5 Simulations

First the data from several papers are discussed, continuing the discussion started in chapter 1. In Kafetzaki (1993) numerical calculations were carried out using model DN, Caboussat (1998) made numerical calculations using mainly model DNM. In both numerical calculations and in the simulations to follow we choose the distribution of $(p_{jk}, k \geq 0, j \geq 1)$ to be Poisson($j\theta$). The simulated results are presented in 5.3 and are as expected from theoretical predictions. The new models we suggest in 5.4 are easy to simulate but would need completely new methods to analyse.

Remark: We choose the distribution of $(p_{jk}, k \geq 0, j \geq 1)$ to be Poissonian with parameter $(j\theta)$. The reasons for this simplification are: description with only one parameter (θ), easier calculations, appropriate to the biological situation because of the following reasons: We have various effects leading to a thinning of the original number of infective stages. One such effect is that there is only a very small probability that a given cercaria succeeds in infecting a host.

5.1 The data

Looking at the data, we see that there is huge heterogeneity amongst the individuals in that the number of worms per human varies tremendously. The distribution of worms per human is highly aggregated, as can be seen in Cheever (1968), Sturrock (1973), Forsyth and Bradley (1966). Data on schistosomiasis mansoni in Cheever (1968) from autopsies have a proportion of noninfected individuals of 104/196, and the ratio of variance/mean is 537. Distributions with a ratio of variance/mean of more than 1 are called overdispersed distributions.

One aim of our eight models is then the following: we want to show that such extreme heterogeneity between individuals can be expected, even though all individuals behave in the same way.

Of particular interest for our models DLM and DNM (with mortality of individuals) is the prevalence curve. It shows the proportion of individuals of each age that are infected with at least one worm. In data from Pesigan et al. (1958) this curve is as follows.

Diagram 5.1: An example of an age-prevalence curve of schistosome infection in a human community; the prevalence of schistosomiasis japonicum in

various age groups of a human community at Palo in the Philippines (data from Pesigan et al. (1958)). Solid points, observed values; solid line, curve fitted by eye.

We see a clear increase in the proportion of infected until the age of about 15 years followed by a levelling off. As is seen in section 5.3, we have the same type of behaviour in our simulations. But this is only true for schistosomiasis japonicum. For schistosomiasis mansoni we see that the proportion of infected people increases dramatically until the age of about 15 and then decreases again until the age of 30, when it stabilises (see Smithers and Terry (1969), Warren (1973)).

5.2 Theoretical background of the simulations

The main mathematical ideas for such simulations can be summarised in the following lemma. These ideas have been used frequently without mention in the proofs in this thesis.

Lemma 5.1 *Let $(X_1, X_2, X_3, \ldots, X_n)$ be n independent random variables, where X_i has an exponential distribution with parameter μ_i, and define $Y := \min(X_1, X_2, X_3, \ldots, X_n)$, $\mu := \sum_{i=1}^{n} \mu_i$. Then we have*
a) $\mathbb{P}[Y \leq t] = 1 - e^{-\mu t}$,
b) $\mathbb{P}[X_i = Y] = \mu_i/\mu$.

Remark to Lemma 5.1 In a) we state that the random variable Y has an exponential distribution with parameter μ; in b) we state that the probability of the i-th exponential variable being "responsible" for the minimum is proportional to the parameter of that random variable.

Proof of Lemma 5.1 Let us first prove this lemma for $n = 2$.

a) As the random variables are assumed to be independent of one another, we can argue as follows:

$$\begin{aligned}\mathbb{P}[Y \leq t] &= 1 - \mathbb{P}[\{X_1 > t\} \cap \{X_2 > t\}] = 1 - \mathbb{P}[X_1 > t]\mathbb{P}[X_2 > t] \\ &= 1 - e^{-(\mu_1+\mu_2)t}.\end{aligned}$$

b)

$$\begin{aligned}\mathbb{P}[X_1 < X_2] &= \int_0^\infty \mathbb{P}[X_1 < X_2 | X_2 = x] e^{-\mu_2 x} \mu_2 dx \\ &= \int_0^\infty (1 - e^{-\mu_1 x}) e^{-\mu_2 x} \mu_2 dx \\ &= \int_0^\infty e^{-\mu_2 x} \mu_2 dx - \int_0^\infty e^{-(\mu_1+\mu_2)x} \mu_2 dx \\ &= 1 - \frac{\mu_2}{\mu_1 + \mu_2} = \frac{\mu_1}{\mu_1 + \mu_2}.\end{aligned}$$

We now just have to justify why we could work with $n = 2$. But for $n = 3$ we can write $\min(X_1, X_2, X_3) = \min(\min(X_1, X_2), X_3)$. As we have seen in a) for $n = 2$, the minimum of two independent exponential random variables is again an exponential random variable. Therefore the proof for $n > 2$ follows by induction.

□

We demonstrate how to simulate such models using the model SNM. In Kafetzaki (1993) the strategy for simulating the model SN was demonstrated in her chapter 5.2. In what follows the strategy for simulating the model SN is included by choosing the death rate $\kappa = 0$. Models SL and SLM can be simulated analogously.

First we illustrate how such models are simulated. Then we discuss what is to be measured and why and in what way.

So let us assume that there are M individuals in system SNM. Let $X(i,t)$ be the number of parasites in person i at time t, where $i = 1, \ldots, M$ and $t \in [0, \infty)$. There are three types of events that can occur:

A) a parasite dies,

B) a new infection takes place,

C) a person dies.

Parasites die independently of one another and their lifetime is modelled by an exponential distribution with parameter μ. Then the infection process is modelled with Poisson processes of rate λ, so that the elapsed time between two (potential) infections of a single human has an exponential distribution with parameter λ. Finally, the lifetime of humans is modelled by an exponential distribution with parameter κ. Say that $x_0^{(M)}$ denotes the proportion of non infected individuals in the system ($x_0^{(M)} := \sum_{i=1}^{M} I[X(i,t) = 0]/M$). Then, if we want to know the time until the next event takes place, we can apply Lemma 5.1 a), and conclude that the elapsed time until the next event has an exponential distribution with parameter

$$TR := \mu \sum_{i=1}^{M} X(i,t) + M\lambda x_0^{(M)}(1 - x_0^{(M)}) + M\kappa,$$

where "TR" stands for "total rate". Here we still count infections with 0 parasites but only of uninfected individuals.

1. So the first step in simulating the behaviour of model SNM is to generate a realisation of an exponential random variable with parameter TR. Then we know when the event happened.

2. Then we have to decide what type of event that is. With probability $\big(\mu \sum_{i=1}^{M} X(i,t)\big)/TR$ a parasite dies, with probability $\big(M\lambda x_0^{(M)}(1-x_0^{(M)})\big)/TR$

an infection takes place, and with probability $M\kappa/TR$ a person dies; this is due to Lemma 5.1 b).

3. Then we have to decide which person is involved (or which persons are involved in the case of an infection):

If we have an event of type A), then it is person i that lost a parasite with probability $X(i,t)/\sum_{l=1}^{M} X(l,t)$.

If we have an event of type B), we choose uniformly amongst the non-infected a person, say person k, and then independently again uniformly we choose person j amongst the infected individuals. Then the initial number of parasites that is transmitted to person k has a Poisson distribution with parameter $X(j,t)\theta$. More generally, not assuming that $p_{1\cdot}$ is Poisson, we have an infection in person k with l worms with probability $p_{X(j,t),l}$.

Finally, if we have an event of type C), it is person i that has died with probability $1/M$.

After each step we register the elapsed time. Then we make the necessary changes in $X(i,t)$ for $i \in \{1,2,\ldots,M\}$.

It might be necessary to explain how we simulate uniform distributions and exponential distributions: usually there exists a generator for uniform random numbers on the interval [0,1]. If there should only exist a random number generator who produces say random numbers from 1 to 2^{32}, we use that generator and divide the realisation by 2^{32}, hence, we have approximately a U[0,1]-random variable. Then we get an exponential random variable with parameter 1 by producing a U[0,1]-random variable x and then taking $-ln(x)$. The reader can easily check that $-ln(x)/\eta$ has an exponential distribution with parameter η.

The program is listed at the end of this thesis. It can be found via anonymous ftp on "ftp.amath.unizh.ch" in the directory "pub/Luchsinger" or you point your internet browser to "ftp://iamassi.unizh.ch/pub/Luchsinger". It is written in the programming language C and the computations have been carried out on a "SUN ULTRA 5" computer system.

We show various simulated results in section 5.3. One question asked is: what is the "average" number of infected individuals? Another question is: what is the "average" proportion of individuals with j worms, $j \geq 0$? Many more questions can be asked.

We focus on the second question to justify that the simulations carried out can be used to answer the questions above. The program listed at the end of this thesis was used to answer that question too. We really want to know, what are the numbers $\overline{\xi}_j$ for $j \geq 0$ in model DNM. So this is the way we are going to interpret the word "average".

Numerically this question can be answered directly. These calculations for model DNM have been carried out in Caboussat (1998). The corresponding

calculations in model DN have been carried out in chapter 5 of Kafetzaki (1993).

But through simulations we are not directly answering *that* question, because we use model SNM for the simulations instead of model DNM. In fact, we even use model SNM *with minor changes*. These changes are necessary in order to simulate model SNM on the computer. The necessary changes are:

1. 0 is not an absorbing state anymore. If our process reaches zero, we do not take into account that particular simulation; therefore we condition on the process not dying out until the end of the simulation. The process never reached zero with our choices of parameters.
2. The number of co-ordinates is limited to 100.
3. The Poisson probabilities p_{jk} are limited such that

$$p_{j,100} := \sum_{k \geq 100} p_{jk}.$$

For j small this is not relevant, for larger j, restrictions 2 and 3 become increasingly important. The largest j that ever appeared in the simulations was 100. But as can be seen in Tables 5.5 and 5.6, there were only few occasions where an individual was carrying 100 parasites.

We denote model SNM with these three changes by SNM*. Then the argumentation is as follows: As M is finite and we only have finitely many co-ordinates in the simulations, we have only finitely many states for the *simulated* Markovian process SNM*. The state-space of SNM* is closed (not really, but we condition on the process not dying out until the end of the simulation). If the state-space of SNM* is closed, then SNM* is a recurrent Markovian process and there exists a unique stationary distribution m. If we define $m_j(t)$ to be the proportion of the total time that a person chosen at random had j worms until time t, then almost surely $m_j(t)$ converges to that m_j. We then choose this m_j to be an approximation of $\bar{\xi}_j$. We now have to ask ourselves if this is justified.

Theorems 3.5 and 3.12 could be used as a justification that for large M this system behaves more and more like system DNM. But we do not know yet whether in model DNM ξ converges towards $\bar{\xi}$, although we believe that this is so and simulations confirm our belief (see "Open questions" in chapter 4). So there is a gap in our line of reasoning. Nevertheless, as the results of the simulations and of numerical calculations are close, we accept this interpretation.

5.3 Numerical and simulated results compared with real data

Although the exact values of $\lambda, \theta, \mu, \kappa$ and the p_{jk} are not known and vary in time and from region to region, the physical, biological meaning stays the same. We can use data to estimate these parameters. We did not estimate the

parameters ourselves, but chose them after studying the data. Then we can make simulations using these estimations and compare the simulated results with real data. If the simulated results mirror real data well, we say that the model is "good".

5.3.1 Diagrams of Kafetzaki (1993) revisited

We present one diagram that can be compared with the simulation results in section 5.3.2 using model SNM*. More simulation results using model DN (or SN) can be found in Kafetzaki (1993).

Diagram 5.2 [Kafetzaki (1993), Diagram 6.1]: The simulated distribution of parasites per individual in model SN (with minor changes) conditional on the individual being infected. The values of the parameters are $\lambda = 3, \mu = 2$ and $\theta = 1.5$. More explanations to this diagram follow in the text just below.

In Diagram 5.2 the values for the rates are $\lambda = 3$ and $\mu = 2$. In the simulations for model SNM* we choose $\lambda = 0.3$ and $\mu = 0.25$. We can nevertheless compare these results with each other as in model SN we can change the time-scale to give $\lambda = 0.3$ and $\mu = 0.2$ which is quite close to our choices. The difference between θ in both models is minor (1.5 and 1.8). Diagram 5.2 must be compared with Diagram 5.4 (not conditional on the individual being infected). We see almost the same shape. The difference comes from slightly different ways of changing the original models SN and SNM respectively such that they could be simulated on a computer, slightly different values for μ and θ and the introduction of the death-rate $\kappa = 0.025$. In Diagram 5.2 we actually have 4 lines on top of each other. Line 1 is with $M = 40$ individuals in the system, line 2 is with $M = 60$ individuals in the system and line 3 is with $M = 80$

individuals in the system. Line 4 indicates numerically calculated values using model DN. All results are very close to each other; therefore the four lines can not be distinguished. This must be so due to Theorems 3.1 and 3.2 if we let M converge to infinity.

5.3.2 Simulation results in model SNM*

For the following simulations we let our program run for a time of 1,000,000 time units [years]. We round the numbers to three digits. The simulation results converged very fast: the changes in the data as presented below were in the third digit, if at all, when we increased the running time of the program from 100,000 to 1,000,000 time units.

5.3.2.1 The prevalence curve

We simulated the prevalence of the infection for values $\lambda = 0.3, \theta = 1.8, \mu = 0.25$ and $\kappa = 0.025$. This lead to the following simulated prevalence of the stationary distribution:

Diagram 5.3: The simulated age-prevalence curve for parameters $\lambda = 0.3, \theta = 1.8, \mu = 0.25, \kappa = 0.025$. The simulated proportion of infected over all ages was 0.476; the theoretical value in model DNM with these parameters is $1 - R_0^{-1} = 0.491$.

If we compare this prevalence curve with the prevalence curve using real data (Diagram 5.1), we see that we have much the same shape. The parameters could be altered to make a better fit. In Diagram 5.1 the curve decreases with increasing age after the age of about 20 to 24 years. This might be due to a different λ for older people; note also that other prevalence curves for schistosomiasis japonicum stayed stable on a high level after the age of about 15 to 20 years.

For larger R_0 the curve increases more at the beginning and stabilises at a higher level.

Intuitively we expected the age-prevalence curve to grow monotonely and asymptotically to a specific value. The instability at higher ages should disappear if we increase the running time of the program. On the other hand we do not have an immediate explanation for the peak at the age of 12 *in the simulation results.*

5.3.2.2 The distribution of worms per individual (all age classes)

In comparison to model DN we include the age of an individual in model DNM. The age plays a role because the younger an individual, the more likely it is not infected (see Diagram 5.3). Therefore we first present the distribution of the parasite burden per individual over all age classes. Then we look at the distribution of the number of worms at age 0, 2, 4, 6, 10, 15, 30 (where age x means age between $[x, x+1)$). With increasing age, the effects of being uninfected at birth becomes less and less important.

Diagram 5.4: The simulated distribution of parasites per individual over all age-classes for parameters $\lambda = 0.3, \theta = 1.8, \mu = 0.25, \kappa = 0.025$.

The exact simulated numbers in Diagram 5.4 cannot be distinguished in that diagram, therefore we repeat the first few.

# parasites	simulated $\overline{\xi}_j$
0	0.524
1	0.223
2	0.098
3	0.052
4	0.030
5	0.019
6	0.013
7	0.009
8	0.006
9	0.005
10	0.004
11	0.003
12	0.002

Table 5.5: The simulated distribution of parasites per individual (parameters as in Diagram 5.4).

In fact, in this simulation the proportion of infected individuals with j parasites decreased monotonely with j until the maximum number $j = 100$. We expected this behaviour, as we know from the beginning of chapter 4 that $\overline{\xi}_{j+1} < \overline{\xi}_j$ for all $j \geq 1$, as long as $\mu > \kappa$. The simulated average number of parasites per individual $\sum_{j\geq 1} j\overline{\xi}_j$ was 1.36 and the simulated second moment $\sum_{j\geq 1} j^2\overline{\xi}_j$ was 10.7.

5.3.2.3 The distribution of worms per individual at ages 0, 2, 4, 6, 10, 15, 30

Let us look at the distribution of parasites per individual at several ages for parameters $\lambda = 0.3, \theta = 1.8, \mu = 0.25, \kappa = 0.025$.

p:y	0	2	4	6	10	15	30
0	.940	.743	.616	.541	.486	.484	.490
1	.012	.065	.121	.170	.233	.254	.252
2	.012	.055	.086	.104	.113	.106	.103
3	.009	.038	.054	.060	.059	.054	.053
4	.006	.025	.034	.036	.034	.031	.030
5	.004	.017	.022	.023	.021	.019	.019
6	.003	.012	.015	.016	.014	.013	.013
7	.002	.009	.011	.011	.009	.009	.009
8	.002	.007	.008	.008	.007	.006	.006
9	.001	.005	.006	.006	.005	.005	.005
10	.001	.004	.005	.004	.004	.003	.004
11	.001	.003	.004	.003	.003	.003	.003
12	.001	.003	.003	.003	.002	.002	.002
av	.313	1.12	1.43	1.51	1.46	1.40	1.39
2m	4.16	12.3	13.5	12.7	11.0	10.5	10.5

Table 5.6: The simulated distribution of parasites per individual (parameters as in Diagram 5.4) at ages 0, 2, 4, 6, 10, 15, 30. Row i, $0 \leq i \leq 12$ shows the proportion of individuals with i numbers of parasites (of that age). The row "av" gives the simulated average number of parasites per individual $\sum_{j\geq 1} j\overline{\xi}_j$ (of that age). The row "2m" gives the simulated second moment $\sum_{j\geq 1} j^2\overline{\xi}_j$ (of that age).

Let us take a closer look at Table 5.6. As can be expected and is already seen in Diagram 5.3, the proportion of uninfected individuals decreases with increasing age. The reason for this behaviour is that being uninfected at birth becomes less and less important.

There are two (wrong) suggestions that might be made after looking at Table 5.6. First one might think that the distribution of parasites per individual, given the individual is infected, is the same over all age-classes. If one looks carefully at the numbers above one immediately sees that this is not so. Secondly, one might suggest that with increasing age (letting age tend to ∞), the distribution of worms per individual might be the same as in model DN (with $\kappa = 0$ and λ, θ, μ as before). This idea could be motivated by saying that if we condition on individuals being old, the "cleaning" of parasites that happens through death and "rebirth" becomes less and less important. But on the other hand we have interaction amongst the age groups which will alter the distribution of parasites in all age-classes.

Looking at the last two rows, we see an increase from age 0 to age 6 in the simulated average number of parasites per individual and from then onwards a slight decrease. The simulated second moment increases from 0 to 4 and

then decreases slightly. We do not have a mathematical interpretation of this behaviour.

The threshold results were also confirmed through simulations (not explicitely mentioned here).

Further simulations were carried out in Baeriswyl (1999) using mainly model SNM. Firstly, the distribution of eggs released per time unit and individual was modelled and compared with real data. Secondly, model SNM was altered: an additional randomness was added such that the number of *eggs released* determines the number of worms that develop in a newly infected individual. The aim of this work is to be able to estimate the number of worms in an individual from the number of eggs released by that individual.

5.4 Conclusion and outlook, new models

5.4.1 Conclusion and outlook

5.4.1.1 The distribution of the number of worms per human

One aim of our models is to show that one can have a large heterogeneity amongst the individuals even though individuals behave in the same way. It may even be that this disease should be modelled with parameters such that the dispersion is infinite. As was shown in Theorem 4.5, such a dispersion can be modelled with model DN. In earlier models, the dispersion was relatively low.

5.4.1.2 The prevalence curve

Introducing mortality of humans in model DN leads to model DNM. Model DNM mirrors well the prevalence curve for schistosomiasis japonicum (comparison of Diagrams 5.1 and 5.3).

Therefore our models are good with respect to these important features. Nevertheless improvements can be made. They are summarised in the following section.

5.4.2 New Models

We only mention new models which are closely related to our models. The following models nevertheless require different methods of analysis. On the other hand they can easily be simulated. We did not carry out any simulations of the models to follow. When specifying the changes to the models we consistently used model DNM to demonstrate what has to be altered. It is also possible to combine some of the following changes.

5.4.2.1 A model where mortality increases with parasite burden MORTINC

Medical doctors suggest that in some way mortality increases the higher the parasite burden. This might be another way to get closer to reality. Demonstrating the changes in comparison to DNM, we have the new model as follows:

$$\begin{aligned}\frac{d\xi_j}{dt} &= (j+1)\mu\xi_{j+1} - j\mu\xi_j + \lambda\xi_0 \sum_{l\geq 1} \xi_l p_{lj} - \kappa_j \xi_j;\ j \geq 1,\\ \frac{d\xi_0}{dt} &= \mu\xi_1 - \lambda\xi_0(1 - \sum_{l\geq 0} \xi_l p_{l0}) + \sum_{l\geq 1} \kappa_l \xi_l.\end{aligned} \tag{MORTINC}$$

We could suggest that there exists a κ such that for all $j \geq 1$ we have $\kappa_j \leq \kappa$ and surely we choose that $\kappa_{j-1} \leq \kappa_j$ for $j \geq 1$.

Another possibility is to choose an increase in mortality of humans proportional to the parasite burden, therefore $\kappa_j = j\kappa$. Models of infectious disease with trickle-infection where host mortality is proportional to parasite burden have been studied in Kretzschmar (1989), Diekmann and Kretzschmar (1991) and Kretzschmar (1993).

5.4.2.2 Almost independent "islands" with random visits ISLAND

In some parts of the world where this epidemic spreads it may well be that a region can be divided into subregions, between which there is not much interaction, due to geographical distance, mountains, ethnic reasons and so on. Additionally our main four parameters $\lambda, \theta, \mu, \kappa$ and even the distributions $(p_{lk}, l \geq 1, k \geq 0)$ might differ from subregion to subregion.

So let us assume we have J regions. In region i, $1 \leq i \leq J$, the parameters above are $(\lambda^{(i)}, \theta^{(i)}, \mu^{(i)}, \kappa^{(i)})$ and if we want more freedom we can also have different p_{lk}, so in this case some $p_{lk}^{(i)}$ for $l \geq 1$ and $k \geq 0$. Notice that in reality these parameters can vary from subregion to subregion: clearly the contact rate λ can be different; then μ and κ can be different due to different medical treatment; finally θ and the probabilities p_{lk} can differ through environmental circumstances. Clearly θ cannot be altered without altering some of the p_{lk}. Additionally we define a $J \times J$ matrix of visiting rates V, such that V_{ij}, $i \neq j$, is the rate at which a person from subregion i visits subregion j and has a potentially infectious contact. We do clearly *not* assume that this matrix V is symmetric. If the distributions $p_{lk}^{(i)}$ vary with i we assume in model ISLAND that a person travelling from i to j can only infect individuals in j and not get infected himself too. On the other hand, if $p_{lk}^{(i)}$ is the same for all i, we can interpret this model such that those cases where a person from subregion i travels to subregion j and gets infected himself are included in the infections

that are caused by individuals traveling from j to i and infecting individuals there. On the diagonal we have $V_{ii} = \lambda_i$. Let $\xi_j^{(i)}(t)$ denote the proportion of individuals of the total region that live in subregion i and are infected with j worms at time t; we assume that $\sum_{i=1}^{J} \sum_{j\geq 0} \xi_j^{(i)}(0) = 1$. So we have J systems of differential equations of the following kind:

$$\frac{d\xi_j^{(i)}}{dt} = (j+1)\mu\xi_{j+1}^{(i)} - j\mu\xi_j^{(i)} + \sum_{k=1}^{J} V_{ki}\xi_0^{(i)} \sum_{l\geq 1} \xi_l^{(k)} p_{lj}^{(i)} - \kappa\xi_j^{(i)};\ j \geq 1,$$

$$\frac{d\xi_0^{(i)}}{dt} = \mu\xi_1^{(i)} - \sum_{j\geq 1}\sum_{k=1}^{J} V_{ki}\xi_0^{(i)} \sum_{l\geq 1} \xi_l^{(k)} p_{lj}^{(i)} + \kappa(1 - \xi_0^{(i)}) \qquad \text{(ISLAND)}$$

for $1 \leq i \leq J$. This model allows us to model situations where the relevant R_i (see previous chapters) in one subregion is smaller than 1, but the epidemic is maintained even there at a maybe low prevalence through the flux of infections from other subregions into that particular region.

The model ISLAND is a so called "household model" (one thinks more in terms of "households" than "islands" as a motivation). They have been studied in various papers. Ball, Mollison and Scalia-Tomba (1997) is the main reference, and further contributions can be found in Becker and Dietz (1995) and Ball (1986). In comparison to homogeneous mixing models, in which each individual makes contacts with every other individual with the same probability in a time interval, household models allow to differentiate between global rates of infection ($V_{ij}, i \neq j$, above) and local rates of infection (λ_i).

5.4.2.3 Concomitant immunity after 2 infections ACQUIRED

The following model might fit real data well. The main idea is that concomitant immunity develops only after the second infection. In detail, an uninfected person gets a group-infection first, then all or at least some of these worms might die, and then a second group-infection can occur. After that second infection, he is immune to further infections, as long as he has some worms alive in his body. He keeps this (acquired) concomitant immunity for the rest of his life.

We denote by $\xi_j^{(1)},\ j \geq 1$, the proportion of individuals with a current infection burden of j parasites during their first infection, $\xi_0^{(1)}$ the proportion of individuals who did not have an infection so far in their life; $\xi_j^{(2)},\ j \geq 1$, the proportion of individuals with a current infection burden of j parasites who have been infected at least twice and finally, $\xi_0^{(2)}$ the proportion of individuals who have been infected at least once and have recovered. We assume that

$\sum_{j\geq 1}\sum_{k=1}^{2}\xi_j^{(k)}(0)=1$. Then we have for $j\geq 1$

$$\begin{aligned}\frac{d\xi_j^{(1)}}{dt} =&(j+1)\mu\xi_{j+1}^{(1)}-j\mu\xi_j^{(1)}+\lambda\sum_{u=0}^{j}\xi_{j-u}^{(1)}\sum_{k=1}^{2}\sum_{l\geq 1}\xi_l^{(k)}p_{lu}\\ &-\lambda(1-\xi_0^{(1)}-\xi_0^{(2)})\xi_j^{(1)}-\kappa\xi_j^{(1)},\\ \frac{d\xi_0^{(1)}}{dt} =&-\lambda\xi_0^{(1)}\sum_{j\geq 1}\sum_{k=1}^{2}\sum_{l\geq 1}\xi_l^{(k)}p_{lj}+\kappa(1-\xi_0^{(1)})\end{aligned}$$

for the first infection, and then

(ACQUIRED)

$$\begin{aligned}\frac{d\xi_j^{(2)}}{dt} &= (j+1)\mu\xi_{j+1}^{(2)}-j\mu\xi_j^{(2)}+\lambda\xi_0^{(2)}\sum_{k=1}^{2}\sum_{l\geq 1}\xi_l^{(k)}p_{lj}-\kappa\xi_j^{(2)};\ j\geq 1,\\ \frac{d\xi_0^{(2)}}{dt} &= \mu(\xi_1^{(1)}+\xi_1^{(2)})-\lambda\xi_0^{(2)}\sum_{j\geq 1}\sum_{k=1}^{2}\sum_{l\geq 1}\xi_l^{(k)}p_{lj}-\kappa\xi_0^{(2)}\end{aligned}$$

for all further infections. As there is a flux of $\mu\xi_1^{(1)}$ from $\xi^{(1)}$ to $\xi^{(2)}$ and a flux of $\kappa\sum_{j\geq 0}\xi_j^{(2)}$ from $\xi^{(2)}$ to $\xi^{(1)}$, there might be a stationary solution to the system of differential equations ACQUIRED.

5.5 Open questions

1. A whole group of questions arises through trying to find equilibria, thresholds and so on (as we did in chapters 2, 3 and 4 for our eight models) in the new models defined in section 5.4.2. As mentioned above these new models need different methods of analysis. On the other hand, simulations using stochastic models could be carried out easily.