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Fungal disease dynamics in insect societies: Optimal killing rates and the ambivalent effect of high social interaction rates

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HIGHLIGHTS

- The dynamics of obligate killing pathogens in social insect colonies are modelled.
- Contact to dead hosts leads to high-level pathogen transfer.
- Contact between live hosts involves low-level transfer, leading to a dilution effect.
- We determine conditions for pathogen invasion by a basic reproduction number R_0.
- Social contact spreads the pathogen, but may dilute it below disease-causing levels.

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ABSTRACT

Entomopathogenic fungi are potent biocontrol agents that are widely used against insect pests, many of which are social insects. Nevertheless, theoretical investigations of their particular life history are scarce. We develop a model that takes into account the main distinguishing features between traditionally studied diseases and obligate killing pathogens, like the (biocontrol-relevant) insect-pathogenic fungi *Metarhizium* and *Beauveria*. First, obligate killing entomopathogenic fungi produce new infectious particles (conidiospores) only after host death and not yet on the living host. Second, the killing rates of entomopathogenic fungi depend strongly on the initial exposure dosage, thus we explicitly consider the pathogen load of individual hosts. Further, we make the model applicable not only to solitary host species, but also to group living species by incorporating social interactions between hosts, like the collective disease defences of insect societies. Our results identify the optimal killing rate for the pathogen that minimises its invasion threshold. Furthermore, we find that the rate of contact between hosts has an ambivalent effect: dense interaction networks between individuals are considered to facilitate disease outbreaks because of increased pathogen transmission. In social insects, this is compensated by their collective disease defences, i.e., social immunity. For the type of pathogens considered here, we show that even without social immunity, high contact rates between live individuals dilute the pathogen in the host colony and hence can reduce individual pathogen loads below disease-causing levels.

1. Introduction

Obligate killing entomopathogenic fungi like the well-known green muscardine disease (*Metarhizium anisopliae*, Zimmermann, 2007) and white muscardine disease (*Beauveria bassiana*, Barbarin et al., 2012) are frequently used in biocontrol of pest insects such as migratory locusts (Wilson et al., 2002) and mosquitoes (Blanford et al., 2005; Scholte et al., 2005; Thomas and Read, 2007). They are also used against social insects (e.g., termites, Almeida et al., 1997 and ants, Jaccoud et al., 1999), which are particularly successful invasive species (Chapman and Bourke, 2001; Cremer et al., 2008) with a high economic burden (Lowe et al., 2000; Pimentel et al., 2000).

Despite the wide application in biocontrol of the above-mentioned entomopathogenic fungi, there is a lack of epidemiological models covering the distinctive features of their particular life history. Specific models are crucial to predict the effects of the use of these fungi as biocontrol agents against pest insects. Most epidemiological models, e.g. the *SI* model and its extensions, are based on the infection modes typical of diseases such as malaria, influenza, and measles, where the pathogens multiply in the living host such that an increased exposure dose can be spread between individuals.

Obligate killing fungi like *Metarhizium* and *Beauveria*, however, form infectious stages (asexually produced conidiospores) only after having killed their host. These conidiospores can then infect

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new hosts through direct contact of an insect with a sporulating (infectious) cadaver, or by conidiospores being dispersed and then picked up mostly from the soil around the cadaver. Conidiospores adhere to the insect body surface, germinate, and penetrate the cuticle (Thomas and Read, 2007; Vestergaard et al., 1999). Inside the body, the fungus grows and produces toxins to kill its host. After host death, fungal hyphae and later also a new generation of conidiospores grow out of the dead body.

In addition to picking up the disease from infectious cadavers or from the soil, hosts can contract the pathogen by contact with other individuals at an early stage after exposure, that carry conidiospores on their body which have not yet strongly adhered to the insect cuticle (Vestergaard et al., 1999) and hence can still be transferred (Konrad et al., 2012). However, there is no multiplication of infectious particles on the surface of a living host, so that contact between two live hosts, at least one of which carries transferable conidiospores on its body, can only lead to a redistribution of the existing conidiospores on both individuals. Thus, transmission via social contact between live hosts leads to a transfer of usually low numbers of infectious particles (Konrad et al., 2012), whereas contraction rates from cadavers are typically very high, at least for ants (Hughes et al., 2004).

Exposure dosage is an important predictor for the likelihood of successful pathogen infection of the host. The entomopathogenic fungi most widely used for biocontrol, *Metarhizium* and *Beauveria*, are host generalists rather than specialists (Boomsma et al., 2013). Hence, they require high conidiospore doses for successful host infection (Schmid-Hempel and Frank, 2007). Low-level exposure can lead to micro-infections resulting in a protective immune stimulation rather than disease (Konrad et al., 2012; Rosengaus et al., 1999).

The first aim of our work was therefore to develop a deterministic epidemiological model that accounts for the particular life history of obligate killing entomopathogenic fungi like *Metarhizium* and *Beauveria*. Our model captures their characteristics by deviation from traditional models in a crucial aspect. New infectious particles are brought into the colony by contact with individuals that died from the infection (infectious cadavers). Contact between living hosts does not increase the total number of pathogen particles present in the colony, but simply spreads them between hosts. This means that contact with infectious cadavers leads to a high exposure dose, whereas contact with a live host typically leads to a low exposure dose. As a consequence, we explicitly consider individual host pathogen load by dividing the host colony into multiple exposure classes.

The second aim was to account for host sociality and to include the high interaction rates among group members as well as their collectively performed sanitary actions. As social insects are characterised by groups of closely related individuals living in high densities and performing frequent social interactions, pathogens would be expected to be easily transmitted across individuals and spread through the host colony (Schmid-Hempel, 1998). To counteract this risk, social insects have developed a variety of collective disease defence mechanisms, their social immunity (Cremer et al., 2007; Evans and Spivak, 2010; Wilson-Rich et al., 2009), which complement the individual immunity of each group member. One of the most important sanitary behaviours expressed against entomopathogenic fungi is grooming, during which the insects remove infectious particles from the body surface of either themselves (self-grooming) or their nestmates (allogrooming) (Hughes et al., 2002; Rosengaus et al., 1999) and even chemically disinfect them (Tragust et al., 2013). Accordingly, we consider the following factors that influence resistance against pathogens: first, individual immunity comprises sanitary behaviour (e.g., self-grooming) and the immune system of the hosts. Second, social contact may simply denote physical contact or food exchange between individuals. In addition, it can include collective or mutually expressed sanitary actions (e.g., allogrooming) and hence include social immunity into our model. Note that even though we include social features in our model, it can be applied to solitary insects by setting the corresponding parameters to zero.

After model establishment, we derive the conditions under which an entomopathogen can invade a social insect colony. This is done by calculating a basic reproduction number for the pathogen (Heesterbeek, 2002; May et al., 2001). If this number exceeds unity, the disease can spread through the colony; if it is less than one, the colony is protected from disease outbreak. This allows us to determine parameter regimes in which these two scenarios occur. Our result allows for predictions on the evolution of killing rates of obligate killing pathogens. To complete its life cycle, a certain killing rate is necessary for the pathogen to persist. Furthermore, our results show that even in the absence of sanitary actions, increased contact between individuals is not necessarily to the disadvantage of the host colony.

2. The model

In this section, we set up a model that describes the dynamics between obligate killing pathogens and a social host colony. This model is similar to traditional SI models in dividing the host colony into multiple compartments. The difference to existing, e.g. age structured, models lies within the interactions and transitions between the different compartments. For $x = 0, 1, \ldots, x_{max}$, let $n_x(t)$ denote the number of hosts carrying pathogen load x at time t. With this notation, n_0 is the class of unexposed individuals and $\{n_1, \ldots, n_{x_{max}}\}$ can be pooled into what is usually the class of exposed individuals. Useful abbreviations will be $N(t) = \sum_{x=0}^{x_{max}} n_x(t)$ for the total number of live individuals and $\mathbf{n}(t) = (n_x(t))_{x=0}^{x_{max}}$ for the vector displaying the composition of the colony into the classes of different exposure levels. Suppose that the colony is sufficiently large and well mixed in order to use mass action assumptions in the modelling below (i.e., the rate of interactions between two classes x_1 and x_2 is proportional to the product $n_{x_1} \cdot n_{x_2}$, see Hethcote, 2000).

Individual immunity and social interactions—the host dynamics: We distinguish between individual immunity and social interactions. Individual immunity summarises the immune system of each individual, as well as individual sanitary behaviour. Social contact comprises interactions between individuals that may or may not include sanitary actions.

Assume that any given individual undertakes individual immunity measures at rate r_s (for simplicity, let all parameters be independent of exposure level). Then, let a host that carries z conidiospores and performs individual immunity measures have a chance of $0 \le G_z^x \le 1$ to end up with x conidiospores. Thus, the individual immunity vectors $\mathbf{G}^x = (G_z^x)_{z=0}^{x_{max}}$ (for $x = 0, \ldots, x_{max}$) must have the property $\sum_{x=0}^{x_{max}} G_z^x = 1$ (i.e., the matrix consisting of the $\{\mathbf{G}^1, \ldots, \mathbf{G}^{x_{max}}\}$ is stochastic) and $G_z^x = 0$ for $x > z$, since pathogen load does not increase by individual immunity.

Let r_c be the rate of social contact between individuals and let S_{zy}^x denote the probability that an individual carrying pathogen load z ends up with pathogen load x given that it has social contact with an individual having pathogen load y. These values are collected into social interaction matrices $\mathbf{S}^x = \left(S_{zy}^x\right)_{z,y=0}^{x_{max}}$ (for $x = 0, \ldots, x_{max}$) which must fulfil $\sum_{x=0}^{x_{max}} S_{zy}^x = 1$, since the matrices $\mathbf{S}^x$ are probability matrices. Furthermore, total pathogen load must not increase by social contact. As a consequence, $S_{zy}^x = 0$ for $x > z+y$, but this is not sufficient. Note that interactions between hosts always spread the pathogen among individuals (social contact), but only if sanitary actions are taken, it decreases the host colony's total pathogen load.

Including the pathogen: The above considerations cover all interactions between the classes n_x, $x = 1, \ldots, x_{x_{max}}$. The rates at which hosts with pathogen load x die from the pathogen are denoted by the killing rate σ_x, and we collect them in a vector $\boldsymbol{\sigma} = (\sigma_x)_{x=0}^{x_{max}}$. Naturally, the σ_x are increasing in x. By $\nu(t)$, we denote the number of dead individuals.