S^n S^m]$, $[S^n I^m]$, $[I^n I^m]$) for all observed n/m combinations. Appendix E lists the corresponding system of 178 differential equations.

Initial conditions: In order to run simulations with the pair-wise model, we need to define some initial conditions (i.e. values of each variable at time $t=0$). Since we have 178 variables, we needed 178 initial values. Appendix F has the SAS® code used to obtain these initial values from the Manitoba data.

First, only cases of chlamydia in 1990 were selected from the cases table. Then, each contact's information, including the newly assigned unique indicator (from the contacts table) was linked to the corresponding case using the identification numbers given by Manitoba Health referring to the case that named them. Of the 5515 resulting links, 681 (approximately 12%) were removed because they could not be matched up in a dyad (i.e. contacts had no corresponding cases or vice versa). These 681 observations with missing information did not seem different from the others with respect to age or sequence (repeaters) but there were more females in the missing group (60% vs 24%) who also had zero numbers of sexual contacts (58% vs 5%) which would explain why they had no one to match up with. This group of people had characteristics consistent with patients who tested positive on screening tests, and who may have been infected by a previous partner. In five records, the case identifier was listed reflexively as the contact. In network terms, this represents a loop, which in this context, is nonsensical must be and due to data-entry errors. Therefore, they were excluded from the analysis leaving 4829 dyads, of which 482 were duplicate partnerships. In the end, there were 4347 unique dyads involving 6838 individuals. The network was then constructed and the degree (i.e. number of sexual partners) for each individual was obtained from Pajek. Finally, counts and cross-tabulations were produced with SAS® in order to calculate the initial values of most

variables. The total population used to calculate the proportions of individuals was 1,105,668 which was the total population in Manitoba in 1990 (Statistics Canada).

Since there is no information on the number of sexual partners (i.e. no known degree distribution) for susceptible individuals, it had to be estimated in order to get initial values for these variables as did the number of pairings between two susceptible individuals. The initial number of initially susceptible individuals was calculated by subtracting the total number of initially infected individuals from the total population ($1,105,668 - 3,669 = 1,101,999$) who then needed to be assigned degrees. Two different methods were used:

Case 1: the distribution of susceptible individuals over the different degrees 'n' (n=1 to 12), was proportional to the distribution of susceptible individuals in the observed 1990 Manitoba data. Since there were a total of 3,169 susceptible individuals in the data, the ratio of individuals in the data to the total population is approximately 1:347 (from 3,169:1,101,999) (Appendix G). In this case, the majority of initially susceptible individuals have one or two sexual partners and none have more than six.

Case 2: the distribution of susceptible individuals over the different degrees 'n' (n=1 to 12), was proportional to the distribution of infected individuals in the observed 1990 Manitoba data. Since there were a total of 3,669 infected individuals in the data, the ratio of individuals in the data to the total population is approximately 1:300 (from 3,669:1,101,999). In this case, initially susceptible individuals have any number of partners between 1 and 12.

In a sense, these two cases represent two extreme distributions of the number of sexual partners for initially susceptible individuals; case 1 is more conservative and case 2 is more liberal. The true distribution of degrees in initially susceptible individuals is most likely somewhere in the middle.

Next, the number of $S^n S^m$ pairs (for $n=1$ to 12 and $m=1$ to 12) need to be determined. This was done by assigning individuals to given pairs while respecting the degree distribution over S^1 to S^{12} . Again, two different methods were used:

- i) Individuals of degree one (i.e. with one sexual partner, S^1) were assigned to $S^1 S^m$ pairs ($m=1$ to 12) first. Then, individuals with degree two followed by individuals with degree three and so on until all initially susceptible individuals are assigned to pairs.
- ii) Conversely, individuals of degree 12 were assigned to $S^{12} S^m$ pairs ($m=1$ to 12) first. Then, individuals with degree 11 followed by individuals with degree 10 and so on until all initially susceptible individuals are assigned to pairs.

Assigning individuals to pairs in increasing degree order, (i), results in fewer pairs of low degree combinations (such as $S^1 S^2$) and more of high degree combinations (such as $S^8 S^{11}$) than assigning individuals to pairs in decreasing degree order, (ii). Again, these two cases represent two extremes; (i) is more liberal and (ii) is more conservative, with the true distribution of pairings is somewhere in the middle.

In all, four different scenarios were explored when estimating initial values for susceptible individuals and pairs where both partners are susceptible (see table 3).

Table 3: Description of the four initial condition scenarios explored for the pair-wise model.

		Degree distribution	
		Case 1 Like the susceptible individuals in the data	Case 2 Like the infected individuals in the data
Order in which individuals were assigned to SS pairs	i S1 to S12	Somewhat conservative (most individuals have fewer partners but individuals with a higher number of partners are paired together more often)	Most promiscuous (more individuals have many partners and individuals with a higher number of partners are paired together more often)
	ii S12 to S1	Most conservative (most individuals have fewer partners and individuals with a higher number of partners are paired together less often)	Somewhat promiscuous (more individuals have many partners but individuals with a higher number of partners are paired together less often)

Assumptions: Based on the available data and the particular disease, our model has some underlying assumptions in addition to those previously mentioned – it also assumes that the network doesn’t change, all contacts are concurrent and rates of intercourse are constant.

The assumption of closed population is reasonable when modelling chlamydia. As stated earlier, the mean duration of infection for chlamydia has been found to be 10 months (Jolly et al., 2005). Therefore, the timescale of the disease is much faster than the

timescale of births and deaths, making any variation in population negligible in the disease model (Brauer, 2008).

Incubation and latent periods for chlamydia are poorly defined (Holmes et al., 2008) and not enough is known about immunity to quantify it. Clearly, a single infection will not result in immunity, since re-infection is common. It has been suggested that there can be some temporary degree of immunity (Brunham & Rekart, 2008) but there is not enough detailed research yet. Therefore, assuming no latent or immune classes in the model is reasonable given the information available (Holmes et al., 2008).

Trying to model the changes in network structure (i.e. edges) in addition to the changes in individuals' disease status has been attempted (Ferguson & Garnett, 2000), but it is very complex and beyond the scope of this project. Therefore, the assumption of a constant network is necessary to maintain a manageable model. Given this assumption, only data from 1990 will be used for initial conditions to minimize the time period covered by the model. Assuming a sexual network remaining constant over a shorter time period is more realistic.

Since the number of sexual partners in the study population ranges from 1 to 12, if all possible n/m combinations of $[S^n S^m]$, $[I^n I^m]$ and $[S^n I^m]$ are considered, 324 variables result in a model with as many differential equations. In order to reduce the model to a reasonable size, some of the equations will be excluded from analysis based on the constant network. Not all possible n/m combinations for $n=1$ to 12 and $m=1$ to 12 exist in the study population (Table 2). Many of the possible degree combinations are not observed at all in the study population; especially those with a high number of partners. For example, there are no pairings between an individual with 6 sexual partners and one

with 8 sexual partners (6/8 degree combination). Since the network is assumed constant, the number of partners and links don't change, only disease statuses change over time. Therefore, if there are no pairs with a 6/8 degree combination at time $t=0$ then there will be none for the entire running time of the model. Even if the corresponding differential equation was coded into the model, since its initial value is zero, it would remain zero. Based on this, the differential equations for pairs that are not present in the 1990 data (i.e. initial conditions of the model) will be excluded from the model altogether.

Table 4: Number of pairs between an individual with 'm' sexual partners and one with 'n' sexual partners for each possible combination of $m=1$ to 12 and $n=1$ to 12*.

m n	1	2	3	4	5	6	7	8	9	10	11	12
1	1630	1256	512	298	136	53	43	38	32	8	9	10
2		101	80	37	20	11	4	7	4	1	1	1
3			12	13	7	1	1	1	0	0	0	0
4				5	3	4	0	1	0	1	0	1
5					2	0	0	0	0	0	0	0
6						1	1	0	0	0	0	0
7							0	0	0	0	0	0
8								0	0	0	1	0
9									0	0	0	0
10										0	0	0
11											0	0
12												0

* Since disease status is not considered, the pair $m=1/n=4$ is equivalent to the pair $m=4/n=1$

One problem with this assumption is that the data provides information on only individuals who were infected with chlamydia and their contacts (i.e. [SI] and [II] pairs);

there is no information on the pairings between two susceptible individuals (i.e. [SS]). Since excluding the n/m combinations absent from the data altogether, also excludes the corresponding pairs of susceptible individuals, it could be argued that existing [SS] pairs are mistakenly excluded; $[S^6S^8]$ for example. If in fact there was an $[S^6S^8]$ pair, then it would be possible for one of these individuals to be infected by one or more of their other partners and become an $[I^6S^8]$ or $[S^6I^8]$ pair. However, degree combinations that did not occur in the chlamydia data will be assumed not to occur in the $[S^nS^m]$ population. For example, if there existed an individual with six sexual partners paired with an individual with eight sexual partners in the general population, it is very likely that one of the individuals would have become infected (i.e. would be present in the 1990 chlamydia data). The validity of this assumption is arguable but it is necessary for the model to be reduced to a reasonable size. And it is reasonable, given that the degree combinations affected by this assumption are higher-order pairings. The number of equations in the model after the removal of all the degree combinations not present in the data is 178 compared with the 324 of all possible combinations.

Finally, the assumptions that all partnerships are active simultaneously and that each has the same rate of intercourse are necessary, in the absence of anything to the contrary.

Comparing the models

Each of the model simulations were run until the system reached an equilibrium (i.e. proportions stabilized and remained constant). At this point, infection has not ceased to occur, but rather the rate at which individuals become infected is equal to the rate at

which individuals recover, therefore the proportions remain constant unless some condition is changed.

The prediction of interest is for a two-year period, therefore the prevalence (i.e. [I]) was recorded at $t=24$ months for each simulation.

Using the Manitoba data, actual incidence rates of chlamydia for 1991 and 1992 were calculated. The network was built the same way it was for 1990; using SAS® and Pajek software packages and the number of newly infected individuals was calculated. There were 3,779 newly infected individuals in 1991 and 2,968 in 1992. The total population of Manitoba was 1,109,614 in 1991 and 1,112,696 in 1992 (Statistics Canada). Based on these numbers, the cumulative incidence was 341 per 100,000 for 1991 and 267 per 100,000 for 1992.

The Manitoba data gave us the cumulative incidences (CI), but the model simulations predicted prevalence over time. Therefore, in order to compare the simulation results to the data, we must convert the cumulative incidences (CI) to prevalences. Assuming a constant incidence rate per year, an average duration (D) of 10 months for chlamydia and Aschengrau & Seage's (2003) formulas, we get a prevalence (P) of 276 per 100,000 in 1990, 284 per 100,000 in 1991 and 222 per 100,000 in 1992.

Formulas: $IR = CI_i/t_i$, where $t_i=1$ year since our CI was for 1 year; and
 $P = IR \times D$

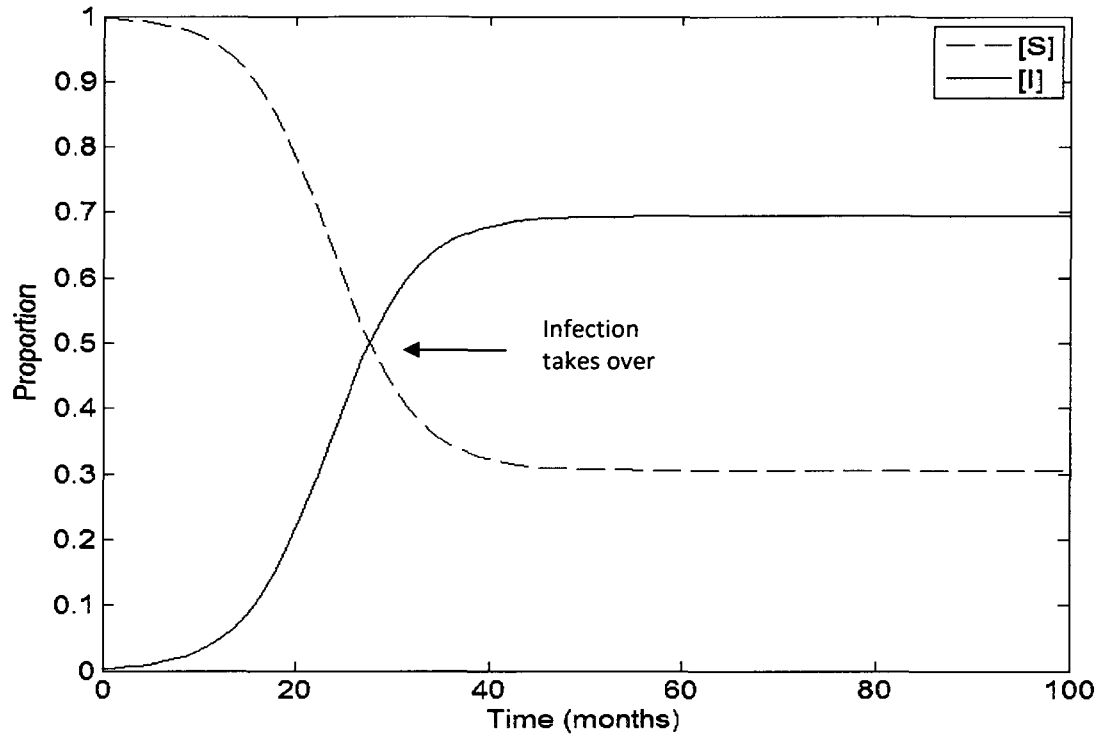
Results

Recall that $[S]$ represents the proportion of the total population that is susceptible, and $[I]$ represents the proportion of the total population that is infected. Since the entire population is either susceptible or infected at any time, the sum $[S]$ and $[I]$ must always be equal to one. In other words, as either $[S]$ or $[I]$ increases, the other must decrease. This makes sense because we have a closed population and two classes. No new individuals enter the population, so if people leave one class, they necessarily enter the other class. Also, note that plotting $[I]$ plots the prevalence over time (i.e. the proportion of infected individuals at time t , accounting for recovered individuals).

Simple SIS model

Figure 6 displays the solutions to the simple SIS model obtained from the simulation, using the same initial values of $[S]$ and $[I]$ as the pair-wise model. The simulation was carried out until the values of $[S]$ and $[I]$ reached equilibrium which happened around 70 months.

Figure 6: Solutions of the simple SIS model. Initial values were: $[S]= 1,101,999/1,105,668$ and $[I]=3669/1105668$.



The simulation predicts that the infection will take over after approximately 33 months at which point both $[I]$ and $[S]$ are 0.5, indicating that half of the population is infected. $[I]$ continues to increase until almost five and a half years (65 months) later when it levels off.

Pair-wise model

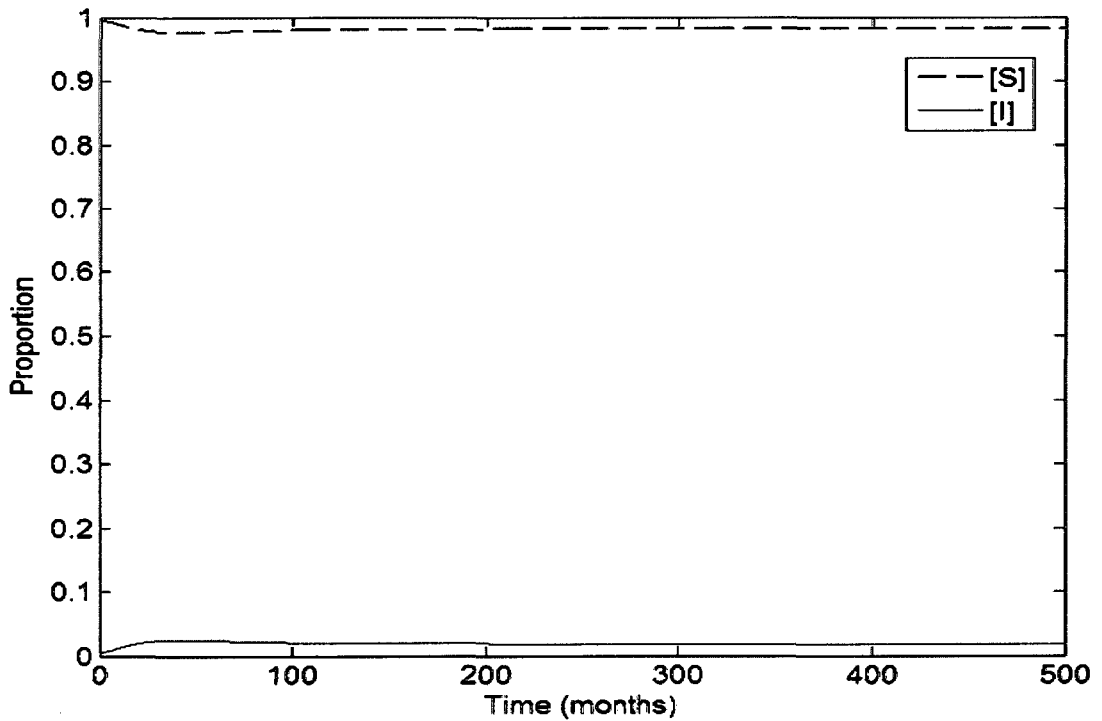
Figures 7 and 8 are the solutions to the pair-wise model obtained from the simulations. The proportions of susceptible and infected individuals were summed over all values of 'n' (i.e. $[S]$ is the sum of all $[S^n]$ and $[I]$ is the sum of all $[I^n]$ for $n=1$ to 12).

Figure 7 is case 1; where the distribution of the proportions of susceptible individuals $[S^n]$, $n=1$ to 12, is proportional to the distribution observed in the susceptible individuals of the Manitoba data. This results in most individuals having few partners.

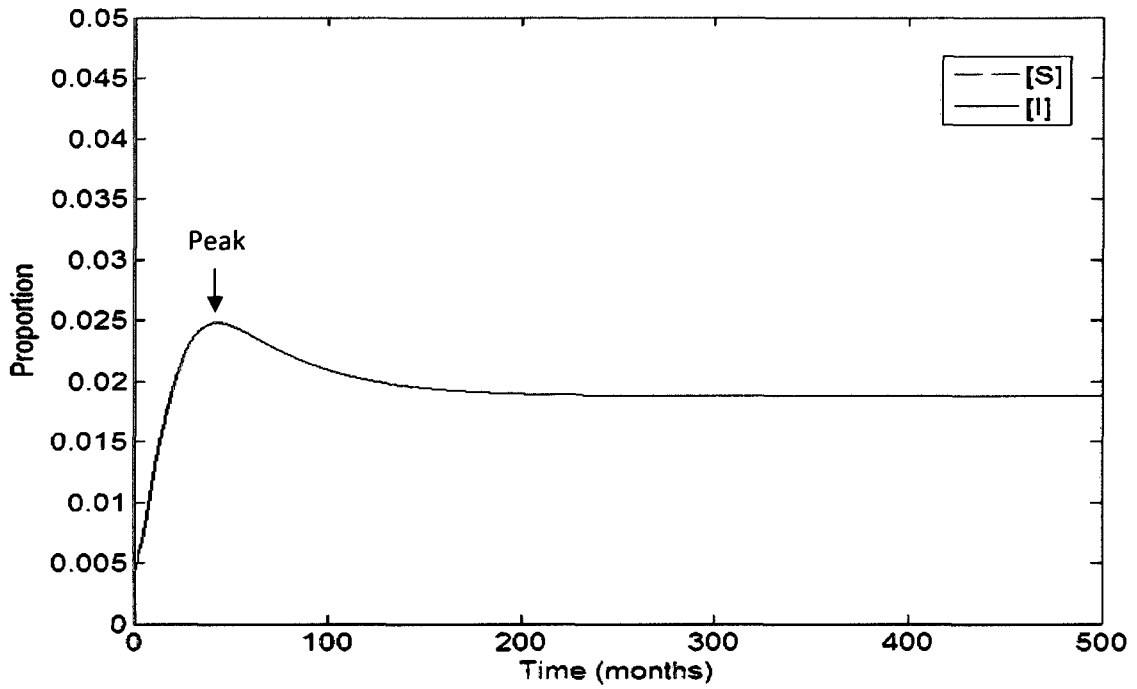
Furthermore, in case 1i, the order in which individuals are assigned to pairs is S^1 to S^{12} , resulting in individuals with the highest number of partners pairing up together more often, while case 1ii is the reverse (S^{12} to S^1), resulting in individuals with the highest number of partners pairing up together less often.

Figure 7: Solutions of the pair-wise model; case 1. Initial values were: $[S]=1,101,999/1,105,668$ and $[I]=3669/1105668$. See Appendix D for the specific values of $[S^n]$ s and $[I^n]$ s.

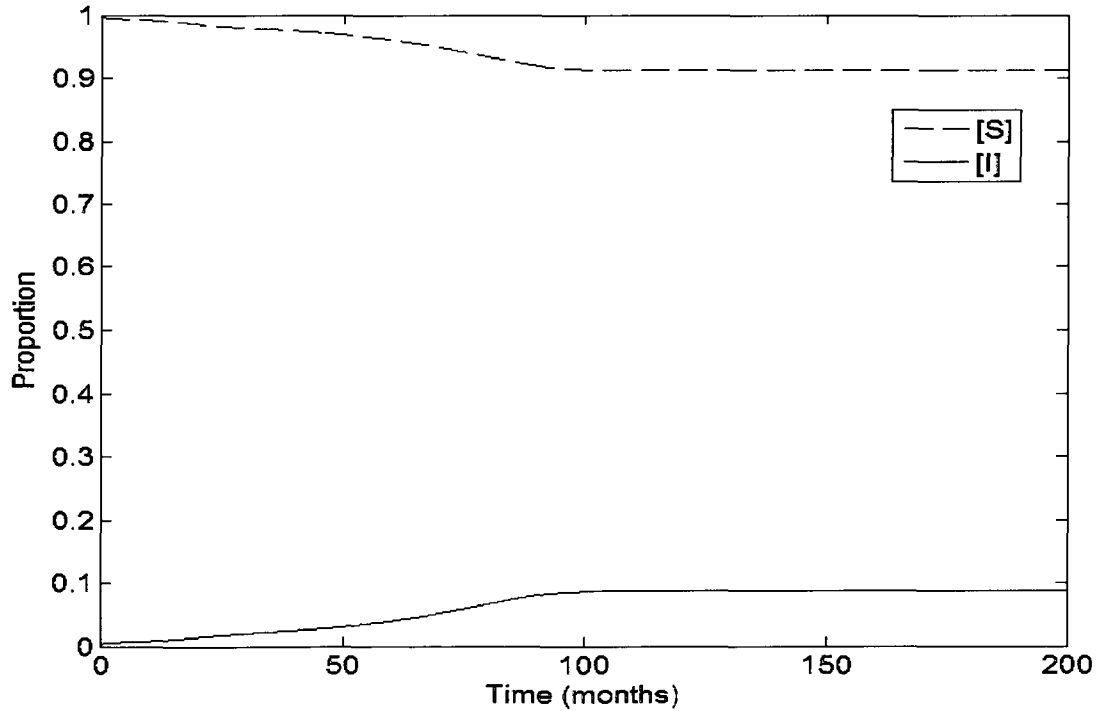
- a) Case 1i: The distribution of initial values for $[S^n]$ is proportional to that of the susceptible individuals in the data and the order in which individuals are assigned to pairs is from S^1 to S^{12}



b) Close-up of the solution for [I]; case 1i.



c) Case 1ii: The distribution of initial values for $[S^n]$ is proportional to that of the susceptible individuals in the data and the order in which individuals are assigned to pairs is from S^{12} to S^1

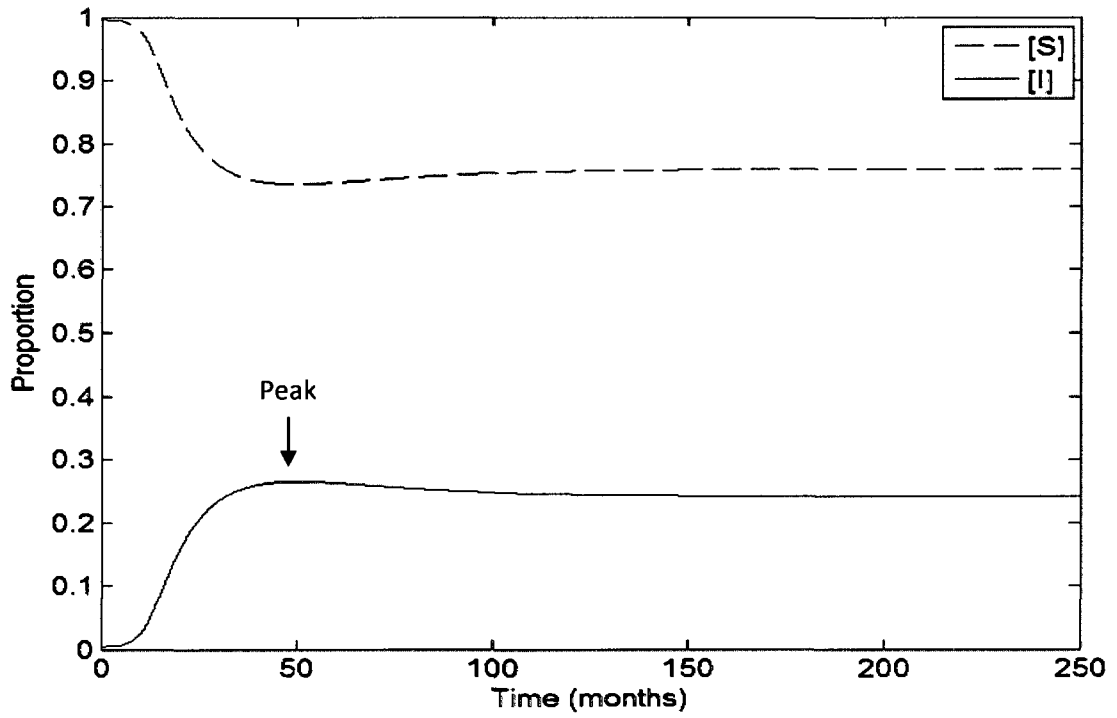


In case 1 (both i and ii), the simulations predict that the infection never takes over. For the case 1i, the proportion of infected individuals, $[I]$, gradually increases to its peak value of 0.0248 at around 42 months, then it decreases and eventually reaches its equilibrium point after almost 500 months. In case 1ii, on the other hand, the proportion of infected individuals, $[I]$, gradually increases to its equilibrium after about 160 months (without peaking first).

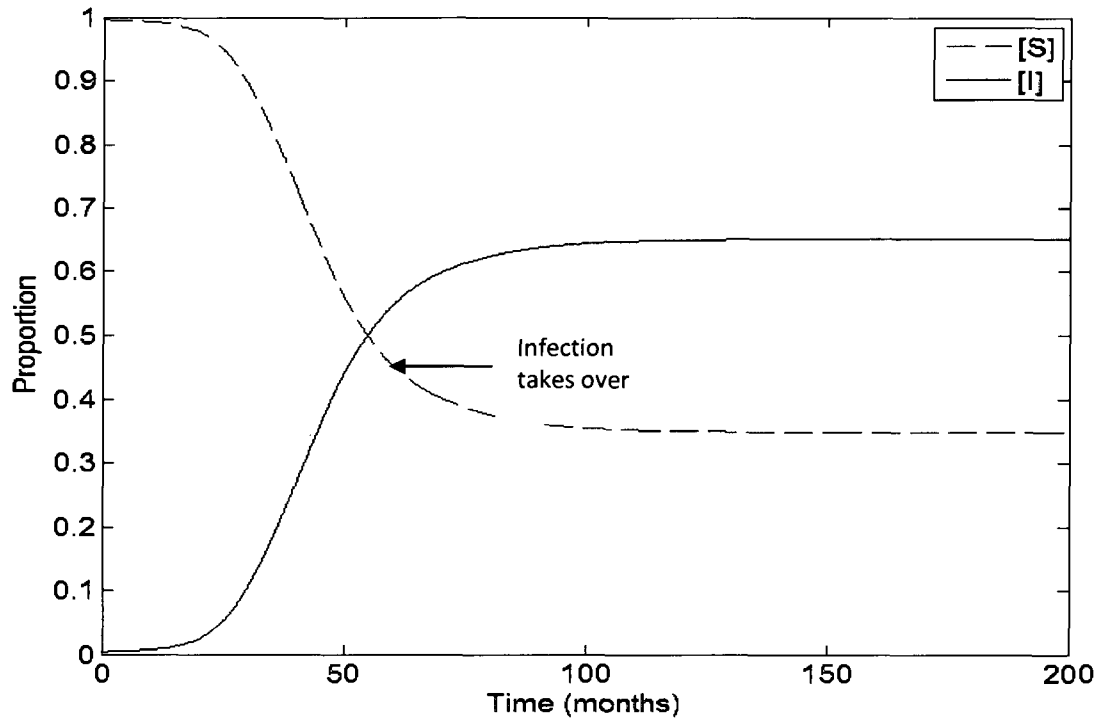
Figure 8 is case 2; where the distribution of the proportions of susceptible individuals $[S^n]$, $n=1$ to 12, is proportional to the distribution observed in the infected individuals of the Manitoba data. This results in more individuals having many partners. Furthermore, in case 2i, the order in which individuals are assigned to pairs is S^1 to S^{12} , resulting in individuals with the highest number of partners pairing up together more often, while case 2ii is the reverse (S^{12} to S^1), resulting in individuals with the highest number of partners pairing up together less often.

Figure 8: Solutions of the pair-wise model; case 2. Initial values were: $[S]=1,101,999/1,105,668$ and $[I]=3669/1105668$. See Appendix D for the specific values of $[S^n]$ s and $[I^n]$ s.

- a) Case 2i: The distribution of initial values for $[S^n]$ is proportional to that of the infected individuals in the data and the order in which individuals are assigned to pairs is from S^1 to S^{12}



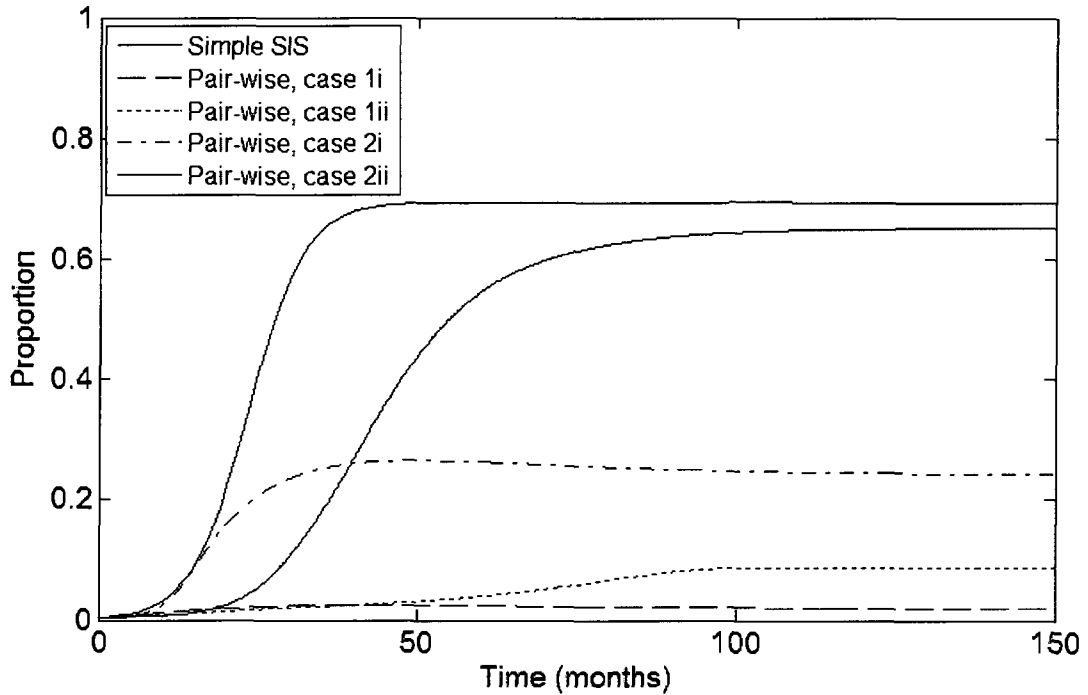
- b) Case 2ii: The distribution of initial values for $[S^n]$ is proportional to that of the infected individuals in the data and the order in which individuals are assigned to pairs is from S^{12} to S^1



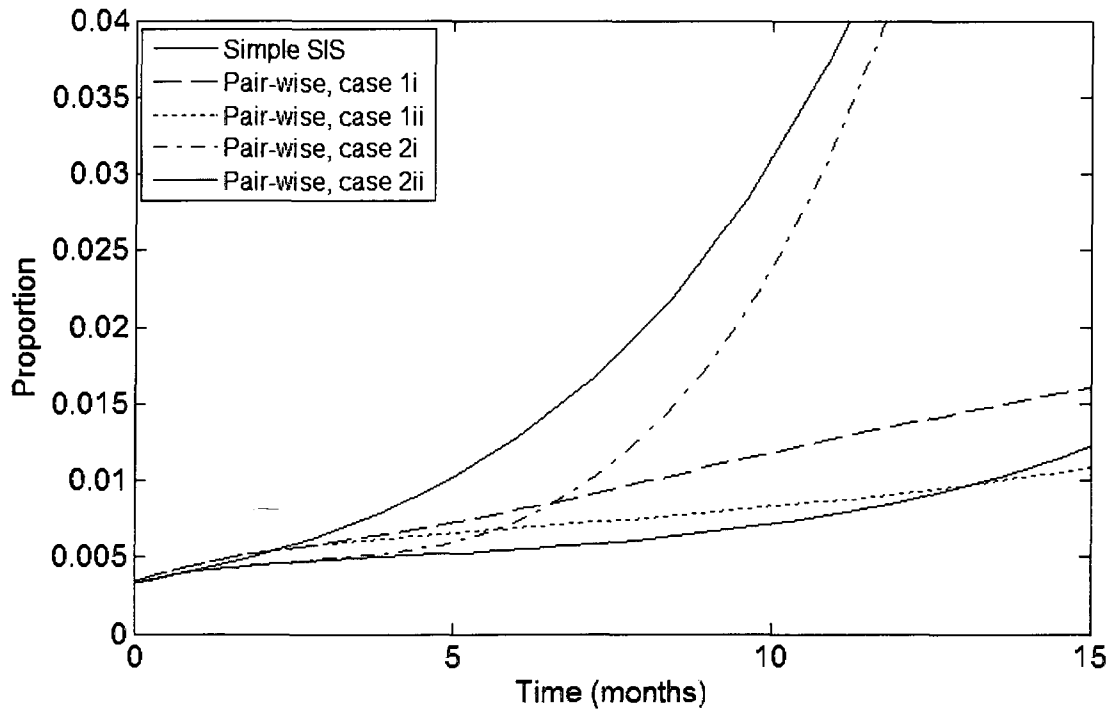
In case 2, the simulations predict that the infection never takes over for case 2i, but is able to take over after approximately 50 months for case 2ii. In case 2i, the proportion of infected individuals, $[I]$, increases to its peak value of 0.2646 at around 50 months, then it decreases and eventually reaches its equilibrium point after almost 250 months. In case 2ii, the proportion of infected individuals, $[I]$, gradually increases, reaching its equilibrium after about 150 months.

Figure 9: Solutions of all five simulations together. Initial values were:
 $[S] = 1,101,999/1,105,668$ and $[I] = 3669/1105668$. See Appendix D for the specific values of $[S^n]$ s and $[I^n]$ s.

a) Simulation run for 150 months



b) Close up of the $[I]$ solutions from the first 15 months for all five simulations.

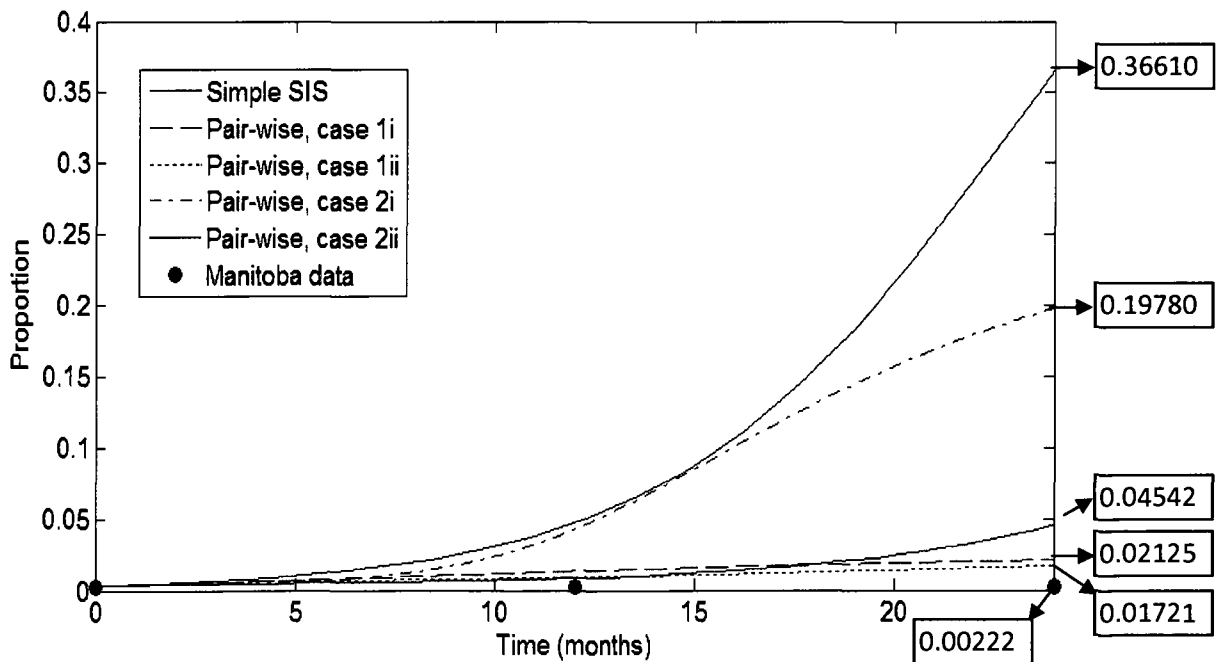


Figures 9 and 10 show the solutions from all five model predictions on the same graph for easy comparison. Clearly, the pair-wise model is very sensitive to the initial conditions. Although the initial values are only slightly altered, the predictions are very different. Recall that the total actual model and the number of initially susceptible and infected individuals are exactly the same in all four pair-wise model simulations. The only change is in the distribution of sexual partnerships.

Accuracy of the predictions

Figure 10 plots the solutions for [I] (i.e. the prevalence) from all three simulations over two years along with the prevalence calculated from the Manitoba data for 1990, 1991 and 1992 for easy comparison.

Figure 10: Solutions of all simulations along with the prevalence from the Manitoba data for 24 months time. Initial values were: [S]= 1,101,999/1,105,668 and [I]=3669/1105668. See Appendix D for the specific values of [Sⁿ]s and [Iⁿ]s.



According to the simulations, using the simple SIS model, the predicted prevalence of chlamydia for 1992 is 36,610 per 100,000. Using the pair-wise model, the predicted prevalence of chlamydia for 1992 is 1,721 or 2,125 or 4,542 or 19,780 per 100,000, depending on the initial conditions. Clearly, the prevalence predicted by any of the model simulations is much higher than the observed prevalence of 222 per 100,000 (Manitoba data). A statistical test isn't necessary to say that all five model predictions are significantly different than the actual observed prevalence.

Discussion

Summary of the findings

Of the five simulations, none was very accurate at predicting the prevalence of chlamydia in 1992. All five model simulations were fairly close together for the first four or five months. However, past this point, three of the pair-wise model solutions did remain fairly close to each other, while the other two solutions predicted that the infection would take hold and the proportion of infected individuals would increase quite quickly until approximately 15 months. After 15 months, the pair-wise model's solutions start to stabilize but the simple SIS model maintains its fast increase. When looking at the particular predictions of interest (i.e. after 2 years' time), the simple SIS model grossly overestimated the proportion of infected individuals. Although the pair-wise model's predictions also greatly overestimate the prevalence, they were much closer to the observed prevalence from the 1992 data. The simple SIS predicts almost twice as many chlamydia cases than the largest of the pair-wise model's predictions (36,610 per 100,000 for the simple SIS vs. 19,780 per 100,000 for the pair-wise, case 2i).

On the other hand, when looking at the predicted equilibrium values, the pair-wise model made very different predictions depending on the initial distribution of susceptible individuals. In fact, as seen in the simulation for case 2ii, the infection was able to take over and about 65.0% of the population would be infected at equilibrium. This is similar to the simple SIS model's prediction that 70% of the population will be infected at equilibrium. However, the time it takes for the pair-wise model predictions to reach its equilibrium, is much longer than for the simple SIS model allowing time to implement control measures before it reaches that point.

The findings make sense when considering the main reason why the simple SIS model was inappropriate. The simple SIS model assumes that sexual contacts are random across the entire population, so an infected individual does not run out of susceptible contacts to whom they can transmit infection. Therefore, depending on the disease parameters, the infection process is able to proceed smoothly and quickly. However, when the local sexual contact network was taken into account, an infected individual's susceptible contacts, to whom they can transmit infection, is finite. As the infection process not only depends on the disease parameters but also on the number and structure of susceptible contacts that infected individuals have, this is clearly reflected in the different shapes of the pair-wise model predictions.

Because the vast majority of individuals are susceptible (i.e. uninfected), their sexual contact structure, about which we know very little, has the most influence on the transmission of STIs. This is why the pair-wise model is so sensitive to changes in the initial conditions. Cases 1i, 1ii, 2i and 2ii did not differ in the number of initially infected or susceptible individuals but the distribution of sexual partners and partnerships of initially susceptible individuals (i.e. their network structure) was different. Although one might think that the network structure of susceptible individuals is not relevant, infection eventually reaches some of these individuals, involving them directly in the spread of disease.

Looking at the shape of the simple SIS model's solution for the proportion of infected individuals, $[I]$, we see that from the start, the infection spreads and the speed at which it does increases (i.e. the slope of the curve is getting steeper, therefore not only is the number of infected individuals increasing but the rate of change in $[I]$ is also

increasing). Eventually, the speed of infection starts to decrease (i.e. the slope starts getting flatter) and equilibrium is reached.

The shape of the different pair-wise model's solutions of infected individuals, [I], reveals the influence of network structure. Regardless of the case, the pair-wise model predicted that the speed at which infection spreads in the first 4 months is actually decreasing. Although the curve is increasing with time (i.e. infection is spreading), the speed of infection decreases (i.e. the slope is getting flatter). Presumably, infected individuals are infecting their neighbours, essentially "using up" all their susceptible contacts, which limits the speed at which infection can spread. In case 1ii where most of initially susceptible individuals had only 1 or 2 sexual partners (six at the most), and most of the individuals with more partners were paired together less often, this continues until infection is spreading so slowly that infected individuals actually recover faster than susceptible individuals are getting infected. At this point, the proportion of infected individuals peaks, then decreases, eventually leveling off. In case 1i, initially susceptible individuals again only had 1 or 2 sexual partners (six at the most), but this time, most of the individuals with more partners are paired together more often. Therefore, when one gets infected, they don't "use-up" all their susceptible contacts as quickly, and the speed at which infection spreads doesn't slow down to the point where infected individuals recover faster than susceptible individuals are infected therefore there is no peak. After approximately 50 months, infection speeds up and eventually slows back down as the solution reaches equilibrium around 160 months. In cases 2i and 2ii, initially susceptible individuals had up to 12 sexual partners, therefore the speed of infection only decreased until the susceptible individuals with many sexual partners, known as hubs (Barabási &

Albert, 1999) became infected and were able to “fast-track” infection by infecting all their partners who in turn infect their partners and so on. At this point, the infection is spreading much faster and is able to take hold of the population, behaving more like the simple SIS model’s predictions. This is especially true for case 2i because case in 2ii, where individuals with a higher number of partners are paired together less often, this “fast-tracking” is limited by the smaller number of high degree partnerships compared to case 2i. Although infection “accelerates” faster in case 2i, once these individuals with many sexual contacts (who are paired more often with other individuals with many other partners) infect all their contacts, they can no longer contribute to the spread of infection. This limits the proportion of infected individuals at equilibrium to just under 25%, compared to 65% in case 2ii.

Strengths and limitations

Like all mathematical models, the pair-wise model has its strengths and limitations. The biggest and most obvious strength of this model is that it takes into account the network of sexual relationships between individuals when modelling the dynamics of STIs. Although the pair-wise model was not accurate, it was a much better approximation of the actual data than the traditional simple SIS model. It gives a reasonable estimate of what can be expected from the disease, which is extremely useful when developing prevention strategies and proposing effective control measures. It can also be an invaluable tool when deciding which strategies to fund, since the relative outcomes of different approaches can be tested and compared without having to actually implement them.

As stated earlier, the quality of a mathematical model depends on the accuracy of its assumptions and hence also its limitations. First, the assumption that all partnerships are concurrent is problematic because a series of monogamous partnerships will allow for transmission across all pairings when that is not the case. For example, if person A is in a relationship with person B then breaks it off and enters a relationship with person C, transmission from person C to person B cannot occur. If we assume that all partnerships are concurrent, however, we are assuming that partnership AB is active at the same time as partnership AC, allowing for infection to be transmitted from person C to B. The chronology of partnerships and the timing of infection are critical to the infection process and the pair-wise model does not take this into account.

Second, assuming that the network is constant is another problem. In reality, partnerships form and dissolve on a regular basis. In addition, they form and dissolve at varying rates. There are long-term partnerships, short-term partnerships, on-and-off partnerships, and one-time partnerships. Since the structure of the network is used to build the pair-wise model, any changes in its structure essentially changes the model and potentially its predictions.

Third, assuming a constant transmission probability, β , is incorrect. The probability of transmission actually depends on many factors, such as the rate of sexual contact within a partnership, the probability of transmission per contact, the type of contact, the use of protection, whether or not a person is treated or the time until a person is treated, which can be longer if the person is asymptomatic or shorter if they are screened. The value of this “constant” parameter, β , was an average, taking into account all the factors listed above. However, since these factors vary so much from person to person, and from

partnership to partnership, an average is difficult to compute and may not even be a valid approach.

Fourth, as mentioned earlier, it has been suggested that there may be some kind of temporary or transient immunity (Brunham & Rekart, 2008). If this is the case, excluding it from the model could greatly affect the predictions of the model. The difficulty in incorporating immunity is that it must first be quantified.

In addition to the accuracy of its assumptions, the quality of the model's predictions depends on the quality of the data used to build it. The Manitoba databases used to build the pair-wise model are incomplete due to the fact that contact tracing ends when a non-infected person is reached and they do not capture undiagnosed infections. Consequently, the number of sexual partners of susceptible individuals in the data was underestimated because it was implied only from the number of different cases that named that individual. If a susceptible individual in a SI pair had degree 3 (i.e. three sexual partners), it is because that individual was named as a contact by three separate cases, but the individual could in fact have two additional sexual partners that were never infected (therefore not in the data and unaccounted for). This means that the individual was actually a susceptible individual of degree 5 but was erroneously counted as a susceptible individual of degree 3. In addition, the information on susceptible individuals not involved with an infected individual was not available at all. Given that the model was sensitive to the initial values of susceptible individuals and their contact structure, underestimation of sex partners in susceptible individuals is an important limitation which can be remedied by use of survey data. In 2007, the Canadian Community Health Survey collected some information on the number of sexual partners in the general population in selected

provinces (result not yet available from Statistics Canada). If this information was available to determine initial conditions, they could be more reliable in the future.

Another reason for incomplete network data is loss to follow-up or untraceable contacts. When the 1990 Manitoba data was collected, a case had the option to inform their contacts of chlamydia infection on their own if they were judged capable of doing so. No contact information was taken in this situation; therefore, there is no way to know if those contacts were actually followed up. Even when contact data was collected, the contacts were not all located for various reasons. This could be a source of bias, because it is believed that people who are evading follow-up may be higher risk individuals and high risk contacts were more likely to use an alias (Jolly et al., 2005).

Finally, some of the missing contact information was due to the fact that not all contacts were named in the first place, since cases were simply asked to recall their sexual contacts. Although the information is missing, there appears to be no systematic bias in the contacts recalled vs. those not recalled (Brewer, Garrett, & Kulasingam, 1999).

Because of these data limitations, methods for making generalizations from incomplete data need to be formulated in order to confidently interpret partial network data in the future.

Implications of the findings

Although our hypothesis that the pair-wise network model would accurately predict the prevalence of chlamydia in 1992, based on the 1990 data, was wrong, we believe that the results demonstrate the importance of taking network structure into account when modelling chlamydia or any other STI. Although the pair-wise model also overestimated

the prevalence of chlamydia, the predictions in all cases were much lower than the prediction of the simple SIS model. Therefore, using the simple SIS model to test and compare control measures and prevention strategies is wrong and could actually hinder our efforts to eliminate chlamydia. The simple SIS model may underestimate the successfulness of certain strategies because it overestimates the infection rate and spread of STIs. Although the pair-wise model also overestimated the infection process, it did so on a much smaller scale. Consequently, a strategy that would work if implemented could be deemed unsuccessful by the simple SIS but not the pair-wise model. If decision-makers continue to rely on the simple SIS, they could dismiss valid cost-effective strategies.

In addition, the sensitivity of the model's predictions to the initial conditions concerning the network structure underlines the critical importance of the network structure on the spread of STIs. Information on the sexual network of the target population must be collected and incorporated into any model used to study the spread of STIs for the model to be helpful.

Finally, the results demonstrate the importance of testing any disease model with real data. Using mathematical tools to model disease dynamics is not only about building a model that is theoretically sound and using it to help researchers and decision-makers. It must also be validated with actual data.

Conclusions

The main conclusion to take away from this research is that, although the pair-wise model itself was not extremely accurate in predicting the prevalence of STIs, its prediction was much closer to the actual prevalence than the prediction of the simple SIS model. The reason for this is because some important assumptions of the simple SIS model, mainly homogeneity within classes and random-mixing, are violated. Since STIs spread through sexual contact, transmission can only occur to a finite number of sexual partners, which limits the ability of infection to spread. Therefore, it is essential to consider the network structure when examining the spread of STIs in a population. The pair-wise model did take into account the local sexual network structure and its predictions clearly demonstrate that the structure can drastically influence the way STIs spread in the population.

Looking Ahead

Some of the assumptions of the pair-wise model were problematic but nonetheless it demonstrated how important it is to take the network structure into account when studying the dynamics of STIs. Therefore, other models must be developed to overcome the pair-wise model's shortcomings. For example, Ferguson & Garrett (2000) have presented a model with dynamic pairs (i.e. pairs form and dissolve at given rates). New pair-wise models should integrate this concept of changing partnerships along with transient immunity, treatment, screening and condom use, and see if this improves accuracy. On the other hand, because network structure is so important, if reliable data is not available, the predictions will be unreliable, regardless of the accuracy of the model. Therefore, it is just as important to ensure that quality data is collected and as complete as

possible. The bottom line, however, is that new models need to account for network structure in order to make accurate and useful predictions.

Appendices

APPENDIX A

ODEs of the pair-wise network model:

$$\frac{d}{dt}[S^n] = g[I^n] - \beta \sum_q [S^n I^q]$$

$$\frac{d}{dt}[I^n] = -g[I^n] + \beta \sum_q [S^n I^q]$$

$$\frac{d}{dt}[S^n S^m] = -\beta \sum_q [S^n S^m I^q] - \beta \sum_q [I^q S^n S^m] + g[S^n I^m] + g[I^n S^m]$$

$$\frac{d}{dt}[S^n I^m] = \beta \sum_q [S^n S^m I^q] - \beta \sum_q [I^q S^n I^m] - \beta [S^n I^m] - g[S^n I^m] + g[I^n I^m]$$

$$\frac{d}{dt}[I^n S^m] = \beta \sum_q [I^q S^n S^m] - \beta \sum_q [I^n S^m I^q] - \beta [I^n S^m] - g[I^n S^m] + g[I^n I^m]$$

$$\frac{d}{dt}[I^n I^m] = \beta \sum_q [I^n S^m I^q] + \beta \sum_q [I^q S^n I^m] + \beta [I^n S^m] + \beta [S^n I^m] - 2g[I^n I^m]$$

where, $[S^n]$ is the number of susceptible individuals with 'n' partners

$[I^n]$ is the number of infected individuals with 'n' partners

$[S^n I^m]$ is the number of pairs made up of a susceptible individual with 'n' partners and an infectious individual with 'm' partners

$[S^n S^m I^q]$ is the number of triples made up of a susceptible individual with 'm' partners paired with both a susceptible individual with 'n' partners and an infected individual with 'q' partners

$\sum_q [I^n S^m I^q]$ is the number of $[I^n S^m I^q]$ triples summed over all possible values of q

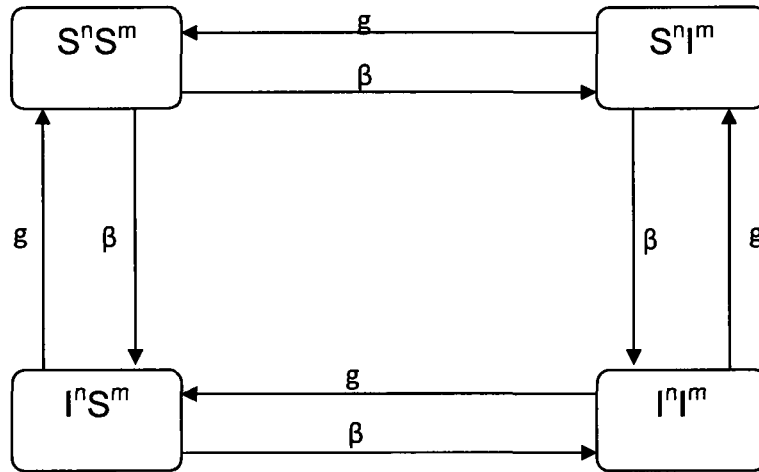
'g' is the recovery rate

'β' is the transmission probability

The triple terms are approximated by the following:

$$[B^n C^m D^p] \approx \frac{(m-1) \times [B^n C^m] \times [C^m D^p]}{m \times [C^m]}$$

Flow diagram of the pair-wise network model:



APPENDIX B

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Notification of Sexually Transmitted Disease – Confidential

Manitoba Health Sexually Transmitted Disease Control 4th Floor - 300 Carlton Street Winnipeg, Manitoba R3B 3M9 (204) 788-6738

Region No. (leave blank)

TELEPHONE HOME WORK

POSTAL CODE

DATE TESTED Y / M / D

UNSEX Y / M / D

GONORRHEA **CHLAMYDIA** **SYPHILIS**

TYPE: GENITO-URINARY OTHER (SPECIFY) _____

TYPE: PRIMARY SECONDARY EARLY LATENT LATE LATENT

CLINICAL FINDINGS (DESCRIBE): _____

TREATMENT GIVEN (SPECIFY): _____

LABORATORY TESTS: _____

SMEAR POS NEG CULTURE POS NEG

GONZOZYME POS NEG CHLAMYDIAZYME POS NEG

HAS A BLOOD TEST BEEN TAKEN FOR SYPHILIS YES NO

TREATMENT GIVEN (SPECIFY): _____

DATE: Y / M / D

PREVIOUS TREATMENT FOR: GONORRHEA YES NO

DATE: Y / M / D CHLAMYDIA YES NO

PREVIOUS TREATMENT FOR SYPHILIS YES NO

BY WHOM: _____ DATE: Y / M / D

OTHER SEXUALLY TRANSMITTED DISEASES

AIDS CHANCROID LGV

DO YOU WISH: CONSULTATIVE SERVICE NOTIFICATION FORMS PATIENT LITERATURE

PHYSICIAN'S SIGNATURE: _____ ADDRESS: _____

CONFIDENTIAL

Contact Information

Manitoba Health Sexually Transmitted Disease Control 4th Floor - 300 Carlton Street Winnipeg, Manitoba R3B 3M9 (204) 788-6738

TELEPHONE HOME WORK

POSTAL CODE

DATE OF AGE Y / M / D

DATE OF EXPOSURE (FIRST) Y / M / D TO Y / M / D

MARITAL STATUS: MARRIED/CL SINGLE OTHER _____

RELATIONSHIP: MARITAL PICK-UP FRIEND PROSTITUTE FEE _____

CHARACTERISTICS: HEIGHT _____ WEIGHT _____ EYE COLOUR _____ HAIR _____ COMPLEXION _____ OTHER _____

PLACE OF MEETING: _____ PLACE OF EXPOSURE: _____ DATE OF EXPOSURE (FIRST) Y / M / D TO Y / M / D

FREQUENCY OF SEX CONTACT: _____ TYPE: O-G G-G R-G

REMARKS: _____

FOR PUBLIC HEALTH USE ONLY

NAME OF INFORMANT: _____ DATE: _____ MONTH: _____

ADDRESS: _____ DATE/TYPE SPECIMEN: _____

GONORRHEA CHLAMYDIA SYPHILIS OTHER _____

DATE	STS BLOOD/CSF	GC SMEAR / CULTURE	CHLAMYDIA TEST	CLINICAL FINDINGS	TREATMENT

EXAMINED BY: _____ SUBMITTED BY: _____

COMMENTS: _____

CONFIDENTIAL

Contact Information

Manitoba Health Sexually Transmitted Disease Control 4th Floor - 300 Carlton Street Winnipeg, Manitoba R3B 3M9 (204) 788-6738

TELEPHONE HOME WORK

POSTAL CODE

DATE OF AGE Y / M / D

DATE OF EXPOSURE (FIRST) Y / M / D TO Y / M / D

MARITAL STATUS: MARRIED/CL SINGLE OTHER _____

RELATIONSHIP: MARITAL PICK-UP FRIEND PROSTITUTE FEE _____

CHARACTERISTICS: HEIGHT _____ WEIGHT _____ EYE COLOUR _____ HAIR _____ COMPLEXION _____ OTHER _____

PLACE OF MEETING: _____ PLACE OF EXPOSURE: _____ DATE OF EXPOSURE (FIRST) Y / M / D TO Y / M / D

FREQUENCY OF SEX CONTACT: _____ TYPE: O-G G-G R-G

REMARKS: _____

FOR PUBLIC HEALTH USE ONLY

NAME OF INFORMANT: _____ DATE: _____ MONTH: _____

ADDRESS: _____ DATE/TYPE SPECIMEN: _____

GONORRHEA CHLAMYDIA SYPHILIS OTHER _____

APPENDIX C



The Ottawa | L'Hôpital
Hospital | d'Ottawa

Research Ethics Board
Conseil d'éthique en recherches
798-5555 ext 14146, 14902 or 15072
Fax No. - 761-4311
<http://www.ohri.ca/ohreb/>

Monday, July 28, 2008

Ms. Nadine Enright
University of Ottawa
Department of Epidemiology
451 Smyth Road, Room 3227
Ottawa, ON
K1H 8M5

Dear Ms. Enright:

Re: Protocol # 2008423-01H Testing the Pair-Wise Network Model: Does it Accurately Predict the Dynamics of STIs on a Network?


Protocol approval valid until - Monday, July 27, 2009

Thank you for your email dated July 14, 2008. I am pleased to inform you that this protocol underwent expedited review by the Ottawa Hospital Research Ethics Board (OHREB) and is approved. Approval has been granted for the Research Protocol dated January 25, 2008. No changes, amendments or addenda may be made to the protocol without the OHREB's review and approval.

If the study is to continue beyond the expiry date noted above, a Renewal Form should be submitted to the OHREB approximately six weeks prior to the current expiry date. If the study has been completed by this date, a Termination Report should be submitted.

The Ottawa Hospital Research Ethics Board is constituted in accordance with, and operates in compliance with the requirements of the Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans; Health Canada Good Clinical Practice: Consolidated Guideline; Part C Division 5 of the Food and Drug Regulations of Health Canada; and the provisions of the Ontario Health Information Protection Act 2004 and its applicable Regulations.

Yours sincerely,

 Raphael Saginur, M.D.
Chairman
Ottawa Hospital Research Ethics Board

/cb/jm



The Ottawa Hospital | L'Hôpital
d'Ottawa

*Research Ethics Board
Conseil d'éthique en recherches
613-798-5555, ext. 14146, 14902 or
15072
Fax No. - 613-761-4311*

July 15, 2008

To Whom It May Concern:

This is to confirm that Mary Ann Laviolette, Ethics Co-ordinator for the Ottawa Hospital Research Ethics Board is hereby authorized to sign ethics correspondence in my absence.

I will be away July 26th to July 31st, 2008, as well as August 4th to August 15th, 2008 inclusive.

Mary Ann Laviolette is also authorized to sign Health Canada Attestation forms at all times.

Yours sincerely,

Raphael Saginur, M.D.
Chairman
Ottawa Hospital Research Ethics Board

APPENDIX D

Simple.m

```
% S = y(1)
% I = y(2)

function dydt=simple(t,y)

global tau
global g

dydt=[g*y(2)-tau*y(1)*y(2); tau*y(1)*y(2)-g*y(2)];
```

Ssolver.m

```
clear all

%define parameters & set values

global tau %define it
        tau=0.3; %give value

global g %define it
        g=0.1; %give value

%set the running time for the syst
ti=0;
tf=70;
tspan=[ti,tf];

%setting initial valaues for y vector
y0=[1101999/1105668;3669/1105668]'; %' is for transpose

%utilize the main routine or solver of Matlab
[t,y]=ode45(@simple,tspan,y0);

plot(t,y(:,1),t,y(:,2))
xlabel('Time (months)')
ylabel('Proportion')
legend ('[S]', '[I]')
```

Thesis.m

```
% S1 = y(1)
% S2 = y(2)
% S3 = y(3)
% S4 = y(4)
% S5 = y(5)
% S6 = y(6)
% S7 = y(7)
% S8 = y(8)
% S9 = y(9)
% S10 = y(10)
% S11 = y(11)
% S12 = y(12)

% I1 = y(13)
% I2 = y(14)
% I3 = y(15)
% I4 = y(16)
% I5 = y(17)
% I6 = y(18)
% I7 = y(19)
% I8 = y(20)
% I9 = y(21)
% I10 = y(22)
% I11 = y(23)
% I12 = y(24)

% S1I1 = y(25)
% S1I2 = y(26)
% S1I3 = y(27)
% S1I4 = y(28)
% S1I5 = y(29)
% S1I6 = y(30)
% S1I7 = y(31)
% S1I8 = y(32)
% S1I9 = y(33)
% S1I10 = y(34)
% S1I11 = y(35)
% S1I12 = y(36)
% S2I1 = y(37)
% S2I2 = y(38)
% S2I3 = y(39)
% S2I4 = y(40)
% S2I5 = y(41)
% S2I6 = y(42)
% S2I7 = y(43)
% S2I8 = y(44)
% S2I9 = y(45)
% S2I10 = y(46)
% S2I11 = y(47)
% S2I12 = y(48)
% S3I1 = y(49)
% S3I2 = y(50)
% S3I3 = y(51)
```

☞	S3I4	= y(52)
☞	S3I5	= y(53)
☞	S3I6	= y(54)
☞	S3I7	= y(55)
☞	S3I8	= y(56)
☞	S4I1	= y(57)
☞	S4I2	= y(58)
☞	S4I3	= y(59)
☞	S4I4	= y(60)
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☞	S6I1	= y(72)
☞	S6I2	= y(73)
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☞	S6I4	= y(75)
☞	S6I5	= y(76)
☞	S6I6	= y(77)
☞	S6I7	= y(78)
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☞	S10I4	= y(92)
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☞	S11I2	= y(94)
☞	S11I8	= y(95)
☞	S12I1	= y(96)
☞	S12I2	= y(97)
☞	S12I4	= y(178)
☞	S1S1	= y(98)
☞	S1S2	= y(99)
☞	S1S3	= y(100)
☞	S1S4	= y(101)
☞	S1S5	= y(102)
☞	S1S6	= y(103)
☞	S1S7	= y(104)

음	S1S8	= y(105)
음	S1S9	= y(106)
음	S1S10	= y(107)
음	S1S11	= y(108)
음	S1S12	= y(109)
음	S2S2	= y(110)
음	S2S3	= y(111)
음	S2S4	= y(112)
음	S2S5	= y(113)
음	S2S6	= y(114)
음	S2S7	= y(115)
음	S2S8	= y(116)
음	S2S9	= y(117)
음	S2S10	= y(118)
음	S2S11	= y(119)
음	S2S12	= y(120)
음	S3S3	= y(121)
음	S3S4	= y(122)
음	S3S5	= y(123)
음	S3S6	= y(124)
음	S3S7	= y(125)
음	S3S8	= y(126)
음	S4S4	= y(127)
음	S4S5	= y(128)
음	S4S6	= y(129)
음	S4S8	= y(130)
음	S4S10	= y(131)
음	S4S12	= y(132)
음	S5S5	= y(133)
음	S5S6	= y(134)
음	S6S6	= y(135)
음	S6S7	= y(136)
음	S8S11	= y(137)
음	I1I1	= y(138)
음	I1I2	= y(139)
음	I1I3	= y(140)
음	I1I4	= y(141)
음	I1I5	= y(142)
음	I1I6	= y(143)
음	I1I7	= y(144)
음	I1I8	= y(145)
음	I1I9	= y(146)
음	I1I10	= y(147)
음	I1I11	= y(148)
음	I1I12	= y(149)
음	I2I2	= y(150)
음	I2I3	= y(151)
음	I2I4	= y(152)
음	I2I5	= y(153)
음	I2I6	= y(154)
음	I2I7	= y(155)
음	I2I8	= y(156)
음	I2I9	= y(157)
음	I2I10	= y(158)

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% I2I11 = y(159)
% I2I12 = y(160)
% I3I3 = y(161)
% I3I4 = y(162)
% I3I5 = y(163)
% I3I6 = y(164)
% I3I7 = y(165)
% I3I8 = y(166)
% I4I4 = y(167)
% I4I5 = y(168)
% I4I6 = y(169)
% I4I8 = y(170)
% I4I10 = y(171)
% I4I12 = y(172)
% I5I5 = y(173)
% I5I6 = y(174)
% I6I6 = y(175)
% I6I7 = y(176)
% I8I11 = y(177)
function dydt=thesis(t,y)

global beta
global g

dydt=[
g*y(13)-
beta*(y(25)+y(26)+y(27)+y(28)+y(29)+y(30)+y(31)+y(32)+y(33)+y(34)+y(35)
)+y(36)); %y1

g*y(14)-
beta*(y(37)+y(38)+y(39)+y(40)+y(41)+y(42)+y(43)+y(44)+y(45)+y(46)+y(47)
)+y(48)); %y2

g*y(15)-beta*(y(49)+y(50)+y(51)+y(52)+y(53)+y(54)+y(55)+y(56)); %y3

g*y(16)-beta*(y(57)+y(58)+y(59)+y(60)+y(61)+y(62)+y(63)+y(64)+y(65));
%y4

g*y(17)-beta*(y(66)+y(67)+y(68)+y(69)+y(70)+y(71)); %y5

g*y(18)-beta*(y(72)+y(73)+y(74)+y(75)+y(76)+y(77)+y(78)); %y6

g*y(19)-beta*(y(79)+y(80)+y(81)+y(82)); %y7

g*y(20)-beta*(y(83)+y(84)+y(85)+y(86)+y(87)); %y8

g*y(21)-beta*(y(88)+y(89)); %y9

g*y(22)-beta*(y(90)+y(91)+y(92)); %y10

g*y(23)-beta*(y(93)+y(94)+y(95)); %y11

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g*y(24)-beta*(y(96)+y(97)+y(178)); %y12
-
g*y(13)+beta*(y(25)+y(26)+y(27)+y(28)+y(29)+y(30)+y(31)+y(32)+y(33)+y(
34)+y(35)+y(36)); %y13
-
g*y(14)+beta*(y(37)+y(38)+y(39)+y(40)+y(41)+y(42)+y(43)+y(44)+y(45)+y(
46)+y(47)+y(48)); %y14
-g*y(15)+beta*(y(49)+y(50)+y(51)+y(52)+y(53)+y(54)+y(55)+y(56)); %y15
-g*y(16)+beta*(y(57)+y(58)+y(59)+y(60)+y(61)+y(62)+y(63)+y(64)+y(65));
%y16
-g*y(17)+beta*(y(66)+y(67)+y(68)+y(69)+y(70)+y(71)); %y17
-g*y(18)+beta*(y(72)+y(73)+y(74)+y(75)+y(76)+y(77)+y(78)); %y18
-g*y(19)+beta*(y(79)+y(80)+y(81)+y(82)); %y19
-g*y(20)+beta*(y(83)+y(84)+y(85)+y(86)+y(87)); %y20
-g*y(21)+beta*(y(88)+y(89)); %y21
-g*y(22)+beta*(y(90)+y(91)+y(92)); %y22
-g*y(23)+beta*(y(93)+y(94)+y(95)); %y23
-g*y(24)+beta*(y(96)+y(97)+y(178)); %y24
-beta*y(25)-g*y(25)+g*y(138); %y25
beta*y(99)*(y(37)+y(38)+y(39)+y(40)+y(41)+y(42)+y(43)+y(44)+y(45)+y(46
)+y(47)+y(48))/(2*y(2)+0.0001)-beta*y(26)-g*y(26)+g*y(139); %y26
beta*2*y(100)*(y(49)+y(50)+y(51)+y(52)+y(53)+y(54)+y(55)+y(56))/(3*y(3
)+0.0001)-beta*y(27)-g*y(27)+g*y(140); %y27
beta*3*y(101)*(y(57)+y(58)+y(59)+y(60)+y(61)+y(62)+y(63)+y(64)+y(65))/
(4*y(4)+0.0001)-beta*y(28)-g*y(28)+g*y(141); %y28
beta*4*y(102)*(y(66)+y(67)+y(68)+y(69)+y(70)+y(71))/(5*y(5)+0.0001)-
beta*y(29)-g*y(29)+g*y(142); %y29
beta*5*y(103)*(y(72)+y(73)+y(74)+y(75)+y(76)+y(77)+y(78))/(6*y(6)+0.00
01)-beta*y(30)-g*y(30)+g*y(143); %y30
beta*6*y(104)*(y(79)+y(80)+y(81)+y(82))/(7*y(7)+0.0001)-beta*y(31)-
g*y(31)+g*y(144); %y31

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$$\text{beta} \cdot 7 \cdot y(105) \cdot (y(83) + y(84) + y(85) + y(86) + y(87)) / (8 \cdot y(8) + 0.0001) - \text{beta} \cdot y(32) - g \cdot y(32) + g \cdot y(145); \%y32$$

$$\text{beta} \cdot 8 \cdot y(106) \cdot (y(88) + y(89)) / (9 \cdot y(9) + 0.0001) - \text{beta} \cdot y(33) - g \cdot y(33) + g \cdot y(146); \%y33$$

$$\text{beta} \cdot 9 \cdot y(107) \cdot (y(90) + y(91) + y(92)) / (10 \cdot y(10) + 0.0001) - \text{beta} \cdot y(34) - g \cdot y(34) + g \cdot y(147); \%y34$$

$$\text{beta} \cdot 10 \cdot y(108) \cdot (y(93) + y(94) + y(95)) / (11 \cdot y(11) + 0.0001) - \text{beta} \cdot y(35) - g \cdot y(35) + g \cdot y(148); \%y35$$

$$\text{beta} \cdot 11 \cdot y(109) \cdot (y(96) + y(97) + y(178)) / (12 \cdot y(12) + 0.0001) - \text{beta} \cdot y(36) - g \cdot y(36) + g \cdot y(149); \%y36$$

$$-$$

$$\text{beta} \cdot y(37) \cdot (y(37) + y(38) + y(39) + y(40) + y(41) + y(42) + y(43) + y(44) + y(45) + y(46) + y(47) + y(48)) / (2 \cdot y(2) + 0.0001) - \text{beta} \cdot y(37) - g \cdot y(37) + g \cdot y(139); \%y37$$

$$\text{beta} \cdot y(110) \cdot (y(37) + y(38) + y(39) + y(40) + y(41) + y(42) + y(43) + y(44) + y(45) + y(46) + y(47) + y(48)) / (2 \cdot y(2) + 0.0001) - \text{beta} \cdot y(38) \cdot (y(37) + y(38) + y(39) + y(40) + y(41) + y(42) + y(43) + y(44) + y(45) + y(46) + y(47) + y(48)) / (2 \cdot y(2) + 0.0001) - \text{beta} \cdot y(38) - g \cdot y(38) + g \cdot y(150); \%y38$$

$$\text{beta} \cdot 2 \cdot y(111) \cdot (y(49) + y(50) + y(51) + y(52) + y(53) + y(54) + y(55) + y(56)) / (3 \cdot y(3) + 0.0001) - \text{beta} \cdot y(39) \cdot (y(37) + y(38) + y(39) + y(40) + y(41) + y(42) + y(43) + y(44) + y(45) + y(46) + y(47) + y(48)) / (2 \cdot y(2) + 0.0001) - \text{beta} \cdot y(39) - g \cdot y(39) + g \cdot y(151); \%y39$$

$$\text{beta} \cdot 3 \cdot y(112) \cdot (y(57) + y(58) + y(59) + y(60) + y(61) + y(62) + y(63) + y(64) + y(65)) / (4 \cdot y(4) + 0.0001) - \text{beta} \cdot y(40) \cdot (y(37) + y(38) + y(39) + y(40) + y(41) + y(42) + y(43) + y(44) + y(45) + y(46) + y(47) + y(48)) / (2 \cdot y(2) + 0.0001) - \text{beta} \cdot y(40) - g \cdot y(40) + g \cdot y(152); \%y40$$

$$\text{beta} \cdot 4 \cdot y(113) \cdot (y(66) + y(67) + y(68) + y(69) + y(70) + y(71)) / (5 \cdot y(5) + 0.0001) - \text{beta} \cdot y(41) \cdot (y(37) + y(38) + y(39) + y(40) + y(41) + y(42) + y(43) + y(44) + y(45) + y(46) + y(47) + y(48)) / (2 \cdot y(2) + 0.0001) - \text{beta} \cdot y(41) - g \cdot y(41) + g \cdot y(153); \%y41$$

$$\text{beta} \cdot 5 \cdot y(114) \cdot (y(72) + y(73) + y(74) + y(75) + y(76) + y(77) + y(78)) / (6 \cdot y(6) + 0.0001) - \text{beta} \cdot y(42) \cdot (y(37) + y(38) + y(39) + y(40) + y(41) + y(42) + y(43) + y(44) + y(45) + y(46) + y(47) + y(48)) / (2 \cdot y(2) + 0.0001) - \text{beta} \cdot y(42) - g \cdot y(42) + g \cdot y(154); \%y42$$

$$\text{beta} \cdot 6 \cdot y(115) \cdot (y(79) + y(80) + y(81) + y(82)) / (7 \cdot y(7) + 0.0001) - \text{beta} \cdot y(43) \cdot (y(37) + y(38) + y(39) + y(40) + y(41) + y(42) + y(43) + y(44) + y(45) + y(46) + y(47) + y(48)) / (2 \cdot y(2) + 0.0001) - \text{beta} \cdot y(43) - g \cdot y(43) + g \cdot y(155); \%y43$$

$$\text{beta} \cdot 7 \cdot y(116) \cdot (y(83) + y(84) + y(85) + y(86) + y(87)) / (8 \cdot y(8) + 0.0001) - \text{beta} \cdot y(44) \cdot (y(37) + y(38) + y(39) + y(40) + y(41) + y(42) + y(43) + y(44) + y(45) + y(46) + y(47) + y(48)) / (2 \cdot y(2) + 0.0001) - \text{beta} \cdot y(44) - g \cdot y(44) + g \cdot y(156); \%y44$$

$$\text{beta}^8 y(117) * (y(88) + y(89)) / (9 * y(9) + 0.0001) -$$
$$\text{beta}^8 y(45) * (y(37) + y(38) + y(39) + y(40) + y(41) + y(42) + y(43) + y(44) + y(45) + y(46) + y(47) + y(48)) / (2 * y(2) + 0.0001) - \text{beta}^8 y(45) - g^8 y(45) + g^8 y(157); \%y45$$

$$\text{beta}^9 y(118) * (y(90) + y(91) + y(92)) / (10 * y(10) + 0.0001) -$$
$$\text{beta}^9 y(46) * (y(37) + y(38) + y(39) + y(40) + y(41) + y(42) + y(43) + y(44) + y(45) + y(46) + y(47) + y(48)) / (2 * y(2) + 0.0001) - \text{beta}^9 y(46) - g^9 y(46) + g^9 y(158); \%y46$$

$$\text{beta}^{10} y(119) * (y(93) + y(94) + y(95)) / (11 * y(11) + 0.0001) -$$
$$\text{beta}^{10} y(47) * (y(37) + y(38) + y(39) + y(40) + y(41) + y(42) + y(43) + y(44) + y(45) + y(46) + y(47) + y(48)) / (2 * y(2) + 0.0001) - \text{beta}^{10} y(47) - g^{10} y(47) + g^{10} y(159); \%y47$$

$$\text{beta}^{11} y(120) * (y(96) + y(97) + y(178)) / (12 * y(12) + 0.0001) -$$
$$\text{beta}^{11} y(48) * (y(37) + y(38) + y(39) + y(40) + y(41) + y(42) + y(43) + y(44) + y(45) + y(46) + y(47) + y(48)) / (2 * y(2) + 0.0001) - \text{beta}^{11} y(48) - g^{11} y(48) + g^{11} y(160); \%y48$$

$$- \text{beta}^2 y(49) * (y(49) + y(50) + y(51) + y(52) + y(53) + y(54) + y(55) + y(56)) /$$
$$(3 * y(3) + 0.0001) - \text{beta}^2 y(49) - g^2 y(49) + g^2 y(140); \%y49$$

$$\text{beta}^2 y(111) * (y(37) + y(38) + y(39) + y(40) + y(41) + y(42) + y(43) + y(44) + y(45) + y(46) + y(47) + y(48)) / (2 * y(2) + 0.0001) -$$
$$\text{beta}^2 y(50) * (y(49) + y(50) + y(51) + y(52) + y(53) + y(54) + y(55) + y(56)) / (3 * y(3) + 0.0001) - \text{beta}^2 y(50) - g^2 y(50) + g^2 y(151); \%y50$$

$$\text{beta}^2 y(121) * (y(49) + y(50) + y(51) + y(52) + y(53) + y(54) + y(55) + y(56)) / (3 * y(3) + 0.0001) -$$
$$\text{beta}^2 y(51) * (y(49) + y(50) + y(51) + y(52) + y(53) + y(54) + y(55) + y(56)) / (3 * y(3) + 0.0001) - \text{beta}^2 y(51) - g^2 y(51) + g^2 y(161); \%y51$$

$$\text{beta}^3 y(122) * (y(57) + y(58) + y(59) + y(60) + y(61) + y(62) + y(63) + y(64) + y(65)) /$$
$$(4 * y(4) + 0.0001) - \text{beta}^2 y(52) * (y(49) + y(50) + y(51) + y(52) + y(53) + y(54) + y(55) + y(56)) / (3 * y(3) + 0.0001) - \text{beta}^2 y(52) - g^2 y(52) + g^2 y(162); \%y52$$

$$\text{beta}^4 y(123) * (y(66) + y(67) + y(68) + y(69) + y(70) + y(71)) / (5 * y(5) + 0.0001) -$$
$$\text{beta}^2 y(53) * (y(49) + y(50) + y(51) + y(52) + y(53) + y(54) + y(55) + y(56)) / (3 * y(3) + 0.0001) - \text{beta}^2 y(53) - g^2 y(53) + g^2 y(163); \%y53$$

$$\text{beta}^5 y(124) * (y(72) + y(73) + y(74) + y(75) + y(76) + y(77) + y(78)) / (6 * y(6) + 0.0001) -$$
$$\text{beta}^2 y(54) * (y(49) + y(50) + y(51) + y(52) + y(53) + y(54) + y(55) + y(56)) / (3 * y(3) + 0.0001) - \text{beta}^2 y(54) - g^2 y(54) + g^2 y(164); \%y54$$

$$\text{beta}^6 y(125) * (y(79) + y(80) + y(81) + y(82)) / (7 * y(7) + 0.0001) -$$
$$\text{beta}^2 y(55) * (y(49) + y(50) + y(51) + y(52) + y(53) + y(54) + y(55) + y(56)) / (3 * y(3) + 0.0001) - \text{beta}^2 y(55) - g^2 y(55) + g^2 y(165); \%y55$$

$$\text{beta}^7 y(126) * (y(83) + y(84) + y(85) + y(86) + y(87)) / (8 * y(8) + 0.0001) -$$
$$\text{beta}^2 y(56) * (y(49) + y(50) + y(51) + y(52) + y(53) + y(54) + y(55) + y(56)) / (3 * y(3) + 0.0001) - \text{beta}^2 y(56) - g^2 y(56) + g^2 y(166); \%y56$$

$$- \text{beta}^3 y(57) * (y(57) + y(58) + y(59) + y(60) + y(61) + y(62) + y(63) + y(64) + y(65)) / (4 * y(4) + 0.0001) - \text{beta}^3 y(57) - g^3 y(57) + g^3 y(141); \%y57$$

$$\begin{aligned} & \text{beta} * y(112) * (y(37) + y(38) + y(39) + y(40) + y(41) + y(42) + y(43) + y(44) + y(45) + y(46) \\ & + y(47) + y(48)) / (2 * y(2) + 0.0001) - \\ & \text{beta} * 3 * y(58) * (y(57) + y(58) + y(59) + y(60) + y(61) + y(62) + y(63) + y(64) + y(65)) / (\\ & 4 * y(4) + 0.0001) - \text{beta} * y(58) - g * y(58) + g * y(152); \quad \%y58 \end{aligned}$$

$$\begin{aligned} & \text{beta} * 2 * y(122) * (y(49) + y(50) + y(51) + y(52) + y(53) + y(54) + y(55) + y(56)) / (3 * y(3) \\ & + 0.0001) - \\ & \text{beta} * 3 * y(59) * (y(57) + y(58) + y(59) + y(60) + y(61) + y(62) + y(63) + y(64) + \\ & y(65)) / (4 * y(4) + 0.0001) - \text{beta} * y(59) - g * y(59) + g * y(162); \quad \%y59 \end{aligned}$$

$$\begin{aligned} & \text{beta} * 3 * y(127) * (y(57) + y(58) + y(59) + y(60) + y(61) + y(62) + y(63) + y(64) + y(65)) / \\ & (4 * y(4) + 0.0001) - \text{beta} * 3 * y(60) * (y(57) + y(58) + y(59) + y(60) + y(61) + y(62) + \\ & y(63) + y(64) + y(65)) / (4 * y(4) + 0.0001) - \text{beta} * y(60) - g * y(60) + g * y(167); \quad \%y60 \end{aligned}$$

$$\begin{aligned} & \text{beta} * 4 * y(128) * (y(66) + y(67) + y(68) + y(69) + y(70) + y(71)) / (5 * y(5) + 0.0001) - \\ & \text{beta} * 3 * y(61) * (y(57) + y(58) + y(59) + y(60) + y(61) + y(62) + y(63) + y(64) + y(65)) / (\\ & 4 * y(4) + 0.0001) - \text{beta} * y(61) - g * y(61) + g * y(168); \quad \%y61 \end{aligned}$$

$$\begin{aligned} & \text{beta} * 5 * y(129) * (y(72) + y(73) + y(74) + y(75) + y(76) + y(77) + y(78)) / (6 * y(6) + 0.00 \\ & 01) - \\ & \text{beta} * 3 * y(62) * (y(57) + y(58) + y(59) + y(60) + y(61) + y(62) + y(63) + y(64) + y(65)) / (\\ & 4 * y(4) + 0.0001) - \text{beta} * y(62) - g * y(62) + g * y(169); \quad \%y62 \end{aligned}$$

$$\begin{aligned} & \text{beta} * 7 * y(130) * (y(83) + y(84) + y(85) + y(86) + y(87)) / (8 * y(8) + 0.0001) - \\ & \text{beta} * 3 * y(63) * (y(57) + y(58) + y(59) + y(60) + y(61) + y(62) + y(63) + y(64) + y(65)) / (\\ & 4 * y(4) + 0.0001) - \text{beta} * y(63) - g * y(63) + g * y(170); \quad \%y63 \end{aligned}$$

$$\begin{aligned} & \text{beta} * 9 * y(131) * (y(90) + y(91) + y(92)) / (10 * y(10) + 0.0001) - \\ & \text{beta} * 3 * y(64) * (y(57) + y(58) + y(59) + y(60) + y(61) + y(62) + y(63) + y(64) + y(65)) / (\\ & 4 * y(4) + 0.0001) - \text{beta} * y(64) - g * y(64) + g * y(171); \quad \%y64 \end{aligned}$$

$$\begin{aligned} & \text{beta} * 11 * y(132) * (y(96) + y(97) + y(178)) / (12 * y(12) + 0.0001) - \\ & \text{beta} * 3 * y(65) * (y(57) + y(58) + y(59) + y(60) + y(61) + y(62) + y(63) + y(64) + y(65)) / (\\ & 4 * y(4) + 0.0001) - \text{beta} * y(65) - g * y(65) + g * y(172); \quad \%y65 \end{aligned}$$

$$\begin{aligned} & -\text{beta} * 4 * y(66) * (y(66) + y(67) + y(68) + y(69) + y(70) + y(71)) / (5 * y(5) + 0.0001) - \\ & \text{beta} * y(66) - g * y(66) + g * y(142); \quad \%y66 \end{aligned}$$

$$\begin{aligned} & \text{beta} * y(113) * (y(37) + y(38) + y(39) + y(40) + y(41) + y(42) + y(43) + y(44) + y(45) + y(46) \\ & + y(47) + y(48)) / (2 * y(2) + 0.0001) - \\ & \text{beta} * 4 * y(67) * (y(66) + y(67) + y(68) + y(69) + y(70) + y(71)) / (5 * y(5) + 0.0001) - \\ & \text{beta} * y(67) - g * y(67) + g * y(153); \quad \%y67 \end{aligned}$$

$$\begin{aligned} & \text{beta} * 2 * y(123) * (y(49) + y(50) + y(51) + y(52) + y(53) + y(54) + y(55) + y(56)) / (3 * y(3) \\ & + 0.0001) - \\ & \text{beta} * 4 * y(68) * (y(66) + y(67) + y(68) + y(69) + y(70) + y(71)) / (5 * y(5) + 0.0001) - \\ & \text{beta} * y(68) - g * y(68) + g * y(163); \quad \%y68 \end{aligned}$$

$$\begin{aligned} & \text{beta} * 3 * y(128) * (y(57) + y(58) + y(59) + y(60) + y(61) + y(62) + y(63) + y(64) + y(65)) / \\ & (4 * y(4) + 0.0001) - \\ & \text{beta} * 4 * y(69) * (y(66) + y(67) + y(68) + y(69) + y(70) + y(71)) / (5 * y(5) + 0.0001) - \\ & \text{beta} * y(69) - g * y(69) + g * y(168); \quad \%y69 \end{aligned}$$

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beta*4*y(133) * (y(66)+y(67)+y(68)+y(69)+y(70)+y(71)) / (5*y(5)+0.0001) -
beta*4*y(70) * (y(66)+y(67)+y(68)+y(69)+y(70)+y(71)) / (5*y(5)+0.0001) -
beta*y(70)-g*y(70)+g*y(173); %y70

beta*5*y(134) * (y(72)+y(73)+y(74)+y(75)+y(76)+y(77)+y(78)) / (6*y(6)+0.0001) -
beta*4*y(71) * (y(66)+y(67)+y(68)+y(69)+y(70)+y(71)) / (5*y(5)+0.0001) -
beta*y(71)-g*y(71)+g*y(174); %y71

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beta*5*y(72) * (y(72)+y(73)+y(74)+y(75)+y(76)+y(77)+y(78)) / (6*y(6)+0.0001) -
beta*y(72)-g*y(72)+g*y(143); %y72

beta*y(114) * (y(37)+y(38)+y(39)+y(40)+y(41)+y(42)+y(43)+y(44)+y(45)+y(46)+y(47)+y(48)) / (2*y(2)+0.0001) -
beta*5*y(73) * (y(72)+y(73)+y(74)+y(75)+y(76)+y(77)+y(78)) / (6*y(6)+0.0001) -
beta*y(73)-g*y(73)+g*y(154); %y73

beta*2*y(124) * (y(49)+y(50)+y(51)+y(52)+y(53)+y(54)+y(55)+y(56)) / (3*y(3)+0.0001) -
beta*5*y(74) * (y(72)+y(73)+y(74)+y(75)+y(76)+y(77)+y(78)) / (6*y(6)+0.0001) -
beta*y(74)-g*y(74)+g*y(164); %y74

beta*3*y(129) * (y(57)+y(58)+y(59)+y(60)+y(61)+y(62)+y(63)+y(64)+y(65)) / (4*y(4)+0.0001) -
beta*5*y(75) * (y(72)+y(73)+y(74)+y(75)+y(76)+y(77)+y(78)) / (6*y(6)+0.0001) -
beta*y(75)-g*y(75)+g*y(169); %y75

beta*4*y(134) * (y(66)+y(67)+y(68)+y(69)+y(70)+y(71)) / (5*y(5)+0.0001) -
beta*5*y(76) * (y(72)+y(73)+y(74)+y(75)+y(76)+y(77)+y(78)) / (6*y(6)+0.0001) -
beta*y(76)-g*y(76)+g*y(174); %y76

beta*5*y(135) * (y(72)+y(73)+y(74)+y(75)+y(76)+y(77)+y(78)) / (6*y(6)+0.0001) -
beta*5*y(77) * (y(72)+y(73)+y(74)+y(75)+y(76)+y(77)+y(78)) / (6*y(6)+0.0001) -
beta*y(77)-g*y(77)+g*y(175); %y77

beta*6*y(136) * (y(79)+y(80)+y(81)+y(82)) / (7*y(7)+0.0001) -
beta*5*y(78) * (y(72)+y(73)+y(74)+y(75)+y(76)+y(77)+y(78)) / (6*y(6)+0.0001) -
beta*y(78)-g*y(78)+g*y(176); %y78

-beta*6*y(79) * (y(79)+y(80)+y(81)+y(82)) / (7*y(7)+0.0001) -beta*y(79) -
g*y(79)+g*y(144); %y79

beta*y(115) * (y(37)+y(38)+y(39)+y(40)+y(41)+y(42)+y(43)+y(44)+y(45)+y(46)+y(47)+y(48)) / (2*y(2)+0.0001) -
beta*6*y(80) * (y(79)+y(80)+y(81)+y(82)) / (7*y(7)+0.0001) -beta*y(80) -
g*y(80)+g*y(155); %y80

beta*2*y(125) * (y(49)+y(50)+y(51)+y(52)+y(53)+y(54)+y(55)+y(56)) / (3*y(3)+0.0001) -
beta*6*y(81) * (y(79)+y(80)+y(81)+y(82)) / (7*y(7)+0.0001) -
beta*y(81)-g*y(81)+g*y(165); %y81

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beta*5*y(136) * (y(72)+y(73)+y(74)+y(75)+y(76)+y(77)+y(78)) / (6*y(6)+0.0001) - beta*6*y(82) * (y(79)+y(80)+y(81)+y(82)) / (7*y(7)+0.0001) - beta*y(82) - g*y(82)+g*y(176); %y82

-beta*7*y(83) * (y(83)+y(84)+y(85)+y(86)+y(87)) / (8*y(8)+0.0001) - beta*y(83) - g*y(83)+g*y(145); %y83

beta*y(116) * (y(37)+y(38)+y(39)+y(40)+y(41)+y(42)+y(43)+y(44)+y(45)+y(46)+y(47)+y(48)) / (2*y(2)+0.0001) - beta*7*y(84) * (y(83)+y(84)+y(85)+y(86)+y(87)) / (8*y(8)+0.0001) - beta*y(84) - g*y(84)+g*y(156); %y84

beta*2*y(126) * (y(49)+y(50)+y(51)+y(52)+y(53)+y(54)+y(55)+y(56)) / (3*y(3)+0.0001) - beta*7*y(85) * (y(83)+y(84)+y(85)+y(86)+y(87)) / (8*y(8)+0.0001) - beta*y(85) - g*y(85)+g*y(166); %y85

beta*3*y(130) * (y(57)+y(58)+y(59)+y(60)+y(61)+y(62)+y(63)+y(64)+y(65)) / (4*y(4)+0.0001) - beta*7*y(86) * (y(83)+y(84)+y(85)+y(86)+y(87)) / (8*y(8)+0.0001) - beta*y(86) - g*y(86)+g*y(170); %y86

beta*10*y(137) * (y(93)+y(94)+y(95)) / (11*y(11)+0.0001) - beta*7*y(87) * (y(83)+y(84)+y(85)+y(86)+y(87)) / (8*y(8)+0.0001) - beta*y(87) - g*y(87)+g*y(177); %y87

-beta*8*y(88) * (y(88)+y(89)) / (9*y(9)+0.0001) - beta*y(88) - g*y(88)+g*y(146); %y88

beta*y(117) * (y(37)+y(38)+y(39)+y(40)+y(41)+y(42)+y(43)+y(44)+y(45)+y(46)+y(47)+y(48)) / (2*y(2)+0.0001) - beta*8*y(89) * (y(88)+y(89)) / (9*y(9)+0.0001) - beta*y(89) - g*y(89)+g*y(157); %y89

-beta*9*y(90) * (y(90)+y(91)+y(92)) / (10*y(10)+0.0001) - beta*y(90) - g*y(90)+g*y(147); %y90

beta*y(118) * (y(37)+y(38)+y(39)+y(40)+y(41)+y(42)+y(43)+y(44)+y(45)+y(46)+y(47)+y(48)) / (2*y(2)+0.0001) - beta*9*y(91) * (y(90)+y(91)+y(92)) / (10*y(10)+0.0001) - beta*y(91) - g*y(91)+g*y(158); %y91

beta*3*y(131) * (y(57)+y(58)+y(59)+y(60)+y(61)+y(62)+y(63)+y(64)+y(65)) / (4*y(4)+0.0001) - beta*9*y(92) * (y(90)+y(91)+y(92)) / (10*y(10)+0.0001) - beta*y(92) - g*y(92)+g*y(171); %y92

-beta*10*y(93) * (y(93)+y(94)+y(95)) / (11*y(11)+0.0001) - beta*y(93) - g*y(93)+g*y(148); %y93

beta*y(119) * (y(37)+y(38)+y(39)+y(40)+y(41)+y(42)+y(43)+y(44)+y(45)+y(46)+y(47)+y(48)) / (2*y(2)+0.0001) - beta*10*y(94) * (y(93)+y(94)+y(95)) / (11*y(11)+0.0001) - beta*y(94) - g*y(94)+g*y(159); %y94

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beta*7*y(137) * (y(83)+y(84)+y(85)+y(86)+y(87)) / (8*y(8)+0.0001) -
beta*10*y(95) * (y(93)+y(94)+y(95)) / (11*y(11)+0.0001) -beta*y(95) -
g*y(95)+g*y(177); %y95

-beta*11*y(96) * (y(96)+y(97)+y(178)) / (12*y(12)+0.0001) -beta*y(96) -
g*y(96)+g*y(149); %y96

beta*y(120) * (y(37)+y(38)+y(39)+y(40)+y(41)+y(42)+y(43)+y(44)+y(45)+y(4
6)+y(47)+y(48)) / (2*y(2)+0.0001) -
beta*11*y(97) * (y(96)+y(97)+y(178)) / (12*y(12)+0.0001) -beta*y(97) -
g*y(97)+g*y(160); %y97

g*y(25); %y98

-beta*y(99) * (y(37)+y(38)+y(39)+y(40)+y(41)+y(42)+y(43)+y(44)+y(45) +
y(46)+y(47)+y(48)) / (2*y(2)+0.0001)+g*y(26)+g*y(37); %y99

-beta*2*y(100) * (y(49)+y(50)+y(51)+y(52)+y(53)+y(54)+y(55)+y(56)) /
(3*y(3)+0.0001)+g*y(27)+g*y(49); %y100

-
beta*3*y(101) * (y(57)+y(58)+y(59)+y(60)+y(61)+y(62)+y(63)+y(64)+y(65)) /
(4*y(4)+0.0001)+g*y(28)+g*y(57); %y101

-beta*4*y(102) * (y(66)+y(67)+y(68)+y(69)+y(70)+y(71)) / (5*y(5)+0.0001)+
g*y(29)+g*y(66); %y102

-beta*5*y(103) * (y(72)+y(73)+y(74)+y(75)+y(76)+y(77)+y(78)) /
(6*y(6)+0.0001)+g*y(30)+g*y(72); %y103

-
beta*6*y(104) * (y(79)+y(80)+y(81)+y(82)) / (7*y(7)+0.0001)+g*y(31)+g*y(79
); %y104

-
beta*7*y(105) * (y(83)+y(84)+y(85)+y(86)+y(87)) / (8*y(8)+0.0001)+g*y(32)+
g*y(83); %y105

-beta*8*y(106) * (y(88)+y(89)) / (9*y(9)+0.0001)+g*y(33)+g*y(88); %y106

-beta*9*y(107) * (y(90)+y(91)+y(92)) / (10*y(10)+0.0001)+g*y(34)+g*y(90);
%y107

-beta*10*y(108) * (y(93)+y(94)+y(95)) / (11*y(11)+0.0001)+g*y(35)+g*y(93);
%y108

-
beta*11*y(109) * (y(96)+y(97)+y(178)) / (12*y(12)+0.0001)+g*y(36)+g*y(96);
%y109

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$$-\text{beta} \cdot y(110) \cdot (y(37) + y(38) + y(39) + y(40) + y(41) + y(42) + y(43) + y(44) + y(45) + y(46) + y(47) + y(48)) / (y(2) + 0.0001) + g \cdot y(38); \%y110$$

$$-\text{beta} \cdot 2 \cdot y(111) \cdot (y(49) + y(50) + y(51) + y(52) + y(53) + y(54) + y(55) + y(56)) / (3 \cdot y(3) + 0.0001) -$$

$$\text{beta} \cdot y(111) \cdot (y(37) + y(38) + y(39) + y(40) + y(41) + y(42) + y(43) + y(44) + y(45) + y(46) + y(47) + y(48)) / (2 \cdot y(2) + 0.0001) + g \cdot y(39) + g \cdot y(50); \%y111$$

-

$$\text{beta} \cdot 3 \cdot y(112) \cdot (y(57) + y(58) + y(59) + y(60) + y(61) + y(62) + y(63) + y(64) + y(65)) / (4 \cdot y(4) + 0.0001) -$$

$$\text{beta} \cdot y(112) \cdot (y(37) + y(38) + y(39) + y(40) + y(41) + y(42) + y(43) + y(44) + y(45) + y(46) + y(47) + y(48)) / (2 \cdot y(2) + 0.0001) + g \cdot y(40) + g \cdot y(58); \%y112$$

$$-\text{beta} \cdot 4 \cdot y(113) \cdot (y(66) + y(67) + y(68) + y(69) + y(70) + y(71)) / (5 \cdot y(5) + 0.0001) -$$

$$\text{beta} \cdot y(113) \cdot (y(37) + y(38) + y(39) + y(40) + y(41) + y(42) + y(43) + y(44) + y(45) + y(46) + y(47) + y(48)) / (2 \cdot y(2) + 0.0001) + g \cdot y(41) + g \cdot y(67); \%y113$$

-

$$\text{beta} \cdot 5 \cdot y(114) \cdot (y(72) + y(73) + y(74) + y(75) + y(76) + y(77) + y(78)) / (6 \cdot y(6) + 0.0001) -$$

$$\text{beta} \cdot y(114) \cdot (y(37) + y(38) + y(39) + y(40) + y(41) + y(42) + y(43) + y(44) + y(45) + y(46) + y(47) + y(48)) / (2 \cdot y(2) + 0.0001) + g \cdot y(42) + g \cdot y(73); \%y114$$

$$-\text{beta} \cdot 6 \cdot y(115) \cdot (y(79) + y(80) + y(81) + y(82)) / (7 \cdot y(7) + 0.0001) -$$

$$\text{beta} \cdot y(115) \cdot (y(37) + y(38) + y(39) + y(40) + y(41) + y(42) + y(43) + y(44) + y(45) + y(46) + y(47) + y(48)) / (2 \cdot y(2) + 0.0001) + g \cdot y(43) + g \cdot y(80); \%y115$$

$$-\text{beta} \cdot 7 \cdot y(116) \cdot (y(83) + y(84) + y(85) + y(86) + y(87)) / (8 \cdot y(8) + 0.0001) -$$

$$\text{beta} \cdot y(116) \cdot (y(37) + y(38) + y(39) + y(40) + y(41) + y(42) + y(43) + y(44) + y(45) + y(46) + y(47) + y(48)) / (2 \cdot y(2) + 0.0001) + g \cdot y(44) + g \cdot y(84); \%y116$$

$$-\text{beta} \cdot 8 \cdot y(117) \cdot (y(88) + y(89)) / (9 \cdot y(9) + 0.0001) -$$

$$\text{beta} \cdot y(117) \cdot (y(37) + y(38) + y(39) + y(40) + y(41) + y(42) + y(43) + y(44) + y(45) + y(46) + y(47) + y(48)) / (2 \cdot y(2) + 0.0001) + g \cdot y(45) + g \cdot y(89); \%y117$$

$$-\text{beta} \cdot 9 \cdot y(118) \cdot (y(90) + y(91) + y(92)) / (10 \cdot y(10) + 0.0001) -$$

$$\text{beta} \cdot y(118) \cdot (y(37) + y(38) + y(39) + y(40) + y(41) + y(42) + y(43) + y(44) + y(45) + y(46) + y(47) + y(48)) / (2 \cdot y(2) + 0.0001) + g \cdot y(46) + g \cdot y(91); \%y118$$

$$-\text{beta} \cdot 10 \cdot y(119) \cdot (y(93) + y(94) + y(95)) / (11 \cdot y(11) + 0.0001) -$$

$$\text{beta} \cdot y(119) \cdot (y(37) + y(38) + y(39) + y(40) + y(41) + y(42) + y(43) + y(44) + y(45) + y(46) + y(47) + y(48)) / (2 \cdot y(2) + 0.0001) + g \cdot y(47) + g \cdot y(94); \%y119$$

$$-\text{beta} \cdot 11 \cdot y(120) \cdot (y(96) + y(97) + y(178)) / (12 \cdot y(12) + 0.0001) -$$

$$\text{beta} \cdot y(120) \cdot (y(37) + y(38) + y(39) + y(40) + y(41) + y(42) + y(43) + y(44) + y(45) + y(46) + y(47) + y(48)) / (2 \cdot y(2) + 0.0001) + g \cdot y(48) + g \cdot y(97); \%y120$$

$$-\text{beta} \cdot 4 \cdot y(121) \cdot (y(49) + y(50) + y(51) + y(52) + y(53) + y(54) + y(55) + y(56)) / (3 \cdot y(3) + 0.0001) + g \cdot y(51); \%y121$$

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$$\text{beta} \cdot 3 \cdot y(122) \cdot (y(57) + y(58) + y(59) + y(60) + y(61) + y(62) + y(63) + y(64) + y(65)) /$$

$(4*y(4)+0.0001)-beta*2*y(122)*(y(49)+y(50)+y(51)+y(52)+y(53)+y(54)+y(55)+y(56))/(3*y(3)+0.0001)+g*y(52)+g*y(59); \%y122$

$-beta*4*y(123)*(y(66)+y(67)+y(68)+y(69)+y(70)+y(71))/(5*y(5)+0.0001)-beta*2*y(123)*(y(49)+y(50)+y(51)+y(52)+y(53)+y(54)+y(55)+y(56))/(3*y(3)+0.0001)+g*y(53)+g*y(68); \%y123$

-

$beta*5*y(124)*(y(72)+y(73)+y(74)+y(75)+y(76)+y(77)+y(78))/(6*y(6)+0.0001)-beta*2*y(124)*(y(49)+y(50)+y(51)+y(52)+y(53)+y(54)+y(55)+y(56))/(3*y(3)+0.0001)+g*y(54)+g*y(74); \%y124$

$-beta*6*y(125)*(y(79)+y(80)+y(81)+y(82))/(7*y(7)+0.0001)-beta*2*y(125)*(y(49)+y(50)+y(51)+y(52)+y(53)+y(54)+y(55)+y(56))/(3*y(3)+0.0001)+g*y(55)+g*y(81); \%y125$

$-beta*7*y(126)*(y(83)+y(84)+y(85)+y(86)+y(87))/(8*y(8)+0.0001)-beta*2*y(126)*(y(49)+y(50)+y(51)+y(52)+y(53)+y(54)+y(55)+y(56))/(3*y(3)+0.0001)+g*y(56)+g*y(85); \%y126$

-

$beta*3*y(127)*(y(57)+y(58)+y(59)+y(60)+y(61)+y(62)+y(63)+y(64)+y(65))/(2*y(4)+0.0001)+g*y(60); \%y127$

$-beta*4*y(128)*(y(66)+y(67)+y(68)+y(69)+y(70)+y(71))/(5*y(5)+0.0001)-beta*3*y(128)*(y(57)+y(58)+y(59)+y(60)+y(61)+y(62)+y(63)+y(64)+y(65))/(4*y(4)+0.0001)+g*y(61)+g*y(69); \%y128$

-

$beta*5*y(129)*(y(72)+y(73)+y(74)+y(75)+y(76)+y(77)+y(78))/(6*y(6)+0.0001)-beta*3*y(129)*(y(57)+y(58)+y(59)+y(60)+y(61)+y(62)+y(63)+y(64)+y(65))/(4*y(4)+0.0001)+g*y(62)+g*y(75); \%y129$

$-beta*7*y(130)*(y(83)+y(84)+y(85)+y(86)+y(87))/(8*y(8)+0.0001)-beta*3*y(130)*(y(57)+y(58)+y(59)+y(60)+y(61)+y(62)+y(63)+y(64)+y(65))/(4*y(4)+0.0001)+g*y(63)+g*y(86); \%y130$

$-beta*9*y(131)*(y(90)+y(91)+y(92))/(10*y(10)+0.0001)-beta*3*y(131)*(y(57)+y(58)+y(59)+y(60)+y(61)+y(62)+y(63)+y(64)+y(65))/(4*y(4)+0.0001)+g*y(64)+g*y(92); \%y131$

$-beta*11*y(132)*(y(96)+y(97)+y(178))/(12*y(12)+0.0001)-beta*3*y(132)*(y(57)+y(58)+y(59)+y(60)+y(61)+y(62)+y(63)+y(64)+y(65))/(4*y(4)+0.0001)+g*y(65)+g*y(178); \%y132$

$-beta*8*y(133)*(y(66)+y(67)+y(68)+y(69)+y(70)+y(71))/(5*y(5)+0.0001)+g*y(70); \%y133$

-

$beta*5*y(134)*(y(72)+y(73)+y(74)+y(75)+y(76)+y(77)+y(78))/(6*y(6)+0.0001)-$

beta*4*y(134) * (y(66)+y(67)+y(68)+y(69)+y(70)+y(71)) / (5*y(5)+0.0001)+g*
y(71)+g*y(76); %y134

-beta*5*y(135) * (y(72)+y(73)+y(74)+y(75)+y(76)+y(77)+y(78)) /
(3*y(6)+0.0001)+g*y(77); %y135

-beta*6*y(136) * (y(79)+y(80)+y(81)+y(82)) / (7*y(7)+0.0001) -
beta*5*y(136) * (y(72)+y(73)+y(74)+y(75)+y(76)+y(77)+y(78)) / (6*y(6)+0.00
01)+g*y(78)+g*y(82); %y136

-beta*10*y(137) * (y(93)+y(94)+y(95)) / (11*y(11)+0.0001) -
beta*7*y(137) * (y(83)+y(84)+y(85)+y(86)+y(87)) / (8*y(8)+0.0001)+g*y(87) +
g*y(95); %y137

beta*y(25)-2*g*y(138); %y138

beta*y(37) * (y(37)+y(38)+y(39)+y(40)+y(41)+y(42)+y(43)+y(44)+y(45)+y(46
) +y(47)+y(48)) / (2*y(2)+0.0001)+beta*y(37)+beta*y(26)-2*g*y(139); %y139

beta*2*y(49) * (y(49)+y(50)+y(51)+y(52)+y(53)+y(54)+y(55)+y(56)) / (3*y(3)
+0.0001)+beta*y(49)+beta*y(27)-2*g*y(140); %y140

beta*3*y(57) * (y(57)+y(58)+y(59)+y(60)+y(61)+y(62)+y(63)+y(64)+y(65)) / (
4*y(4)+0.0001)+beta*y(57)+beta*y(28)-2*g*y(141); %y141

beta*4*y(66) * (y(66)+y(67)+y(68)+y(69)+y(70)+y(71)) / (5*y(5)+0.0001)+bet
a*y(66)+beta*y(29)-2*g*y(142); %y142

beta*5*y(72) * (y(72)+y(73)+y(74)+y(75)+y(76)+y(77)+y(78)) / (6*y(6)+0.000
1)+beta*y(72)+beta*y(30)-2*g*y(143); %y143

beta*6*y(79) * (y(79)+y(80)+y(81)+y(82)) / (7*y(7)+0.0001)+beta*y(79)+beta
*y(31)-2*g*y(144); %y144

beta*7*y(83) * (y(83)+y(84)+y(85)+y(86)+y(87)) / (8*y(8)+0.0001)+beta*y(83
) +beta*y(32)-2*g*y(145); %y145

beta*8*y(88) * (y(88)+y(89)) / (9*y(9)+0.0001)+beta*y(88)+beta*y(33) -
2*g*y(146); %y146

beta*9*y(90) * (y(90)+y(91)+y(92)) / (10*y(10)+0.0001)+beta*y(90)+beta*y(3
4)-2*g*y(147); %y147

beta*10*y(93) * (y(93)+y(94)+y(95)) / (11*y(11)+0.0001)+beta*y(93)+beta*y(
35)-2*g*y(148); %y148

beta*11*y(96) * (y(96)+y(97)+y(178)) / (12*y(12)+0.0001)+beta*y(96)+beta*y
(36)-2*g*y(149); %y149

beta*y(38) * (y(37)+y(38)+y(39)+y(40)+y(41)+y(42)+y(43)+y(44)+y(45)+y(46
) +y(47)+y(48)) / (y(2)+0.0001)+beta*y(38)-2*g*y(150); %y150

$\text{beta} * 2 * y(50) * (y(49) + y(50) + y(51) + y(52) + y(53) + y(54) + y(55) + y(56)) / (3 * y(3) + 0.0001) + \text{beta} * y(39) * (y(37) + y(38) + y(39) + y(40) + y(41) + y(42) + y(43) + y(44) + y(45) + y(46) + y(47) + y(48)) / (2 * y(2) + 0.0001) + \text{beta} * y(50) + \text{beta} * y(39) - 2 * g * y(151); \%y151$

$\text{beta} * 3 * y(58) * (y(57) + y(58) + y(59) + y(60) + y(61) + y(62) + y(63) + y(64) + y(65)) / (4 * y(4) + 0.0001) + \text{beta} * y(40) * (y(37) + y(38) + y(39) + y(40) + y(41) + y(42) + y(43) + y(44) + y(45) + y(46) + y(47) + y(48)) / (2 * y(2) + 0.0001) + \text{beta} * y(58) + \text{beta} * y(40) - 2 * g * y(152); \%y152$

$\text{beta} * 4 * y(67) * (y(66) + y(67) + y(68) + y(69) + y(70) + y(71)) / (5 * y(5) + 0.0001) + \text{beta} * y(41) * (y(37) + y(38) + y(39) + y(40) + y(41) + y(42) + y(43) + y(44) + y(45) + y(46) + y(47) + y(48)) / (2 * y(2) + 0.0001) + \text{beta} * y(67) + \text{beta} * y(41) - 2 * g * y(153); \%y153$

$\text{beta} * 5 * y(73) * (y(72) + y(73) + y(74) + y(75) + y(76) + y(77) + y(78)) / (6 * y(6) + 0.0001) + \text{beta} * y(42) * (y(37) + y(38) + y(39) + y(40) + y(41) + y(42) + y(43) + y(44) + y(45) + y(46) + y(47) + y(48)) / (2 * y(2) + 0.0001) + \text{beta} * y(73) + \text{beta} * y(42) - 2 * g * y(154); \%y154$

$\text{beta} * 6 * y(80) * (y(79) + y(80) + y(81) + y(82)) / (7 * y(7) + 0.0001) + \text{beta} * y(43) * (y(37) + y(38) + y(39) + y(40) + y(41) + y(42) + y(43) + y(44) + y(45) + y(46) + y(47) + y(48)) / (2 * y(2) + 0.0001) + \text{beta} * y(80) + \text{beta} * y(43) - 2 * g * y(155); \%y155$

$\text{beta} * 7 * y(84) * (y(83) + y(84) + y(85) + y(86) + y(87)) / (8 * y(8) + 0.0001) + \text{beta} * y(44) * (y(37) + y(38) + y(39) + y(40) + y(41) + y(42) + y(43) + y(44) + y(45) + y(46) + y(47) + y(48)) / (2 * y(2) + 0.0001) + \text{beta} * y(84) + \text{beta} * y(44) - 2 * g * y(156); \%y156$

$\text{beta} * 8 * y(89) * (y(88) + y(89)) / (9 * y(9) + 0.0001) + \text{beta} * y(45) * (y(37) + y(38) + y(39) + y(40) + y(41) + y(42) + y(43) + y(44) + y(45) + y(46) + y(47) + y(48)) / (2 * y(2) + 0.0001) + \text{beta} * y(89) + \text{beta} * y(45) - 2 * g * y(157); \%y157$

$\text{beta} * 9 * y(91) * (y(90) + y(91) + y(92)) / (10 * y(10) + 0.0001) + \text{beta} * y(46) * (y(37) + y(38) + y(39) + y(40) + y(41) + y(42) + y(43) + y(44) + y(45) + y(46) + y(47) + y(48)) / (2 * y(2) + 0.0001) + \text{beta} * y(91) + \text{beta} * y(46) - 2 * g * y(158); \%y158$

$\text{beta} * 10 * y(94) * (y(93) + y(94) + y(95)) / (11 * y(11) + 0.0001) + \text{beta} * y(47) * (y(37) + y(38) + y(39) + y(40) + y(41) + y(42) + y(43) + y(44) + y(45) + y(46) + y(47) + y(48)) / (2 * y(2) + 0.0001) + \text{beta} * y(94) + \text{beta} * y(47) - 2 * g * y(159); \%y159$

$\text{beta} * 11 * y(97) * (y(96) + y(97) + y(98)) / (12 * y(12) + 0.0001) + \text{beta} * y(48) * (y(37) + y(38) + y(39) + y(40) + y(41) + y(42) + y(43) + y(44) + y(45) + y(46) + y(47) + y(48)) / (2 * y(2) + 0.0001) + \text{beta} * y(97) + \text{beta} * y(48) - 2 * g * y(160); \%y160$

$\text{beta} * 4 * y(51) * (y(49) + y(50) + y(51) + y(52) + y(53) + y(54) + y(55) + y(56)) / (3 * y(3) + 0.0001) + \text{beta} * y(51) - 2 * g * y(161); \%y161$

$\text{beta} * 3 * y(59) * (y(57) + y(58) + y(59) + y(60) + y(61) + y(62) + y(63) + y(64) + y(65)) / (4 * y(4) + 0.0001) + \text{beta} * 2 * y(52) * (y(49) + y(50) + y(51) + y(52) + y(53) + y(54) + y(55) + y(56)) / (3 * y(3) + 0.0001) + \text{beta} * y(59) + \text{beta} * y(52) - 2 * g * y(162); \%y162$

$\text{beta} * 4 * y(68) * (y(66) + y(67) + y(68) + y(69) + y(70) + y(71)) / (5 * y(5) + 0.0001) + \text{beta} * 2 * y(53) * (y(49) + y(50) + y(51) + y(52) + y(53) + y(54) + y(55) + y(56)) / (3 * y(3) + 0.0001) + \text{beta} * y(68) + \text{beta} * y(53) - 2 * g * y(163); \%y163$

$$\text{beta}^5 * y(74) * (y(72) + y(73) + y(74) + y(75) + y(76) + y(77) + y(78)) / (6 * y(6) + 0.0001) + \text{beta}^2 * y(54) * (y(49) + y(50) + y(51) + y(52) + y(53) + y(54) + y(55) + y(56)) / (3 * y(3) + 0.0001) + \text{beta} * y(74) + \text{beta} * y(54) - 2 * g * y(164); \%y164$$

$$\text{beta}^6 * y(81) * (y(79) + y(80) + y(81) + y(82)) / (7 * y(7) + 0.0001) + \text{beta}^2 * y(55) * (y(49) + y(50) + y(51) + y(52) + y(53) + y(54) + y(55) + y(56)) / (3 * y(3) + 0.0001) + \text{beta} * y(81) + \text{beta} * y(55) - 2 * g * y(165); \%y165$$

$$\text{beta}^7 * y(85) * (y(83) + y(84) + y(85) + y(86) + y(87)) / (8 * y(8) + 0.0001) + \text{beta}^2 * y(56) * (y(49) + y(50) + y(51) + y(52) + y(53) + y(54) + y(55) + y(56)) / (3 * y(3) + 0.0001) + \text{beta} * y(85) + \text{beta} * y(56) - 2 * g * y(166); \%y166$$

$$\text{beta}^3 * y(60) * (y(57) + y(58) + y(59) + y(60) + y(61) + y(62) + y(63) + y(64) + y(65)) / (2 * y(4) + 0.0001) + \text{beta} * y(60) - 2 * g * y(167); \%y167$$

$$\text{beta}^4 * y(69) * (y(66) + y(67) + y(68) + y(69) + y(70) + y(71)) / (5 * y(5) + 0.0001) + \text{beta}^3 * y(61) * (y(57) + y(58) + y(59) + y(60) + y(61) + y(62) + y(63) + y(64) + y(65)) / (4 * y(4) + 0.0001) + \text{beta} * y(69) + \text{beta} * y(61) - 2 * g * y(168); \%y168$$

$$\text{beta}^5 * y(75) * (y(72) + y(73) + y(74) + y(75) + y(76) + y(77) + y(78)) / (6 * y(6) + 0.0001) + \text{beta}^3 * y(62) * (y(57) + y(58) + y(59) + y(60) + y(61) + y(62) + y(63) + y(64) + y(65)) / (4 * y(4) + 0.0001) + \text{beta} * y(75) + \text{beta} * y(62) - 2 * g * y(169); \%y169$$

$$\text{beta}^7 * y(86) * (y(83) + y(84) + y(85) + y(86) + y(87)) / (8 * y(8) + 0.0001) + \text{beta}^3 * y(63) * (y(57) + y(58) + y(59) + y(60) + y(61) + y(62) + y(63) + y(64) + y(65)) / (4 * y(4) + 0.0001) + \text{beta} * y(86) + \text{beta} * y(63) - 2 * g * y(170); \%y170$$

$$\text{beta}^9 * y(92) * (y(90) + y(91) + y(92)) / (10 * y(10) + 0.0001) + \text{beta}^3 * y(64) * (y(57) + y(58) + y(59) + y(60) + y(61) + y(62) + y(63) + y(64) + y(65)) / (4 * y(4) + 0.0001) + \text{beta} * y(92) + \text{beta} * y(64) - 2 * g * y(171); \%y171$$

$$\text{beta}^{11} * y(178) * (y(96) + y(97) + y(178)) / (12 * y(12) + 0.0001) + \text{beta}^3 * y(65) * (y(57) + y(58) + y(59) + y(60) + y(61) + y(62) + y(63) + y(64) + y(65)) / (4 * y(4) + 0.0001) + \text{beta} * y(178) + \text{beta} * y(65) - 2 * g * y(172); \%y172$$

$$\text{beta}^8 * y(70) * (y(66) + y(67) + y(68) + y(69) + y(70) + y(71)) / (5 * y(5) + 0.0001) + \text{beta} * y(70) - 2 * g * y(173); \%y173$$

$$\text{beta}^5 * y(76) * (y(72) + y(73) + y(74) + y(75) + y(76) + y(77) + y(78)) / (6 * y(6) + 0.0001) + \text{beta}^4 * y(71) * (y(66) + y(67) + y(68) + y(69) + y(70) + y(71)) / (5 * y(5) + 0.0001) + \text{beta} * y(76) + \text{beta} * y(71) - 2 * g * y(174); \%y174$$

$$\text{beta}^5 * y(77) * (y(72) + y(73) + y(74) + y(75) + y(76) + y(77) + y(78)) / (3 * y(6) + 0.0001) + \text{beta} * y(77) - 2 * g * y(175); \%y175$$

$$\text{beta}^6 * y(82) * (y(79) + y(80) + y(81) + y(82)) / (7 * y(7) + 0.0001) + \text{beta}^5 * y(78) * (y(72) + y(73) + y(74) + y(75) + y(76) + y(77) + y(78)) / (6 * y(6) + 0.0001) + \text{beta} * y(82) + \text{beta} * y(78) - 2 * g * y(176); \%y176$$

$$\text{beta}^{10} * y(95) * (y(93) + y(94) + y(95)) / (11 * y(11) + 0.0001) + \text{beta}^7 * y(87) * (y(83) + y(84) + y(85) + y(86) + y(87)) / (8 * y(8) + 0.0001) + \text{beta} * y(95) + \text{beta} * y(87) - 2 * g * y(177); \%y177$$

```

beta*3*y(132)*(y(57)+y(58)+y(59)+y(60)+y(61)+y(62)+y(63)+y(64)+y(65))/
(4*y(4)+0.0001)-beta*11*y(178)*(y(96)+y(97)+y(178))/(12*y(12)+0.0001)-
beta*y(178)-g*y(178)+g*y(172); %y178
];

```

Tsolver1_1.m (case 1i)

```

clear all

%define parameters & set values

global beta %define it
    beta=0.3; %give value

global g %define it
    g=0.1; %give value

    %set the running time for the syst
ti=0;
tf=70;
tspan=[ti,tf];

%setting initial valaues for y vector
y0=[1077362/1105668; % S1 = y(1)
22902/1105668; % S2 = y(2)
1041/1105668; % S3 = y(3)
347/1105668; % S4 = y(4)
0/1105668; % S5 = y(5)
347/1105668; % S6 = y(6)
0; % S7 = y(7)
0; % S8 = y(8)
0; % S9 = y(9)
0; % S10 = y(10)
0; % S11 = y(11)
0; % S12 = y(12)

2557/1105668; % I1 = y(13)
746/1105668; % I2 = y(14)
210/1105668; % I3 = y(15)
91/1105668; % I4 = y(16)
34/1105668; % I5 = y(17)
11/1105668; % I6 = y(18)
7/1105668; % I7 = y(19)
6/1105668; % I8 = y(20)
4/1105668; % I9 = y(21)
1/1105668; % I10 = y(22)
1/1105668; % I11 = y(23)
1/1105668; % I12 = y(24)

```

1352/567602; % S1I1 = y(25)
878/567602; % S1I2 = y(26)
379/567602; % S1I3 = y(27)
223/567602; % S1I4 = y(28)
110/567602; % S1I5 = y(29)
41/567602; % S1I6 = y(30)
36/567602; % S1I7 = y(31)
30/567602; % S1I8 = y(32)
25/567602; % S1I9 = y(33)
7/567602; % S1I10 = y(34)
7/567602; % S1I11 = y(35)
10/567602; % S1I12 = y(36)
64/567602; % S2I1 = y(37)
27/567602; % S2I2 = y(38)
13/567602; % S2I3 = y(39)
12/567602; % S2I4 = y(40)
7/567602; % S2I5 = y(41)
3/567602; % S2I6 = y(42)
2/567602; % S2I7 = y(43)
2/567602; % S2I8 = y(44)
0/567602; % S2I9 = y(45)
1/567602; % S2I10 = y(46)
0/567602; % S2I11 = y(47)
1/567602; % S2I12 = y(48)
2/567602; % S3I1 = y(49)
3/567602; % S3I2 = y(50)
1/567602; % S3I3 = y(51)
1/567602; % S3I4 = y(52)
2/567602; % S3I5 = y(53)
0; % S3I6 = y(54)
0; % S3I7 = y(55)
0/567602; % S3I8 = y(56)
1/567602; % S4I1 = y(57)
0/567602; % S4I2 = y(58)
0/567602; % S4I3 = y(59)
1/567602; % S4I4 = y(60)
0/567602; % S4I5 = y(61)
1/567602; % S4I6 = y(62)
0; % S4I8 = y(63)
0; % S4I10 = y(64)
1/567602; % S4I12 = y(65)
0; % S5I1 = y(66)
0/567602; % S5I2 = y(67)
0; % S5I3 = y(68)
0; % S5I4 = y(69)
0; % S5I5 = y(70)
0; % S5I6 = y(71)
1/567602; % S6I1 = y(72)
1/567602; % S6I2 = y(73)
0; % S6I3 = y(74)
2/567602; % S6I4 = y(75)
0; % S6I5 = y(76)
1/567602; % S6I6 = y(77)
1/567602; % S6I7 = y(78)

```

0;      % S7I1   = y(79)
0;      % S7I2   = y(80)
0;      % S7I3   = y(81)
0;      % S7I6   = y(82)
0;      % S8I1   = y(83)
0;      % S8I2   = y(84)
0;      % S8I3   = y(85)
0;      % S8I4   = y(86)
0;      % S8I11  = y(87)
0;      % S9I1   = y(88)
0;      % S9I2   = y(89)
0;      % S10I1  = y(90)
0;      % S10I2  = y(91)
0;      % S10I4  = y(92)
0;      % S11I1  = y(93)
0;      % S11I2  = y(94)
0;      % S11I8  = y(95)
0;      % S12I1  = y(96)
0;      % S12I2  = y(97)

531047/566504; % S1S1   = y(98)
11314/566504; % S1S2   = y(99)
514/566504;   % S1S3   = y(100)
171/566504;   % S1S4   = y(101)
0;      % S1S5   = y(102)
171/566504;   % S1S6   = y(103)
0;      % S1S7   = y(104)
0;      % S1S8   = y(105)
0;      % S1S9   = y(106)
0;      % S1S10  = y(107)
0;      % S1S11  = y(108)
0;      % S1S12  = y(109)
15969/566504; % S2S2   = y(110)
1452/566504; % S2S3   = y(111)
484/566504;   % S2S4   = y(112)
0;      % S2S5   = y(113)
484/566504;   % S2S6   = y(114)
0;      % S2S7   = y(115)
0;      % S2S8   = y(116)
0;      % S2S9   = y(117)
0;      % S2S10  = y(118)
0;      % S2S11  = y(119)
0;      % S2S12  = y(120)
345/566504;   % S3S3   = y(121)
229/566504;   % S3S4   = y(122)
0;      % S3S5   = y(123)
229/566504;   % S3S6   = y(124)
0;      % S3S7   = y(125)
0;      % S3S8   = y(126)
125/566504;   % S4S4   = y(127)
0;      % S4S5   = y(128)
250/566504;   % S4S6   = y(129)
0;      % S4S8   = y(130)
0;      % S4S10  = y(131)
0;      % S4S12  = y(132)

```

```

0; % S5S5 = y(133)
0; % S5S6 = y(134)
471/566504; % S6S6 = y(135)
0; % S6S7 = y(136)
0; % S8S11 = y(137)

278/566504; % I1I1 = y(138)
314/566504; % I1I2 = y(139)
131/566504; % I1I3 = y(140)
74/566504; % I1I4 = y(141)
26/566504; % I1I5 = y(142)
11/566504; % I1I6 = y(143)
7/566504; % I1I7 = y(144)
8/566504; % I1I8 = y(145)
7/566504; % I1I9 = y(146)
1/566504; % I1I10 = y(147)
2/566504; % I1I11 = y(148)
0; % I1I12 = y(149)
74/566504; % I2I2 = y(150)
64/566504; % I2I3 = y(151)
25/566504; % I2I4 = y(152)
13/566504; % I2I5 = y(153)
7/566504; % I2I6 = y(154)
2/566504; % I2I7 = y(155)
5/566504; % I2I8 = y(156)
4/566504; % I2I9 = y(157)
0; % I2I10 = y(158)
1/566504; % I2I11 = y(159)
0; % I2I12 = y(160)
11/566504; % I3I3 = y(161)
12/566504; % I3I4 = y(162)
5/566504; % I3I5 = y(163)
1/566504; % I3I6 = y(164)
1/566504; % I3I7 = y(165)
1/566504; % I3I8 = y(166)
4/566504; % I4I4 = y(167)
3/566504; % I4I5 = y(168)
1/566504; % I4I6 = y(169)
1/566504; % I4I8 = y(170)
1/566504; % I4I10 = y(171)
0; % I4I12 = y(172)
2/566504; % I5I5 = y(173)
0; % I5I6 = y(174)
0; % I6I6 = y(175)
0; % I6I7 = y(176)
1/566504; % I8I11 = y(177)
0]'; % S12I4 = y(178) %' is for transpose

%utilize the main routine or solver of Matlab
[t,y]=ode45(@thesis,tspan,y0);

%plot (t,y)
plot(t,y(:,1)+y(:,2)+y(:,3)+y(:,4)+y(:,5)+y(:,6)+y(:,7)+y(:,8)+y(:,9)+y(
:,10)+y(:,11)+y(:,12),t,y(:,13)+y(:,14)+y(:,15)+y(:,16)+y(:,17)+y(:,18)+y(
:,19)+y(:,20)+y(:,21)+y(:,22)+y(:,23)+y(:,24))

```

```

xlabel('Time (months)')
ylabel('Proportion')
legend ('[S]', '[I]')

```

Tsolver1_2.m (case lii)

```

clear all

%define parameters & set values

global beta %define it
    beta=0.3; %give value

global g %define it
    g=0.1; %give value

    %set the running time for the syst
ti=0;
tf=70;
tspan=[ti,tf];

%setting initial values for y vector
y0=[768399/1105668; % S1 = y(1)
223800/1105668; % S2 = y(2)
63000/1105668; % S3 = y(3)
27300/1105668; % S4 = y(4)
10200/1105668; % S5 = y(5)
3300/1105668; % S6 = y(6)
2100/1105668; % S7 = y(7)
1800/1105668; % S8 = y(8)
1200/1105668; % S9 = y(9)
300/1105668; % S10 = y(10)
300/1105668; % S11 = y(11)
300/1105668; % S12 = y(12)

2557/1105668; % I1 = y(13)
746/1105668; % I2 = y(14)
210/1105668; % I3 = y(15)
91/1105668; % I4 = y(16)
34/1105668; % I5 = y(17)
11/1105668; % I6 = y(18)
7/1105668; % I7 = y(19)
6/1105668; % I8 = y(20)
4/1105668; % I9 = y(21)
1/1105668; % I10 = y(22)
1/1105668; % I11 = y(23)
1/1105668; % I12 = y(24)

```

1352/819024; % S1I1 = y(25)
878/819024; % S1I2 = y(26)
379/819024; % S1I3 = y(27)
223/819024; % S1I4 = y(28)
110/819024; % S1I5 = y(29)
41/819024; % S1I6 = y(30)
36/819024; % S1I7 = y(31)
30/819024; % S1I8 = y(32)
25/819024; % S1I9 = y(33)
7/819024; % S1I10 = y(34)
7/819024; % S1I11 = y(35)
10/819024; % S1I12 = y(36)
64/819024; % S2I1 = y(37)
27/819024; % S2I2 = y(38)
13/819024; % S2I3 = y(39)
12/819024; % S2I4 = y(40)
7/819024; % S2I5 = y(41)
3/819024; % S2I6 = y(42)
2/819024; % S2I7 = y(43)
2/819024; % S2I8 = y(44)
0/819024; % S2I9 = y(45)
1/819024; % S2I10 = y(46)
0/819024; % S2I11 = y(47)
1/819024; % S2I12 = y(48)
2/819024; % S3I1 = y(49)
3/819024; % S3I2 = y(50)
1/819024; % S3I3 = y(51)
1/819024; % S3I4 = y(52)
2/819024; % S3I5 = y(53)
0; % S3I6 = y(54)
0; % S3I7 = y(55)
0/819024; % S3I8 = y(56)
1/819024; % S4I1 = y(57)
0/819024; % S4I2 = y(58)
0/819024; % S4I3 = y(59)
1/819024; % S4I4 = y(60)
0/819024; % S4I5 = y(61)
1/819024; % S4I6 = y(62)
0; % S4I8 = y(63)
0; % S4I10 = y(64)
1/819024; % S4I12 = y(65)
0; % S5I1 = y(66)
0/819024; % S5I2 = y(67)
0; % S5I3 = y(68)
0; % S5I4 = y(69)
0; % S5I5 = y(70)
0; % S5I6 = y(71)
1/819024; % S6I1 = y(72)
1/819024; % S6I2 = y(73)
0; % S6I3 = y(74)
2/819024; % S6I4 = y(75)
0; % S6I5 = y(76)
1/819024; % S6I6 = y(77)
1/819024; % S6I7 = y(78)

```

0;      %      S7I1      = y(79)
0;      %      S7I2      = y(80)
0;      %      S7I3      = y(81)
0;      %      S7I6      = y(82)
0;      %      S8I1      = y(83)
0;      %      S8I2      = y(84)
0;      %      S8I3      = y(85)
0;      %      S8I4      = y(86)
0;      %      S8I11     = y(87)
0;      %      S9I1      = y(88)
0;      %      S9I2      = y(89)
0;      %      S10I1     = y(90)
0;      %      S10I2     = y(91)
0;      %      S10I4     = y(92)
0;      %      S11I1     = y(93)
0;      %      S11I2     = y(94)
0;      %      S11I8     = y(95)
0;      %      S12I1     = y(96)
0;      %      S12I2     = y(97)

512108/566504;      %      S1S1      = y(98)
43633/566504;      %      S1S2      = y(99)
3038/566504;      %      S1S3      = y(100)
1349/566504;      %      S1S4      = y(101)
0;      %      S1S5      = y(102)
2028/566504;      %      S1S6      = y(103)
0;      %      S1S7      = y(104)
0;      %      S1S8      = y(105)
0;      %      S1S9      = y(106)
0;      %      S1S10     = y(107)
0;      %      S1S11     = y(108)
0;      %      S1S12     = y(109)
950/566504;      %      S2S2      = y(110)
66/566504;      %      S2S3      = y(111)
30/566504;      %      S2S4      = y(112)
0;      %      S2S5      = y(113)
43/566504;      %      S2S6      = y(114)
0;      %      S2S7      = y(115)
0;      %      S2S8      = y(116)
0;      %      S2S9      = y(117)
0;      %      S2S10     = y(118)
0;      %      S2S11     = y(119)
0;      %      S2S12     = y(120)
3/566504;      %      S3S3      = y(121)
2/566504;      %      S3S4      = y(122)
0;      %      S3S5      = y(123)
2/566504;      %      S3S6      = y(124)
0;      %      S3S7      = y(125)
0;      %      S3S8      = y(126)
1/566504;      %      S4S4      = y(127)
0;      %      S4S5      = y(128)
1/566504;      %      S4S6      = y(129)
0;      %      S4S8      = y(130)
0;      %      S4S10     = y(131)
0;      %      S4S12     = y(132)

```

```

0;      %   S5S5   = y(133)
0;      %   S5S6   = y(134)
1/566504; %   S6S6   = y(135)
0;      %   S6S7   = y(136)
0;      %   S8S11  = y(137)

278/819024; %   I1I1   = y(138)
314/819024; %   I1I2   = y(139)
131/819024; %   I1I3   = y(140)
74/819024; %   I1I4   = y(141)
26/819024; %   I1I5   = y(142)
11/819024; %   I1I6   = y(143)
7/819024; %   I1I7   = y(144)
8/819024; %   I1I8   = y(145)
7/819024; %   I1I9   = y(146)
1/819024; %   I1I10  = y(147)
2/819024; %   I1I11  = y(148)
0;      %   I1I12  = y(149)
74/819024; %   I2I2   = y(150)
64/819024; %   I2I3   = y(151)
25/819024; %   I2I4   = y(152)
13/819024; %   I2I5   = y(153)
7/819024; %   I2I6   = y(154)
2/819024; %   I2I7   = y(155)
5/819024; %   I2I8   = y(156)
4/819024; %   I2I9   = y(157)
0;      %   I2I10  = y(158)
1/819024; %   I2I11  = y(159)
0;      %   I2I12  = y(160)
11/819024; %   I3I3   = y(161)
12/819024; %   I3I4   = y(162)
5/819024; %   I3I5   = y(163)
1/819024; %   I3I6   = y(164)
1/819024; %   I3I7   = y(165)
1/819024; %   I3I8   = y(166)
4/819024; %   I4I4   = y(167)
3/819024; %   I4I5   = y(168)
1/819024; %   I4I6   = y(169)
1/819024; %   I4I8   = y(170)
1/819024; %   I4I10  = y(171)
0;      %   I4I12  = y(172)
2/819024; %   I5I5   = y(173)
0;      %   I5I6   = y(174)
0;      %   I6I6   = y(175)
0;      %   I6I7   = y(176)
1/819024; %   I8I11  = y(177)
0]';    %   S12I4  = y(178)  %' is for transpose

%utilize the main routine or solver of Matlab
[t,y]=ode45(@thesis,tspan,y0);

%plot (t,y)
plot(t,y(:,1)+y(:,2)+y(:,3)+y(:,4)+y(:,5)+y(:,6)+y(:,7)+y(:,8)+y(:,9)+y(
:,10)+y(:,11)+y(:,12),t,y(:,13)+y(:,14)+y(:,15)+y(:,16)+y(:,17)+y(:,18)+y(
(:,19)+y(:,20)+y(:,21)+y(:,22)+y(:,23)+y(:,24))

```

```
xlabel('Time (months)')
ylabel('Proportion')
legend ('[S]', '[I]')
```

Tsolver2_1.m (case 2i)

```
clear all

%define parameters & set values

global beta %define it
    beta=0.327; %give value

global g %define it
    g=0.1; %give value

    %set the running time for the syst
ti=0;
tf=200;
tspan=[ti,tf];

%setting initial valaues for y vector
y0=[768399/1105668; % S1 = y(1)
223800/1105668; % S2 = y(2)
63000/1105668; % S3 = y(3)
27300/1105668; % S4 = y(4)
10200/1105668; % S5 = y(5)
3300/1105668; % S6 = y(6)
2100/1105668; % S7 = y(7)
1800/1105668; % S8 = y(8)
1200/1105668; % S9 = y(9)
300/1105668; % S10 = y(10)
300/1105668; % S11 = y(11)
300/1105668; % S12 = y(12)

2557/1105668; % I1 = y(13)
746/1105668; % I2 = y(14)
210/1105668; % I3 = y(15)
91/1105668; % I4 = y(16)
34/1105668; % I5 = y(17)
11/1105668; % I6 = y(18)
7/1105668; % I7 = y(19)
6/1105668; % I8 = y(20)
4/1105668; % I9 = y(21)
1/1105668; % I10 = y(22)
1/1105668; % I11 = y(23)
1/1105668; % I12 = y(24)

1352/804725; % S1I1 = y(25)
878/804725; % S1I2 = y(26)
379/804725; % S1I3 = y(27)
223/804725; % S1I4 = y(28)
```

110/804725;	%	S1I5	= y(29)
41/804725;	%	S1I6	= y(30)
36/804725;	%	S1I7	= y(31)
30/804725;	%	S1I8	= y(32)
25/804725;	%	S1I9	= y(33)
7/804725;	%	S1I10	= y(34)
7/804725;	%	S1I11	= y(35)
10/804725;	%	S1I12	= y(36)
64/804725;	%	S2I1	= y(37)
27/804725;	%	S2I2	= y(38)
13/804725;	%	S2I3	= y(39)
12/804725;	%	S2I4	= y(40)
7/804725;	%	S2I5	= y(41)
3/804725;	%	S2I6	= y(42)
2/804725;	%	S2I7	= y(43)
2/804725;	%	S2I8	= y(44)
0/804725;	%	S2I9	= y(45)
1/804725;	%	S2I10	= y(46)
0/804725;	%	S2I11	= y(47)
1/804725;	%	S2I12	= y(48)
2/804725;	%	S3I1	= y(49)
3/804725;	%	S3I2	= y(50)
1/804725;	%	S3I3	= y(51)
1/804725;	%	S3I4	= y(52)
2/804725;	%	S3I5	= y(53)
0;	%	S3I6	= y(54)
0;	%	S3I7	= y(55)
0/804725;	%	S3I8	= y(56)
1/804725;	%	S4I1	= y(57)
0/804725;	%	S4I2	= y(58)
0/804725;	%	S4I3	= y(59)
1/804725;	%	S4I4	= y(60)
0/804725;	%	S4I5	= y(61)
1/804725;	%	S4I6	= y(62)
0;	%	S4I8	= y(63)
0;	%	S4I10	= y(64)
1/804725;	%	S4I12	= y(65)
0;	%	S5I1	= y(66)
0/804725;	%	S5I2	= y(67)
0;	%	S5I3	= y(68)
0;	%	S5I4	= y(69)
0;	%	S5I5	= y(70)
0;	%	S5I6	= y(71)
1/804725;	%	S6I1	= y(72)
1/804725;	%	S6I2	= y(73)
0;	%	S6I3	= y(74)
2/804725;	%	S6I4	= y(75)
0;	%	S6I5	= y(76)
1/804725;	%	S6I6	= y(77)
1/804725;	%	S6I7	= y(78)
0;	%	S7I1	= y(79)
0;	%	S7I2	= y(80)
0;	%	S7I3	= y(81)
0;	%	S7I6	= y(82)
0;	%	S8I1	= y(83)

0;	☞	S8I2	= y(84)
0;	☞	S8I3	= y(85)
0;	☞	S8I4	= y(86)
0;	☞	S8I11	= y(87)
0;	☞	S9I1	= y(88)
0;	☞	S9I2	= y(89)
0;	☞	S10I1	= y(90)
0;	☞	S10I2	= y(91)
0;	☞	S10I4	= y(92)
0;	☞	S11I1	= y(93)
0;	☞	S11I2	= y(94)
0;	☞	S11I8	= y(95)
0;	☞	S12I1	= y(96)
0;	☞	S12I2	= y(97)
314308/804725;	☞	S1S1	= y(98)
91698/804725;	☞	S1S2	= y(99)
25813/804725;	☞	S1S3	= y(100)
11186/804725;	☞	S1S4	= y(101)
4179/804725;	☞	S1S5	= y(102)
1352/804725;	☞	S1S6	= y(103)
860/804725;	☞	S1S7	= y(104)
737/804725;	☞	S1S8	= y(105)
491/804725;	☞	S1S9	= y(106)
123/804725;	☞	S1S10	= y(107)
123/804725;	☞	S1S11	= y(108)
123/804725;	☞	S1S12	= y(109)
142847/804725;	☞	S2S2	= y(110)
40210/804725;	☞	S2S3	= y(111)
17424/804725;	☞	S2S4	= y(112)
6510/804725;	☞	S2S5	= y(113)
2106/804725;	☞	S2S6	= y(114)
1340/804725;	☞	S2S7	= y(115)
1148/804725;	☞	S2S8	= y(116)
765/804725;	☞	S2S9	= y(117)
191/804725;	☞	S2S10	= y(118)
191/804725;	☞	S2S11	= y(119)
191/804725;	☞	S2S12	= y(120)
45385/804725;	☞	S3S3	= y(121)
19666/804725;	☞	S3S4	= y(122)
7347/804725;	☞	S3S5	= y(123)
2377/804725;	☞	S3S6	= y(124)
1512/804725;	☞	S3S7	= y(125)
1296/804725;	☞	S3S8	= y(126)
23591/804725;	☞	S4S4	= y(127)
8814/804725;	☞	S4S5	= y(128)
2851/804725;	☞	S4S6	= y(129)
1555/804725;	☞	S4S8	= y(130)
259/804725;	☞	S4S10	= y(131)
259/804725;	☞	S4S12	= y(132)
10394/804725;	☞	S5S5	= y(133)
3362/804725;	☞	S5S6	= y(134)
2938/804725;	☞	S6S6	= y(135)
1870/804725;	☞	S6S7	= y(136)
2986/804725;	☞	S8S11	= y(137)

```

278/804725; % I1I1 = y(138)
314/804725; % I1I2 = y(139)
131/804725; % I1I3 = y(140)
74/804725; % I1I4 = y(141)
26/804725; % I1I5 = y(142)
11/804725; % I1I6 = y(143)
7/804725; % I1I7 = y(144)
8/804725; % I1I8 = y(145)
7/804725; % I1I9 = y(146)
1/804725; % I1I10 = y(147)
2/804725; % I1I11 = y(148)
0; % I1I12 = y(149)
74/804725; % I2I2 = y(150)
64/804725; % I2I3 = y(151)
25/804725; % I2I4 = y(152)
13/804725; % I2I5 = y(153)
7/804725; % I2I6 = y(154)
2/804725; % I2I7 = y(155)
5/804725; % I2I8 = y(156)
4/804725; % I2I9 = y(157)
0; % I2I10 = y(158)
1/804725; % I2I11 = y(159)
0; % I2I12 = y(160)
11/804725; % I3I3 = y(161)
12/804725; % I3I4 = y(162)
5/804725; % I3I5 = y(163)
1/804725; % I3I6 = y(164)
1/804725; % I3I7 = y(165)
1/804725; % I3I8 = y(166)
4/804725; % I4I4 = y(167)
3/804725; % I4I5 = y(168)
1/804725; % I4I6 = y(169)
1/804725; % I4I8 = y(170)
1/804725; % I4I10 = y(171)
0; % I4I12 = y(172)
2/804725; % I5I5 = y(173)
0; % I5I6 = y(174)
0; % I6I6 = y(175)
0; % I6I7 = y(176)
1/804725; % I8I11 = y(177)
0]'; % S12I4 = y(178) %' is for transpose

%utilize the main routine or solver of Matlab
[t,y]=ode45(@thesis,tspan,y0);

%plot (t,y)
plot(t,y(:,1)+y(:,2)+y(:,3)+y(:,4)+y(:,5)+y(:,6)+y(:,7)+y(:,8)+y(:,9)+y(:,10)+y(:,11)+y(:,12),'--',t,y(:,13)+y(:,14)+y(:,15)+y(:,16)+y(:,17)+y(:,18)+y(:,19)+y(:,20)+y(:,21)+y(:,22)+y(:,23)+y(:,24),'-')

xlabel('Time (months)','FontSize',14)
ylabel('Proportion','FontSize',14)
legend(['S'],'[I]')

```

Tsolver2_2.m (case 2ii)

```
clear all

%define parameters & set values

global beta %define it
    beta=0.327; %give value

global g %define it
    g=0.1; %give value

%set the running time for the syst
ti=0;
tf=200;
tspan=[ti,tf];

%setting initial valaues for y vector
y0=[768399/1105668; % S1 = y(1)
223800/1105668; % S2 = y(2)
63000/1105668; % S3 = y(3)
27300/1105668; % S4 = y(4)
10200/1105668; % S5 = y(5)
3300/1105668; % S6 = y(6)
2100/1105668; % S7 = y(7)
1800/1105668; % S8 = y(8)
1200/1105668; % S9 = y(9)
300/1105668; % S10 = y(10)
300/1105668; % S11 = y(11)
300/1105668; % S12 = y(12)

2557/1105668; % I1 = y(13)
746/1105668; % I2 = y(14)
210/1105668; % I3 = y(15)
91/1105668; % I4 = y(16)
34/1105668; % I5 = y(17)
11/1105668; % I6 = y(18)
7/1105668; % I7 = y(19)
6/1105668; % I8 = y(20)
4/1105668; % I9 = y(21)
1/1105668; % I10 = y(22)
1/1105668; % I11 = y(23)
1/1105668; % I12 = y(24)

1352/820122; % S1I1 = y(25)
878/820122; % S1I2 = y(26)
379/820122; % S1I3 = y(27)
223/820122; % S1I4 = y(28)
110/820122; % S1I5 = y(29)
41/820122; % S1I6 = y(30)
36/820122; % S1I7 = y(31)
30/820122; % S1I8 = y(32)
25/820122; % S1I9 = y(33)
```

7/820122; % S1I10 = y(34)
7/820122; % S1I11 = y(35)
10/820122; % S1I12 = y(36)
64/820122; % S2I1 = y(37)
27/820122; % S2I2 = y(38)
13/820122; % S2I3 = y(39)
12/820122; % S2I4 = y(40)
7/820122; % S2I5 = y(41)
3/820122; % S2I6 = y(42)
2/820122; % S2I7 = y(43)
2/820122; % S2I8 = y(44)
0/820122; % S2I9 = y(45)
1/820122; % S2I10 = y(46)
0/820122; % S2I11 = y(47)
1/820122; % S2I12 = y(48)
2/820122; % S3I1 = y(49)
3/820122; % S3I2 = y(50)
1/820122; % S3I3 = y(51)
1/820122; % S3I4 = y(52)
2/820122; % S3I5 = y(53)
0; % S3I6 = y(54)
0; % S3I7 = y(55)
0/820122; % S3I8 = y(56)
1/820122; % S4I1 = y(57)
0/820122; % S4I2 = y(58)
0/820122; % S4I3 = y(59)
1/820122; % S4I4 = y(60)
0/820122; % S4I5 = y(61)
1/820122; % S4I6 = y(62)
0; % S4I8 = y(63)
0; % S4I10 = y(64)
1/820122; % S4I12 = y(65)
0; % S5I1 = y(66)
0/820122; % S5I2 = y(67)
0; % S5I3 = y(68)
0; % S5I4 = y(69)
0; % S5I5 = y(70)
0; % S5I6 = y(71)
1/820122; % S6I1 = y(72)
1/820122; % S6I2 = y(73)
0; % S6I3 = y(74)
2/820122; % S6I4 = y(75)
0; % S6I5 = y(76)
1/820122; % S6I6 = y(77)
1/820122; % S6I7 = y(78)
0; % S7I1 = y(79)
0; % S7I2 = y(80)
0; % S7I3 = y(81)
0; % S7I6 = y(82)
0; % S8I1 = y(83)
0; % S8I2 = y(84)
0; % S8I3 = y(85)
0; % S8I4 = y(86)
0; % S8I11 = y(87)
0; % S9I1 = y(88)

```

0;      *      S9I2      = y(89)
0;      *      S10I1     = y(90)
0;      *      S10I2     = y(91)
0;      *      S10I4     = y(92)
0;      *      S11I1     = y(93)
0;      *      S11I2     = y(94)
0;      *      S11I8     = y(95)
0;      *      S12I1     = y(96)
0;      *      S12I2     = y(97)

126485/820122; *      S1S1      = y(98)
230707/820122; *      S1S2      = y(99)
121679/820122; *      S1S3      = y(100)
73987/820122;  *      S1S4      = y(101)
35388/820122;  *      S1S5      = y(102)
13798/820122;  *      S1S6      = y(103)
10667/820122;  *      S1S7      = y(104)
10218/820122;  *      S1S8      = y(105)
8361/820122;   *      S1S9      = y(106)
2261/820122;   *      S1S10     = y(107)
2551/820122;   *      S1S11     = y(108)
2714/820122;   *      S1S12     = y(109)
67307/820122;  *      S2S2      = y(110)
35499/820122;  *      S2S3      = y(111)
21581/820122;  *      S2S4      = y(112)
10324/820122;  *      S2S5      = y(113)
4025/820122;   *      S2S6      = y(114)
3111/820122;   *      S2S7      = y(115)
2976/820122;   *      S2S8      = y(116)
2439/820122;   *      S2S9      = y(117)
659/820122;    *      S2S10     = y(118)
743/820122;    *      S2S11     = y(119)
790/820122;    *      S2S12     = y(120)
9993/820122;   *      S3S3      = y(121)
6075/820122;   *      S3S4      = y(122)
2906/820122;   *      S3S5      = y(123)
1133/820122;   *      S3S6      = y(124)
876/820122;    *      S3S7      = y(125)
837/820122;    *      S3S8      = y(126)
2632/820122;   *      S4S4      = y(127)
1259/820122;   *      S4S5      = y(128)
491/820122;    *      S4S6      = y(129)
363/820122;    *      S4S8      = y(130)
80/820122;     *      S4S10     = y(131)
96/820122;     *      S4S12     = y(132)
470/820122;    *      S5S5      = y(133)
183/820122;    *      S5S6      = y(134)
59/820122;     *      S6S6      = y(135)
46/820122;     *      S6S7      = y(136)
6/820122;      *      S8S11     = y(137)

278/820122;    *      I1I1     = y(138)
314/820122;    *      I1I2     = y(139)
131/820122;    *      I1I3     = y(140)
74/820122;     *      I1I4     = y(141)

```

```

26/820122; % I1I5 = y(142)
11/820122; % I1I6 = y(143)
7/820122; % I1I7 = y(144)
8/820122; % I1I8 = y(145)
7/820122; % I1I9 = y(146)
1/820122; % I1I10 = y(147)
2/820122; % I1I11 = y(148)
0; % I1I12 = y(149)
74/820122; % I2I2 = y(150)
64/820122; % I2I3 = y(151)
25/820122; % I2I4 = y(152)
13/820122; % I2I5 = y(153)
7/820122; % I2I6 = y(154)
2/820122; % I2I7 = y(155)
5/820122; % I2I8 = y(156)
4/820122; % I2I9 = y(157)
0; % I2I10 = y(158)
1/820122; % I2I11 = y(159)
0; % I2I12 = y(160)
11/820122; % I3I3 = y(161)
12/820122; % I3I4 = y(162)
5/820122; % I3I5 = y(163)
1/820122; % I3I6 = y(164)
1/820122; % I3I7 = y(165)
1/820122; % I3I8 = y(166)
4/820122; % I4I4 = y(167)
3/820122; % I4I5 = y(168)
1/820122; % I4I6 = y(169)
1/820122; % I4I8 = y(170)
1/820122; % I4I10 = y(171)
0; % I4I12 = y(172)
2/820122; % I5I5 = y(173)
0; % I5I6 = y(174)
0; % I6I6 = y(175)
0; % I6I7 = y(176)
1/820122; % I8I11 = y(177)
0]'; % S12I4 = y(178) %' is for transpose

%utilize the main routine or solver of Matlab
[t,y]=ode45(@thesis,tspan,y0);

%plot (t,y)
plot(t,y(:,1)+y(:,2)+y(:,3)+y(:,4)+y(:,5)+y(:,6)+y(:,7)+y(:,8)+y(:,9)+y(:,10)+y(:,11)+y(:,12),'--',t,y(:,13)+y(:,14)+y(:,15)+y(:,16)+y(:,17)+y(:,18)+y(:,19)+y(:,20)+y(:,21)+y(:,22)+y(:,23)+y(:,24),'-')

xlabel('Time (months)','FontSize',14)
ylabel('Proportion','FontSize',14)
legend ('[S]','[I]')

```

APPENDIX E

$$\frac{d[\mathbf{S}^1]}{dt} = \mathbf{g}[\mathbf{I}^1] - \beta([\mathbf{S}^1\mathbf{I}^1] + [\mathbf{S}^1\mathbf{I}^2] + [\mathbf{S}^1\mathbf{I}^3] + [\mathbf{S}^1\mathbf{I}^4] + [\mathbf{S}^1\mathbf{I}^5] + [\mathbf{S}^1\mathbf{I}^6] + [\mathbf{S}^1\mathbf{I}^7] + [\mathbf{S}^1\mathbf{I}^8] + [\mathbf{S}^1\mathbf{I}^9] + [\mathbf{S}^1\mathbf{I}^{10}] + [\mathbf{S}^1\mathbf{I}^{11}] + [\mathbf{S}^1\mathbf{I}^{12}])$$

$$\frac{d[\mathbf{S}^2]}{dt} = \mathbf{g}[\mathbf{I}^2] - \beta([\mathbf{S}^2\mathbf{I}^1] + [\mathbf{S}^2\mathbf{I}^2] + [\mathbf{S}^2\mathbf{I}^3] + [\mathbf{S}^2\mathbf{I}^4] + [\mathbf{S}^2\mathbf{I}^5] + [\mathbf{S}^2\mathbf{I}^6] + [\mathbf{S}^2\mathbf{I}^7] + [\mathbf{S}^2\mathbf{I}^8] + [\mathbf{S}^2\mathbf{I}^9] + [\mathbf{S}^2\mathbf{I}^{10}] + [\mathbf{S}^2\mathbf{I}^{11}] + [\mathbf{S}^2\mathbf{I}^{12}])$$

$$\frac{d[\mathbf{S}^3]}{dt} = \mathbf{g}[\mathbf{I}^3] - \beta([\mathbf{S}^3\mathbf{I}^1] + [\mathbf{S}^3\mathbf{I}^2] + [\mathbf{S}^3\mathbf{I}^3] + [\mathbf{S}^3\mathbf{I}^4] + [\mathbf{S}^3\mathbf{I}^5] + [\mathbf{S}^3\mathbf{I}^6] + [\mathbf{S}^3\mathbf{I}^7] + [\mathbf{S}^3\mathbf{I}^8])$$

$$\frac{d[\mathbf{S}^4]}{dt} = \mathbf{g}[\mathbf{I}^4] - \beta([\mathbf{S}^4\mathbf{I}^1] + [\mathbf{S}^4\mathbf{I}^2] + [\mathbf{S}^4\mathbf{I}^3] + [\mathbf{S}^4\mathbf{I}^4] + [\mathbf{S}^4\mathbf{I}^5] + [\mathbf{S}^4\mathbf{I}^6] + [\mathbf{S}^4\mathbf{I}^7] + [\mathbf{S}^4\mathbf{I}^8] + [\mathbf{S}^4\mathbf{I}^{10}] + [\mathbf{S}^4\mathbf{I}^{12}])$$

$$\frac{d[\mathbf{S}^5]}{dt} = \mathbf{g}[\mathbf{I}^5] - \beta([\mathbf{S}^5\mathbf{I}^1] + [\mathbf{S}^5\mathbf{I}^2] + [\mathbf{S}^5\mathbf{I}^3] + [\mathbf{S}^5\mathbf{I}^4] + [\mathbf{S}^5\mathbf{I}^5] + [\mathbf{S}^5\mathbf{I}^6])$$

$$\frac{d[\mathbf{S}^6]}{dt} = \mathbf{g}[\mathbf{I}^6] - \beta([\mathbf{S}^6\mathbf{I}^1] + [\mathbf{S}^6\mathbf{I}^2] + [\mathbf{S}^6\mathbf{I}^3] + [\mathbf{S}^6\mathbf{I}^4] + [\mathbf{S}^6\mathbf{I}^5] + [\mathbf{S}^6\mathbf{I}^6] + [\mathbf{S}^6\mathbf{I}^7])$$

$$\frac{d[\mathbf{S}^7]}{dt} = \mathbf{g}[\mathbf{I}^7] - \beta([\mathbf{S}^7\mathbf{I}^1] + [\mathbf{S}^7\mathbf{I}^2] + [\mathbf{S}^7\mathbf{I}^3] + [\mathbf{S}^7\mathbf{I}^6])$$

$$\frac{d[\mathbf{S}^8]}{dt} = \mathbf{g}[\mathbf{I}^8] - \beta([\mathbf{S}^8\mathbf{I}^1] + [\mathbf{S}^8\mathbf{I}^2] + [\mathbf{S}^8\mathbf{I}^3] + [\mathbf{S}^8\mathbf{I}^4] + [\mathbf{S}^8\mathbf{I}^{11}])$$

$$\frac{d[\mathbf{S}^9]}{dt} = \mathbf{g}[\mathbf{I}^9] - \beta([\mathbf{S}^9\mathbf{I}^1] + [\mathbf{S}^9\mathbf{I}^2])$$

$$\frac{d[\mathbf{S}^{10}]}{dt} = g[\mathbf{I}^{10}] - \beta([\mathbf{S}^{10}\mathbf{I}^1] + [\mathbf{S}^{10}\mathbf{I}^2] + [\mathbf{S}^{10}\mathbf{I}^4])$$

$$\frac{d[\mathbf{S}^{11}]}{dt} = g[\mathbf{I}^{11}] - \beta([\mathbf{S}^{11}\mathbf{I}^1] + [\mathbf{S}^{11}\mathbf{I}^2] + [\mathbf{S}^{11}\mathbf{I}^8])$$

$$\frac{d[\mathbf{S}^{12}]}{dt} = g[\mathbf{I}^{12}] - \beta([\mathbf{S}^{12}\mathbf{I}^1] + [\mathbf{S}^{12}\mathbf{I}^2] + [\mathbf{S}^{12}\mathbf{I}^4])$$

$$\frac{d[\mathbf{I}^1]}{dt} = -g[\mathbf{I}^1] + \beta([\mathbf{S}^1\mathbf{I}^1] + [\mathbf{S}^1\mathbf{I}^2] + [\mathbf{S}^1\mathbf{I}^3] + [\mathbf{S}^1\mathbf{I}^4] + [\mathbf{S}^1\mathbf{I}^5] + [\mathbf{S}^1\mathbf{I}^6] + [\mathbf{S}^1\mathbf{I}^7] + [\mathbf{S}^1\mathbf{I}^8] + [\mathbf{S}^1\mathbf{I}^9] + [\mathbf{S}^1\mathbf{I}^{10}] + [\mathbf{S}^1\mathbf{I}^{11}] + [\mathbf{S}^1\mathbf{I}^{12}])$$

$$\frac{d[\mathbf{I}^2]}{dt} = -g[\mathbf{I}^2] + \beta([\mathbf{S}^2\mathbf{I}^1] + [\mathbf{S}^2\mathbf{I}^2] + [\mathbf{S}^2\mathbf{I}^3] + [\mathbf{S}^2\mathbf{I}^4] + [\mathbf{S}^2\mathbf{I}^5] + [\mathbf{S}^2\mathbf{I}^6] + [\mathbf{S}^2\mathbf{I}^7] + [\mathbf{S}^2\mathbf{I}^8] + [\mathbf{S}^2\mathbf{I}^9] + [\mathbf{S}^2\mathbf{I}^{10}] + [\mathbf{S}^2\mathbf{I}^{11}] + [\mathbf{S}^2\mathbf{I}^{12}])$$

$$\frac{d[\mathbf{I}^3]}{dt} = -g[\mathbf{I}^3] + \beta([\mathbf{S}^3\mathbf{I}^1] + [\mathbf{S}^3\mathbf{I}^2] + [\mathbf{S}^3\mathbf{I}^3] + [\mathbf{S}^3\mathbf{I}^4] + [\mathbf{S}^3\mathbf{I}^5] + [\mathbf{S}^3\mathbf{I}^6] + [\mathbf{S}^3\mathbf{I}^7] + [\mathbf{S}^3\mathbf{I}^8])$$

$$\frac{d[\mathbf{I}^4]}{dt} = -g[\mathbf{I}^4] + \beta([\mathbf{S}^4\mathbf{I}^1] + [\mathbf{S}^4\mathbf{I}^2] + [\mathbf{S}^4\mathbf{I}^3] + [\mathbf{S}^4\mathbf{I}^4] + [\mathbf{S}^4\mathbf{I}^5] + [\mathbf{S}^4\mathbf{I}^6] + [\mathbf{S}^4\mathbf{I}^8] + [\mathbf{S}^4\mathbf{I}^{10}] + [\mathbf{S}^4\mathbf{I}^{12}])$$

$$\frac{d[\mathbf{I}^5]}{dt} = -g[\mathbf{I}^5] + \beta([\mathbf{S}^5\mathbf{I}^1] + [\mathbf{S}^5\mathbf{I}^2] + [\mathbf{S}^5\mathbf{I}^3] + [\mathbf{S}^5\mathbf{I}^4] + [\mathbf{S}^5\mathbf{I}^5] + [\mathbf{S}^5\mathbf{I}^6])$$

$$\frac{d[\mathbf{I}^6]}{dt} = -g[\mathbf{I}^6] + \beta([\mathbf{S}^6\mathbf{I}^1] + [\mathbf{S}^6\mathbf{I}^2] + [\mathbf{S}^6\mathbf{I}^3] + [\mathbf{S}^6\mathbf{I}^4] + [\mathbf{S}^6\mathbf{I}^5] + [\mathbf{S}^6\mathbf{I}^6] + [\mathbf{S}^6\mathbf{I}^7])$$

$$\frac{d[\Gamma^7]}{dt} = -g[\Gamma^7] + \beta([\Gamma^7] + [S^7I^2] + [S^7I^3] + [S^7I^6])$$

$$\frac{d[\Gamma^8]}{dt} = -g[\Gamma^8] + \beta([\Gamma^8] + [S^8I^2] + [S^8I^3] + [S^8I^4] + [S^8I^{11}])$$

$$\frac{d[\Gamma^9]}{dt} = -g[\Gamma^9] + \beta([\Gamma^9] + [S^9I^2])$$

$$\frac{d[\Gamma^{10}]}{dt} = -g[\Gamma^{10}] + \beta([\Gamma^{10}] + [S^{10}I^2] + [S^{10}I^4])$$

$$\frac{d[\Gamma^{11}]}{dt} = -g[\Gamma^{11}] + \beta([\Gamma^{11}] + [S^{11}I^2] + [S^{11}I^8])$$

$$\frac{d[\Gamma^{12}]}{dt} = -g[\Gamma^{12}] + \beta([\Gamma^{12}] + [S^{12}I^2] + [S^{12}I^4])$$

$$\frac{d[S^1I^1]}{dt} = -\beta[S^1I^1] - g[S^1I^1] + g[\Gamma^1I^1]$$

$$\frac{d[S^1I^2]}{dt} = \frac{\beta[S^1S^2]}{2[S^2]}([\Gamma^2] + [S^2I^2] + [S^2I^3] + [S^2I^4] + [S^2I^5] + [S^2I^6] + [S^2I^7] + [S^2I^8] + [S^2I^9] + [S^2I^{10}] + [S^2I^{11}] + [S^2I^{12}]) - \beta[S^1I^2] - g[S^1I^2] + g[\Gamma^1I^2]$$

$$\frac{d[S^1I^3]}{dt} = \frac{2\beta[S^1S^3]}{3[S^3]}([\Gamma^3] + [S^3I^2] + [S^3I^3] + [S^3I^4] + [S^3I^5] + [S^3I^6] + [S^3I^7] + [S^3I^8] - \beta[S^1I^3] - g[S^1I^3] + g[\Gamma^1I^3])$$

$$\frac{d[S^1I^4]}{dt} = \frac{3\beta[S^1S^4]}{4[S^4]}([\Gamma^4] + [S^4I^2] + [S^4I^3] + [S^4I^4] + [S^4I^5] + [S^4I^6] + [S^4I^7] + [S^4I^8] + [S^4I^{10}] + [S^4I^{12}]) - \beta[S^1I^4] - g[S^1I^4] + g[\Gamma^1I^4]$$

$$\frac{d[S^1I^5]}{dt} = \frac{4\beta[S^1S^5](S^5I^1) + [S^5I^2] + [S^5I^3] + [S^5I^4] + [S^5I^5] + [S^5I^6]) - \beta[S^1I^5] - g[S^1I^5] + g[I^1I^5]}{5[S^5]}$$

$$\frac{d[S^1I^6]}{dt} = \frac{5\beta[S^1S^6](S^6I^1) + [S^6I^2] + [S^6I^3] + [S^6I^4] + [S^6I^5] + [S^6I^6] + [S^6I^7]) - \beta[S^1I^6] - g[S^1I^6] + g[I^1I^6]}{6[S^6]}$$

$$\frac{d[S^1I^7]}{dt} = \frac{6\beta[S^1S^7](S^7I^1) + [S^7I^2] + [S^7I^3] + [S^7I^4] + [S^7I^5] + [S^7I^6] - g[S^1I^7] + g[I^1I^7]}{7[S^7]}$$

$$\frac{d[S^1I^8]}{dt} = \frac{7\beta[S^1S^8](S^8I^1) + [S^8I^2] + [S^8I^3] + [S^8I^4] + [S^8I^5] + [S^8I^6] - \beta[S^1I^8] - g[S^1I^8] + g[I^1I^8]}{8[S^8]}$$

$$\frac{d[S^1I^9]}{dt} = \frac{8\beta[S^1S^9](S^9I^1) + [S^9I^2] - \beta[S^1I^9] - g[S^1I^9] + g[I^1I^9]}{9[S^9]}$$

$$\frac{d[S^1I^{10}]}{dt} = \frac{9\beta[S^1S^{10}](S^{10}I^1) + [S^{10}I^2] + [S^{10}I^4]) - \beta[S^1I^{10}] - g[S^1I^{10}] + g[I^1I^{10}]}{10[S^{10}]}$$

$$\frac{d[S^1I^{11}]}{dt} = \frac{10\beta[S^1S^{11}](S^{11}I^1) + [S^{11}I^2] + [S^{11}I^8]) - \beta[S^1I^{11}] - g[S^1I^{11}] + g[I^1I^{11}]}{11[S^{11}]}$$

$$\frac{d[S^1I^{12}]}{dt} = \frac{11\beta[S^1S^{12}](S^{12}I^1) + [S^{12}I^2] + [S^{12}I^4]) - \beta[S^1I^{12}] - g[S^1I^{12}] + g[I^1I^{12}]}{12[S^{12}]}$$

$$\frac{d[S^2I^1]}{dt} = \frac{-\beta[S^2I^1](I^1S^2) + [I^2S^2] + [I^3S^2] + [I^4S^2] + [I^5S^2] + [I^6S^2] + [I^7S^2] + [I^8S^2] + [I^9S^2] + [I^{10}S^2] + [I^{11}S^2] + [I^{12}S^2]) - \beta[S^2I^1] - g[S^2I^1] + g[I^2I^1]}{2[S^2]}$$

$$\begin{aligned}
\frac{d[\underline{S}^2\Gamma^9]}{dt} &= \frac{8\beta[\underline{S}^2\mathbf{S}^9]}{9[\underline{S}^9]}([\underline{S}^9\Gamma^1] + [\underline{S}^9\Gamma^2]) - \frac{\beta[\underline{S}^2\Gamma^9]}{2[\underline{S}^2]}([\Gamma^1\mathbf{S}^2] + [\Gamma^2\mathbf{S}^2] + [\Gamma^3\mathbf{S}^2] + [\Gamma^4\mathbf{S}^2] + [\Gamma^5\mathbf{S}^2] + [\Gamma^6\mathbf{S}^2] + [\Gamma^7\mathbf{S}^2] + [\Gamma^8\mathbf{S}^2] + [\Gamma^9\mathbf{S}^2] + [\Gamma^{10}\mathbf{S}^2] + [\Gamma^{11}\mathbf{S}^2] + \\
&\quad [\Gamma^{12}\mathbf{S}^2]) - \beta[\underline{S}^2\Gamma^9] - \mathbf{g}[\underline{S}^2\Gamma^9] + \mathbf{g}[\Gamma^9\Gamma^9] \\
\frac{d[\underline{S}^2\Gamma^{10}]}{dt} &= \frac{2\beta[\underline{S}^2\mathbf{S}^{10}]}{10[\underline{S}^{10}]}([\underline{S}^{10}\Gamma^1] + [\underline{S}^{10}\Gamma^2] + [\underline{S}^{10}\Gamma^4]) - \frac{\beta[\underline{S}^2\Gamma^{10}]}{2[\underline{S}^2]}([\Gamma^1\mathbf{S}^2] + [\Gamma^2\mathbf{S}^2] + [\Gamma^3\mathbf{S}^2] + [\Gamma^4\mathbf{S}^2] + [\Gamma^5\mathbf{S}^2] + [\Gamma^6\mathbf{S}^2] + [\Gamma^7\mathbf{S}^2] + [\Gamma^8\mathbf{S}^2] + [\Gamma^9\mathbf{S}^2] + [\Gamma^{10}\mathbf{S}^2] + [\Gamma^{11}\mathbf{S}^2] + \\
&\quad [\Gamma^{12}\mathbf{S}^2]) - \beta[\underline{S}^2\Gamma^{10}] - \mathbf{g}[\underline{S}^2\Gamma^{10}] + \mathbf{g}[\Gamma^2\Gamma^{10}] \\
\frac{d[\underline{S}^2\Gamma^{11}]}{dt} &= \frac{10\beta[\underline{S}^2\mathbf{S}^{11}]}{11[\underline{S}^{11}]}([\underline{S}^{11}\Gamma^1] + [\underline{S}^{11}\Gamma^2] + [\underline{S}^{11}\Gamma^8]) - \frac{\beta[\underline{S}^2\Gamma^{11}]}{2[\underline{S}^2]}([\Gamma^1\mathbf{S}^2] + [\Gamma^2\mathbf{S}^2] + [\Gamma^3\mathbf{S}^2] + [\Gamma^4\mathbf{S}^2] + [\Gamma^5\mathbf{S}^2] + [\Gamma^6\mathbf{S}^2] + [\Gamma^7\mathbf{S}^2] + [\Gamma^8\mathbf{S}^2] + [\Gamma^9\mathbf{S}^2] + [\Gamma^{10}\mathbf{S}^2] + \\
&\quad [\Gamma^{11}\mathbf{S}^2] + [\Gamma^{12}\mathbf{S}^2]) - \beta[\underline{S}^2\Gamma^{11}] - \mathbf{g}[\underline{S}^2\Gamma^{11}] + \mathbf{g}[\Gamma^2\Gamma^{11}] \\
\frac{d[\underline{S}^2\Gamma^{12}]}{dt} &= \frac{11\beta[\underline{S}^2\mathbf{S}^{12}]}{12[\underline{S}^{12}]}([\underline{S}^{12}\Gamma^1] + [\underline{S}^{12}\Gamma^2] + [\underline{S}^{12}\Gamma^4]) - \frac{\beta[\underline{S}^2\Gamma^{12}]}{2[\underline{S}^2]}([\Gamma^1\mathbf{S}^2] + [\Gamma^2\mathbf{S}^2] + [\Gamma^3\mathbf{S}^2] + [\Gamma^4\mathbf{S}^2] + [\Gamma^5\mathbf{S}^2] + [\Gamma^6\mathbf{S}^2] + [\Gamma^7\mathbf{S}^2] + [\Gamma^8\mathbf{S}^2] + [\Gamma^9\mathbf{S}^2] + [\Gamma^{10}\mathbf{S}^2] + \\
&\quad [\Gamma^{11}\mathbf{S}^2] + [\Gamma^{12}\mathbf{S}^2]) - \beta[\underline{S}^2\Gamma^{12}] - \mathbf{g}[\underline{S}^2\Gamma^{12}] + \mathbf{g}[\Gamma^2\Gamma^{12}] \\
\frac{d[\underline{S}^3\Gamma^1]}{dt} &= -\frac{2\beta[\underline{S}^3\Gamma^1]}{3[\underline{S}^3]}([\Gamma^1\mathbf{S}^3] + [\Gamma^2\mathbf{S}^3] + [\Gamma^3\mathbf{S}^3] + [\Gamma^4\mathbf{S}^3] + [\Gamma^5\mathbf{S}^3] + [\Gamma^6\mathbf{S}^3] + [\Gamma^7\mathbf{S}^3] + [\Gamma^8\mathbf{S}^3]) - \beta[\underline{S}^3\Gamma^1] - \mathbf{g}[\underline{S}^3\Gamma^1] + \mathbf{g}[\Gamma^3\Gamma^1] \\
\frac{d[\underline{S}^3\Gamma^2]}{dt} &= \frac{\beta[\underline{S}^3\mathbf{S}^2]}{2[\underline{S}^2]}([\underline{S}^2\Gamma^1] + [\underline{S}^2\Gamma^2] + [\underline{S}^2\Gamma^3] + [\underline{S}^2\Gamma^4] + [\underline{S}^2\Gamma^5] + [\underline{S}^2\Gamma^6] + [\underline{S}^2\Gamma^7] + [\underline{S}^2\Gamma^8] + [\underline{S}^2\Gamma^9] + [\underline{S}^2\Gamma^{10}] + [\underline{S}^2\Gamma^{11}] + [\underline{S}^2\Gamma^{12}]) - \frac{2\beta[\underline{S}^3\Gamma^2]}{3[\underline{S}^3]}([\Gamma^1\mathbf{S}^3] + [\Gamma^2\mathbf{S}^3] + \\
&\quad [\Gamma^3\mathbf{S}^3] + [\Gamma^4\mathbf{S}^3] + [\Gamma^5\mathbf{S}^3] + [\Gamma^6\mathbf{S}^3] + [\Gamma^7\mathbf{S}^3] + [\Gamma^8\mathbf{S}^3]) - \beta[\underline{S}^3\Gamma^2] - \mathbf{g}[\underline{S}^3\Gamma^2] + \mathbf{g}[\Gamma^3\Gamma^2] \\
\frac{d[\underline{S}^3\Gamma^3]}{dt} &= \frac{2\beta[\underline{S}^3\mathbf{S}^3]}{3[\underline{S}^3]}([\underline{S}^3\Gamma^1] + [\underline{S}^3\Gamma^2] + [\underline{S}^3\Gamma^3] + [\underline{S}^3\Gamma^4] + [\underline{S}^3\Gamma^5] + [\underline{S}^3\Gamma^6] + [\underline{S}^3\Gamma^7] + [\underline{S}^3\Gamma^8] + [\underline{S}^3\Gamma^9] + [\underline{S}^3\Gamma^{10}] + [\underline{S}^3\Gamma^{11}] + [\underline{S}^3\Gamma^{12}]) - \frac{2\beta[\underline{S}^3\Gamma^3]}{3[\underline{S}^3]}([\Gamma^1\mathbf{S}^3] + [\Gamma^2\mathbf{S}^3] + [\Gamma^3\mathbf{S}^3] + [\Gamma^4\mathbf{S}^3] + [\Gamma^5\mathbf{S}^3] + [\Gamma^6\mathbf{S}^3] + \\
&\quad [\Gamma^7\mathbf{S}^3] + [\Gamma^8\mathbf{S}^3]) - \beta[\underline{S}^3\Gamma^3] - \mathbf{g}[\underline{S}^3\Gamma^3] + \mathbf{g}[\Gamma^3\Gamma^3]
\end{aligned}$$

$$\frac{d[\underline{S}^{11}I^8]}{dt} = \frac{7\beta[\underline{S}^{11}S^8]([\underline{S}^8I^1] + [S^8I^2] + [S^8I^3] + [S^8I^4] + [S^8I^5] + [S^8I^6] + [S^8I^7] + [S^8I^8]) - 10\beta[\underline{S}^{11}I^8]([\underline{I}^1S^{11}] + [I^2S^{11}] + [I^8S^{11}]) - \beta[\underline{S}^{11}I^8] - g[\underline{I}^{11}I^8]}{8[S^8]} + \frac{11[\underline{S}^{11}]}{11[\underline{S}^{11}]}$$

$$\frac{d[\underline{S}^{12}I^1]}{dt} = -\frac{11\beta[\underline{S}^{12}I^1]([\underline{I}^1S^{12}] + [I^2S^{12}] + [I^4S^{12}]) - \beta[\underline{S}^{12}I^1] - g[\underline{I}^{12}I^1]}{12[S^{12}]} + g[\underline{I}^{12}I^1]$$

$$\frac{d[\underline{S}^{12}I^2]}{dt} = \frac{\beta[\underline{S}^{12}S^2]([\underline{S}^2I^1] + [S^2I^2] + [S^2I^3] + [S^2I^4] + [S^2I^5] + [S^2I^6] + [S^2I^7] + [S^2I^8] + [S^2I^9] + [S^2I^{10}] + [S^2I^{11}] + [S^2I^{12}]) - 11\beta[\underline{S}^{12}I^2]([\underline{I}^1S^{12}] + [I^2S^{12}]) + [I^4S^{12}]}{2[S^2]} - \frac{11\beta[\underline{S}^{12}I^2]}{12[S^{12}]} + g[\underline{I}^{12}I^2]$$

$$\frac{d[\underline{S}^{12}I^4]}{dt} = \frac{3\beta[\underline{S}^{12}S^4]([\underline{S}^4I^1] + [S^4I^2] + [S^4I^3] + [S^4I^4] + [S^4I^5] + [S^4I^6] + [S^4I^7] + [S^4I^8] + [S^4I^9] + [S^4I^{10}] + [S^4I^{12}]) - 11\beta[\underline{S}^{12}I^4]([\underline{I}^1S^{12}] + [I^2S^{12}]) - 4[S^4]}{4[S^4]} - \frac{11\beta[\underline{S}^{12}I^4]}{12[S^{12}]} + g[\underline{I}^{12}I^4]$$

$$\frac{d[\underline{S}^1S^1]}{dt} = g[\underline{S}^1I^1]$$

$$\frac{d[\underline{S}^1S^2]}{dt} = -\frac{\beta[\underline{S}^1S^2]([\underline{S}^2I^1] + [S^2I^2] + [S^2I^3] + [S^2I^4] + [S^2I^5] + [S^2I^6] + [S^2I^7] + [S^2I^8] + [S^2I^9] + [S^2I^{10}] + [S^2I^{11}] + [S^2I^{12}]) + g[\underline{I}^1S^2]}{2[S^2]} + g[\underline{I}^1S^2]$$

$$\frac{d[\underline{S}^1S^3]}{dt} = -\frac{2\beta[\underline{S}^1S^3]([\underline{S}^3I^1] + [S^3I^2] + [S^3I^3] + [S^3I^4] + [S^3I^5] + [S^3I^6] + [S^3I^7] + [S^3I^8] + [S^3I^9] + [S^3I^{10}] + [S^3I^{12}]) + g[\underline{I}^1S^3]}{3[S^3]} + g[\underline{I}^1S^3]$$

$$\frac{d[\underline{S}^1S^4]}{dt} = -\frac{3\beta[\underline{S}^1S^4]([\underline{S}^4I^1] + [S^4I^2] + [S^4I^3] + [S^4I^4] + [S^4I^5] + [S^4I^6] + [S^4I^7] + [S^4I^8] + [S^4I^9] + [S^4I^{10}] + [S^4I^{12}]) + g[\underline{I}^1S^4]}{4[S^4]} + g[\underline{I}^1S^4]$$

$$\frac{d[\underline{S}^1S^5]}{dt} = -\frac{4\beta[\underline{S}^1S^5]([\underline{S}^5I^1] + [S^5I^2] + [S^5I^3] + [S^5I^4] + [S^5I^5] + [S^5I^6] + [S^5I^7] + [S^5I^8] + [S^5I^9] + [S^5I^{10}] + [S^5I^{12}]) + g[\underline{I}^1S^5]}{5[S^5]} + g[\underline{I}^1S^5]$$

$$\frac{d[\underline{S}^1 \underline{S}^6]}{dt} = -\frac{5\beta[\underline{S}^1 \underline{S}^6]}{6[\underline{S}^6]}([\underline{S}^6 \underline{I}^1] + [\underline{S}^6 \underline{I}^2] + [\underline{S}^6 \underline{I}^3] + [\underline{S}^6 \underline{I}^4] + [\underline{S}^6 \underline{I}^5] + [\underline{S}^6 \underline{I}^6] + [\underline{S}^6 \underline{I}^7]) + \underline{g}[\underline{S}^1 \underline{I}^6] + \underline{g}[\underline{I}^1 \underline{S}^6]$$

$$\frac{d[\underline{S}^1 \underline{S}^7]}{dt} = -\frac{6\beta[\underline{S}^1 \underline{S}^7]}{7[\underline{S}^7]}([\underline{S}^7 \underline{I}^1] + [\underline{S}^7 \underline{I}^2] + [\underline{S}^7 \underline{I}^3] + [\underline{S}^7 \underline{I}^4] + [\underline{S}^7 \underline{I}^5] + [\underline{S}^7 \underline{I}^6] + [\underline{S}^7 \underline{I}^7]) + \underline{g}[\underline{I}^1 \underline{S}^7]$$

$$\frac{d[\underline{S}^1 \underline{S}^8]}{dt} = -\frac{7\beta[\underline{S}^1 \underline{S}^8]}{8[\underline{S}^8]}([\underline{S}^8 \underline{I}^1] + [\underline{S}^8 \underline{I}^2] + [\underline{S}^8 \underline{I}^3] + [\underline{S}^8 \underline{I}^4] + [\underline{S}^8 \underline{I}^5] + [\underline{S}^8 \underline{I}^6] + [\underline{S}^8 \underline{I}^7]) + \underline{g}[\underline{S}^1 \underline{I}^8] + \underline{g}[\underline{I}^1 \underline{S}^8]$$

$$\frac{d[\underline{S}^1 \underline{S}^9]}{dt} = -\frac{8\beta[\underline{S}^1 \underline{S}^9]}{9[\underline{S}^9]}([\underline{S}^9 \underline{I}^1] + [\underline{S}^9 \underline{I}^2]) + \underline{g}[\underline{S}^1 \underline{I}^9] + \underline{g}[\underline{I}^1 \underline{S}^9]$$

$$\frac{d[\underline{S}^1 \underline{S}^{10}]}{dt} = -\frac{9\beta[\underline{S}^1 \underline{S}^{10}]}{10[\underline{S}^{10}]}([\underline{S}^{10} \underline{I}^1] + [\underline{S}^{10} \underline{I}^2] + [\underline{S}^{10} \underline{I}^4]) + \underline{g}[\underline{S}^1 \underline{I}^{10}] + \underline{g}[\underline{I}^1 \underline{S}^{10}]$$

$$\frac{d[\underline{S}^1 \underline{S}^{11}]}{dt} = -\frac{10\beta[\underline{S}^1 \underline{S}^{11}]}{11[\underline{S}^{11}]}([\underline{S}^{11} \underline{I}^1] + [\underline{S}^{11} \underline{I}^2] + [\underline{S}^{11} \underline{I}^8]) + \underline{g}[\underline{S}^1 \underline{I}^{11}] + \underline{g}[\underline{I}^1 \underline{S}^{11}]$$

$$\frac{d[\underline{S}^1 \underline{S}^{12}]}{dt} = -\frac{11\beta[\underline{S}^1 \underline{S}^{12}]}{12[\underline{S}^{12}]}([\underline{S}^{12} \underline{I}^1] + [\underline{S}^{12} \underline{I}^2] + [\underline{S}^{12} \underline{I}^4]) + \underline{g}[\underline{S}^1 \underline{I}^{12}] + \underline{g}[\underline{I}^1 \underline{S}^{12}]$$

$$\frac{d[\underline{S}^2 \underline{S}^2]}{dt} = -\frac{\beta[\underline{S}^2 \underline{S}^2]}{[\underline{S}^2]}([\underline{S}^2 \underline{I}^1] + [\underline{S}^2 \underline{I}^2] + [\underline{S}^2 \underline{I}^3] + [\underline{S}^2 \underline{I}^4] + [\underline{S}^2 \underline{I}^5] + [\underline{S}^2 \underline{I}^6] + [\underline{S}^2 \underline{I}^7] + [\underline{S}^2 \underline{I}^8] + [\underline{S}^2 \underline{I}^9] + [\underline{S}^2 \underline{I}^{10}] + [\underline{S}^2 \underline{I}^{11}] + [\underline{S}^2 \underline{I}^{12}]) + \underline{g}[\underline{S}^2 \underline{I}^2]$$

$$\frac{d[\underline{S}^2 \underline{S}^3]}{dt} = -\frac{2\beta[\underline{S}^2 \underline{S}^3]}{3[\underline{S}^3]}([\underline{S}^3 \underline{I}^1] + [\underline{S}^3 \underline{I}^2] + [\underline{S}^3 \underline{I}^3] + [\underline{S}^3 \underline{I}^4] + [\underline{S}^3 \underline{I}^5] + [\underline{S}^3 \underline{I}^6] + [\underline{S}^3 \underline{I}^7] + [\underline{S}^3 \underline{I}^8]) - \frac{\beta[\underline{S}^2 \underline{S}^3]}{2[\underline{S}^2]}([\underline{I}^1 \underline{S}^2] + [\underline{I}^2 \underline{S}^2] + [\underline{I}^3 \underline{S}^2] + [\underline{I}^4 \underline{S}^2] + [\underline{I}^5 \underline{S}^2] + [\underline{I}^6 \underline{S}^2] + [\underline{I}^7 \underline{S}^2] + [\underline{I}^8 \underline{S}^2] + [\underline{I}^9 \underline{S}^2] + [\underline{I}^{10} \underline{S}^2] + [\underline{I}^{11} \underline{S}^2] + [\underline{I}^{12} \underline{S}^2]) + \underline{g}[\underline{S}^2 \underline{I}^3] + \underline{g}[\underline{I}^2 \underline{S}^3]$$

$$\frac{d[\Gamma^1\Gamma^5]}{dt} = \frac{4\beta[\Gamma^1\mathbf{S}^5]}{5[\mathbf{S}^5]}([\mathbf{S}^5\Gamma^1] + [\mathbf{S}^5\Gamma^2] + [\mathbf{S}^5\Gamma^3] + [\mathbf{S}^5\Gamma^4] + [\mathbf{S}^5\Gamma^5] + [\mathbf{S}^5\Gamma^6]) + \beta[\Gamma^1\mathbf{S}^5] + \beta[\mathbf{S}^1\mathbf{S}^5] - 2g[\Gamma^1\Gamma^5]$$

$$\frac{d[\Gamma^1\Gamma^6]}{dt} = \frac{5\beta[\Gamma^1\mathbf{S}^6]}{6[\mathbf{S}^6]}([\mathbf{S}^6\Gamma^1] + [\mathbf{S}^6\Gamma^2] + [\mathbf{S}^6\Gamma^3] + [\mathbf{S}^6\Gamma^4] + [\mathbf{S}^6\Gamma^5] + [\mathbf{S}^6\Gamma^6] + [\mathbf{S}^6\Gamma^7]) + \beta[\Gamma^1\mathbf{S}^6] + \beta[\mathbf{S}^1\mathbf{S}^6] - 2g[\Gamma^1\Gamma^6]$$

$$\frac{d[\Gamma^1\Gamma^7]}{dt} = \frac{6\beta[\Gamma^1\mathbf{S}^7]}{7[\mathbf{S}^7]}([\mathbf{S}^7\Gamma^1] + [\mathbf{S}^7\Gamma^2] + [\mathbf{S}^7\Gamma^3] + [\mathbf{S}^7\Gamma^4] + [\mathbf{S}^7\Gamma^5] + [\mathbf{S}^7\Gamma^6] + [\mathbf{S}^7\Gamma^7]) + \beta[\Gamma^1\mathbf{S}^7] - 2g[\Gamma^1\Gamma^7]$$

$$\frac{d[\Gamma^1\Gamma^8]}{dt} = \frac{7\beta[\Gamma^1\mathbf{S}^8]}{8[\mathbf{S}^8]}([\mathbf{S}^8\Gamma^1] + [\mathbf{S}^8\Gamma^2] + [\mathbf{S}^8\Gamma^3] + [\mathbf{S}^8\Gamma^4] + [\mathbf{S}^8\Gamma^5] + [\mathbf{S}^8\Gamma^6] + [\mathbf{S}^8\Gamma^7] + [\mathbf{S}^8\Gamma^8]) + \beta[\Gamma^1\mathbf{S}^8] - 2g[\Gamma^1\Gamma^8]$$

$$\frac{d[\Gamma^1\Gamma^9]}{dt} = \frac{8\beta[\Gamma^1\mathbf{S}^9]}{9[\mathbf{S}^9]}([\mathbf{S}^9\Gamma^1] + [\mathbf{S}^9\Gamma^2]) + \beta[\Gamma^1\mathbf{S}^9] + \beta[\mathbf{S}^1\mathbf{S}^9] - 2g[\Gamma^1\Gamma^9]$$

$$\frac{d[\Gamma^1\Gamma^{10}]}{dt} = \frac{9\beta[\Gamma^1\mathbf{S}^{10}]}{10[\mathbf{S}^{10}]}([\mathbf{S}^{10}\Gamma^1] + [\mathbf{S}^{10}\Gamma^2] + [\mathbf{S}^{10}\Gamma^4]) + \beta[\Gamma^1\mathbf{S}^{10}] + \beta[\mathbf{S}^1\mathbf{S}^{10}] - 2g[\Gamma^1\Gamma^{10}]$$

$$\frac{d[\Gamma^1\Gamma^{11}]}{dt} = \frac{10\beta[\Gamma^1\mathbf{S}^{11}]}{11[\mathbf{S}^{11}]}([\mathbf{S}^{11}\Gamma^1] + [\mathbf{S}^{11}\Gamma^2] + [\mathbf{S}^{11}\Gamma^8]) + \beta[\Gamma^1\mathbf{S}^{11}] + \beta[\mathbf{S}^1\mathbf{S}^{11}] - 2g[\Gamma^1\Gamma^{11}]$$

$$\frac{d[\Gamma^1\Gamma^{12}]}{dt} = \frac{11\beta[\Gamma^1\mathbf{S}^{12}]}{12[\mathbf{S}^{12}]}([\mathbf{S}^{12}\Gamma^1] + [\mathbf{S}^{12}\Gamma^2] + [\mathbf{S}^{12}\Gamma^4]) + \beta[\Gamma^1\mathbf{S}^{12}] + \beta[\mathbf{S}^1\mathbf{S}^{12}] - 2g[\Gamma^1\Gamma^{12}]$$

$$\frac{d[\Gamma^2\Gamma^2]}{dt} = \beta\frac{[\Gamma^2\mathbf{S}^2]}{[\mathbf{S}^2]}([\mathbf{S}^2\Gamma^1] + [\mathbf{S}^2\Gamma^2] + [\mathbf{S}^2\Gamma^3] + [\mathbf{S}^2\Gamma^4] + [\mathbf{S}^2\Gamma^5] + [\mathbf{S}^2\Gamma^6] + [\mathbf{S}^2\Gamma^7] + [\mathbf{S}^2\Gamma^8] + [\mathbf{S}^2\Gamma^9] + [\mathbf{S}^2\Gamma^{10}] + [\mathbf{S}^2\Gamma^{11}] + [\mathbf{S}^2\Gamma^{12}]) + \beta[\mathbf{S}^2\Gamma^2] - 2g[\Gamma^2\Gamma^2]$$

$$\frac{d[\Gamma^2\Gamma^{10}]}{dt} = \frac{9\beta[\Gamma^2\Gamma^{10}](\Gamma^{10}\Gamma^1) + [\Gamma^{10}\Gamma^2] + [\Gamma^{10}\Gamma^4] + \beta[\Gamma^2\Gamma^{10}](\Gamma^1\Gamma^2) + [\Gamma^2\Gamma^2] + [\Gamma^3\Gamma^2] + [\Gamma^4\Gamma^2] + [\Gamma^5\Gamma^2] + [\Gamma^6\Gamma^2] + [\Gamma^7\Gamma^2] + [\Gamma^8\Gamma^2] + [\Gamma^9\Gamma^2] + [\Gamma^{10}\Gamma^2] + [\Gamma^{11}\Gamma^2] + [\Gamma^{12}\Gamma^2]) + \beta[\Gamma^2\Gamma^{10}] + \beta[\Gamma^2\Gamma^{10}] - 2g[\Gamma^2\Gamma^{10}]$$

$$\frac{d[\Gamma^2\Gamma^{11}]}{dt} = \frac{10\beta[\Gamma^2\Gamma^{11}](\Gamma^{11}\Gamma^1) + [\Gamma^{11}\Gamma^2] + [\Gamma^{11}\Gamma^8] + \beta[\Gamma^2\Gamma^{11}](\Gamma^1\Gamma^2) + [\Gamma^2\Gamma^2] + [\Gamma^3\Gamma^2] + [\Gamma^4\Gamma^2] + [\Gamma^5\Gamma^2] + [\Gamma^6\Gamma^2] + [\Gamma^7\Gamma^2] + [\Gamma^8\Gamma^2] + [\Gamma^9\Gamma^2] + [\Gamma^{10}\Gamma^2] + [\Gamma^{11}\Gamma^2] + [\Gamma^{12}\Gamma^2]) + \beta[\Gamma^2\Gamma^{11}] + \beta[\Gamma^2\Gamma^{11}] - 2g[\Gamma^2\Gamma^{11}]$$

$$\frac{d[\Gamma^2\Gamma^{12}]}{dt} = \frac{11\beta[\Gamma^2\Gamma^{12}](\Gamma^{12}\Gamma^1) + [\Gamma^{12}\Gamma^2] + [\Gamma^{12}\Gamma^4] + \beta[\Gamma^2\Gamma^{12}](\Gamma^1\Gamma^2) + [\Gamma^2\Gamma^2] + [\Gamma^3\Gamma^2] + [\Gamma^4\Gamma^2] + [\Gamma^5\Gamma^2] + [\Gamma^6\Gamma^2] + [\Gamma^7\Gamma^2] + [\Gamma^8\Gamma^2] + [\Gamma^9\Gamma^2] + [\Gamma^{10}\Gamma^2] + [\Gamma^{11}\Gamma^2] + [\Gamma^{12}\Gamma^2]) + \beta[\Gamma^2\Gamma^{12}] + \beta[\Gamma^2\Gamma^{12}] - 2g[\Gamma^2\Gamma^{12}]$$

$$\frac{d[\Gamma^3\Gamma^3]}{dt} = \frac{4\beta[\Gamma^3\Gamma^3](\Gamma^3\Gamma^1) + [\Gamma^3\Gamma^2] + [\Gamma^3\Gamma^3] + [\Gamma^3\Gamma^4] + [\Gamma^3\Gamma^5] + [\Gamma^3\Gamma^6] + [\Gamma^3\Gamma^7] + [\Gamma^3\Gamma^8] + \beta[\Gamma^3\Gamma^3] - 2g[\Gamma^3\Gamma^3]$$

$$\frac{d[\Gamma^3\Gamma^4]}{dt} = \frac{3\beta[\Gamma^3\Gamma^4](\Gamma^4\Gamma^1) + [\Gamma^4\Gamma^2] + [\Gamma^4\Gamma^3] + [\Gamma^4\Gamma^4] + [\Gamma^4\Gamma^5] + [\Gamma^4\Gamma^6] + [\Gamma^4\Gamma^7] + [\Gamma^4\Gamma^8] + [\Gamma^4\Gamma^{10}] + [\Gamma^4\Gamma^{12}] + 2\beta[\Gamma^3\Gamma^4](\Gamma^1\Gamma^3) + [\Gamma^2\Gamma^3] + [\Gamma^3\Gamma^3] + [\Gamma^4\Gamma^3] + [\Gamma^5\Gamma^3] + [\Gamma^6\Gamma^3] + [\Gamma^7\Gamma^3] + [\Gamma^8\Gamma^3] + [\Gamma^9\Gamma^3] + [\Gamma^{10}\Gamma^3] + [\Gamma^{11}\Gamma^3] + [\Gamma^{12}\Gamma^3]) + \beta[\Gamma^3\Gamma^4] - 2g[\Gamma^3\Gamma^4]$$

$$\frac{d[\Gamma^3\Gamma^5]}{dt} = \frac{4\beta[\Gamma^3\Gamma^5](\Gamma^5\Gamma^1) + [\Gamma^5\Gamma^2] + [\Gamma^5\Gamma^3] + [\Gamma^5\Gamma^4] + [\Gamma^5\Gamma^5] + [\Gamma^5\Gamma^6] + 2\beta[\Gamma^3\Gamma^5](\Gamma^1\Gamma^3) + [\Gamma^2\Gamma^3] + [\Gamma^3\Gamma^3] + [\Gamma^4\Gamma^3] + [\Gamma^5\Gamma^3] + [\Gamma^6\Gamma^3] + [\Gamma^7\Gamma^3] + [\Gamma^8\Gamma^3] + [\Gamma^9\Gamma^3] + [\Gamma^{10}\Gamma^3] + [\Gamma^{11}\Gamma^3] + [\Gamma^{12}\Gamma^3]) + \beta[\Gamma^3\Gamma^5] - 2g[\Gamma^3\Gamma^5]$$

$$\frac{d[\Gamma^3\Gamma^6]}{dt} = \frac{5\beta[\Gamma^3\Gamma^6](\Gamma^6\Gamma^1) + [\Gamma^6\Gamma^2] + [\Gamma^6\Gamma^3] + [\Gamma^6\Gamma^4] + [\Gamma^6\Gamma^5] + [\Gamma^6\Gamma^6] + [\Gamma^6\Gamma^7] + 2\beta[\Gamma^3\Gamma^6](\Gamma^1\Gamma^3) + [\Gamma^2\Gamma^3] + [\Gamma^3\Gamma^3] + [\Gamma^4\Gamma^3] + [\Gamma^5\Gamma^3] + [\Gamma^6\Gamma^3] + [\Gamma^7\Gamma^3] + [\Gamma^8\Gamma^3] + [\Gamma^9\Gamma^3] + [\Gamma^{10}\Gamma^3] + [\Gamma^{11}\Gamma^3] + [\Gamma^{12}\Gamma^3]) + \beta[\Gamma^3\Gamma^6] - 2g[\Gamma^3\Gamma^6]$$

$$\frac{d[\Gamma^3\Gamma^7]}{dt} = \frac{6\beta[\Gamma^3S^7]}{7[S^7]}([\Gamma^7\Gamma^1] + [\Gamma^7\Gamma^2] + [\Gamma^7\Gamma^3] + [S^7\Gamma^6] + [S^7\Gamma^7] + [S^7\Gamma^8] + [S^7\Gamma^9] + [S^7\Gamma^{10}] + [S^7\Gamma^{11}] + [S^7\Gamma^{12}]) + \frac{2\beta[S^3\Gamma^7]}{3[S^3]}([\Gamma^3S^3] + [\Gamma^4S^3] + [\Gamma^5S^3] + [\Gamma^6S^3] + [\Gamma^7S^3] + [\Gamma^8S^3]) + \beta[\Gamma^3S^7] + \beta[\Gamma^3S^8] + \beta[\Gamma^3S^9] + \beta[\Gamma^3S^{10}] + \beta[\Gamma^3S^{11}] + \beta[\Gamma^3S^{12}] - 2g[\Gamma^3\Gamma^7]$$

$$\frac{d[\Gamma^3\Gamma^8]}{dt} = \frac{7\beta[\Gamma^3S^8]}{8[S^8]}([\Gamma^8\Gamma^1] + [\Gamma^8\Gamma^2] + [\Gamma^8\Gamma^3] + [S^8\Gamma^4] + [S^8\Gamma^5] + [S^8\Gamma^6] + [S^8\Gamma^7] + [S^8\Gamma^8] + [S^8\Gamma^9] + [S^8\Gamma^{10}] + [S^8\Gamma^{11}] + [S^8\Gamma^{12}]) + \frac{2\beta[S^3\Gamma^8]}{3[S^3]}([\Gamma^3S^3] + [\Gamma^4S^3] + [\Gamma^5S^3] + [\Gamma^6S^3] + [\Gamma^7S^3] + [\Gamma^8S^3]) + [\Gamma^3S^8] + [\Gamma^4S^8] + [\Gamma^5S^8] + [\Gamma^6S^8] + [\Gamma^7S^8] + [\Gamma^8S^8] - 2g[\Gamma^3\Gamma^8]$$

$$\frac{d[\Gamma^4\Gamma^4]}{dt} = \frac{3\beta[\Gamma^4S^4]}{2[S^4]}([\Gamma^4\Gamma^1] + [\Gamma^4\Gamma^2] + [\Gamma^4\Gamma^3] + [S^4\Gamma^4] + [S^4\Gamma^5] + [S^4\Gamma^6] + [S^4\Gamma^7] + [S^4\Gamma^8] + [S^4\Gamma^9] + [S^4\Gamma^{10}] + [S^4\Gamma^{11}] + [S^4\Gamma^{12}]) + \beta[S^4\Gamma^4] - 2g[\Gamma^4\Gamma^4]$$

$$\frac{d[\Gamma^4\Gamma^5]}{dt} = \frac{4\beta[\Gamma^4S^5]}{5[S^5]}([\Gamma^5\Gamma^1] + [\Gamma^5\Gamma^2] + [\Gamma^5\Gamma^3] + [S^5\Gamma^4] + [S^5\Gamma^5] + [S^5\Gamma^6] + [S^5\Gamma^7] + [S^5\Gamma^8] + [S^5\Gamma^9] + [S^5\Gamma^{10}] + [S^5\Gamma^{11}] + [S^5\Gamma^{12}]) + \frac{3\beta[S^4\Gamma^5]}{4[S^4]}([\Gamma^4S^4] + [\Gamma^5S^4] + [\Gamma^6S^4] + [\Gamma^7S^4] + [\Gamma^8S^4] + [\Gamma^9S^4] + [\Gamma^{10}S^4] + [\Gamma^{11}S^4] + [\Gamma^{12}S^4]) + \beta[\Gamma^4S^5] + \beta[\Gamma^5S^4] - 2g[\Gamma^4\Gamma^5]$$

$$\frac{d[\Gamma^4\Gamma^6]}{dt} = \frac{5\beta[\Gamma^4S^6]}{6[S^6]}([\Gamma^6\Gamma^1] + [\Gamma^6\Gamma^2] + [\Gamma^6\Gamma^3] + [S^6\Gamma^4] + [S^6\Gamma^5] + [S^6\Gamma^6] + [S^6\Gamma^7] + [S^6\Gamma^8] + [S^6\Gamma^9] + [S^6\Gamma^{10}] + [S^6\Gamma^{11}] + [S^6\Gamma^{12}]) + \frac{3\beta[S^4\Gamma^6]}{4[S^4]}([\Gamma^4S^4] + [\Gamma^5S^4] + [\Gamma^6S^4] + [\Gamma^7S^4] + [\Gamma^8S^4] + [\Gamma^9S^4] + [\Gamma^{10}S^4] + [\Gamma^{11}S^4] + [\Gamma^{12}S^4]) + \beta[\Gamma^4S^6] + \beta[\Gamma^6S^4] - 2g[\Gamma^4\Gamma^6]$$

$$\frac{d[\Gamma^4\Gamma^8]}{dt} = \frac{7\beta[\Gamma^4S^8]}{8[S^8]}([\Gamma^8\Gamma^1] + [\Gamma^8\Gamma^2] + [S^8\Gamma^3] + [S^8\Gamma^4] + [S^8\Gamma^5] + [S^8\Gamma^6] + [S^8\Gamma^7] + [S^8\Gamma^8] + [S^8\Gamma^9] + [S^8\Gamma^{10}] + [S^8\Gamma^{11}] + [S^8\Gamma^{12}]) + \frac{3\beta[S^4\Gamma^8]}{4[S^4]}([\Gamma^4S^4] + [\Gamma^5S^4] + [\Gamma^6S^4] + [\Gamma^7S^4] + [\Gamma^8S^4] + [\Gamma^9S^4] + [\Gamma^{10}S^4] + [\Gamma^{11}S^4] + [\Gamma^{12}S^4]) + \beta[\Gamma^4S^8] + \beta[\Gamma^8S^4] - 2g[\Gamma^4\Gamma^8]$$

$$\frac{d[\Gamma^4\Gamma^{10}]}{dt} = \frac{9\beta[\Gamma^4S^{10}]}{10[S^{10}]}([\Gamma^{10}\Gamma^1] + [S^{10}\Gamma^2] + [S^{10}\Gamma^3] + [S^{10}\Gamma^4] + [S^{10}\Gamma^5] + [S^{10}\Gamma^6] + [S^{10}\Gamma^7] + [S^{10}\Gamma^8] + [S^{10}\Gamma^9] + [S^{10}\Gamma^{10}] + [S^{10}\Gamma^{11}] + [S^{10}\Gamma^{12}]) + \frac{3\beta[S^4\Gamma^{10}]}{4[S^4]}([\Gamma^4S^4] + [\Gamma^5S^4] + [\Gamma^6S^4] + [\Gamma^7S^4] + [\Gamma^8S^4] + [\Gamma^9S^4] + [\Gamma^{10}S^4] + [\Gamma^{11}S^4] + [\Gamma^{12}S^4]) + \beta[\Gamma^4S^{10}] + \beta[\Gamma^{10}S^4] - 2g[\Gamma^4\Gamma^{10}]$$

$$\frac{d[\Gamma^4\Gamma^{12}]}{dt} = \frac{11\beta[\Gamma^4S^{12}]}{12[S^{12}]}([S^{12}\Gamma^1] + [S^{12}\Gamma^2] + [S^{12}\Gamma^3] + [S^{12}\Gamma^4]) + \frac{3\beta[S^4\Gamma^{12}]}{4[S^4]}([\Gamma^1S^4] + [\Gamma^2S^4] + [\Gamma^3S^4] + [\Gamma^4S^4] + [\Gamma^5S^4] + [\Gamma^6S^4] + [\Gamma^8S^4] + [\Gamma^{10}S^4] + [\Gamma^{12}S^4]) + \beta[\Gamma^4S^{12}] + \beta[S^4\Gamma^{12}] - 2g[\Gamma^4\Gamma^{12}]$$

$$\frac{d[\Gamma^5\Gamma^5]}{dt} = \frac{8\beta[\Gamma^5S^5]}{5[S^5]}([S^5\Gamma^1] + [S^5\Gamma^2] + [S^5\Gamma^3] + [S^5\Gamma^4] + [S^5\Gamma^5] + [S^5\Gamma^6] + [S^5\Gamma^7] + [S^5\Gamma^8] + [S^5\Gamma^9] + [S^5\Gamma^{10}] + [S^5\Gamma^{11}] + [S^5\Gamma^{12}]) + \beta[S^5\Gamma^5] - 2g[\Gamma^5\Gamma^5]$$

$$\frac{d[\Gamma^5\Gamma^6]}{dt} = \frac{5\beta[\Gamma^5S^6]}{6[S^6]}([S^6\Gamma^1] + [S^6\Gamma^2] + [S^6\Gamma^3] + [S^6\Gamma^4] + [S^6\Gamma^5] + [S^6\Gamma^6] + [S^6\Gamma^7] + [S^6\Gamma^8] + [S^6\Gamma^9] + [S^6\Gamma^{10}] + [S^6\Gamma^{11}] + [S^6\Gamma^{12}]) + \frac{4\beta[S^5\Gamma^6]}{5[S^5]}([\Gamma^1S^5] + [\Gamma^2S^5] + [\Gamma^3S^5] + [\Gamma^4S^5] + [\Gamma^5S^5] + [\Gamma^6S^5] + [\Gamma^7S^5] + [\Gamma^8S^5] + [\Gamma^9S^5] + [\Gamma^{10}S^5] + [\Gamma^{11}S^5] + [\Gamma^{12}S^5]) + \beta[\Gamma^5S^6] + \beta[S^5\Gamma^6] - 2g[\Gamma^5\Gamma^6]$$

$$\frac{d[\Gamma^6\Gamma^6]}{dt} = \frac{5\beta[\Gamma^6S^6]}{3[S^6]}([S^6\Gamma^1] + [S^6\Gamma^2] + [S^6\Gamma^3] + [S^6\Gamma^4] + [S^6\Gamma^5] + [S^6\Gamma^6] + [S^6\Gamma^7] + [S^6\Gamma^8] + [S^6\Gamma^9] + [S^6\Gamma^{10}] + [S^6\Gamma^{11}] + [S^6\Gamma^{12}]) + \beta[S^6\Gamma^6] - 2g[\Gamma^6\Gamma^6]$$

$$\frac{d[\Gamma^6\Gamma^7]}{dt} = \frac{6\beta[\Gamma^6S^7]}{7[S^7]}([S^7\Gamma^1] + [S^7\Gamma^2] + [S^7\Gamma^3] + [S^7\Gamma^4] + [S^7\Gamma^5] + [S^7\Gamma^6] + [S^7\Gamma^7] + [S^7\Gamma^8] + [S^7\Gamma^9] + [S^7\Gamma^{10}] + [S^7\Gamma^{11}] + [S^7\Gamma^{12}]) + \frac{5\beta[S^6\Gamma^7]}{6[S^6]}([\Gamma^1S^6] + [\Gamma^2S^6] + [\Gamma^3S^6] + [\Gamma^4S^6] + [\Gamma^5S^6] + [\Gamma^6S^6] + [\Gamma^7S^6] + [\Gamma^8S^6] + [\Gamma^9S^6] + [\Gamma^{10}S^6] + [\Gamma^{11}S^6] + [\Gamma^{12}S^6]) + \beta[\Gamma^6S^7] + \beta[S^6\Gamma^7] - 2g[\Gamma^6\Gamma^7]$$

$$\frac{d[\Gamma^8\Gamma^{11}]}{dt} = \frac{10\beta[\Gamma^8S^{11}]}{11[S^{11}]}([S^{11}\Gamma^1] + [S^{11}\Gamma^2] + [S^{11}\Gamma^3] + [S^{11}\Gamma^4] + [S^{11}\Gamma^5] + [S^{11}\Gamma^6] + [S^{11}\Gamma^7] + [S^{11}\Gamma^8] + [S^{11}\Gamma^9] + [S^{11}\Gamma^{10}] + [S^{11}\Gamma^{11}] + [S^{11}\Gamma^{12}]) + \frac{7\beta[S^8\Gamma^{11}]}{8[S^8]}([\Gamma^1S^8] + [\Gamma^2S^8] + [\Gamma^3S^8] + [\Gamma^4S^8] + [\Gamma^5S^8] + [\Gamma^6S^8] + [\Gamma^7S^8] + [\Gamma^8S^8] + [\Gamma^9S^8] + [\Gamma^{10}S^8] + [\Gamma^{11}S^8] + [\Gamma^{12}S^8]) + \beta[\Gamma^8S^{11}] + \beta[S^8\Gamma^{11}] - 2g[\Gamma^8\Gamma^{11}]$$

APPENDIX F

SAS code for calculating initial values

```
/*variables: 'uniq' is the unique indicator to recognize the same
            individuals in either table
            'stdid' in the contacts table is the identification number
            of the case that named them
            'stdid' in the cases table is its identification number
            (to link with contacts table)
            'recno' is a unique number for each "event" or entry into
            the database (even for repeaters)*/

/*Merging the corresponding contact data to the cases data*/

/*renaming variables to tell cases and contacts apart once merged*/
data msc.contacts;
  set msc.contacts;
  con_uniq=uniq;
  con_age=age;
run;

data msc.actors;
  set msc.actors;
  case_uniq=uniq;
  case_age=age;
  case_sex=sex;
run;

/*selecting only the cases from the actor list*/
data msc.actorscase;
  set msc.actors;
  if cas=1 ;
run;

/*merging information from cases database to the cases from actors list
in order to have the year in the actors list
dataset */
proc sort data=msc.actorscase;
  by recno;
run;

proc sort data=msc.cases;
  by recno ;
run;

data msc.actorsyear;
  merge msc.actorscase (in=a) msc.cases;
  by recno;
  if a=1 then output;
run;
```

```

/*Selecting only the chlamydia cases*/
data msc.actorschlam;
  set msc.actorsyear;
  if icd91 in (99.8,99.6,99.7) or icd92 in (99.8,99.6,99.7);
run;

/*Selecting only 1990 records*/
data msc.actorschlam90;
  set msc.actorschlam;
  if year=90;
run;

/*create pairs list:merging corresponding contacts to the actor list
based on 'stdid'*/
proc sort data=msc.actorschlam90;
  by stdid;
run;

proc sort data=msc.contacts;
  by stdid;
run;

data msc.merged;
  merge msc.actorschlam90 (in=a) msc.contacts;
  by stdid;
  if a=1 then output;
run;

/*keep only relevant variables and remove any observation with missing
information ~12% */
data msc.mergedfinal; /* n=4834 */
  set msc.merged; /* n=5515 */
  if con_uniq ne . and case_uniq ne .;
  keep case_uniq con_uniq stdid contsex con_age case_age case_sex;
run;

/*look at removed observations*/
data msc.missinginfo;
  set msc.merged;
  if con_uniq = . or case_uniq = .;
run;

data msc.nomissinginfo;
  set msc.merged;
  if con_uniq ne . and case_uniq ne .;
run;

proc freq data=msc.missinginfo;
  table seq syph sex connum;
run;
proc freq data=msc.nomissinginfo;
  table seq syph sex connum;
run;

```

```

proc means data=msc.missinginfo;
  var connum age;
run;
proc means data=msc.nomissinginfo;
  var connum age;
run;

/*remove duplicate partnerships : singlepairs*/
data msc.singlepairs;
  set msc.mergedfinal;
  minval=min(of case_uniq,con_uniq);
  maxval=max(of case_uniq,con_uniq);
run;
proc sort data=msc.singlepairs;
  by minval maxval;
run;
data msc.singlepairs;
set msc.singlepairs;
  by minval maxval;
  if first.maxval=1;
run;

/*Remove any case that is its own contact*/
data msc.singlepairs;
  set msc.singlepairs;
  if case_uniq=con_uniq then delete;
run;

/*merge degree information obtained from Pajek to the pairs list*/
/* for cases */
proc sort data=msc.singlepairs;
  by case_uniq;
run;
data msc.degreecase;
  set msc.degree90;
  case_uniq=uniq;
  case_deg=degree;
run;
proc sort data=msc.degreecase;
  by case_uniq;
run;
data msc.step1;
  merge msc.singlepairs (in=b) msc.degreecase;
  by case_uniq;
  if b=1 then output;
run;

/*for contacts*/
data msc.degreecontact;
  set msc.degree90;
  con_uniq=uniq;
  con_deg=degree;
run;

```

```

proc sort data=msc.degreecontact;
  by con_uniq;
run;
proc sort data=msc.step1;
  by con_uniq;
run;
data msc.step2;
  merge msc.step1 (in=c) msc.degreecontact;
  by con_uniq;
  if c=1 then output;
run;

/*keep only relevant variables*/
data msc.step2a;
  set msc.step2;
  keep case_deg case_uniq con_uniq con_deg;
run;

/*step2a = singlepairs with degree info*/

/*new dataset imported into sas from excel. Using excel,I added a column
'count'
which returns the number of times that that con_uniq appears in the
case_uniq colums.
If it appears at least once, then that contact was infected. If it
doesn't appear,
then that contact was never infected*/

/*remove duplicate con_uniq*/
proc sort data=msc.testdata ;
  by con_uniq count;
run;

data msc.singletest;
  set msc.testdata;
  by con_uniq count;
  if first.count=1;
run;

/*add the 'count' variable to the single pairs list to be able to
determine which contacts were infected and
which remained susceptible*/
proc sort data=msc.step2a;
  by con_uniq;
run;

data msc.singlepairs2;
  merge msc.step2a (in=e) msc.singletest;
  by con_uniq;
  if e=1 then output;
run;

```

```

/*split singlepairs2 into 2 tables, one with all infected contacts, the
other with all susceptible contacts*/
data msc.infected_con;
  set msc.singlepairs2;
  if count>=1;
run;

data msc.susceptible_con;
  set msc.singlepairs2;
  if count=0;
run;

/*count the number of total pairs by number of partners*/
proc freq data=msc.step2a;
  table case_deg*con_deg/ nopercnt norow nocol;
run;

/*count the number of pairs between a case (infected) and an susceptible
contact*/
proc freq data=msc.susceptible_con;
  table case_deg*con_deg/ nopercnt norow nocol;
run;

/*count the number of pairs between a case (infected) and a infected
contact*/
proc freq data=msc.infected_con;
  table case_deg*con_deg/ nopercnt norow nocol;
run;

/*count number of infected and susceptible individuals based on their
degree*/
/*INFECTED*/
/*combined cases and infected contacts*/
data msc.infected1;
  set msc.step1; /*step1 = singlepairs with case degree*/
  ndeg=case_deg;
  nuniq=case_uniq;
run;
data msc.infected2;
  set msc.infected_con;
  ndeg=con_deg;
  nuniq=con_uniq;
run;
data msc.infected;
  set msc.infected1 msc.infected2;
run;

/*eliminate duplicate uniq from new infected dataset (includes all cases
and infected contacts*/
proc sort data=msc.infected ;
  by nuniq;
run;

```

```
data msc.infected_nodup;
  set msc.infected;
  by nuniq;
  if first.nuniq=1;
run;

/*count infected by degree*/
proc freq data=msc.infected_nodup;
  table ndeg;
run;
/*SUSCEPTIBLE*/
/*eliminate duplicate con_uniq from susceptible contacts dataset*/
proc sort data=msc.susceptible_con ;
  by con_uniq;
run;
data msc.susceptible_nodup;
  set msc.susceptible_con;
  by con_uniq;
  if first.con_uniq=1;
run;
/*count susceptible contacts by degree*/
proc freq data=msc.susceptible_nodup;
  table con_deg;
run;
```

APPENDIX G

Estimating the initial condition of susceptible individuals and pairings of two susceptible individuals.

In both cases 1 and 2, there are 1,101,999 susceptible individuals to distribute among S_n , ($n=1$ to 12), where S_n is the number of susceptible individuals with 'n' sexual partners.

In **case 1**, they are distributed proportionally to the distribution of susceptible individuals from the data which is:

$S_1=3098$	$S_2=66$	$S_3=3$	$S_4=1$
$S_5=0$	$S_6=1$	$S_7=0$	$S_8=0$
$S_9=0$	$S_{10}=0$	$S_{11}=0$	$S_{12}=0$

The ratio of susceptible individuals in the date to susceptible individuals in the entire population is approximately 1:347. Therefore, the distribution of susceptible individuals from the entire population in case 1 is:

$S_1=1,077,362$	$S_2=22,902$	$S_3=1,041$	$S_4=347$
$S_5=0$	$S_6=347$	$S_7=0$	$S_8=0$
$S_9=0$	$S_{10}=0$	$S_{11}=0$	$S_{12}=0$

In **case 2**, they are distributed proportionally to the distribution of infected individuals from the data which is:

$S_1=2557$	$S_2=746$	$S_3=210$	$S_4=91$
$S_5=34$	$S_6=11$	$S_7=7$	$S_8=6$
$S_9=4$	$S_{10}=1$	$S_{11}=1$	$S_{12}=1$

The ratio of infected individuals in the date to susceptible individuals in the entire population is approximately 1:300. Therefore, the distribution of susceptible individuals from the entire population in case 2 is:

$S_1=768,399$	$S_2=223,800$	$S_3=63,000$	$S_4=27,300$
$S_5=10,200$	$S_6=3,300$	$S_7=2,100$	$S_8=1,800$
$S_9=1,200$	$S_{10}=300$	$S_{11}=300$	$S_{12}=300$

Next, the pairs of susceptible individuals, $S_n S_m$ for $n=1$ to 12 and $m=1$ to 12 are determined while respecting the distribution of individuals over S_1 to S_{12} (details included bellow). In cases 1i and 2i, the S_1 individuals are assigned to pairs first. Then, the S_2 individuals, the S_3 individuals, and so on until the S_{12} individuals are assigned to pairs. On the other hand, in cases 1ii and 2ii, the reverse is true. The S_{12} individuals are assigned to pairs first. Then, it is the S_{11} individuals, and so on until the S_1 individuals are assigned to pairs.

Here is an example of the detailed calculations for determining the number of $S_n S_m$ pairs for $n=1$ to 12 and $m=1$ to 12 in case 2ii. The calculations were done using the same reasoning for all four cases.

Determining the number of $S_n S_m$ pairs in case 2ii

Recall that in case 2, the initial number of S_n for $n=1$ to 12 are:

$S_1=768,399$	$S_2=223,800$	$S_3=63,000$	$S_4=27,300$
$S_5=10,200$	$S_6=3,300$	$S_7=2,100$	$S_8=1,800$
$S_9=1,200$	$S_{10}=300$	$S_{11}=300$	$S_{12}=300$

Starting with S_{12} individuals: There are 300 of them to place in pairs. There are no S_{12} individuals in any of the S_i pairs; therefore all 300 must be placed in $S_j S_k$ pairs. Also, since an S_{12} individual has 12 sexual partners, each of them must be placed in 12 different pairs. This means that $300 \times 12 = 3,600$ pairs must involve an S_{12} individual.

Based on our model assumptions, the only $S_j S_k$ pairs involving an S_{12} individual are $S_1 S_{12}$, $S_2 S_{12}$ and $S_4 S_{12}$. The ratio of S_1 , S_2 and S_4 individuals are 2,557 : 746 : 91.

Therefore, placing the 3,600 occurrences of S_{12} individuals amongst $S_1 S_{12}$, $S_2 S_{12}$ and $S_4 S_{12}$ pairs, while respecting the ratio of S_1 , S_2 and S_4 individuals, gives (approximately):

$S_1 S_{12}=2,714$	$S_2 S_{12}=790$	$S_4 S_{12}=96$
--------------------	------------------	-----------------

Next are the S_{11} individuals: There are also 300 of them to place in pairs. Again, there are no S_{11} individuals in any of the S_i pairs; therefore all 300 must be placed in $S_j S_k$ pairs. Since an S_{11} individual has 11 sexual partners, then each of them must be placed in 11 different pairs. This means that $300 \times 11 = 3,300$ pairs must involve an S_{11} individual.

Based on our model assumptions, the $S_j S_k$ pairs involving an S_{11} individual are $S_1 S_{11}$, $S_2 S_{11}$ and $S_8 S_{11}$. The ratio of S_1 , S_2 and S_8 individuals in this case are 2,557 : 746 : 6.

Therefore, placing the 3,300 occurrences of S_{11} individuals amongst $S_1 S_{11}$, $S_2 S_{11}$ and $S_8 S_{11}$ pairs, while respecting the ratio of S_1 , S_2 and S_8 individuals, gives (approximately):

$S_1 S_{11}=2,551$	$S_2 S_{11}=743$	$S_8 S_{11}=6$
--------------------	------------------	----------------

.....

For the S_7 individuals: There are 2,100 of them to place in pairs. Again, there are no S_7 individuals in any of the S_i pairs; therefore all 2,100 must be placed in $S_j S_k$ pairs. Since an S_7 individual has 7 sexual partners, then each of them must be placed in 7 different pairs. This means that $2,100 \times 7 = 14,700$ pairs must involve an S_7 individual.

Based on our model assumptions, the $S_j S_k$ pairs involving an S_7 individual are $S_1 S_7$, $S_2 S_7$, $S_3 S_7$ and $S_6 S_7$. The ratio of S_1 , S_2 , S_3 and S_6 individuals are 2,557 : 746 : 210 : 11.

Therefore, placing the 14,700 occurrences of S_7 individuals amongst $S_1 S_7$, $S_2 S_7$, $S_3 S_7$ and $S_6 S_7$ pairs, while respecting the ratio of S_1 , S_2 , S_3 and S_6 individuals, gives (approximately):

$S_1 S_7=10,667$	$S_2 S_7=3,111$	$S_3 S_7=876$	$S_6 S_7=46$
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For the S_6 individuals: There are 3,300 of them to place in pairs. But, 1 S_6 individual is already in S_i pairs; therefore, only the remaining 3,299 need to be placed in $S_j S_k$ pairs. Since an S_6 individual has 6 sexual partners, then each of them must be placed in 6 different pairs. This means that

3,299*6=19,794 SS pairs must involve an S6 individual. But, the number of S6S7 pairs has already been determined to be 46 (when placing S7 individuals). Therefore, 19,794-46=19,748 SS pairs (other than S6S7) must involve an S6 individual.

Based on our model assumptions, the remaining SS pairs involving an S6 individual are S1S6, S2S6, S3S6, S4S6, S5S6 and S6S6. The ratio of S1, S2, S3, S4, S5 and S6 individuals are 2,557 : 746 : 210 : 91 : 34 : 11.

Therefore, placing the 19,748 occurrences of S6 individuals left to place, amongst S1S6, S2S6, S3S6, S4S6, S5S6 and S6S6 pairs, while respecting the ratio of S1, S2, S3, S4, S5 and S6 individuals, gives (approximately):

S1S6=13,798	S2S6=4,025	S3S6=1,133	S4S6=491
S5S6=183	S6S6=59		

.....

For the S3 individuals: There are 63,000 of them to place in pairs. There are already 66 S3 individuals in SI pairs; therefore, only the remaining 62,997 need to be placed in SS pairs. Since an S3 individual has 3 sexual partners, then each of them must be placed in 3 different pairs. This means that 62,997*3=188,991 SS pairs must involve an S3 individual. But, the number of S3S4, S3S5, S3S6, S3S7 and S3S8 pairs has already been determined to be 6,075, 2,906, 1,133, 876 and 837 respectively. Therefore, 188,991-6,075-2,906-1,133-876-837=177,164 remaining SS pairs must involve an S3 individual.

Based on our model assumptions, those remaining SS pairs involving an S3 individual are S1S3, S2S3 and S3S3. The ratio of S1, S2 and S3 individuals are 2,557 : 746 : 210.

Therefore, placing the 177,164 occurrences of S3 individuals left to place, amongst S1S3, S2S3 and S3S3 pairs, while respecting the ratio of S1, S2 and S3 individuals, gives (approximately):

S1S3=121,679	S2S3=35,499	S3S3=9,993
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And so on

Here is a table of the final numbers for all four cases:

PAIR	Case 1i	Case 1ii	Case 2i	Case 2ii
s1s1	531,047	512,108	266,679	126,485
s1s2	11,314	43,633	155,605	230,707
s1s3	514	3,038	43,803	121,679
s1s4	171	1,349	18,981	73,987
s1s5	0	0	7,091	35,388
s1s6	171	2,028	2,294	13,798
s1s7	0	0	1,460	10,667
s1s8	0	0	1,251	10,218
s1s9	0	0	834	8,361
s1s10	0	0	208	2,261
s1s11	0	0	208	2,551
s1s12	0	0	208	2,714
s2s2	15,969	950	97,902	67,307
s2s3	1,452	66	55,118	35,499
s2s4	484	30	23,884	21,581
s2s5	0	0	8,924	10,324
s2s6	484	43	2,887	4,025
s2s7	0	0	1,837	3,111
s2s8	0	0	1,574	2,976
s2s9	0	0	1,049	2,439
s2s10	0	0	262	659
s2s11	0	0	262	743
s2s12	0	0	262	790
s3s3	345	3	26,345	9,993
s3s4	229	2	22,830	6,075
s3s5	0	0	8,530	2,906
s3s6	229	2	2,759	1,133
s3s7	0	0	1,756	876
s3s8	0	0	1,505	837
s4s4	125	1	13,747	2,632
s4s5	0	0	10,269	1,259
s4s6	250	1	3,322	491
s4s8	0	0	1,812	363
s4s10	0	0	302	80
s4s12	0	0	302	96
s5s5	0	0	6,115	470
s5s6	0	0	3,956	183
s6s6	471	1	1,398	59
s6s7	0	0	1,780	46
s8s11	0	0	2,830	6

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