

# Endemic disease, awareness, and local behavioural response

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## Abstract

The spread of a contagious disease is often accompanied by a rise in awareness of those in the social vicinity of infected individuals, and a subsequent change in behaviour. Such reactions can manifest themselves in lower susceptibility as people try to prevent themselves from catching the disease, but also in lower infectivity because of self-imposed quarantine or better hygiene, shorter durations of infectiousness or longer immunity. We here focus on the scenario of an endemic disease of which members of the population can be either aware or unaware, and consider a broad set of possible reactions. We quantify the impact on the endemicity of a disease in a well-mixed population under the variation of different disease parameters as a consequence of growing awareness in the population. Applying a pair-closure scheme allows us to analyse the effect of local correlations if aware individuals tend to occur near infected cases, and to link this to the amount of overlap between the networks underlying the spread of awareness and disease, respectively. Lastly, we study the consequences on the dynamics when the pathogen and awareness spread at different velocities.

*Keywords:* infectious disease, pair approximation, behaviour change, rumour spread

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## 1. Introduction

The spread of a contagious disease can trigger behavioural responses of people trying to minimise the effect of the disease onto themselves and their peers, and to prevent themselves and others from contracting the disease in the first place [9]. Depending on the best behaviour associated with a given disease, heightened levels of awareness give rise to the usage of face masks [14, 13], practise of better hygiene [10, 17], application of preventive medicine [15], vaccination [4], voluntary quarantine [20], avoidance of congregated places [10], practise of safe sex [1], etc. These actions can change the transmission patterns of the disease in altering the rates of transmission, as well as the durations of infectivity and immunity. The exact impact they can have on the disease dynamics, however, is difficult to quantify and often subject to speculation. Where conclusive observations are missing, mathematical modelling is used to test hypotheses and to identify crucial parameters in the interaction between a spreading disease and an associated behavioural response in the population [6].

The behavioural response to a disease carries elements of a contagious process itself. For people to react in some way, they do not necessarily need to have witnessed the disease first hand. Often, they have heard of it through the media or health authorities. These, however, usually focus on high-profile diseases and report broad statistics which often provide little information to

people trying to assess their individual costs and benefits of behavioural changes. Instead, awareness of the local prevalence of a disease not covered by media or local health authorities is more likely to be raised to by acts of informal information spread [e.g., 19], i.e. by hearing about someone having fallen ill, notes on a nursery door or other forms of local dissemination of awareness. As the information about the presence of a disease spreads in the population, people adapt their behaviour as a result of their awareness of the disease [e.g., 18].

The spread of rumours or other tokens of information in a human population has previously been compared to the spread of a contagious disease as an entity which is passed on from person to person [8]. Both in this context and in the context of spreading diseases, the importance of social network structure has received growing attention in recent years [12]. In our particular context, we are faced with two processes which spread over two, not necessarily overlapping networks and interact through the behavioural response of people as they become aware of the presence of a disease. This is not entirely dissimilar from the interaction between two diseases which has been studied, for example, by Vasco et al. [21].

We recently presented a model for the spread of awareness in response to an epidemic outbreak and analysed the effect this can have on the outbreak [7]. Here, we expand on that idea to study a simplified model of the interaction between local behavioural response and endemic disease. We map the model we introduced previously to a model which knows just two states of awareness – aware and unaware. This allows us to apply a systematic treatment to distinguish between the impact of spreading awareness on the initial phase of an outbreak of a conta-

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gious disease and the long-term impacts on the establishment of the disease, and to ask what happens under different types of behavioural change.

In the following, we introduce the model and study it in a well-mixed population, before considering the impact of local correlations using a pair approximation. All methods employed in this work are *deterministic* in nature, which makes them a good approximation only if infection is abundant enough to make stochastic extinction very unlikely. Therefore, we focus here on endemic disease which, once established, is present in a substantial fraction of the population. To assess the remaining effect of stochasticity, we compare the results with an equivalent stochastic model on a network.

## 2. The model

We divide our model population into two compartments: aware (labelled +) and unaware (−). Awareness spreads within the population analogously to an SIS (Susceptible-Infected-Susceptible) model, in that awareness is spread from the aware to the unaware part of the population at rate  $\alpha$ , and lost again or forgotten with rate  $\lambda$ .

We overlay the model for the spread of awareness with a standard SIRS (Susceptible-Infected-Recovered-Susceptible) model for endemic disease [see, e.g., 2], with associated rates of infection  $\beta$ , recovery  $\gamma$  and loss of immunity  $\delta$ . In total, we therefore end up with 6 distinct compartments:

$S_-$	Susceptible unaware
$I_-$	Infected unaware
$R_-$	Recovered unaware
$S_+$	Susceptible aware
$I_+$	Infected aware
$R_+$	Recovered aware

According to whether an individual is aware or unaware, we examine a variety of consequences on behaviour and, consequently, the disease progression with respect to that individual. In addition to reduced susceptibility as a consequence of protective behaviour adopted in a state of greater alert, we study the impact of reduced infectiousness of infected individuals as they become aware of carrying the disease and voluntarily reduce their number of contacts or take medication which reduces their infectiveness. If we denote the infection rate in an unaware population with  $\beta$ , the reduction in infectivity by a factor  $0 < \sigma_I < 1$  and the reduction in susceptibility by a factor  $0 < \sigma_S < 1$ , we end up with four different infection rates depending on the awareness of the susceptible and infected individuals in contact:

$\beta$	Infection rate from unaware infected to unaware susceptible
$\sigma_S \beta$	Infection rate from unaware infected to aware susceptible
$\sigma_I \beta$	Infection rate from aware infected to unaware susceptible
$\sigma_S \sigma_I \beta$	Infection rate from aware infected to aware susceptible

Generally, the combined effect of reduced susceptibility and infectiousness on the infection rate from aware infected to aware

susceptibles does not need to be multiplicative, but could be a more general  $\sigma_{SI}$ . Here, however, for the purpose of being later able to treat the two effects of reduced susceptibility and reduced infectiousness separately, we decided to regard them as independent effects on the infection rate, so that  $\sigma_{SI} = \sigma_S \sigma_I$ .

The model, in principle, also covers the scenario in which infectivity or susceptibility is increased by awareness (i.e.,  $\sigma_I > 1$  or  $\sigma_S > 1$ ). Although we do not expect this to be a common scenario, and it is beyond the scope of this paper, it is more than a theoretical possibility and could be encountered, for instance, in risk-seeking behaviour, such as deliberate contacts between infected with uninfected individuals in communities where HIV is highly prevalent [3], or in the increased movement of livestock in anticipation of a ban on movement, in the presence of a zoonosis.

In addition to modifying the infection rates, we study the case where awareness changes the duration of infection as people take medication or take other measures to recover more quickly. Denoting the reduction in the duration of infection with  $\epsilon^{-1}$  leads to the modified recovery rates:

$\gamma$	Recovery rate of unaware infected
$\epsilon\gamma$	Recovery rate of aware infected

We also allow the duration of immunity to be multiplied by a factor  $\phi^{-1}$  for people who are aware of the presence of the disease, caused, for example, by continued medication or renewal of vaccination. The resulting modified rates of loss of immunity are:

$\delta$	Rate immunity loss of unaware recovered
$\phi\delta$	Rate of immunity loss of aware recovered

This sums up the parameters of the modified SIRS model, and the way they change according to whether someone is aware or not. As mentioned above, awareness has its own dynamics governed by the following rates:

$\alpha$	Rate of awareness spread
$\lambda$	Rate of awareness loss

Lastly, the presence of awareness is coupled to the presence of the disease by a transition of rate  $\omega$  at which those unaware and infected become aware without contact to others. These are the sources of awareness.

$\omega$	Rate of infected becoming aware
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All compartments and the transitions between them are summarised in Fig. 1.

## 3. Mean-field analysis

Under the assumption of a well-mixed population, interactions between the different compartments happen completely at random, and rates of change are therefore proportional to the total number of individuals in the different compartments. Denoting with  $N_+ = S_+ + I_+ + R_+$  the aware and with  $N_- = S_- + I_- + R_-$  the unaware part of the population of constant size  $N = N_+ + N_-$ ,

the dynamics of the spread of awareness is described by the following ordinary differential equation (ODE):

$$\dot{N}_+ = \alpha N_+ \frac{N_-}{N} - \lambda N_+ + \omega I_-, \quad (1)$$

with the equation for  $N_-$  following trivially from  $N_- + N_+ = N$ . In the absence of infection ( $I_- = 0$ ), the system described by Eq. (1) has two equilibria:

$$N_{+,1} = 0 \quad \text{and} \quad N_{+,2} = (1 - \lambda/\alpha)N, \quad (2)$$

representing situations in which awareness is absent from the population or established in it, respectively. Analogously to the invasion threshold in epidemic models, the stability of the equilibria is determined by the value of the ratio  $R_0^a = \alpha/\lambda$ . If  $R_0^a < 1$ , the unaware equilibrium  $N_{+,1}$  is stable, whereas if  $R_0^a > 1$  it becomes unstable, and the equilibrium  $N_{+,2}$  in which with a part of the population is aware acquires stability.  $R_0^a$  therefore acts as a *basic reproductive number* of awareness, a familiar concept in epidemiology [5].

Combining the model for the spread of awareness with the model for the spread of the disease as given by the SIRS model we end up with a system of 6 ODEs representing the dynamics of the full system:

$$\begin{aligned} \frac{dS_-}{dt} &= -(I_- + \sigma_I I_+) \beta \frac{S_-}{N} - \alpha(S_+ + I_+ + R_+) \frac{S_-}{N} + \lambda S_+ + \delta R_- \\ \frac{dI_-}{dt} &= +(I_- + \sigma_I I_+) \beta \frac{S_-}{N} - \alpha(S_+ + I_+ + R_+) \frac{I_-}{N} + \lambda I_+ - \gamma I_- - \omega I_- \\ \frac{dR_-}{dt} &= -\alpha(S_+ + I_+ + R_+) \frac{R_-}{N} + \lambda R_+ - \delta R_- + \gamma I_- \\ \frac{dS_+}{dt} &= -(I_- + \sigma_I I_+) \sigma_S \beta \frac{S_+}{N} + \alpha(S_+ + I_+ + R_+) \frac{S_+}{N} - \lambda S_+ + \phi \delta R_+ \\ \frac{dI_+}{dt} &= +(I_- + \sigma_I I_+) \sigma_S \beta \frac{S_+}{N} + \alpha(S_+ + I_+ + R_+) \frac{I_+}{N} - \lambda I_+ - \epsilon \gamma I_+ + \omega I_- \\ \frac{dR_+}{dt} &= +\alpha(S_+ + I_+ + R_+) \frac{R_+}{N} - \lambda R_+ - \phi \delta R_+ + \epsilon \gamma I_+ \end{aligned} \quad (3)$$

Summation over the disease states of the system to obtain  $\dot{N}_- = \dot{S}_- + \dot{I}_- + \dot{R}_-$  and  $\dot{N}_+ = \dot{S}_+ + \dot{I}_+ + \dot{R}_+$  recovers the dynamics of the spread of awareness as prescribed by Eq. (1), and summing over the information states to obtain  $\dot{S} = \dot{S}_- + \dot{S}_+$ ,  $\dot{I} = \dot{I}_- + \dot{I}_+$  and  $\dot{R} = \dot{R}_- + \dot{R}_+$  recovers the equations of the classical SIRS model if the disease rates are awareness-independent ( $\sigma_I = \sigma_S = \epsilon = \phi = 1$ ). The condition for disease invasion is then fulfilled when the basic reproductive number  $R_0^d = \beta/\gamma$  exceeds 1 [e.g., 5].

In the full system described by Eqs. (3), we identify four qualitatively different types of mean-field equilibria in which either everyone is susceptible and unaware, or any combination of disease and awareness are endemic (Fig. 2a). If awareness and disease spread completely independently, with awareness-independent disease transition rates and  $\omega = 0$ , the equilibrium structure is fully determined by the values of the threshold parameters  $R_0^d = \beta/\gamma$  and  $R_0^a = \alpha/\lambda$  which assume the role of the epidemic thresholds for the two different processes.

When the interaction between the spreads comes into play, i.e. when any of the disease-related parameters change with

respect to the awareness of a given susceptible-infected pair, the borders between these four regions can change. The way such changes depend on the interplay between the parameters will be discussed in the following.

A special role is assumed by the process of information generation, coupled to the parameter  $\omega$ . If  $\omega > 0$ , there is no longer an equilibrium in which the disease is endemic but awareness is not. Whenever there is any positive fraction of infected in the population, it will also create some level of awareness. To first order, the number of aware individuals thus generated is (see appendix)

$$N_+^\omega \approx \frac{\omega}{|\alpha - \lambda|} \frac{I_-}{N} \quad (4)$$

which is a good approximation as long as

$$\frac{\omega}{\alpha} \frac{I_-}{N} \lesssim \frac{1}{4} \left(1 - \frac{1}{R_0^a}\right)^2. \quad (5)$$

If  $R_0^a \approx 1$ , the contribution of sources of awareness to the aware population is better approximated by

$$N_+^\omega \approx N \sqrt{\frac{\omega}{\alpha} \frac{I_-}{N}}. \quad (6)$$

In the following we study the equilibrium structure of the mean-field model under different scenarios for the impact of awareness on the parameters of the disease dynamics

### 3.1. Equilibrium structure

The trivial equilibrium of our model is one which is free of disease and awareness, at  $S_- = N$  and  $S_+ = I_- = I_+ = R_- = R_+ = 0$ . At that point, the whole population is susceptible to the disease and unaware of it. On contact with the infected part of the population, susceptibles are infected with a rate potentially scaled with the parameters  $\sigma_S$  and  $\sigma_I$ , depending on whether the susceptible and infected individuals in contact are aware of the disease or not, and, once infected, recover at a rate scaled with  $\epsilon$  if they are aware. If  $\omega = 0$ , the stability of the disease- and awareness-free equilibrium depends only on  $\beta/\gamma$  and  $\alpha/\lambda$ , just as in the decoupled case described above, and independently of  $\sigma_S$ ,  $\sigma_I$  and  $\epsilon$ . In that case, the borders of the bottom region in the left corner of the graph discussed above remain as before and they are determined by

$$R_0^d = \frac{\beta}{\gamma} \quad \text{and} \quad R_0^a = \frac{\alpha}{\lambda} \quad (7)$$

If  $R_0^d$  is smaller than 1 but the awareness threshold  $R_0^a$  exceeds 1, the stable equilibrium is one where awareness is endemic but the disease is not ( $S_- = N \cdot \lambda/\alpha$ ,  $S_+ = N - S_-$ ,  $I_- = I_+ = R_+ = R_- = 0$ ). If both  $R_0^d$  and  $R_0^a$  are greater than 1, the dependence of the disease-related parameters comes into play as it becomes harder for the disease to invade the population if there is a sustained level of awareness. This is the case for several of the possible effects of our model, i.e. if aware individuals recover from the infection more quickly, but also if they spread the infection less, or if aware susceptibles are less

prone to catching the disease (Fig. 2b), as we will see in greater detail in the following.

A complete analysis of the ODE system (3) is difficult and does not lead to transparent results. Instead, we will cover some limiting cases to illustrate the effect which different kinds of behavioural change as a result of awareness can have. We here state the results of our analysis of the invasion conditions, the derivations of which can be found in the appendix.

#### Reduced susceptibility

If susceptibles have their susceptibility reduced by a factor  $\sigma_S$ , while the other rates remain unaffected by awareness,  $\sigma_I = \epsilon = \phi = 1$ , the epidemic threshold remains at 1 for  $R_0^a < 1$ , but if  $R_0^a > 1$  it increases to

$$R_0^d > 1 + \frac{(1 - \sigma_S)(R_0^a - 1)}{1 + \sigma_S(R_0^a - 1)}, \quad (8)$$

which depends only on  $R_0^a$  and is independent of the relative speeds of the two processes, and of the rate of information generation  $\omega$ . If  $R_0^a \rightarrow \infty$ , the threshold approaches  $1/\sigma_S$ , as everyone in the population will be aware. Eq. (8) is similar to the result obtained by Vasco et al. [21] in the context of the spread of two interacting diseases.

#### Reduced infectivity

If only infected individuals have their infectivity reduced by a factor  $\sigma_I$ , while the other rates remain unaffected by awareness,  $\sigma_S = \epsilon = \phi = 1$ , the invasion threshold for the disease is changed even if  $R_0^a < 1$  because now the appearance of awareness in infected individuals at rate  $\omega$  changes the disease dynamics even if awareness does not spread much. In that case, the condition for disease invasion changes to

$$R_0^d > 1 + \frac{(1 - \sigma_I)\omega}{\lambda + \gamma + \sigma_I\omega}. \quad (9)$$

This explains why there is a gap between the epidemic threshold and 1 for  $R_0^a < 1$  in Fig. 2b. If awareness can spread, such that  $R_0^a > 1$ , the invasion condition becomes

$$R_0^d > 1 + \frac{(1 - \sigma_I) \left[ R_0^a \left( 1 + \frac{\omega}{\alpha + \gamma} \right) - 1 \right]}{1 + \sigma_I \left[ R_0^a \left( 1 + \frac{\omega}{\alpha + \gamma} \right) - 1 \right]}, \quad (10)$$

which is similar to Eq. (8), but contains an additional term reflecting the impact of the rate  $\omega$  at which infected can become aware by themselves. If  $\omega = 0$ , Eq. (8) and (10) are the same with  $\sigma_S$  and  $\sigma_I$  interchanged.

Note that  $\alpha$ ,  $\lambda$ ,  $\beta$  and  $\gamma$  cannot be eliminated concurrently from inequalities (9) and (10) by expressing the them in terms of  $R_0^d$  and  $R_0^a$  only. The impact of new awareness appearing in those infected is relative to how long they stay infected ( $\gamma^{-1}$ ) and how fast it is spread ( $\alpha$ ).

#### Faster recovery

If only the recovery rate, or the duration of infection, depends on the awareness of a given infectious individual, such

that  $\epsilon > 1$ , but all other parameters are awareness-independent, the invasion condition changes whatever the value of  $R_0^a$  because infected individuals can become aware at rate  $\omega > 0$  and have their period of infectivity shortened, even if awareness does not spread far. If  $R_0^a < 1$ , the condition for disease invasion becomes

$$R_0^d > 1 + \frac{(\epsilon - 1)\omega}{\lambda + \epsilon\gamma + \omega}, \quad (11)$$

which, again, causes a gap between the epidemic threshold and 1 for  $R_0^a < 1$  in Fig. 2b. If  $R_0^a > 1$ , the invasion condition is

$$R_0^d > 1 + \frac{R_0^a - 1 + \frac{\omega}{\alpha + \gamma + \omega}}{R_0^a + \frac{(\epsilon - 1)\gamma}{\alpha + \gamma + \omega}} (\epsilon - 1). \quad (12)$$

Again, the invasion conditions cannot be described by a simple relation between  $R_0^d$  and  $R_0^a$ , but only by a more complex relation of all parameters.

#### Longer preservation of immunity

If the duration of immunity  $\delta^{-1}$  depends on the awareness of individuals, this changes the fraction of infected and recovered in the endemic state, yet it does not affect the transitions between the equilibria. This is, to some extent, an artefact of the deterministic formulation of the model. If awareness is abundant, and it prolongs immunity by a large amount, the number of infected can drop so low that the deterministic approximation used here loses its value and stochastic extinction becomes likely enough to be relevant. However, we will not discuss this further in this paper.

#### Endemic equilibria

While we did not find analytical expressions for the exact levels of the endemic equilibria, they can be derived numerically, a few examples of which are shown in Fig. 2c. Unlike with the invasion conditions shown in Fig. 2b, which display a sharp threshold at  $R_0^a = 1$ , there is a noticeable effect on the endemic equilibrium for  $R_0^a < 1$  as  $R_0^a$  approaches 1 because even if awareness cannot spread independently, a sizable part of the population will become aware, lowering the equilibrium density of infected individuals.

#### 3.2. Pair approximation

While the mean-field approximation is useful in capturing general features of the model system, it does not contain a notion of spatial structure in the population as it assumes random mixing. As awareness spreads in the population in the mean-field model, it does so only by affecting an increasing fraction of the population which the disease encounters. This is reflected by the interaction terms which assume the form

$$\dot{I} = +\beta \frac{1}{N} (I_- + \sigma_I I_+) (S_- + \sigma_S S_+) - \dots \quad (13)$$

This form of interaction includes the assumption that the probability of any one infected to encounter an aware/unaware susceptible is proportional to the fraction of such individuals in the population.

If one wants to take into account effects of local interaction and the notion that awareness can be different around disease cases from other parts of the population, the system is more accurately described at the level of pairs. If we denote by  $[\dots]^d$  the number of pairs of two members of the population in given state with a potentially infectious contact, the interaction term becomes

$$\dot{I} = +\hat{\beta}([S_-I_-]^d + \sigma_I[S_-I_+]^d + \sigma_S[S_+I_-]^d + \sigma_S\sigma_I[S_+I_+]^d) - \dots, \quad (14)$$

where  $\hat{\beta} = \beta/k^d$  is the per-contact default infection rate if  $k^d$  is the number of disease contacts each individual possesses in the population, assumed here to be constant. Under the assumption of random mixing, i.e. if all contacts occur completely at random, we recover the well-mixed case described by the mean-field approximation, and  $[S_{\pm}I_{\pm}]^d = k^d S_{\pm}I_{\pm}/N$ . By describing the system at the level of pairs, however, we can capture situations where  $[S_{\pm}I_{\pm}]^d$  is greater or smaller than in a completely random setting, including cases where, for example, members of the population with a potentially infectious contact in their neighbourhood have a higher awareness with respect to the rest of the population.

The build-up of correlations between states has been shown to be relevant to the description of spreading diseases in structured populations. In the absence of awareness the basic reproductive number of the disease at the level of pairs is given by

$$R_0^d = C_{S_-I_-}^d \frac{\beta}{\gamma}, \quad (15)$$

where

$$C_{S_-I_-}^d = \frac{N [S_-I_-]^d}{k^d S_- I_-} \quad (16)$$

is the correlation between unaware susceptibles and unaware infected on disease edges, i.e. their tendency of being neighbours on the network. This correlation can be shown to reach a quasi-equilibrium very fast with respect to the disease dynamic, yielding the basic reproductive number as given by the pair approximation [11]

$$R_0^d = \left(1 - \frac{2}{k^d}\right) \frac{\beta}{\gamma}. \quad (17)$$

In addition to capturing state correlations, a description on the level of pairs allows us to distinguish between the pathways underlying the spread of the different processes. We thus denote pairs on the disease network of potentially contagious contact with  $[\dots]^d$ , and ones on the network of spreading awareness with  $[\dots]^a$ , so that the interaction terms for the spread of awareness assume the form

$$\dot{S}_+ = \dots + \hat{\alpha}([S_-S_+]^a + [S_-I_+]^a + [S_-R_+]^a) \dots, \quad (18)$$

where  $\hat{\alpha} = \alpha/k^a$  is the per-contact rate of awareness spread if  $k^a$  is the constant number of contacts each individual possesses on the network on which awareness spreads. Analogously to Eq. (15), we can define a basic reproductive number of awareness at pair level

$$R_0^a = C_{-+}^a \frac{\alpha}{\lambda} \quad (19)$$

where

$$C_{-+}^a = \frac{N [N_-N_+]^a}{k^a N_-N_+} \quad (20)$$

is the correlation between aware and unaware individuals on the network underlying the spread of awareness.

The 6 different states on 2 distinct edge types in our model leads to a total number of 42 pair equations. Deriving them by hand is tedious to do and prone to errors. Therefore, we implemented an automated procedure to generate the equations from a given set of states, edge types and transitions. The resulting system of equations can be found in its full form in the online supporting material, while we elaborate on the exact way we treat the overlap between the two networks in the appendix.

Analysing the system of equations produced from the pair approximation, we find that correlations can indeed play an intricate role in the interaction between spreading awareness and disease. The most pronounced difference in the dynamics of the correlations occurs in the initial phase of growth of a disease which breaks out in an almost completely susceptible population. Once the system comes close to equilibrium, the correlations converge to approximately 1, and network effects cease to play a significant role.

We can introduce correlation measures for the local interaction between disease and awareness. Concentrating, for example, on the effect of reduced susceptibility, i.e.  $\sigma_S < 1$  while all other rates are awareness-independent, the local accumulation of awareness around infected cases is captured by the correlation

$$C_{S_+I_-}^d = \frac{N [S_+I_-]^d + [S_+I_+]^d}{k^d S_+(I_- + I_+)}, \quad (21)$$

which gives the tendency of aware susceptibles to be connected to infected individuals on the disease network.

With a large degree of overlap between the two networks, the approach to equilibrium can be different from the non-overlapping case. Generally, if  $R_0^d > 1$  and one starts with a few infected individuals, the disease goes through a phase of exponential increase before the equilibrium is approached. With a large degree of overlap between the two networks, the initial correlation between infected and aware individuals slows down the exponential increase, and the approach to equilibrium can be slower than what the well-mixed view predicts, even when they converge to the same equilibrium (Fig. 3).

To assess the impact of this initial mitigation of the growth of the disease, we tracked the number of individuals infected in a single outbreak as predicted by the pair approximations, as well as by stochastic simulations. The results reveal an effect not predictable by the mean-field approximation but captured by the pair dynamics. If  $R_0^a < 1$ , and the two networks do not overlap, there is no noticeable effect of awareness on outbreak sizes, just as in the mean-field approximation. If, however, the networks do overlap, the pair approximation suggests that an increasing  $R_0^d$  is necessary for an outbreak to grow to a given size, the strongest relative change occurring when  $R_0^a \approx 1$ , i.e. when the spread of awareness is nearly critical (Fig. 4). In that case, the equilibrium number of aware individuals is approximately 0, but any awareness which appears in the population

either establishes itself at a small number (if  $R_0^a \gtrsim 1$ ) or subsides only slowly (if  $R_0^a \lesssim 1$ ). Now, if the networks overlap strongly, awareness appears in infected cases (at rate  $\omega$ ) and spreads around these, so that  $[SI]^d$  pairs tend to be of type  $[S_+I_+]^d$  with the corresponding reduction in transmission rate.

If  $R_0^a < 1$ , the effect on the outbreak size on overlapping networks is caused by minor outbreaks of awareness generated around infected cases, which themselves are sources of awareness. As these outbreaks are generally of small size because  $R_0^a < 1$ , different timescales between the two spreading processes make no big difference. If, on the other hand,  $R_0^a > 1$ , awareness is able to spread and establish itself in the population even without being refreshed by infected cases. Now, for the same combination of  $R_0^d$  and  $R_0^a$ , the relative timescales between the two processes determine how quickly awareness takes over large parts of the population, and consequently how early it can have a strong influence on the disease outbreak. Keeping  $R_0^a$  constant but increasing  $\hat{\alpha}$ , we observe an increased effect on the quenching of the epidemic (Fig. 4).

The results presented here apply to relatively unclustered networks. While we did extend the methods devised by Keeling [11] for pair approximations on clustered networks to our more complex system, these failed to generate convincing results or capture any of the effects we previously showed to operate when disease and awareness interact on clustered networks [7]. In fact, we found that the sheer complexity of the system of equations resulting from the pair approximation we derived made it difficult to go beyond the simple observations presented here.

#### 4. Discussion

We find the impact of spreading awareness on endemic disease to be manifested in two different phenomena. On one hand, it changes the invasion conditions between a disease-free and endemic equilibrium, and can make it impossible for a disease to establish itself in the population. This effect is well captured by the mean-field approximation, as the situation in endemic equilibrium is usually close to well-mixed, and the disease is evenly distributed in the whole population rather than local to a particular part of it.

Reduced infectivity or shorter duration of infection of aware infected, as well as reduced susceptibility of aware susceptibles, or a combination of the three, all make it more difficult for the disease to establish itself in the population. If infected individuals act as sources of awareness, reduced infectivity, for example due to self-imposed quarantine or practise of better hygiene can raise the threshold for disease invasion even if awareness does not spread in the population. The same holds if those infected spread the disease for shorter periods, for example because they take medication to recover quicker. A longer duration of immunity of aware recovered individuals, on the other hand, lowers the disease prevalence in the endemic equilibrium, however it does not change the invasion conditions. As we have shown previously, such effects on the invasion threshold can be observed in a well-mixed population only if awareness does not deteriorate as it spreads through the population [7].

A second effect is the deceleration of the spread of a disease as it approaches equilibrium. In the initial phase of the outbreak, local correlations between disease and awareness can be important. If the networks overlap more, the outbreak is slowed down more effectively, a phenomenon which the mean-field approximation fails to capture, and which is particularly pronounced if the spread of awareness is nearly critical. If awareness spreads sufficiently to establish itself in the population on a larger scale, its initial impact on an outbreak is largely determined by its relative speed with respect to the spreading disease.

Part of the resulting structure of equilibria is similar to what has previously been found for the interaction between two pathogens, where one provides immune enhancement, i.e. improved immune response to the other [21]. In addition, we have shown both the use and limitations of using pair approximation to describe the resulting interaction, especially as potential difference in the contact structures underlying the spread of the representative pathogen comes into play. While the pair approximation allowed for the study of situations of varying network overlap, it necessitated an automated procedure to generate the vast number of equations required. At the same time, the system became so complex that it was almost completely opaque to deeper analysis.

To conclude, we have investigated a simple model for the contemporaneous spread of two processes, where spreading awareness can inhibit the spread of a disease. A systematic investigation of the different possible consequences for the spread of the pathogen yielded the impact on the course of the disease when parts of the population change their behaviour as a result of becoming aware to the presence of the disease. The methods developed here, however, are by no means limited to this particular case, and should provide a useful set of tools for any investigation of multiple and interacting spreading processes, whether it be rumours, opinions, pathogens or multiple strains of the same pathogen.

#### Acknowledgements

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#### Appendix A. Level of awareness generated by sources

Including infecteds as sources of awareness, the equation determining the awareness dynamics reads:

$$\dot{N}_+ = \alpha N_+ \frac{N_-}{N} - \lambda N_+ + \omega I_- \quad (\text{A.1})$$

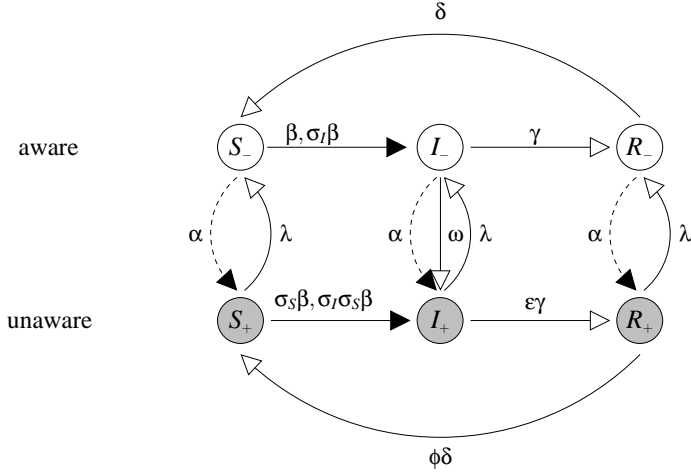


Figure 1: Classes and transitions in the model. An arrow stands for “can turn into”, with filled arrow caps indicating processes subject to contacts on the disease (solid lines) or awareness (dashed lines) networks. Open arrow caps indicate processes that do are not subject to contact.

Substituting  $N_- = N - N_+$  and solving for  $\dot{N}_+ = 0$  yields the two equilibria

$$N_+ = N \left[ \frac{1}{2} \left( 1 - \frac{\lambda}{\alpha} \right) \pm \sqrt{\frac{1}{4} \left( 1 - \frac{\lambda}{\alpha} \right)^2 + \frac{\omega I_-}{\alpha N}} \right], \quad (\text{A.2})$$

subject to the equilibrium value of  $I_-$  which can be determined only from the full system of ODEs (3). If the second summand under the square root of Eq. (A.2) is smaller than the first, or

$$\frac{\omega I_-}{\alpha N} \lesssim \frac{1}{4} \left( 1 - \frac{\lambda}{\alpha} \right)^2, \quad (\text{A.3})$$

Eq. (A.2) is well approximated by expanding around  $(\omega I_-)/(\alpha N) \approx 0$ , to first order

$$N_+ = N \left[ \left( \frac{1}{2} \pm \frac{1}{2} \right) \left( 1 - \frac{\lambda}{\alpha} \right) + \frac{\omega I_-}{|\alpha - \lambda| N} + o \left( \frac{\omega I_-}{\alpha N} \right)^2 \right], \quad (\text{A.4})$$

with the minus sign yielding a stable and positive equilibrium for  $R_0^a < 1$  and the positive sign for  $R_0^a > 1$ . Therefore, if  $R_0^a$  is sufficiently different from 1, the contribution of sources is awareness is approximately

$$N_+^\omega \approx \frac{\omega I_-}{|\alpha - \lambda| N}. \quad (\text{A.5})$$

If, on the other hand, the first summand under the square root of Eq. (A.2) is greater than the the first, or if  $R_0^a \approx 1$ , and

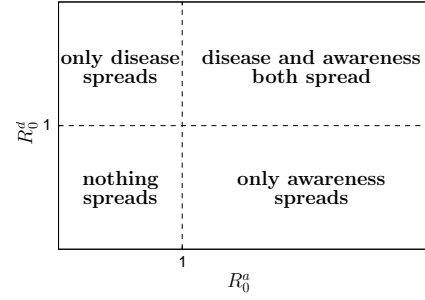
$$\frac{\omega I_-}{\alpha N} \gtrsim \frac{1}{4} \left( 1 - \frac{\lambda}{\alpha} \right)^2, \quad (\text{A.6})$$

a better approximation can be obtained by expanding around  $(1/2)(1 - \lambda/\alpha)$ , yielding

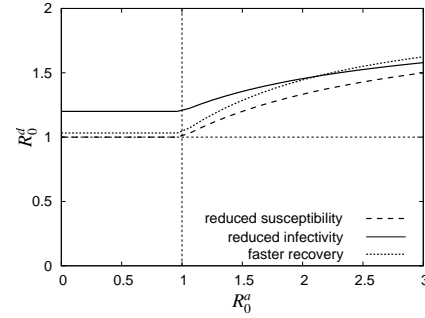
$$N_+ = N \left[ \frac{1}{2} \left( 1 - \frac{\lambda}{\alpha} \right) + \sqrt{\frac{\omega I_-}{\alpha N}} + o \left( \frac{1}{2} \left| 1 - \frac{\lambda}{\alpha} \right| \right)^2 \right], \quad (\text{A.7})$$

such that the contribution of awareness is

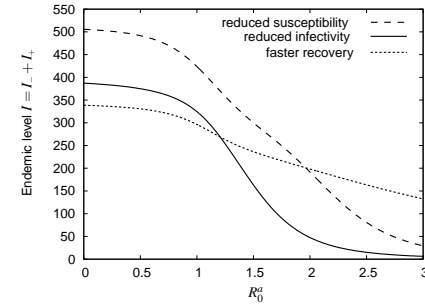
$$N_+^\omega = N \sqrt{\frac{\omega I_-}{\alpha N}} \quad (\text{A.8})$$



(a)



(b)



(c)

Figure 2: Equilibrium structure if disease and awareness spread independently (a), the effect of reduced susceptibility (dashed,  $\sigma_S = 0.5$ ) and infectivity (solid,  $\sigma_I = 0.5$ ), and faster recovery (dotted,  $\epsilon = 2$ ) on the epidemic threshold (b) and endemic equilibria of the total number of infected  $I = I_- + I_+$  at  $R_0^d = 1.5$  (c), all in terms of the basic reproductive number of awareness,  $R_0^a$ . The plots are generated by varying  $\alpha$  for fixed  $\lambda = 1$  and  $\omega = 1$ .

## Appendix B. Mean-field equilibria

Setting the derivatives to zero in the system of equations (3), we find the following equilibria:

*All unaware and susceptible*

$$S_- = N \quad S_+ = I_- = I_+ = R_- = R_+ = 0. \quad (\text{B.1})$$

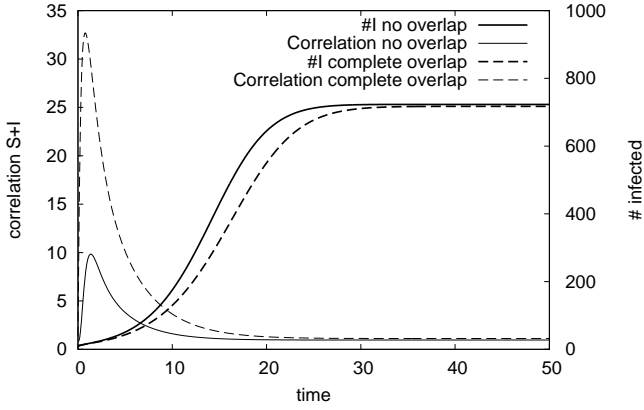


Figure 3: Outbreak of disease and awareness on overlapping (dashed line) and non-overlapping (solid line) networks in pair approximation. Thin lines indicate the correlation  $C_{S+,I}^d$ , thick lines the number of infected. ( $\sigma_S = 0.1$ ,  $\sigma_I = \epsilon = \phi = 1$ ,  $\hat{\beta} = 0.3$ ,  $\hat{\alpha} = 0.1$ ,  $\lambda = \gamma = \delta = 1$ ,  $\omega = 10$ )

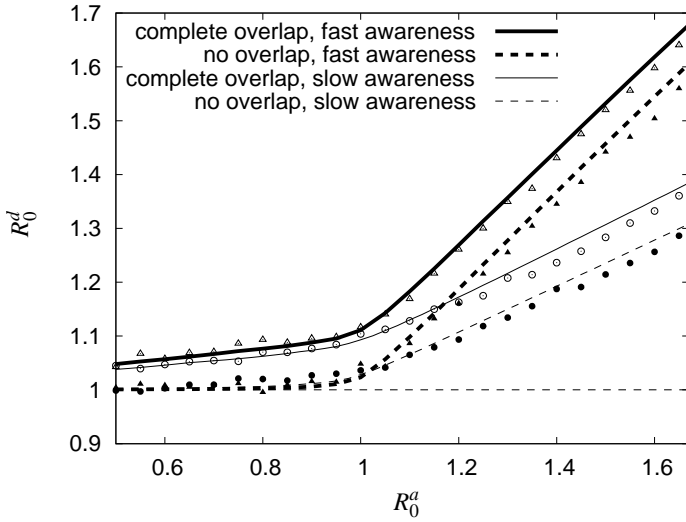


Figure 4: Iso-line of 4% infected in an outbreak for overlapping (solid, open triangles/circles) and non-overlapping (dashed, closed triangles/circles) networks as described by the pair approximations (lines) and measured in stochastic simulations (points), for awareness spreading slow (thin lines, circles,  $\hat{\alpha} = \hat{\beta}$ ) or fast (thick lines, triangles,  $\hat{\alpha} = 5\hat{\beta}$ ). The shown values of  $R_0^d$  and  $R_0^a$  are the basic reproductive numbers of disease and awareness, respectively, as given by the pair approximation. The value of 4% was chosen so the lines converge to  $R_0^d = 1$  if  $R_0^a = 0$ .

The corresponding eigenvalues are

$$\begin{aligned}
 \xi_1 &= 0 \\
 \xi_2 &= \alpha - \lambda \\
 \xi_3 &= -\delta \\
 \xi_4 &= -\phi\delta - \lambda \\
 \xi_5 &= \frac{1}{2} \left( \beta - (\epsilon + 1)\gamma - \lambda - \omega - \sqrt{(\beta + (\epsilon - 1)\gamma + \lambda - \omega)^2 + 4\sigma_I\beta\omega} \right) \\
 \xi_6 &= \frac{1}{2} \left( \beta - (\epsilon + 1)\gamma - \lambda - \omega + \sqrt{(\beta + (\epsilon - 1)\gamma + \lambda - \omega)^2 + 4\sigma_I\beta\omega} \right)
 \end{aligned} \tag{B.2}$$

Eigenvalues with positive real part, as associated with instability, can arise if  $\alpha > \lambda$  (eigenvalue  $\xi_2$ ), or if (eigenvalue  $\xi_6$ )

$$\begin{aligned}
 0 &< (\beta + (\epsilon - 1)\gamma + \lambda - \omega)^2 + 4\sigma_I\beta\omega - (\beta - (\epsilon + 1)\gamma - \lambda - \omega)^2 \\
 0 &< (\beta - \gamma - \omega)(\epsilon\gamma + \lambda) + \sigma_I\beta\omega \\
 0 &< \beta \left( 1 + \sigma_I \frac{\omega}{\epsilon\gamma + \lambda} \right) - \gamma - \omega,
 \end{aligned} \tag{B.3}$$

which, with  $R_0^d = \beta/\gamma$  yields Inequalities (9) and (11).

*No infection, awareness endemic*

$$S_- = \frac{\lambda}{\alpha} N \quad S_+ = \left(1 - \frac{\lambda}{\alpha}\right) N \quad I_- = I_+ = R_- = R_+ = 0. \tag{B.4}$$

The corresponding eigenvalues are

$$\begin{aligned}
 \varphi_1 &= 0 \\
 \varphi_2 &= \lambda - \alpha \\
 \varphi_3 &= \frac{1}{2} \left( -\alpha - (1 + \phi)\delta + \sqrt{(\alpha + (1 - \phi)\delta)^2 - 4(1 - \phi)\delta\lambda} \right) \\
 \varphi_4 &= \frac{1}{2} \left( -\alpha - (1 + \phi)\delta - \sqrt{(\alpha + (1 - \phi)\delta)^2 - 4(1 - \phi)\delta\lambda} \right),
 \end{aligned} \tag{B.5}$$

and another pair of eigenvalues which are too complex to offer straightforward interpretation, for which reason we state them only under the scenarios used in the main text. Besides these, the only eigenvalue which can have positive real part is  $\varphi_2$ , if  $\lambda > \alpha$ . Since we assume awareness to prolong the duration of immunity,  $\phi < 1$ , and therefore  $\varphi_3 < 0$  and  $\varphi_4 < 0$ .

- **Reduced susceptibility**

$$0 \leq \sigma_S < 1, \quad \sigma_I = \epsilon = \phi = 1 \tag{B.6}$$

yields

$$\begin{aligned}
 \varphi_5 &= \sigma_S\beta - \gamma + (1 - \sigma_S)\beta\frac{\lambda}{\alpha} \\
 \varphi_6 &= -\alpha - \gamma - \omega,
 \end{aligned} \tag{B.7}$$

with instability following if Inequality (8) holds.

- **Reduced infectivity**

$$0 \leq \sigma_I < 1, \quad \sigma_S = \epsilon = \phi = 1 \tag{B.8}$$

yields two more eigenvalues which are tedious to write down but from which Inequality (10) follows.

- **Shorter duration of infection**

$$\epsilon > 1, \quad \sigma_S = \sigma_I = \phi = 1 \tag{B.9}$$

yields two more eigenvalues which again are tedious to write down but from which Inequality (12) follows.



- **Longer duration of immunity**

$$0 \leq \phi < 1, \sigma_S = \sigma_I = \epsilon = 1 \quad (\text{B.10})$$

yields

$$\begin{aligned} \varphi_5 &= \beta - \gamma \\ \varphi_6 &= -\alpha - \gamma - \omega, \end{aligned} \quad (\text{B.11})$$

which do not change the invasion conditions from a model without awareness.

#### All unaware, infection endemic

As discussed in the main text, in this equilibrium there is no awareness at all only if  $\omega = 0$ . In that case,

$$S_- = \frac{\gamma}{\beta} N \quad I_- = \frac{\beta - \gamma}{\beta} \frac{\delta}{\gamma + \delta} \quad R_- = \frac{\beta - \gamma}{\beta} \frac{\gamma}{\gamma + \delta} \quad S_+ = I_+ = R_+ = \frac{E^d \cap E^a}{|E^d \cap E^a|} \quad (\text{B.12})$$

and the eigenvalues are

$$\begin{aligned} \eta_1 &= 0 \\ \eta_2 &= \alpha - \lambda \\ \eta_3 &= \frac{1}{2} \left( -\frac{(\beta + \delta)\delta}{\gamma + \delta} - \sqrt{\left[ \frac{(\beta + \delta)\delta}{\gamma + \delta} \right]^2 - 4(\beta - \gamma)\delta} \right) \\ \eta_4 &= \frac{1}{2} \left( -\frac{(\beta + \delta)\delta}{\gamma + \delta} + \sqrt{\left[ \frac{(\beta + \delta)\delta}{\gamma + \delta} \right]^2 - 4(\beta - \gamma)\delta} \right), \end{aligned} \quad (\text{B.13})$$

and two more eigenvalues which are too complicated to allow for simple insights but can be shown to be greater than 0 only if  $\gamma > \beta$ , which also holds for  $\eta_4$ , while  $\eta_3$  is always less than 0. The other possibility for instability can be found in  $\eta_2$ , which becomes greater than 0 if  $\lambda > \alpha$ .

#### Infection and awareness both endemic

While equilibria with both infection and awareness spreading can be observed in numerical simulations, we did not find corresponding simple analytic expressions. However, as the invasion thresholds to the other areas in the parameter space have been identified, little additional insight could be expected here.

### Appendix C. Pair approximation

We here derive and state the equations obtained by closing the system at the level of pairs. In principle, one needs to distinguish between three different types of contacts for each pair of states: those describing contacts which have a disease link only but cannot spread awareness, those that spread awareness but cannot spread the disease, and lastly those that can spread both. We here employ the simplified notations  $[\dots]^d$  and  $[\dots]^a$  to describe *all* state pairs being able to spread disease and awareness, respectively, irrespective of whether they also spread the other (see Fig. C.5). We then approximate the number of disease contacts of a given pair of states which can also spread awareness by multiplication with

$$q_{ald} = \frac{|E^d \cap E^a|}{|E^d|}, \quad (\text{C.1})$$

where  $|E^d|$  is the total number of edges on the disease network and  $|E^d \cap E^a|$  the number of edges pertaining to both networks. The fraction  $q_{ald}$  therefore gives the probability of a randomly chosen pair of neighbours with a disease edge between them to also be able to spread awareness. Analogously, we define

$$q_{dla} = \frac{|E^d \cap E^a|}{|E^a|}, \quad (\text{C.2})$$

which we will use to approximate the number of awareness contacts of a given pair of state which can also spread the disease. Thus, if disease and awareness contacts are completely distinct and the two networks share no edges at all,  $q_{ald} = q_{dla} = 0$  because  $E^d \cap E^a = \emptyset$ . Moreover,  $q_{ald} = 1$  if  $E^a \subseteq E^d$  and  $q_{dla} = 1$  if  $E^d \subseteq E^a$ . If all contacts can spread both processes and the two networks overlap completely,  $q_{ald} = 1$  and  $q_{dla} = 1$ . Note, however, that this measure is not symmetric and generally  $q_{ald} \neq q_{dla}$  (Fig. C.6).

To close the system at the level of pairs, we approximate state triples using a pair approximation framework [16]. We use  $[ABC]^{xy}$  to denote the number of triples in state  $A$ ,  $B$  and  $C$ , where  $A$  and  $B$  are connected by an edge of type  $x$  and  $B$  and  $C$  are connected by an edge of type  $y$ ,  $x$  and  $y$  standing for either  $d$  or  $a$  (see Fig. C.5). Following Keeling [11], the pair approximation then yields

$$[ABC]^{xy} \approx \frac{k^y - q_{ylx}}{k^y} \frac{[AB]^x [BC]^y}{[B]} = \zeta^{xy} \frac{[AB]^x [BC]^y}{[B]}, \quad (\text{C.3})$$

where  $k^d = \frac{|E^d|}{N}$  and  $k^a = \frac{|E^a|}{N}$  are the average number of connections of each individual on the disease and awareness network, respectively, and

$$\zeta^{xy} \equiv \frac{k^y - q_{ylx}}{k^y} \quad (\text{C.4})$$

is a correctional factor because  $A$  and  $C$  cannot be the same node. Note that the consistency condition

$$[ABC]^{xy} = [CBA]^{yx} \quad (\text{C.5})$$

implies

$$q_{ylx} k^x = q_{xly} k^y = \frac{|E^d \cap E^a|}{N}, \quad (\text{C.6})$$

which always holds according to Eq. C.2.

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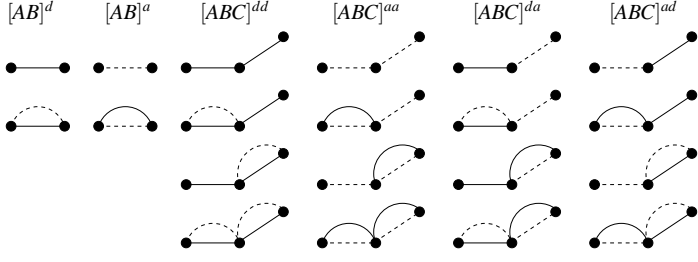


Figure C.5: Possible pairs and triples as contained in the quantities indicated in the column headers. Solid lines indicate disease ( $d$ ) edges and dashed lines awareness ( $a$ ) edges. The term  $[ABC]^{da}$  denotes the number of connected triples (in states  $A$ ,  $B$  and  $C$ ), where  $A$  and  $B$  are connected by *at least* a  $d$ -edge, and  $B$  and  $C$  are connected by *at least* an  $a$ -edge. The figure shows all possible connected triples that are counted by this term, and the same for other terms.

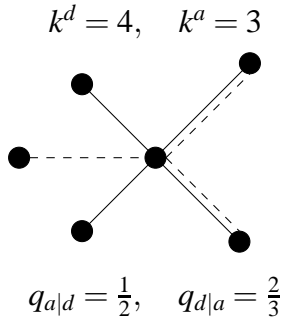


Figure C.6: Example of a small network with  $q_{d|a} \neq q_{a|d}$ . Solid lines indicate disease edges and dashed lines awareness edges.

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## Pair equations

The equations of the pair approximation will be included as a separate pdf as supporting online material. They are listed here for completeness:

$$\begin{aligned} \frac{d}{dt}[S_-] &= -\hat{\beta}[S_-I_-]^d - \sigma_I \hat{\beta}[S_-I_+]^d \\ &\quad + \delta[R_-] \\ &\quad + \lambda[S_+] \\ &\quad - \hat{\alpha}[S_-S_+]^a - \hat{\alpha}[S_-I_+]^a - \hat{\alpha}[S_-R_+]^a \end{aligned}$$

$$\begin{aligned} \frac{d}{dt}[I_-] &= +\hat{\beta}[S_-I_-]^d + \sigma_I \hat{\beta}[S_-I_+]^d \\ &\quad - \gamma[I_-] \\ &\quad + \lambda[I_+] \\ &\quad - \omega[I_-] \\ &\quad - \hat{\alpha}[I_-S_+]^a - \hat{\alpha}[I_-I_+]^a - \hat{\alpha}[I_-R_+]^a \end{aligned}$$

$$\begin{aligned} \frac{d}{dt}[R_-] &= +\gamma[I_-] \\ &\quad - \delta[R_-] \\ &\quad + \lambda[R_+] \\ &\quad - \hat{\alpha}[R_-S_+]^a - \hat{\alpha}[R_-I_+]^a - \hat{\alpha}[R_-R_+]^a \end{aligned}$$

$$\begin{aligned} \frac{d}{dt}[S_+] &= -\sigma_S \sigma_I \hat{\beta}[S_+I_+]^d - \sigma_S \hat{\beta}[I_-S_+]^d \\ &\quad + \phi \delta[R_+] \\ &\quad - \lambda[S_+] \\ &\quad + \hat{\alpha}[S_-S_+]^a + \hat{\alpha}[S_-I_+]^a + \hat{\alpha}[S_-R_+]^a \end{aligned}$$

$$\begin{aligned} \frac{d}{dt}[I_+] &= +\sigma_S \sigma_I \hat{\beta}[S_+I_+]^d + \sigma_S \hat{\beta}[I_-S_+]^d \\ &\quad - \epsilon \gamma[I_+] \\ &\quad - \lambda[I_+] \\ &\quad + \omega[I_-] \\ &\quad + \hat{\alpha}[I_-S_+]^a + \hat{\alpha}[I_-I_+]^a + \hat{\alpha}[I_-R_+]^a \end{aligned}$$

$$\begin{aligned} \frac{d}{dt}[R_+] &= +\epsilon \gamma[I_+] \\ &\quad - \phi \delta[R_+] \\ &\quad - \lambda[R_+] \\ &\quad + \hat{\alpha}[R_-S_+]^a + \hat{\alpha}[R_-I_+]^a + \hat{\alpha}[R_-R_+]^a \end{aligned}$$

$$\begin{aligned} \frac{d}{dt}[S_-S_-]^d &= 2 \left( -\hat{\beta}[S_-S_-I_-]^{dd} - \sigma_I \hat{\beta}[S_-S_-I_+]^{dd} \right. \\ &\quad + \delta[S_-R_-]^d \\ &\quad + \lambda[S_-S_+]^d \\ &\quad \left. - \hat{\alpha}[S_-S_-S_+]^{da} - \hat{\alpha}[S_-S_-I_+]^{da} - \hat{\alpha}[S_-S_-R_+]^{da} \right) \end{aligned}$$

$$\begin{aligned} \frac{d}{dt}[S_-S_-]^a &= 2 \left( -\hat{\beta}[S_-S_-I_-]^{ad} - \sigma_I \hat{\beta}[S_-S_-I_+]^{ad} \right. \\ &\quad \left. + \delta[S_-R_-]^a \right) \end{aligned}$$

$$\begin{aligned}
& +\lambda [S_{-S_+}]^a \\
& -\hat{\alpha} [S_{-S_+}]^{aa} - \hat{\alpha} [S_{-S_+I_+}]^{aa} - \hat{\alpha} [S_{-S_+R_+}]^{aa} \\
& ) \\
\frac{d}{dt} [S_{-I_+}]^d &= -\hat{\beta} [S_{-I_+}]^d + \hat{\beta} [S_{-S_+I_+}]^{dd} - \hat{\beta} [I_{+S_+I_+}]^{dd} \\
& +\sigma_I \hat{\beta} [S_{-S_+I_+}]^{dd} - \sigma_I \hat{\beta} [I_{+S_+I_+}]^{dd} \\
& -\gamma [S_{-I_+}]^d \\
& +\delta [I_{-R_+}]^d \\
& +\lambda [I_{-S_+}]^d + \lambda [S_{-I_+}]^d \\
& -\omega [S_{-I_+}]^d \\
& -\hat{\alpha} [S_{+S_+I_+}]^{ad} - \hat{\alpha} [I_{+S_+I_+}]^{ad} - \hat{\alpha} [R_{+S_+I_+}]^{ad} \\
& -\hat{\alpha} [S_{-I_+S_+}]^{da} - \hat{\alpha} [S_{-I_+I_+}]^{da} - \hat{\alpha} [S_{-I_+R_+}]^{da} \\
\frac{d}{dt} [S_{-I_+}]^a &= +\hat{\beta} [S_{-S_+I_+}]^{ad} - \hat{\beta} [I_{+S_+I_+}]^{da} + \sigma_I \hat{\beta} [S_{-S_+I_+}]^{ad} - \sigma_I \hat{\beta} [I_{+S_+I_+}]^{da} \\
& -\gamma [S_{-I_+}]^a \\
& +\delta [I_{-R_+}]^a \\
& +\lambda [I_{-S_+}]^a + \lambda [S_{-I_+}]^a \\
& -\omega [S_{-I_+}]^a \\
& -\hat{\alpha} [S_{+S_+I_+}]^{aa} - \hat{\alpha} [I_{+S_+I_+}]^{aa} - \hat{\alpha} [R_{+S_+I_+}]^{aa} \\
& -\hat{\alpha} [S_{-I_+S_+}]^{aa} - \hat{\alpha} [S_{-I_+I_+}]^{aa} - \hat{\alpha} [S_{-I_+R_+}]^{aa} \\
& -q_{d|a} \hat{\beta} [S_{-I_+}]^a \\
\frac{d}{dt} [S_{-R_+}]^d &= -\hat{\beta} [I_{-S_+R_+}]^{dd} - \sigma_I \hat{\beta} [I_{+S_+R_+}]^{dd} \\
& +\gamma [S_{-I_+}]^d \\
& -\delta [S_{-R_+}]^d + \delta [R_{-R_+}]^d \\
& +\lambda [R_{-S_+}]^d + \lambda [S_{-R_+}]^d \\
& -\hat{\alpha} [S_{+S_+R_+}]^{ad} - \hat{\alpha} [I_{+S_+R_+}]^{ad} - \hat{\alpha} [R_{+S_+R_+}]^{ad} \\
& -\hat{\alpha} [S_{-R_+S_+}]^{da} - \hat{\alpha} [S_{-R_+I_+}]^{da} - \hat{\alpha} [S_{-R_+R_+}]^{da} \\
\frac{d}{dt} [S_{-R_+}]^a &= -\hat{\beta} [I_{-S_+R_+}]^{da} - \sigma_I \hat{\beta} [I_{+S_+R_+}]^{da} \\
& +\gamma [S_{-I_+}]^a \\
& -\delta [S_{-R_+}]^a + \delta [R_{-R_+}]^a \\
& +\lambda [R_{-S_+}]^a + \lambda [S_{-R_+}]^a \\
& -\hat{\alpha} [S_{+S_+R_+}]^{aa} - \hat{\alpha} [I_{+S_+R_+}]^{aa} - \hat{\alpha} [R_{+S_+R_+}]^{aa} \\
& -\hat{\alpha} [S_{-R_+S_+}]^{aa} - \hat{\alpha} [S_{-R_+I_+}]^{aa} - \hat{\alpha} [S_{-R_+R_+}]^{aa} \\
\frac{d}{dt} [S_{-S_+}]^d &= -\hat{\beta} [I_{-S_+S_+}]^{dd} - \sigma_S \sigma_I \hat{\beta} [S_{-S_+I_+}]^{dd} - \sigma_I \hat{\beta} [I_{+S_+S_+}]^{dd} - \sigma_S \hat{\beta} [S_{-S_+I_+}]^{dd} \\
& +\delta [R_{-S_+}]^d + \phi \delta [S_{-R_+}]^d \\
& -\lambda [S_{-S_+}]^d + \lambda [S_{+S_+}]^d \\
& +\hat{\alpha} [S_{-S_+S_+}]^{da} - \hat{\alpha} [S_{+S_+S_+}]^{ad} + \hat{\alpha} [S_{-S_+I_+}]^{da} \\
& -\hat{\alpha} [I_{+S_+S_+}]^{ad} + \hat{\alpha} [S_{-S_+R_+}]^{da} - \hat{\alpha} [R_{+S_+S_+}]^{ad} \\
& -q_{d|a} \hat{\alpha} [S_{-S_+}]^d \\
\frac{d}{dt} [S_{-S_+}]^a &= -\hat{\beta} [I_{-S_+S_+}]^{da} - \sigma_S \sigma_I \hat{\beta} [S_{-S_+I_+}]^{ad} - \sigma_I \hat{\beta} [I_{+S_+S_+}]^{da} - \sigma_S \hat{\beta} [S_{-S_+I_+}]^{ad} \\
& +\delta [R_{-S_+}]^a + \phi \delta [S_{-R_+}]^a \\
& -\lambda [S_{-S_+}]^a + \lambda [S_{+S_+}]^a \\
& -\hat{\alpha} [S_{-S_+}]^a + \hat{\alpha} [S_{-S_+S_+}]^{aa} - \hat{\alpha} [S_{+S_+S_+}]^{aa} + \hat{\alpha} [S_{-S_+I_+}]^{aa} \\
& -\hat{\alpha} [I_{+S_+S_+}]^{aa} + \hat{\alpha} [S_{-S_+R_+}]^{aa} - \hat{\alpha} [R_{+S_+S_+}]^{aa} \\
\frac{d}{dt} [S_{-I_+}]^d &= -\hat{\beta} [I_{-S_+I_+}]^{dd} + \sigma_S \sigma_I \hat{\beta} [S_{-S_+I_+}]^{dd} - \sigma_I \hat{\beta} [S_{-I_+}]^d \\
& -\sigma_I \hat{\beta} [I_{+S_+I_+}]^{dd} + \sigma_S \hat{\beta} [S_{-S_+I_+}]^{dd} \\
& -\epsilon \gamma [S_{-I_+}]^d \\
& +\delta [R_{-I_+}]^d \\
& +\lambda [S_{+I_+}]^d - \lambda [S_{-I_+}]^d \\
& +\omega [S_{-I_+}]^d \\
& -\hat{\alpha} [S_{+S_+I_+}]^{ad} - \hat{\alpha} [I_{+S_+I_+}]^{ad} - \hat{\alpha} [R_{+S_+I_+}]^{ad} \\
& +\hat{\alpha} [S_{-I_+S_+}]^{da} + \hat{\alpha} [S_{-I_+I_+}]^{da} + \hat{\alpha} [S_{-I_+R_+}]^{da} \\
& -q_{d|a} \hat{\alpha} [S_{-I_+}]^d \\
\frac{d}{dt} [S_{-I_+}]^a &= -\hat{\beta} [I_{-S_+I_+}]^{da} + \sigma_S \sigma_I \hat{\beta} [S_{-S_+I_+}]^{ad} - \sigma_I \hat{\beta} [I_{+S_+I_+}]^{da} \\
& -\epsilon \gamma [S_{-I_+}]^a \\
& +\delta [R_{-I_+}]^a \\
& +\lambda [S_{+I_+}]^a - \lambda [S_{-I_+}]^a \\
& +\omega [S_{-I_+}]^a \\
& -\hat{\alpha} [S_{+S_+I_+}]^{aa} - \hat{\alpha} [S_{-I_+}]^a - \hat{\alpha} [I_{+S_+I_+}]^{aa} - \hat{\alpha} [R_{+S_+I_+}]^{aa} \\
& +\hat{\alpha} [S_{-I_+S_+}]^{aa} + \hat{\alpha} [S_{-I_+I_+}]^{aa} + \hat{\alpha} [S_{-I_+R_+}]^{aa} \\
& -q_{d|a} \sigma_I \hat{\beta} [S_{-I_+}]^a \\
\frac{d}{dt} [S_{-R_+}]^d &= -\hat{\beta} [I_{-S_+R_+}]^{dd} - \sigma_I \hat{\beta} [I_{+S_+R_+}]^{dd} \\
& +\epsilon \gamma [S_{-I_+}]^d \\
& +\delta [R_{-R_+}]^d - \phi \delta [S_{-R_+}]^d \\
& +\lambda [S_{+R_+}]^d - \lambda [S_{-R_+}]^d \\
& -\hat{\alpha} [S_{+S_+R_+}]^{ad} - \hat{\alpha} [I_{+S_+R_+}]^{ad} - \hat{\alpha} [R_{+S_+R_+}]^{ad} \\
& +\hat{\alpha} [S_{-R_+S_+}]^{da} + \hat{\alpha} [S_{-R_+I_+}]^{da} + \hat{\alpha} [S_{-R_+R_+}]^{da} \\
& -q_{d|a} \hat{\alpha} [S_{-R_+}]^d \\
\frac{d}{dt} [S_{-R_+}]^a &= -\hat{\beta} [I_{-S_+R_+}]^{da} - \sigma_I \hat{\beta} [I_{+S_+R_+}]^{da} \\
& +\epsilon \gamma [S_{-I_+}]^a \\
& +\delta [R_{-R_+}]^a - \phi \delta [S_{-R_+}]^a \\
& +\lambda [S_{+R_+}]^a - \lambda [S_{-R_+}]^a \\
& -\hat{\alpha} [S_{+S_+R_+}]^{aa} - \hat{\alpha} [I_{+S_+R_+}]^{aa} - \hat{\alpha} [S_{-R_+}]^a - \hat{\alpha} [R_{+S_+R_+}]^{aa} \\
& +\hat{\alpha} [S_{-R_+S_+}]^{aa} + \hat{\alpha} [S_{-R_+I_+}]^{aa} + \hat{\alpha} [S_{-R_+R_+}]^{aa} \\
\frac{d}{dt} [I_{-I_+}]^d &= 2 \left( +\hat{\beta} [S_{-I_+}]^d + \hat{\beta} [I_{-S_+I_+}]^{dd} + \sigma_I \hat{\beta} [I_{+S_+I_+}]^{dd} \right. \\
& \left. -\gamma [I_{-I_+}]^d \right. \\
& +\lambda [I_{-I_+}]^d \\
& -\omega [I_{-I_+}]^d \\
& \left. -\hat{\alpha} [I_{-I_+S_+}]^{da} - \hat{\alpha} [I_{-I_+I_+}]^{da} - \hat{\alpha} [I_{-I_+R_+}]^{da} \right) \\
\frac{d}{dt} [I_{-I_+}]^a &= 2 \left( +\hat{\beta} [I_{-S_+I_+}]^{da} + \sigma_I \hat{\beta} [I_{+S_+I_+}]^{da} \right. \\
& \left. -\gamma [I_{-I_+}]^a \right. \\
& +\lambda [I_{-I_+}]^a \\
& -\omega [I_{-I_+}]^a \\
& \left. -\hat{\alpha} [I_{-I_+S_+}]^{aa} - \hat{\alpha} [I_{-I_+I_+}]^{aa} - \hat{\alpha} [I_{-I_+R_+}]^{aa} \right. \\
& \left. +q_{d|a} \hat{\beta} [S_{-I_+}]^a \right)
\end{aligned}$$

$$\begin{aligned}
\frac{d}{dt} [I_{-R_-}]^d &= +\hat{\beta} [I_{-S_-} R_-]^{dd} + \sigma_I \hat{\beta} [I_{+S_-} R_-]^{dd} && +\omega [I_{-I_-}]^a - \omega [I_{+I_-}]^a \\
&+ \gamma [I_{-I_-}]^d - \gamma [I_{+I_-}]^d && + \hat{\alpha} [I_{-I_- S_-}]^{aa} - \hat{\alpha} [S_{+I_-} I_-]^{aa} - \hat{\alpha} [I_{+I_-}]^a + \hat{\alpha} [I_{-I_- I_-}]^a \\
&-\delta [I_{-R_-}]^d && - \hat{\alpha} [I_{+I_- I_-}]^{aa} + \hat{\alpha} [I_{-I_- R_-}]^{aa} - \hat{\alpha} [R_{+I_- I_-}]^{aa} \\
&+ \lambda [R_{-I_-}]^d + \lambda [I_{+R_-}]^d && + q_{d|a} \sigma_I \hat{\beta} [S_{-I_-}]^a + q_{d|a} \sigma_S \hat{\beta} [I_{-S_-}]^a \\
&-\omega [I_{-R_-}]^d && \\
&-\hat{\alpha} [S_{+I_-} R_-]^{ad} - \hat{\alpha} [I_{+I_-} R_-]^{ad} - \hat{\alpha} [R_{+I_-} R_-]^{ad} && \\
&-\hat{\alpha} [I_{-R_- S_-}]^{da} - \hat{\alpha} [I_{-R_- I_-}]^{da} - \hat{\alpha} [I_{-R_- R_-}]^{da} && \\
\frac{d}{dt} [I_{-R_-}]^a &= +\hat{\beta} [I_{-S_-} R_-]^{da} + \sigma_I \hat{\beta} [I_{+S_-} R_-]^{da} && \\
&+ \gamma [I_{-I_-}]^a - \gamma [I_{+I_-}]^a && \\
&-\delta [I_{-R_-}]^a && \\
&+ \lambda [R_{-I_-}]^a + \lambda [I_{+R_-}]^a && \\
&-\omega [I_{-R_-}]^a && \\
&-\hat{\alpha} [S_{+I_-} R_-]^{aa} - \hat{\alpha} [I_{+I_-} R_-]^{aa} - \hat{\alpha} [R_{+I_-} R_-]^{aa} && \\
&-\hat{\alpha} [I_{-R_- S_-}]^{aa} - \hat{\alpha} [I_{-R_- I_-}]^{aa} - \hat{\alpha} [I_{-R_- R_-}]^{aa} && \\
\frac{d}{dt} [I_{-S_+}]^d &= +\hat{\beta} [I_{-S_-} S_+]^{dd} - \sigma_S \sigma_I \hat{\beta} [I_{-S_+} I_+]^{dd} + \sigma_I \hat{\beta} [I_{+S_-} S_+]^{dd} && \\
&-\sigma_S \hat{\beta} [I_{-S_+}]^d - \sigma_S \hat{\beta} [I_{-S_+} I_+]^{dd} && \\
&-\gamma [I_{-S_+}]^d && \\
&+\phi \delta [I_{-R_+}]^d && \\
&-\lambda [I_{-S_+}]^d + \lambda [S_{+I_+}]^d && \\
&-\omega [I_{-S_+}]^d && \\
&+\hat{\alpha} [S_{+S_-} I_-]^{ad} + \hat{\alpha} [I_{+S_-} I_-]^{ad} + \hat{\alpha} [R_{+S_-} I_-]^{ad} && \\
&-\hat{\alpha} [S_{+I_-} S_+]^{ad} - \hat{\alpha} [I_{+I_-} S_+]^{ad} - \hat{\alpha} [R_{+I_-} S_+]^{ad} && \\
&-q_{a|d} \hat{\alpha} [I_{-S_+}]^d && \\
\frac{d}{dt} [I_{-S_+}]^a &= +\hat{\beta} [I_{-S_-} S_+]^{da} - \sigma_S \sigma_I \hat{\beta} [I_{-S_+} I_+]^{ad} + \sigma_I \hat{\beta} [I_{+S_-} S_+]^{da} - \sigma_S \hat{\beta} [I_{-S_+} I_+]^{ad} && \\
&-\gamma [I_{-S_+}]^a && \\
&+\phi \delta [I_{-R_+}]^a && \\
&-\lambda [I_{-S_+}]^a + \lambda [S_{+I_+}]^a && \\
&-\omega [I_{-S_+}]^a && \\
&+\hat{\alpha} [S_{+S_-} I_-]^{aa} + \hat{\alpha} [I_{+S_-} I_-]^{aa} + \hat{\alpha} [R_{+S_-} I_-]^{aa} - \hat{\alpha} [I_{-S_+}]^a && \\
&-\hat{\alpha} [S_{+I_-} S_+]^{aa} - \hat{\alpha} [I_{+I_-} S_+]^{aa} - \hat{\alpha} [R_{+I_-} S_+]^{aa} && \\
&-q_{a|a} \sigma_S \hat{\beta} [I_{-S_+}]^a && \\
\frac{d}{dt} [I_{+I_+}]^d &= +\hat{\beta} [I_{-S_-} I_+]^{dd} + \sigma_S \sigma_I \hat{\beta} [I_{-S_+} I_+]^{dd} + \sigma_I \hat{\beta} [S_{-I_+}]^d && \\
&+\sigma_I \hat{\beta} [I_{+S_-} I_+]^{dd} + \sigma_S \hat{\beta} [I_{-S_+}]^d + \sigma_S \hat{\beta} [I_{-S_+} I_+]^{dd} && \\
&-\gamma [I_{+I_+}]^d - \epsilon \gamma [I_{-I_+}]^d && \\
&-\lambda [I_{+I_+}]^d + \lambda [I_{-I_+}]^d && \\
&+\omega [I_{-I_+}]^d - \omega [I_{+I_+}]^d && \\
&+\hat{\alpha} [I_{-I_-} S_+]^{da} - \hat{\alpha} [S_{+I_-} I_+]^{ad} + \hat{\alpha} [I_{-I_-} I_+]^{da} && \\
&-\hat{\alpha} [I_{+I_-} I_+]^{ad} + \hat{\alpha} [I_{-I_-} R_+]^{da} - \hat{\alpha} [R_{+I_-} I_+]^{ad} && \\
&-q_{a|d} \hat{\alpha} [I_{-I_+}]^d && \\
\frac{d}{dt} [I_{+I_+}]^a &= +\hat{\beta} [I_{-S_-} I_+]^{da} + \sigma_S \sigma_I \hat{\beta} [I_{-S_+} I_+]^{ad} + \sigma_I \hat{\beta} [I_{+S_-} I_+]^{da} + \sigma_S \hat{\beta} [I_{-S_+} I_+]^{ad} && \\
&-\gamma [I_{+I_+}]^a - \epsilon \gamma [I_{-I_+}]^a && \\
&-\lambda [I_{+I_+}]^a + \lambda [I_{-I_+}]^a && \\
\frac{d}{dt} [I_{+R_+}]^d &= +\hat{\beta} [I_{-S_-} R_+]^{dd} + \sigma_I \hat{\beta} [I_{+S_-} R_+]^{dd} && \\
&-\gamma [I_{+R_+}]^d + \epsilon \gamma [I_{-I_+}]^d && \\
&-\phi \delta [I_{+R_+}]^d && \\
&+\lambda [I_{+R_+}]^d - \lambda [I_{-R_+}]^d && \\
&-\omega [I_{+R_+}]^d && \\
&-\hat{\alpha} [S_{+I_-} R_+]^{ad} - \hat{\alpha} [I_{+I_-} R_+]^{ad} - \hat{\alpha} [R_{+I_-} R_+]^{ad} && \\
&+\hat{\alpha} [I_{-R_- S_+}]^{da} + \hat{\alpha} [I_{-R_- I_+}]^{da} + \hat{\alpha} [I_{-R_- R_+}]^{da} && \\
&-q_{a|d} \hat{\alpha} [I_{+R_+}]^d && \\
\frac{d}{dt} [I_{+R_+}]^a &= +\hat{\beta} [I_{-S_-} R_+]^{da} + \sigma_I \hat{\beta} [I_{+S_-} R_+]^{da} && \\
&-\gamma [I_{+R_+}]^a + \epsilon \gamma [I_{-I_+}]^a && \\
&-\phi \delta [I_{+R_+}]^a && \\
&+\lambda [I_{+R_+}]^a - \lambda [I_{-R_+}]^a && \\
&-\omega [I_{+R_+}]^a && \\
&-\hat{\alpha} [S_{+I_-} R_+]^{aa} - \hat{\alpha} [I_{+I_-} R_+]^{aa} - \hat{\alpha} [I_{-R_+}]^a - \hat{\alpha} [R_{+I_-} I_+]^{aa} && \\
&+\hat{\alpha} [I_{-R_- S_+}]^{aa} + \hat{\alpha} [I_{-R_- I_+}]^{aa} + \hat{\alpha} [I_{-R_- R_+}]^{aa} && \\
\frac{d}{dt} [R_{-R_-}]^d &= 2(+\gamma [I_{-R_-}]^d && \\
&-\delta [R_{-R_-}]^d && \\
&+\lambda [R_{-R_-}]^d && \\
&-\hat{\alpha} [R_{-R_- S_+}]^{da} - \hat{\alpha} [R_{-R_- I_+}]^{da} - \hat{\alpha} [R_{-R_- R_+}]^{da} && \\
\frac{d}{dt} [R_{-R_-}]^a &= 2(+\gamma [I_{-R_-}]^a && \\
&-\delta [R_{-R_-}]^a && \\
&+\lambda [R_{-R_-}]^a && \\
&-\hat{\alpha} [R_{-R_- S_+}]^{aa} - \hat{\alpha} [R_{-R_- I_+}]^{aa} - \hat{\alpha} [R_{-R_- R_+}]^{aa} && \\
) &&& \\
\frac{d}{dt} [R_{-S_+}]^d &= -\sigma_S \sigma_I \hat{\beta} [R_{-S_-} I_+]^{dd} - \sigma_S \hat{\beta} [R_{-S_+} I_+]^{dd} && \\
&+\gamma [I_{-S_+}]^d && \\
&-\delta [R_{-S_+}]^d + \phi \delta [R_{-R_+}]^d && \\
&-\lambda [R_{-S_+}]^d + \lambda [S_{+R_+}]^d && \\
&+\hat{\alpha} [S_{+S_-} R_-]^{ad} + \hat{\alpha} [I_{+S_-} R_-]^{ad} + \hat{\alpha} [R_{+S_-} R_-]^{ad} && \\
&-\hat{\alpha} [S_{+R_- S_+}]^{ad} - \hat{\alpha} [I_{+R_- S_+}]^{ad} - \hat{\alpha} [R_{+R_- S_+}]^{ad} && \\
&-q_{a|d} \hat{\alpha} [R_{-S_+}]^d && \\
\frac{d}{dt} [R_{-S_+}]^a &= -\sigma_S \sigma_I \hat{\beta} [R_{-S_-} I_+]^{ad} - \sigma_S \hat{\beta} [R_{-S_+} I_+]^{ad} && \\
&+\gamma [I_{-S_+}]^a && \\
&-\delta [R_{-S_+}]^a + \phi \delta [R_{-R_+}]^a && \\
&-\lambda [R_{-S_+}]^a + \lambda [S_{+R_+}]^a && \\
&+\hat{\alpha} [S_{+S_-} R_-]^{aa} + \hat{\alpha} [I_{+S_-} R_-]^{aa} + \hat{\alpha} [R_{+S_-} R_-]^{aa} - \hat{\alpha} [R_{-S_+}]^a && \\
&-\hat{\alpha} [S_{+R_- S_+}]^{aa} - \hat{\alpha} [I_{+R_- S_+}]^{aa} - \hat{\alpha} [R_{+R_- S_+}]^{aa} && \\
\end{aligned}$$

$$\begin{aligned}
\frac{d}{dt} [R_- I_+]^d &= +\sigma_S \sigma_I \hat{\beta} [R_- S_+ I_+]^{dd} + \sigma_S \hat{\beta} [R_- S_+ I_-]^{dd} & +\omega [I_- S_+]^d \\
&+ \gamma [I_+ I_+]^d - \epsilon \gamma [R_- I_+]^d & + \hat{\alpha} [S_+ S_- I_+]^{ad} + \hat{\alpha} [I_+ S_- I_+]^{ad} + \hat{\alpha} [R_+ S_- I_+]^{ad} \\
& - \delta [R_- I_+]^d & + \hat{\alpha} [S_+ I_+ S_+]^{ad} + \hat{\alpha} [I_+ I_- S_+]^{ad} + \hat{\alpha} [R_+ I_- S_+]^{ad} \\
& - \lambda [R_- I_+]^d + \lambda [I_+ R_+]^d & + q_{ad} \hat{\alpha} [S_- I_+]^d + q_{ad} \hat{\alpha} [I_- S_+]^d \\
& + \omega [I_- R_-]^d & \\
& + \hat{\alpha} [S_+ I_- R_-]^{ad} + \hat{\alpha} [I_+ I_- R_-]^{ad} + \hat{\alpha} [R_+ I_- R_-]^{ad} & \frac{d}{dt} [S_+ I_+]^a = +\sigma_S \sigma_I \hat{\beta} [S_+ S_+ I_+]^{ad} - \sigma_S \sigma_I \hat{\beta} [I_+ S_+ I_+]^{da} + \sigma_S \hat{\beta} [S_+ S_+ I_-]^{ad} \\
& - \hat{\alpha} [S_+ R_- I_+]^{ad} - \hat{\alpha} [I_+ R_- I_+]^{ad} - \hat{\alpha} [R_+ R_- I_+]^{ad} & - \epsilon \gamma [S_+ I_+]^a \\
& - q_{ad} \hat{\alpha} [R_- I_+]^d & + \phi \delta [I_+ R_+]^a \\
& & - \lambda [S_+ I_+]^a - \lambda [S_+ I_+]^a \\
& & + \omega [I_- S_+]^a \\
\frac{d}{dt} [R_- I_+]^a &= +\sigma_S \sigma_I \hat{\beta} [R_- S_+ I_+]^{ad} + \sigma_S \hat{\beta} [R_- S_+ I_-]^{ad} & + \hat{\alpha} [S_+ S_- I_+]^{aa} + \hat{\alpha} [S_- I_+]^a + \hat{\alpha} [I_+ S_- I_+]^{aa} + \hat{\alpha} [R_+ S_- I_+]^{ad} \\
& + \gamma [I_+ I_+]^a - \epsilon \gamma [R_- I_+]^a & + \hat{\alpha} [I_- S_+]^a + \hat{\alpha} [S_+ I_+ S_+]^{aa} + \hat{\alpha} [I_+ I_- S_+]^{aa} + \hat{\alpha} [R_+ I_- S_+]^{ad} \\
& - \delta [R_- I_+]^a & - q_{ad} \sigma_S \sigma_I \hat{\beta} [S_+ I_+]^a \\
& - \lambda [R_- I_+]^a + \lambda [I_+ R_+]^a & \\
& + \omega [I_- R_-]^a & \\
& + \hat{\alpha} [S_+ I_- R_-]^{aa} + \hat{\alpha} [I_+ I_- R_-]^{aa} + \hat{\alpha} [R_+ I_- R_-]^{aa} - \hat{\alpha} [S_+ I_+ R_+]^{da} & = -\sigma_S \sigma_I \hat{\beta} [I_+ S_+ R_+]^{dd} - \sigma_S \hat{\beta} [I_- S_+ R_+]^{dd} \\
& - \hat{\alpha} [R_- I_+]^a - \hat{\alpha} [I_+ R_- I_+]^{aa} - \hat{\alpha} [R_+ R_- I_+]^{aa} & + \epsilon \gamma [S_+ I_+]^d \\
& & - \phi \delta [S_+ R_+]^d + \phi \delta [R_+ R_+]^d \\
\frac{d}{dt} [R_- R_+]^d &= +\gamma [I_- R_+]^d + \epsilon \gamma [R_- I_+]^d & - \lambda [S_+ R_+]^d - \lambda [S_+ R_+]^d \\
& - \delta [R_- R_+]^d - \phi \delta [R_- R_+]^d & + \hat{\alpha} [S_+ S_- R_+]^{ad} + \hat{\alpha} [I_+ S_- R_+]^{ad} + \hat{\alpha} [R_+ S_- R_+]^{ad} \\
& - \lambda [R_- R_+]^d + \lambda [R_+ R_+]^d & + \hat{\alpha} [S_+ R_- S_+]^{ad} + \hat{\alpha} [I_+ R_- S_+]^{ad} + \hat{\alpha} [R_+ R_- S_+]^{ad} \\
& + \hat{\alpha} [R_- R_- S_+]^{da} - \hat{\alpha} [S_+ R_- R_+]^{ad} + \hat{\alpha} [R_- R_- I_+]^{da} & + q_{ad} \hat{\alpha} [S_- R_+]^d + q_{ad} \hat{\alpha} [R_- S_+]^d \\
& - \hat{\alpha} [I_+ R_- R_+]^{ad} + \hat{\alpha} [R_- R_- R_+]^{da} - \hat{\alpha} [R_+ R_- R_+]^{ad} & \\
& - q_{ad} \hat{\alpha} [R_- R_+]^d & \frac{d}{dt} [S_+ R_+]^a = -\sigma_S \sigma_I \hat{\beta} [I_+ S_+ R_+]^{da} - \sigma_S \hat{\beta} [I_- S_+ R_+]^{da} \\
& & + \epsilon \gamma [S_+ I_+]^a \\
\frac{d}{dt} [R_- R_+]^a &= +\gamma [I_- R_+]^a + \epsilon \gamma [R_- I_+]^a & - \phi \delta [S_+ R_+]^a + \phi \delta [R_+ R_+]^a \\
& - \delta [R_- R_+]^a - \phi \delta [R_- R_+]^a & - \lambda [S_+ R_+]^a - \lambda [S_+ R_+]^a \\
& - \lambda [R_- R_+]^a + \lambda [R_+ R_+]^a & + \hat{\alpha} [S_+ S_- R_+]^{aa} + \hat{\alpha} [I_+ S_- R_+]^{aa} + \hat{\alpha} [S_- R_+]^a + \hat{\alpha} [R_+ S_- R_+]^{ad} \\
& + \hat{\alpha} [R_- R_- S_+]^{aa} - \hat{\alpha} [S_+ R_- R_+]^{aa} + \hat{\alpha} [R_- R_- I_+]^{aa} - \hat{\alpha} [I_+ R_- R_+]^{aa} & + \hat{\alpha} [R_- S_+]^a + \hat{\alpha} [S_+ R_- S_+]^{aa} + \hat{\alpha} [I_+ R_- S_+]^{aa} + \hat{\alpha} [R_+ R_- S_+]^{ad} \\
& - \hat{\alpha} [R_- R_+]^a + \hat{\alpha} [R_- R_- R_+]^{aa} - \hat{\alpha} [R_+ R_- R_+]^{aa} & \\
& & \frac{d}{dt} [I_+ I_+]^d = 2 \left( +\sigma_S \sigma_I \hat{\beta} [S_+ I_+]^d + \sigma_S \sigma_I \hat{\beta} [I_+ S_+ I_+]^{dd} + \sigma_S \hat{\beta} [I_- S_+ I_+]^{dd} \right. \\
\frac{d}{dt} [S_+ S_+]^d &= 2 \left( -\sigma_S \sigma_I \hat{\beta} [S_+ S_+ I_+]^{dd} - \sigma_S \hat{\beta} [S_+ S_+ I_-]^{dd} & - \epsilon \gamma [I_+ I_+]^d \\
& + \phi \delta [S_+ R_+]^d & - \lambda [I_+ I_+]^d \\
& - \lambda [S_+ S_+]^d & + \omega [I_+ I_+]^d \\
& + \hat{\alpha} [S_+ S_- S_+]^{ad} + \hat{\alpha} [I_+ S_- S_+]^{ad} + \hat{\alpha} [R_+ S_- S_+]^{ad} & + \hat{\alpha} [S_+ I_+ I_+]^{ad} + \hat{\alpha} [I_+ I_+ I_+]^{ad} + \hat{\alpha} [R_+ I_+ I_+]^{ad} \\
& + q_{ad} \hat{\alpha} [S_- S_+]^d \left. \right) & + q_{ad} \hat{\alpha} [I_- I_+]^d \left. \right) \\
\frac{d}{dt} [S_+ S_+]^a &= 2 \left( -\sigma_S \sigma_I \hat{\beta} [S_+ S_+ I_+]^{ad} - \sigma_S \hat{\beta} [S_+ S_+ I_-]^{ad} & \frac{d}{dt} [I_+ I_+]^a = 2 \left( +\sigma_S \sigma_I \hat{\beta} [I_+ S_+ I_+]^{da} + \sigma_S \hat{\beta} [I_- S_+ I_+]^{da} \right. \right. \\
& + \phi \delta [S_+ R_+]^a & - \epsilon \gamma [I_+ I_+]^a \\
& - \lambda [S_+ S_+]^a & - \lambda [I_+ I_+]^a \\
& + \hat{\alpha} [S_- S_+]^a + \hat{\alpha} [S_+ S_- S_+]^{aa} + \hat{\alpha} [I_+ S_- S_+]^{aa} + \hat{\alpha} [R_+ S_- S_+]^{aa} & + \omega [I_- I_+]^a \\
& \left. \right) & + \hat{\alpha} [S_+ I_+ I_+]^{aa} + \hat{\alpha} [I_+ I_+]^a + \hat{\alpha} [I_+ I_- I_+]^{aa} + \hat{\alpha} [R_+ I_+ I_+]^{ad} \\
& & + q_{ad} \sigma_S \sigma_I \hat{\beta} [S_+ I_+]^a \left. \right) \\
\frac{d}{dt} [S_+ I_+]^d &= -\sigma_S \sigma_I \hat{\beta} [S_+ I_+]^d + \sigma_S \sigma_I \hat{\beta} [S_+ S_+ I_+]^{dd} - \sigma_S \sigma_I \hat{\beta} [I_+ S_+ I_+]^{dd} & \frac{d}{dt} [I_+ R_+]^d = +\sigma_S \sigma_I \hat{\beta} [I_+ S_+ R_+]^{dd} + \sigma_S \hat{\beta} [I_- S_+ R_+]^{dd} \\
& + \sigma_S \hat{\beta} [S_+ S_+ I_-]^{dd} - \sigma_S \hat{\beta} [I_- S_+ I_+]^{dd} & + \epsilon \gamma [I_+ I_+]^d - \epsilon \gamma [I_+ R_+]^d \\
& - \epsilon \gamma [S_+ I_+]^d & - \phi \delta [I_+ R_+]^d \\
& + \phi \delta [I_+ R_+]^d & \\
& - \lambda [S_+ I_+]^d - \lambda [S_+ I_+]^d & 
\end{aligned}$$

$$\begin{aligned}
& -\lambda [I_+ R_+]^d - \lambda [I_+ R_+]^d \\
& + \omega [I_+ R_+]^d \\
& + \hat{\alpha} [S_+ I_+ R_+]^{ad} + \hat{\alpha} [I_+ I_+ R_+]^{ad} + \hat{\alpha} [R_+ I_+ R_+]^{ad} \\
& + \hat{\alpha} [S_+ R_+ I_+]^{ad} + \hat{\alpha} [I_+ R_+ I_+]^{ad} + \hat{\alpha} [R_+ R_+ I_+]^{ad} \\
& + q_{ad} \hat{\alpha} [I_+ R_+]^d + q_{ad} \hat{\alpha} [R_+ I_+]^d \\
\frac{d}{dt} [I_+ R_+]^a & = +\sigma_S \sigma_I \hat{\beta} [I_+ S_+ R_+]^{da} + \sigma_S \hat{\beta} [I_+ S_+ R_+]^{da} \\
& + \epsilon \gamma [I_+ I_+]^a - \epsilon \gamma [I_+ R_+]^a \\
& - \phi \delta [I_+ R_+]^a \\
& - \lambda [I_+ R_+]^a - \lambda [I_+ R_+]^a \\
& + \omega [I_+ R_+]^a \\
& + \hat{\alpha} [S_+ I_+ R_+]^{aa} + \hat{\alpha} [I_+ I_+ R_+]^{aa} + \hat{\alpha} [I_+ R_+]^a + \hat{\alpha} [R_+ I_+ R_+]^{aa} \\
& + \hat{\alpha} [S_+ R_+ I_+]^{aa} + \hat{\alpha} [R_+ I_+]^a + \hat{\alpha} [I_+ R_+ I_+]^{aa} + \hat{\alpha} [R_+ R_+ I_+]^{aa} \\
\frac{d}{dt} [R_+ R_+]^d & = 2(+\epsilon \gamma [I_+ R_+]^d \\
& - \phi \delta [R_+ R_+]^d \\
& - \lambda [R_+ R_+]^d \\
& + \hat{\alpha} [S_+ R_+ R_+]^{ad} + \hat{\alpha} [I_+ R_+ R_+]^{ad} + \hat{\alpha} [R_+ R_+ R_+]^{ad} \\
& + q_{ad} \hat{\alpha} [R_+ R_+]^d) \\
\frac{d}{dt} [R_+ R_+]^a & = 2(+\epsilon \gamma [I_+ R_+]^a \\
& - \phi \delta [R_+ R_+]^a \\
& - \lambda [R_+ R_+]^a \\
& + \hat{\alpha} [S_+ R_+ R_+]^{aa} + \hat{\alpha} [I_+ R_+ R_+]^{aa} + \hat{\alpha} [R_+ R_+]^a + \hat{\alpha} [R_+ R_+ R_+]^{aa} \\
& )
\end{aligned}$$