Title: Dynamic parasite aggregation reduces parasite regulation of host populations and the stability of host-parasite interactions

Running title: Parasite aggregation and host regulation

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Abstract

Macroparasites can have significant effects on the dynamics of host populations that include limiting the growth of a host population and altering the stability of a host-parasite equilibrium. An important factor determining the dynamical effects that parasites have on host populations is how aggregated the distribution of parasites is across hosts in the population. While canonical host-macroparasite models assume that parasite aggregation is fixed, empirical and theoretical-work suggests that fixed aggregation is likely the exception rather than the rule. Here I assumed that parasite aggregation varies according to an empirically-supported constraint-based model, in contrast to the canonical assumption of fixed parasite aggregation. I then explored how this assumption alters the ability of parasites to regulate and suppress host populations, as well as stabilize the equilibrium of host-parasite interactions. The model with dynamic aggregation predicts that parasites are less likely to regulate host populations and the host-parasite equilibrium is less likely to be stable compared to the models that assume fixed aggregation. These results suggest that the theoretical ability of parasites to regulate host populations and stabilize the host-parasite equilibrium may be more rare than previously thought, providing an additional explanation for the general lack of empirical evidence for parasites as a primary factor regulating host populations.

Keywords: suppression, feasible sets, constraint-based models, pathogenicity, negative binomial distribution, macroparasite

1 Introduction

Macroparasites can alter the dynamics of wildlife populations (Hudson et al., 1998; Tompkins and Begon, 1999; Albon et al., 2002). One notable way that macroparasites can do this is by suppressing host population abundance (Anderson and May, 1978; Rosà and Pugliese, 2002;

Albon et al., 2002; Tompkins et al., 2002). In simplest terms this means that the presence of a parasite reduces a host population to a lower abundance than would be observed by a similar host population without the parasite. The ability of a parasite to suppress a host population has important implications for managing wildlife populations of conservation and economic interest (Murdoch et al., 1985; Peterson, 2004; Tompkins et al., 2011).

In addition to suppressing the host population, particular macroparasite traits can stabilize or destabilize a host-parasite equilibrium (May and Anderson, 1978; Rosà and Pugliese, 2002; Tompkins et al., 2002). For example, density-dependent interactions of parasites within a host can stabilize the host-parasite equilibrium (Anderson and May, 1978), whereas parasite-induced reductions in host fecundity can destabilize the equilibrium (May and Anderson, 1978; Diekmann and Kretzschmar, 1991). While these different dynamical effects have been shown theoretically, empirical examples of parasites directly affecting host dynamics remain limited to a few high-profile studies (Scott, 1988; Hudson et al., 1998; Albon et al., 2002; Redpath et al., 2006). In part, this is due to the logistical difficulties of manipulative experiments that are needed to definitively link parasites to changes in host population dynamics (Tompkins et al., 2002, 2011). Because of this difficulty, epidemiological models are critical for predicting the conditions under which parasites may be expected to suppress and stabilize host-parasite systems (Dobson and Hudson, 1992; Albon et al., 2002; Tompkins et al., 2002).

In addition, epidemiological models can provide insight into the conditions under which a parasite can regulate a host population. Following previous work in host-macroparasite systems, I specifically define regulation as the ability of a parasite to prevent a host population from growing without bound (Anderson and May, 1978; Rosà and Pugliese, 2002). While in reality other ecological factors will limit host population size if parasites fail to do so, this simple definition of regulation is often used in host-macroparasite models (Diekmann and Kretzschmar, 1991; Albon et al., 2002; Rosà and Pugliese, 2002). In this study I distinguish regulation from suppression, which refers to the ability of a parasite to reduce equilibrium host abundance, conditional on reg-

ulation. Particular attributes of macroparasites affect their ability to regulate a host population in models. For example, increasing parasite reproductive rate increases the ability of parasites to regulate host populations, while increasing parasite virulence decreases the ability of parasites to regulate host populations (Anderson and May, 1978).

Parasite aggregation is an attribute of host-macroparasite systems that has implications for the potential of a parasite to regulate a host population (i.e. prevent unbounded growth), suppress a host population (i.e. reduce the equilibrium host abundance) and stabilize the host-parasite equilibrium (Anderson and May, 1978; Kretzschmar and Adler, 1993). Aggregation is the nearly ubiquitous pattern in parasite ecology that many hosts have few parasites and few hosts have many parasites (Shaw and Dobson, 1995; Shaw et al., 1998). Specifically, this means that host-parasite distributions often have a variance to mean ratio greater than one and are highly right-skewed. In host-parasite models, increasing aggregation decreases a parasite's ability to regulate a host population, but, if regulation is possible, then increasing aggregation increases the stability of the host-parasite equilibrium, but decreases the suppression of the host population by the parasite (Anderson and May, 1978). The effect of aggregation on regulation, suppression, and stability also interacts with other processes operating in the host-parasite system. For example, highly aggregated and highly virulent parasites are unable to regulate a host population as many parasites are removed from the population upon the death of a host, which occurs frequently (Anderson and May, 1978). On the other hand, if parasites reduce host fecundity, then higher levels of aggregation are needed to stabilize the host-parasite equilibrium (Tompkins et al., 2002). Thus aggregation plays an important role in host-parasite dynamics both independently and through its interaction with other host- and parasite-related vital rates.

Many mechanisms can affect parasite aggregation, including clumped infections (Isham, 1995), parasite-induced mortality (Barbour and Pugliese, 2000), host heterogeneity (Wilson et al., 2002; Gourbière et al., 2015), the balance between parasite immigration rate and birth rate (Fowler and Hollingsworth, 2016), and host immunity (Morrill and Forbes, 2012). Due to multiple inter-

acting mechanisms shaping patterns of parasite aggregation, one might assume that predicting aggregation would require highly system-specific models. Surprisingly, this is not the case. Recent work has shown that because many mechanisms interact to affect aggregation, general statistical rules may be able to predict observed patterns of aggregation across different host-parasite systems (Wilber et al., 2017). For example, simple constraint-based models developed in community ecology can predict patterns of aggregation across a range of amphibian (host)-trematode (macroparasite) systems (Wilber et al., 2017; Johnson and Wilber, 2017). Constraint-based models are rooted in the concept of maximum entropy and predict the most likely distribution given a set of constraints (Haegeman and Etienne, 2010; Harte, 2011; Locey and White, 2013; Harte and Newman, 2014). In host-parasite systems, there are two inherent constraints on any observed parasite distribution: the total number of parasites P and the total number of hosts H in the distribution (Wilber et al., 2017). This means that the only possible distribution of P parasites amongst H hosts that could be observed is one that is consistent with these constraints. The most-likely distribution given these constraints is the one that can be realized in the largest number of ways (Jaynes, 1982).

An important prediction from constraint-based models is that the level of parasite aggregation changes as the total number of hosts H and parasites P change (Locey and McGlinn, 2013; Johnson and Wilber, 2017). This is important because theoretical results have shown that when aggregation varies with H and P, the conditions for a stable equilibrium in host-parasite systems are altered, compared to the canonical assumption of fixed aggregation (Adler and Krestzschmar, 1992; Kretzschmar and Adler, 1993; Rosà and Pugliese, 2002). For example, Kretzschmar and Adler (1993) showed that aggregation itself is not sufficient to stabilize a host-parasite system. Rather, aggregation needs to be an increasing function of mean parasite load (P/H) to stabilize the host-parasite equilibrium. Despite this well-known importance of aggregation that depends on P and H, there is no theory that predicts the precise shape of this relationship. Constraint-based theory provides such a prediction.

In this study I explore the effects of the constraint-based aggregation on the dynamics of host-parasite systems. In particular, this study asks two questions. First, how does a constraint-based model for parasite aggregation affect the ability of a parasite to regulate and suppress a host population? Second, how does constraint-based aggregation affect the stability of the host-parasite equilibrium? This study shows that empirically-supported constraint-based models of aggregation reduce the parameter space in which parasites are predicted to regulate host populations and stabilize the host-parasite equilibrium, compared to the standard assumption of fixed aggregation.

2 Material and methods

2.1 Overview

The goal of this study was to understand whether constraint-based aggregation changed how aggregation affected host-parasite dynamics, compared to the canonical assumption of fixed parasite aggregation. To this end, I extended a simple host-macroparasite model developed in previous studies (described below, Anderson and May, 1978; Kretzschmar and Adler, 1993; Rosà and Pugliese, 2002). This simple model excludes important processes affecting host-macroparasite systems such as host heterogeneity (beyond that captured by heterogeneity in parasite intensity), clumped infections, adaptive immunity, and logistic host growth, all of which have been explored previously (Isham, 1995; Pugliese and Rosà, 1995; Pugliese et al., 1998; Rosà and Pugliese, 2002). These processes were excluded to allow for direct comparison between the dynamics of host-macroparasite systems following constraint-based aggregation and those predicted by the canonical host-macroparasite model with fixed aggregation (Anderson and May, 1978; Rosà and Pugliese, 2002). By first analyzing the behavior of the simple model in the absence of the mechanisms mentioned above, the impact of constraint-based aggregation on host-parasite dynamics can be understood without the confounding effects of other stabilizing and destabilizing mecha-

nisms.

In the following sections I describe two host-macroparasite models, one with fixed aggregation and one with aggregation following constraint-based predictions. When introducing the model with constraint-based aggregation, I discuss the theoretical and empirical justification for this model of aggregation. I then compare and contrast predictions from the two models regarding the ability of a parasite to regulate and suppress the host population and stabilize the host-parasite equilibrium.

2.2 The host-macroparasite model

Consider the following host-macroparasite model where H is the abundance of hosts in a population and P is the abundance of directly reproducing macroparasites across all hosts in the population (Anderson and May, 1978; Diekmann and Kretzschmar, 1991; Rosà and Pugliese, 2002)

$$\frac{dH}{dt} = -dH - \alpha P + \sum_{i=0}^{\infty} r_i(b - \xi i) \tag{1}$$

$$\frac{dP}{dt} = -(d+\mu)P + \phi H - \alpha \sum_{i=0}^{\infty} i^2 r_i \tag{2}$$

b is host birth rate, d is host death rate, α is the rate of parasite-induced host mortality, μ is parasite death rate, and ϕ is the rate at which parasites are acquired from the environment. ϕ takes the functional form $\frac{\lambda P}{H_0+H}$, which is a result of assuming that dynamics of the free-living stage of the parasite occur on a much faster time scale than the within-host dynamics (Anderson and May, 1978; Kretzschmar and Adler, 1993; Rosà and Pugliese, 2002). $\sum_{i=0}^{\infty} i^2 \frac{r_i}{H} = E[i^2]$ is the second moment of the host-parasite distribution where r_i is the number of hosts having i parasites. This term is a result of the assumption that parasite-induced death rate increases linearly with the number of parasites per host. ξ is the per parasite reduction in host birth rate and it assumed to depend linearly on parasite load i (May and Anderson, 1978, , but see

Diekmann and Kretzschmar (1991) for an alternative formulation). This two dimensional system of equations is a representation of an infinite series of ordinary differential equations (ODEs) that tracks the number of hosts with $i = 0, 1, \ldots, \infty$ parasites (Anderson and May, 1978; Kretzschmar and Adler, 1993). The relationship between equations 1 and 2 and the infinite series of ODEs are discussed at length elsewhere (Rosà and Pugliese, 2002; Cornell, 2010).

An alternative formulation of the above equations in terms of the total number of hosts H and the mean number of parasites per host $x = \frac{P}{H}$ is given by (Kretzschmar and Adler, 1993)

$$\frac{dH}{dt} = H(b - d - \alpha x - \xi x) \tag{3}$$

$$\frac{dx}{dt} = x(\frac{\lambda H}{H_0 + H} - (b + \mu) - \alpha\pi(x) + \xi x) \tag{4}$$

where I have used the identities $\frac{dx}{dt} = \frac{1}{H}(\frac{dP}{dt} - \frac{dH}{dt}x)$, $\sum_{i=0}^{\infty} r_i(b - \xi i) = bH - \xi P$, and $\sum_{i=0}^{\infty} i^2 \frac{r_i}{H} = x(\pi(x) + x)$ where $\pi(x)$ is the variance to mean ratio. The advantage of this set of equations is that they conceptually simplify many of analyses that follow. Moreover, they express parasite aggregation in terms of the variance to mean ratio, a standard metric of aggregation.

This model assumes that there is no density-dependence in host birth or death rates. This means that host population size can only be regulated by parasites and, upon escaping parasite control, hosts will increase exponentially (for $b > d$, Anderson and May, 1978). This is a useful simplification for precisely defining parasite regulation – preventing a host population from increasing exponentially (Rosà and Pugliese, 2002). This model also assumes that the host population is homogeneous. In reality host populations have stage- and age-structure and hosts vary in immunity and behavior, all of which have implications on host-parasite dynamics and the patterns of parasite aggregation (Pacala and Dobson, 1988; Isham, 1995; Chan and Isham, 1998; Wilson et al., 2002; Calabrese et al., 2011; Johnson and Hoverman, 2014).

2.3 Modeling parasite aggregation

To close the system of equations given above, it is often assumed that the parasite distribution follows a negative binomial distribution, a flexible two parameter distribution that fits observed, aggregated host-parasite distributions (Anderson and May, 1978; Shaw et al., 1998). The variance to mean ratio of a negative binomial distribution is given by $\pi(x) = 1 + \frac{1}{k}x$, where $k \in (0, \infty)$ is the aggregation parameter. Decreasing k increases the variance to mean ratio for a given mean and increases aggregation. Plugging the negative binomial distribution equation for $\pi(x)$ into equations 3 and 4 leads to the host-macroparasite model with fixed k (henceforth the Fixed k Model). Variants of this model have been analyzed extensively in the host-parasite literature (May and Anderson, 1978; Diekmann and Kretzschmar, 1991; Rosà and Pugliese, 2002).

However, the assumption that k is fixed is generally not consistent with empirical observations (Scott, 1987; Boag et al., 2001). Rather, aggregation, in terms of the parameter k or the variance to mean ratio, depends on the mean number of parasites per host as well as the number of hosts (Kretzschmar and Adler, 1993; Poulin, 1993, 2013). Deterministic host-parasite models have captured the dynamic nature of aggregation using two different approaches. One approach uses a three dimensional approximation of the infinite series of differential equations such that aggregation (typically the variance to mean ratio) is explicitly modeled as a dynamic state variable (Adler and Krestzschmar, 1992; Kretzschmar and Adler, 1993; Rosà and Pugliese, 2002). While useful, this approach does not obviate the need to assume some distribution (often a negative binomial) to close the three-dimensional system of equations (Rosà and Pugliese, 2002; Cornell, 2010).

Another approach is to use the two dimensional approximation given by equations 3 and 4, and then allow aggregation defined by the the variance to mean ratio $\pi(x)$ to be a generic function of both the mean parasites per host and the total number of hosts in a population (Kretzschmar and Adler, 1993). The advantage to this approach is flexibility – aggregation can

be driven by both the dynamics of the system affecting H and x and the assumed relationship $\pi(x, H)$. However, this flexibility is also a disadvantage as it is not clear empirically or theoretically what form $\pi(x, H)$ should take. In the following two sections I discuss how constraint-based theory predicts a form for $\pi(x, H)$ from that is both derived from first principles and has empirical support.

2.4 Constraint-based aggregation

Theoretical justification

What if you were told that some area had H hosts and P parasites and were then asked to predict the distribution of these parasites across hosts. Given only this information, what would be your best guess? A reasonable first step would be to eliminate any potential configuration of parasites across hosts that did not satisfy the constraints P and H. All of the remaining configurations comprise what is known as the feasible set of solutions, subject to the constraints P and H (Haegeman and Loreau, 2008, 2009; Locey and White, 2013). By configuration, I specifically mean the set $\{p_1, p_2, \ldots, p_H\}$ where p_i is the number of parasites harbored by the host of rank i, $p_1 \geq p_2 \geq \cdots \geq p_H$ and $\sum_{i=1}^{H} p_i = P$. Intuitively, we might expect the "best" configuration to be the one that occurs the largest number of times in the feasible set. This can be equivalently expressed as the configuration that maximizes information entropy, subject to the constraints P and H (Jaynes, 1982, 2003). For the sake of intuition, I will continue using the language of multiplicity (e.g. largest number of times) rather than entropy.

Before identifying the configuration that occurs the largest number of times in the feasible set, the weights on each configuration in the feasible set must be specified (Haegeman and Etienne, 2010). For example, consider $P = 3$ and $H = 3$. The feasible set contains the configurations $\{\{3, 0, 0\}, \{2, 1, 0\}, \{1, 1, 1\}\}$. There are three reasonable weighting options that make the same number of assumptions. The first option is to assume that parasites and hosts are labeled such

that the weight of any particular configuration is given by the multinomial coefficient $\binom{P}{p_1, p_2, \ldots, p_H}$. With this assumption, the configuration {3, 0, 0} could arise three different ways, {2, 1, 0} 18 different ways, and {1, 1, 1} six different ways. The second option is to assume that hosts are labeled and parasites are unlabeled, such that the weight of any particular configuration is given by $\frac{H!}{\Pi_{i \in A} r_i!}$ (Brualdi, 2010), where A is a set containing the unique parasite abundances found in a configuration, i is a particular member of that set, and r_i is the number of hosts in the configuration that have parasite abundance i. Note that $\sum_{i \in A} r_i = H$. Given this assumption, the configuration {3, 0, 0} could arise three different ways, {2, 1, 0} six different ways, and {1, 1, 1} one way. Third, one could assume unlabeled hosts and unlabeled parasites, in which case all configurations in the feasible set are equally likely. In terms of the most likely configuration, option 1 and option 2 prefer the configuration {2, 1, 0}, while option 3 is indifferent. In this simple example option 1 and option 2 yield the same prediction, but this is not the case as H and P increase (Wilber et al., 2017).

These three approaches also predict the probability that a given host has i parasites, $[i|P, H]$ – the host-parasite distribution that is explicitly used in equations 1 and 2 to predict host-parasite dynamics. Let F be the feasible set given P and H and m be a configuration within the feasible set, then $[i|P, H] = \sum_{m \in F} [i|m, P, H][m|P, H]$ where $[m|P, H]$ is proportional to the weight of configuration m in the feasible set. Just given P and H, weighting option 1 predicts that $[i|P, H]$ follows a Binomial distribution, which is the finite equivalent of the Poisson distribution. The Poisson distribution is commonly used as a null hypothesis in parasite ecology (Shaw and Dobson, 1995; Shaw et al., 1998; Wilson et al., 2002). Weighting option 2 (i.e. "the composition model") predicts that $[i|P, H]$ follows the finite equivalent of negative binomial distribution with an aggregation parameter $k = 1$ (Haegeman and Etienne, 2010). Finally, option 3 (i.e. "the partition model") does not have a known closed form solution, but can easily be generated via simulation (Locey and McGlinn, 2013). Examples of these three distributions are shown in Figure 1. In general, the partition model and composition models predict substantially more aggregated distributions than

the Poisson distribution, with the partition model being more aggregated than the composition model (Fig. 1).

To summarize, given only knowledge of the constraints P and H and an *a priori* weighting scheme, the most likely distribution of parasites across hosts can be predicted. The three predicted distributions are optimal in the sense that they are the most uniform distributions that contain all of the information in P, H, and the weighting scheme (Jaynes, 2003; Harte, 2011). On theoretical grounds alone, it is not entirely clear which of these distributions should be preferred. One could argue that considering labeled parasites is inconsistent with a host-perspective of parasitism, in which a particular host is "sampled" and assigned a number of unlabeled parasites. Similarly, one could argue that labeling parasites makes the assumption of independence between parasites, while unlabeled parasites assumes ignorance without precluding independence. On biological grounds, the distributions can be generated via multiple different biological mechanisms. For example, the Poisson distribution can be generated by a death-immigration model in which parasites infect hosts and die at some rate independent of all other parasites (Anderson and Gordon, 1982). Similarly, the composition model can be generated via a "rich get richer" infection scheme in which previously infected hosts are more likely to be infected again (Harte, 2011). However, when empirical data correspond to one of these distribution, it does not mean that one of these generating models is the underlying cause of the distribution because, by definition, there are many processes that can lead to these patterns as they are the most likely distributions given P, H, and a particular weighting scheme. With many potential biological or theoretical rationales to justify the use of one of these models, it has been suggested that comparison to empirical data is a reasonable way to distinguish between these alternative distributions (Haegeman and Loreau, 2009; Haegeman and Etienne, 2010; Xiao et al., 2015).

Empirical support

The Poisson distribution is almost universally rejected as an adequate model for host-parasite distributions as observed distributions are almost always more aggregated (Shaw and Dobson, 1995; Shaw et al., 1998). The composition model and the partition model have only recently been tested against 842 host-parasite distributions from various amphibian (host)-trematode (parasite) systems (Wilber et al., 2017). Wilber et al. (2017) found 1) both options drastically out-performed the Poisson distribution 2) both options described *c.* 85% of the variation in the observed host-parasite distributions and 3) the partition model slightly outperformed the composition model. Moreover, Johnson and Wilber (2017) found that the partition model was able to describe 90% of the variation in the relationship between mean parasite intensity and variance in parasite intensity, using the exact same number of assumptions as a Poisson distribution. These empirical results indicate that the assumption of unlabeled parasites in the composition model and partition model is more reasonable than the assumption of labeled parasites in the Poisson model.

For the remainder of the study I focus on the partition model as a null model of aggregation and its impacts on host-parasite dynamics. In addition to being supported by currently available empirical data (Wilber et al., 2017), the partition model predicts that the level of aggregation of parasites across hosts varies with both mean load and the number of hosts in the population (Fig. 2A, B). This has been noted and observed in other theoretical and empirical studies of parasite aggregation (Scott, 1987; Kretzschmar and Adler, 1993; Poulin, 1993, 2013). Note that the composition model is also a candidate null hypothesis for parasite aggregation based on empirical data. As this distribution is equivalent to a negative binomial distribution with $k = 1$ for large H, I consider this distribution to be in the family of Fixed k Models for host-macroparasite dynamics, against which I compare the partition model and its affects on host-parasite dynamics.

2.5 Incorporating constraint-based aggregation

As the partition model has no known closed form solution, I used a simulation-based approach to approximate the partition model's prediction for $\pi(x, H)$. To do this, I drew 1000 random configurations of P parasites among H hosts from the feasible set of the partition model with $P = 3, \ldots, 500$ and $H = 3, \ldots, 500$ (248,004 combinations). For any given (P, H) pair, this resulting draw of configurations resulted in matrix with 1000 rows (i.e. 1000 random configurations) and H columns. From this sample, the variance of the distribution $[i|P, H]$ can be estimated by flattening the 1000 x H matrix into a vector and calculating the variance of this vector, $\hat{\sigma}^2_{P,H}$. This "flattening" numerically performs the marginalization $[i|P, H] = \sum_{m \in F}[i|m, P, H][m|P, H]$ such that the resulting vector is a random sample from $[i|P, H]$ from which the variance can be computed. The variance to mean ratio for the partition model is then given by $\hat{\pi}_{pm}(x, H) = \hat{\sigma}^2_{P,H}/x$.

The above steps provide $\hat{\pi}_{pm}(x, H)$ values for all discrete combinations of P and H on a 498 x 498 grid (P and H are both between 3 - 500). However, to use this surface with equations 3 and 4, $\hat{\pi}_{pm}(x, H)$ needed to be defined when P and H were not integers. To do this, I approximated $\hat{\pi}_{pm}(x, H)$ with the equation $\hat{\pi}_{pm}(x, H) \approx cH^b x^z$ (Fig. 2A), where $b = 0.57$, $c = -0.33$, and $z = 0.49$ based on fitting $cH^b x^z$ to the simulated partition model data with least-squares (Fig. 2A). This equation states that the variance to mean ratio scales approximately as a power law relationship with mean parasite load, with a constant of proportionality that scales as a power law with the number of hosts H. This approximation becomes more precise as H increases. An alternative approach for approximating $\hat{\pi}_{pm}(x, H)$ is to interpolate over the simulated 498 by 498 grid. I found that the power law approximation provides the same qualitative results as interpolating and gives a more intuitive understanding of how the variance to mean ratio is changing with mean x and H under the partition model.

Fig. 2B shows the predicted $\hat{\pi}_{pm}(x, H)$ surface from the power law approximation. The

partition model predicts that the variation to mean ratio increases with increasing mean parasite load (similar to the negative binomial distribution where $\pi(x, H) = 1 + (1/k)x$) and the variation to mean ratio increases with increasing number of hosts H.

Plugging $\hat{\pi}_{pm}(x, H)$ back into equations 3 and 4 yields what I will refer to as the Feasible Aggregation Model. To answer the questions regarding how constraint-based aggregation affects host-parasite dynamics, I compared the ability of parasites to regulate and suppress a host population as well as the stability of host-parasite equilibrium under both the Fixed k Model and the Feasible Aggregation Model. All analyses were performed in Python v. 3.6.4 and the code to replicate the analyses is provided at https://github.com/mqwilber/parasite_regulation.

3 Results

3.1 Question 1: How do parasites regulate and suppress a host population?

To facilitate comparison with previous results, I first assume that parasites have no effect on host fecundity ($\xi = 0$) and only affect host mortality ($\alpha > 0$). I relax this assumption in the following section. Under this assumption, the Fixed k Model predicts that parasites are able to regulate a host population when $\alpha \neq 0$ and $\lambda > b + \mu + \alpha + \frac{(b-d)}{k}$ (Anderson and May, 1978). As aggregation increases (k decreases) it becomes more difficult for parasites to regulate the host population (Fig. 3).

To compare this result to the ability of the Feasible Aggregation Model to regulate the host population, I numerically determined whether or not an equilibrium existed for the Feasible Aggregation Model given a set of parameters. The ability of a parasite to regulate a host population under the Feasible Aggregation Model is reduced compared the Fixed k Model (Fig. 3A, B). However, when parasite reproductive rate λ is low and parasites are highly aggregated under the Fixed k Model (e.g. $k = 0.2$), there are regions where the Fixed k Model exhibits regulation but the Feasible Aggregation Model does not. This is only a small portion of the parameter space

and as the reproductive rate of the parasite (λ) increases, the Feasible Aggregation Model again shows a reduced region in which parasites can regulate the host population (Fig. 3A-B).

These differences between the Fixed k Model and the Feasible Aggregation Model can be understood in terms of how the aggregation, the total abundance of hosts, and mean parasite load interact to affect host suppression, given that a host equilibrium H^* exists. Under the Fixed k Model, an increase in α increases the equilibrium host abundance H^* (Fig. 4A), decreases mean parasite load (Fig. 4C), and decreases the variance to mean ratio (Fig. 3D). Under the Feasible Aggregation Model an increase in α also leads to an increase in H^* (Fig. 4A) and a decrease in mean parasite load. However, while a decrease in mean parasite load decreases aggregation under the Feasible Aggregation Model similar to the Fixed k Model, the increase in H^* increases the variance to mean ratio in the Feasible Aggregation Model (Fig. 2), resulting in less of a reduction in the variance to mean ratio under the Feasible Aggregation Model and less host suppression (Fig 4A, D). Further increases in α lead to even smaller reductions in the variance to mean ratio and subsequently less host suppression (increased H^*), until eventually there is a complete inability of parasites to regulate the host population under the Feasible Aggregation Model.

This reduced suppression under the Feasible Aggregation Model can also be understood by examining parasite efficiency, defined as the negative log percentage of unparasitized hosts divided by equilibrium parasite abundance (Singh et al., 2009). Fig. 4B shows that while parasites are initially more efficient under the Feasible Aggregation Model than the Fixed k Model with $k = 1$, their level of efficiency decreases rapidly under the Feasible Aggregation Model with increasing pathogenicity. This decreasing efficiency with increasing pathogenicity leads to reduced host suppression under the Feasible Aggregation Model and a failure to regulate host populations at lower levels of parasite pathogenicity (α). In contrast, parasite efficiency actually increases over this parameter range for the Fixed k Model. This means that parasites are able to more effectively suppress the host population parasite when efficiency is higher under Fixed

k Model than the Feasible Aggregation Model. Eventually, parasite efficiency also begins to decrease with increasing parasite pathogenicity under the Fixed k Model, but does so at higher levels of parasite pathogenicity than the Feasible Aggregation Model.

3.2 Question 2: How does dynamic aggregation affect the stability of the host-parasite equilibrium?

3.2.1 Stability properties without a parasite reduction in host fecundity ($\xi = 0$)

To understand the nature of the dynamics in the regulated region of Figure 3, I performed a local stability analysis on both the Fixed k Model and the Feasible Aggregation Model. The results from the Fixed k Model are well-known – when a parasite with aggregation $0 < k < \infty$ is able to regulate a host population, the resulting system has a locally stable equilibrium (Fig. 3, Anderson and May, 1978). The Feasible Aggregation Model shows similar behavior – when the host-macroparasite system is regulated the resulting host-parasite equilibrium is locally stable for the entire parameter space considered (Fig. 2). Because the parameter space in which the parasite can regulate the host population is reduced under the Feasible Aggregation Model compared to the Fixed k Model (Fig. 3), the parameter space in which the host-parasite equilibrium is stable is also reduced under the Feasible Aggregation Model.

The stability of the Feasible Aggregation Model is consistent with the observation that aggregation is a stabilizing mechanism in host-macroparasite systems (Anderson and May, 1978). While the Feasible Aggregation Model predicts that the parasite distribution varies with H and x, the distribution is almost always aggregated (variance / mean > 1, Fig. 2). However, aggregation by itself is not sufficient to stabilize the equilibrium of a host-parasite interaction. Rather aggregation as given by the variance to mean ratio must be an increasing function of mean parasite load (Kretzschmar and Adler, 1993). $\pi(x, H)$ from the partition model satisfies this stability criterion and therefore, given an equilibrium exists for a Feasible Aggregation Model and parasites

do not affect host fecundity, this equilibrium should be stable.

3.2.2 Stability properties with a parasite reduction in host fecundity ($\xi > 0$)

In the previous section I considered the stability of the host-parasite interaction when there was no parasite-induced reduction in host fecundity ($\xi = 0$). However, in many host-macroparasite systems parasites have larger effects on host fecundity than on host mortality (e.g. Tompkins and Begon, 1999). Therefore, I also consider the stability and dynamics for both the Fixed k and Feasible Aggregation Model when $\xi > 0$.

Parasite-induced reduction in host fecundity is a destabilizing mechanism in host-parasite systems (May and Anderson, 1978; Diekmann and Kretzschmar, 1991; Dobson and Hudson, 1992). Including parasite-induced reduction in fecundity into the Fixed k Model leads to a region of the parameter space in which the host-macroparasite equilibrium exists, but is unstable (to the left of the stability region in Fig. 5). Decreasing k (increasing aggregation) reduces the region in which the equilibrium is unstable (reduces the area of the left hand region in Fig. 5C compared to figure Fig. 5E for the Fixed k Model), but increases the region in which parasites are unable to regulate the host population (right hand region of Fig. 5C compared to Fig. 5E). Thus aggregation promotes the stability of the host-macroparasite equilibrium, but decreases the overall parameter space in which an equilibrium can occur (May and Anderson, 1978).

In comparison to the Fixed k Model with $k \leq 1$ (empirically realistic values of k, Shaw and Dobson, 1995), the Feasible Aggregation Model predicts a larger region in which the host-macroparasite has a positive equilibrium that is unstable and, consistent with the results in the previous section, a larger region in which the host population is unregulated (provided that both λ and k are not too small, Fig. 3A and Fig. 5E). The reason for the increased region of instability in the Feasible Aggregation Model compared to the Fixed k Model with $k \leq 1$ is because of the dynamic link between the equilibrium number of hosts, mean parasite intensity and parasite aggregation. In the Feasible Aggregation Model, as parasite pathogenicity (α) decreases,

mean parasite load increases, and the equilibrium number of hosts decreases (Fig. 4). However, because decreasing H^* decreases aggregation under the Feasible Aggregation Model for a fixed mean (which does not happen under the Fixed k Model), the variance to mean ratio does not increase as quickly. This allows aggregation to remain lower under the Feasible Aggregation Model than the Fixed k Model for a given mean parasite intensity as α decreases. Because increasing aggregation stabilizes the host-parasite equilibrium conditional on regulation, this lower level of aggregation leads to reduced stability under Feasible Aggregation Model compared to the Fixed k Model. As parasite reduction in host fecundity ξ is a destabilizing factor, maintaining stability of the host-parasite equilibrium with increasing ξ requires increased aggregation for a given mean parasite load (May and Anderson, 1978). Aggregation tends to be lower under the Feasible Aggregation when parasite pathogenicity is low compared to the Fixed k Model.

4 Discussion

This study couples constraint-based models of parasite aggregation with dynamic host-macroparasite models to show that when parasites follow first principle predictions of aggregation, the ability of a parasite to regulate host populations and stabilize the host-parasite equilibrium is reduced compared to the canonical assumption of fixed aggregation. These results build on previous studies that show that assuming dynamic parasite aggregation can fundamentally change the behavior of host-macroparasite systems (Kretzschmar and Adler, 1993; Rosà and Pugliese, 2002). However, it has been unclear whether there is a consistent way that real host-macroparasite systems deviate from the assumption of fixed aggregation. Because constraint-based models provide a empirically-supported prediction regarding how parasite aggregation changes with P and H, they may provide a more reasonable starting point when modeling host-macroparasite dynamics than a fixed level of aggregation. If data or known mechanisms of the system suggest that aggregation is in fact fixed (e.g. McCallum, 1982) then this should be modeled accordingly, rather

than assumed as the default behavior of host-macroparasite models.

While the Feasible Aggregation Model explored here reduced the parameter space in which parasites could regulate host populations, this does not necessarily mean that parasites are less likely to regulate host populations in nature. This is because the reduced parameter space may still be the parameter space in which most host-macroparasite systems reside. In fact, many macroparasites have little effect on the survival probability of their hosts and instead affect other host vital rates such as reproduction (e.g. Dobson and Hudson, 1992; Tompkins and Begon, 1999). Moreover, many macroparasites have high reproductive rates (Anderson and May, 1991), which makes it easier for parasites to regulate host populations under the Feasible Aggregation Model. However, the models presented here do suggest that common patterns of parasite aggregation might make the ability of parasites to regulate host populations more rare than previously thought.

In addition to reducing the ability of parasites to regulate a host population, the Feasible Aggregation Model, compared to the Fixed k Model, also reduced the stability of the host-parasite equilibrium when parasites reduced host fecundity. It is well-known that by reducing host fecundity macroparasites can augment cycles in host populations (Dobson and Hudson, 1992; Hudson et al., 1998; Rosà and Pugliese, 2002). The Feasible Aggregation Model shows that when parasites reduce the fecundity of their host there is an increased region of the parameter space in which an unstable host-parasite equilibrium exists, compared to the assumptions from the Fixed k Model with k in an empirically realistic range of less than 1 (Shaw et al., 1998). In some of this parameter space, perturbations from the unstable Feasible Aggregation Model equilibrium resulted in diverging population cycles when the Fixed k Model predicted a stable host-parasite equilibrium.

The propensity of fixed k models to underestimate the region of host-macroparasite cycles compared to more mechanistically based host-macroparasite models has been previously noted (Rosà and Pugliese, 2002). Rosà and Pugliese showed that fixed k models under-predicted the pa-

rameter regions in which oscillatory dynamics were expected if the true mechanism leading to aggregated parasite distributions was clumped infections. However, Rosà and Pugliese (2002) also showed that if heterogeneity in host susceptibility was the aggregating mechanism, then a Fixed k Model over-predicted the region of oscillatory dynamics. The Feasible Aggregation Model differs from the extensions explored by Rosà and Pugliese (2002) as no processes are explicitly generating the aggregation predicted by the partition model. However, because many different processes result in aggregation patterns that follow the partition model, the systematic under-prediction of oscillatory dynamics by the Fixed k Model may be a general result. On the other hand, both models ignore other well-known destabilizing mechanisms in host-macroparasite systems, such as time delays in the macroparasite life cycle (May and Anderson, 1978), such that a more mechanistic approach to parasite aggregation will be needed to understand how often the Fixed k Model over-predicts or under-predicts the stability of the host-parasite equilibrium.

This highlights a notable short-coming of the Feasible Aggregation Model: it does not directly model the mechanisms leading to parasite aggregation. This is a limitation because it is well-established that many host-parasite mechanisms affect aggregation (Anderson and Gordon, 1982). For example, increasing parasite pathogenicity α can in turn affect the shape of the host-parasite distribution (Crofton, 1971; Barbour and Pugliese, 2000), above and beyond any effects on aggregation via changes in the total number of parasites and the total number of hosts (Johnson and Wilber, 2017). While changes in aggregation independent of changes in P and H do occur in host-parasite systems (Johnson and Wilber, 2017), changes in aggregation are often well-described by changes in P and H (Wilber et al., 2017). Therefore, the assumption that mechanisms affect aggregation primarily through their affects on P and H may not be unreasonable. Moreover, the Feasible Aggregation Model assumption is less stringent than the commonly used Fixed k Model, which also does not directly model the mechanisms leading to aggregation (Anderson and May, 1978; Dobson and Hudson, 1992; Townsend et al., 2009). By allowing the level of aggregation to change with P and H, the Feasible Aggregation Model is mimicking a

three-dimensional system of equations where the level of parasite aggregation is also included as a dynamic variable (Adler and Krestzschmar, 1992; Kretzschmar and Adler, 1993; Rosà and Pugliese, 2002).

All of these models (i.e. the Fixed k Model, the Feasible Aggregation Model, and the three dimensional model) assume that parasites instantaneously redistribute themselves to either maintain the same level of aggregation or change aggregation according to some function. Considering the biological realism of this assumption, it is clearly impossible for a intra-host helminth population to instantaneously redistribute itself following a change in the host or parasite population. While the biological realism and implications of this assumed instantaneous redistribution of macroparasites is rarely considered in host-macroparasite models, they are much-discussed topics in host-parasitoid systems (e.g. Murdoch and Stewart-Oaten, 1989; Rohani et al., 1994; Hassell, 2000; Briggs and Hoopes, 2004). Depending on the assumptions made about the time scale at which parasitoids redistribute themselves among patches of hosts and whether this redistribution depends on host density, the strength of parasitoid aggregation as a stabilizing mechanism can change (Murdoch and Stewart-Oaten, 1989; Rohani et al., 1994; Hassell, 2000). For example, while density-dependent aggregation is a putative stabilizing mechanisms in discrete time host-parasitoid models (Hassell and May, 1973), Murdoch and Stewart-Oaten (1989) and Rohani et al. (1994) showed that this stabilizing effect was reduced when parasitoids were able to continually redistribute themselves among patches in response to host density within a season. This interaction between the stability properties of a system and the time scale at which putative stabilizing process are assumed to act has been shown in other models as well (e.g. Singh and Nisbet, 2007) and highlights that it is important to identify not just how macroparasite aggregation changes with P and H, but also the time scale at which this change in aggregation occurs after changes in P and H. Incorporating time delays in the response of aggregation to changes in host and parasite abundance is one possible approach to account for this mismatch in time scale. Depending on the nature of the time delay, it could potentially increase or decrease the predicted

stability of the host-parasite equilibrium in the Feasible Aggregation Model (Nunney, 1985).

In conclusion, variable parasite aggregation can have large effects on the predicted dynamics of host-parasite systems. Constraint-based models provide a empirically-supported null hypothesis to account for the variation in parasite aggregation and show that models that assume fixed aggregation may over-predict both the ability of parasites to regulate a host population and the stability of the host-parasite equilibrium. Given the lack of evidence that macroparasites are the dominant factor regulating many host populations (Tompkins et al., 2011), these results provide a theoretical rationale, to complement the often-discussed logistical difficulties of detecting parasite regulation empirically (Scott and Dobson, 1989; Tompkins et al., 2011), that may help explain some of these null results.

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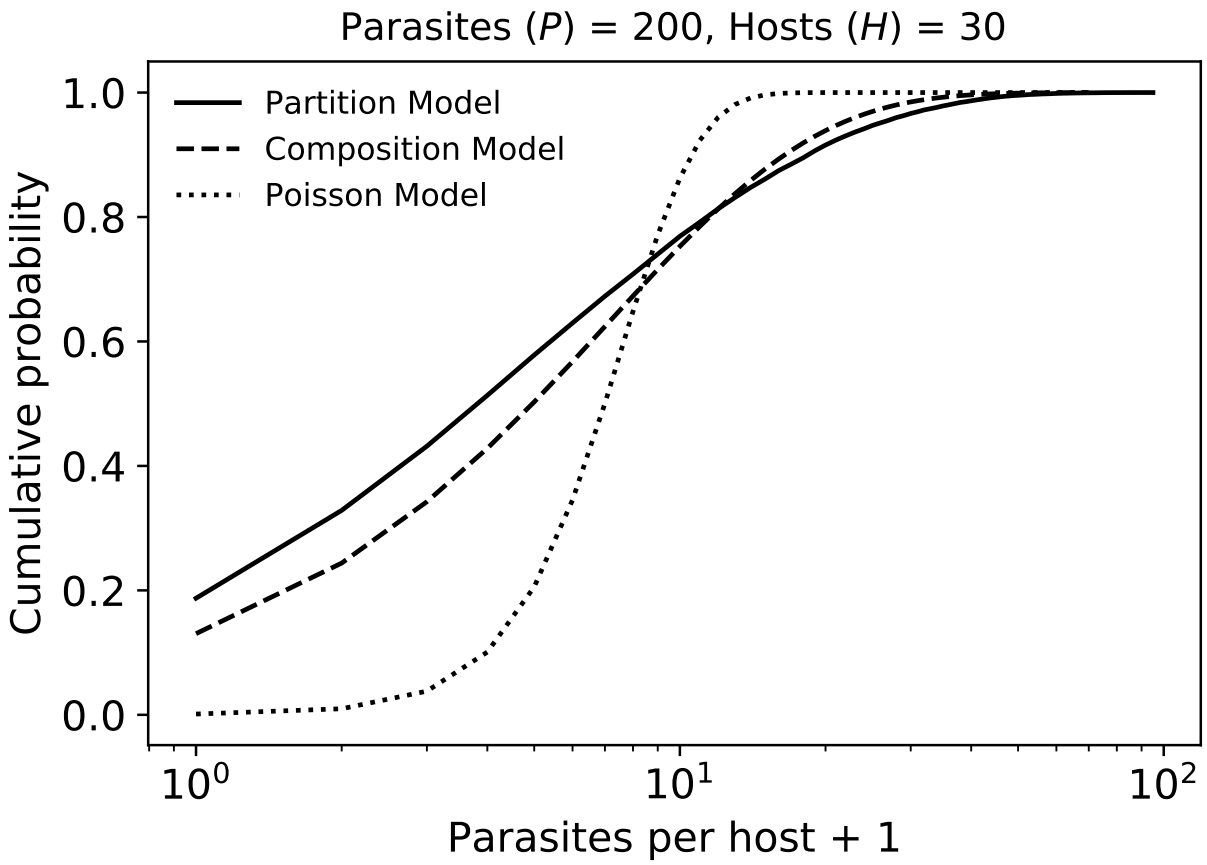

Figure 1: The predicted cumulative distribution function for the partition model, composition model, and Poisson model with $P = 200$ parasites and $H = 30$ hosts. All of these models require the same number of assumptions and the partition and composition model predict more aggregated distributions than the Poisson model.

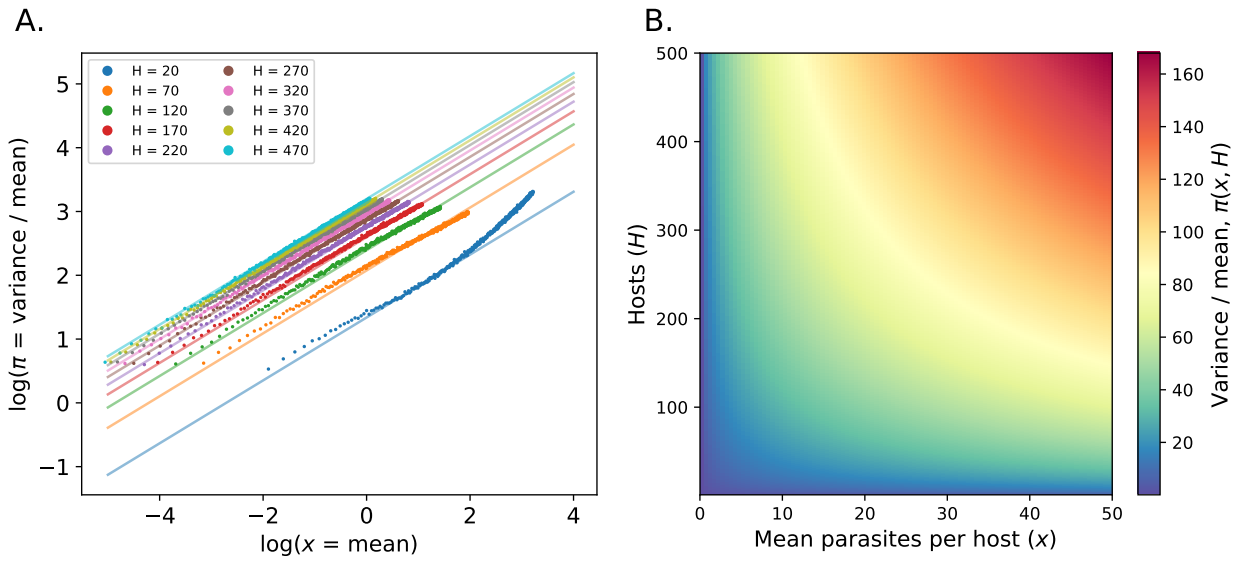

Figure 2: **A.** The simulated variance to mean relationship from the partition model. Dots of the same color all have the same value of H but different means. The colored lines give the approximated power law variance to mean relationship $\pi_{pm}(x, H) = -0.33H^{0.57}x^{0.49}$ for each value of H shown. The approximation is increasingly accurate as H increases, but tends to underestimate the variance to mean ratio when $H < 30$. **B.** The approximate $\pi_{pm}(x, H)$ surface for the partition model using the power law approximation. This is the surface that was used when evaluating equations 3 and 4.

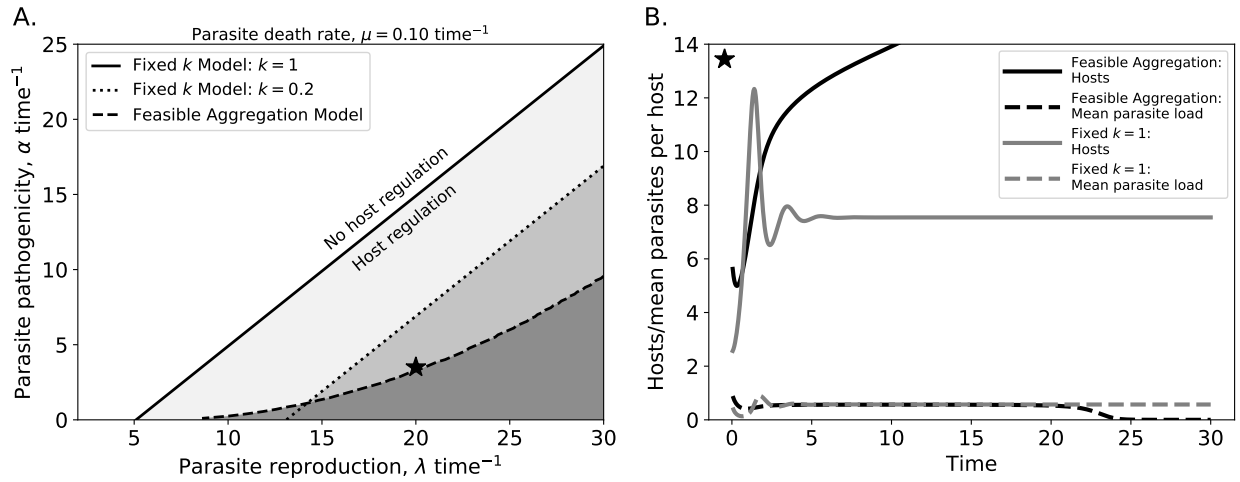

Figure 3: **A.** The boundaries at which a parasite can regulate a host population under the Fixed k Model and the Feasible Aggregation Model. Below the line of a particular model is where a parasite can regulate a host population. For the parameter space shown, when a parasite was able to regulate the host population the system had a locally stable equilibrium (the host-parasite equilibriums in all gray shaded regions are stable). B. An example of the host-parasite dynamics when the models have values of λ and α given by the black star in A. In the Feasible Aggregation Model, parasites are not able to regulate the host population which grows faster than the parasite population, eventually resulting in the mean parasites per host decreasing to 0. For clarity, the dynamical predictions for the Fixed k Model with $k = 0.2$ are not shown. All other parameters are $\mu = 0.1$ and 3 time^{-1}, $H_0 = 10$, $b = 3$ time^{-1}, $d = 1$ time^{-1}, and $\xi = 0$.

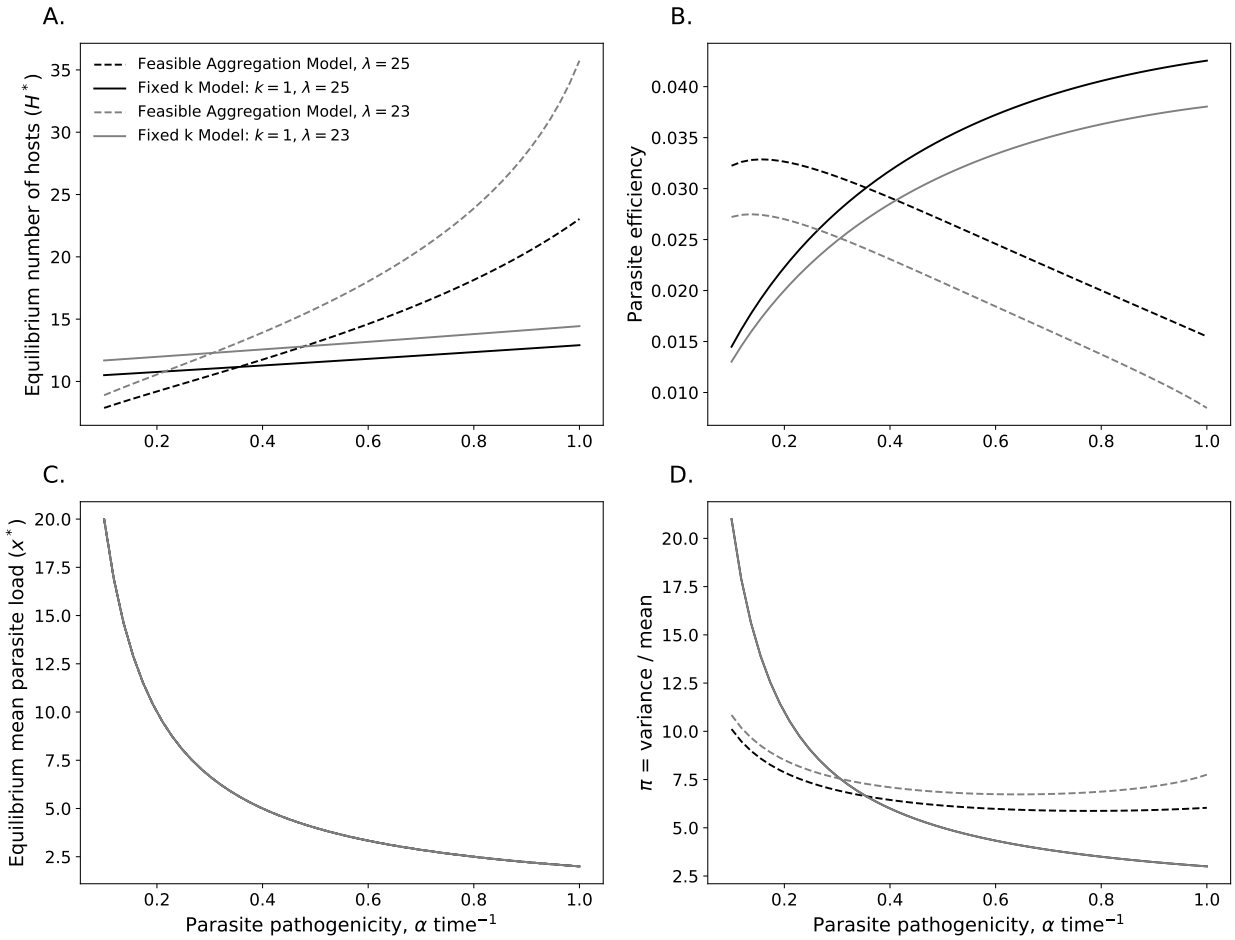

Figure 4: **A.** The host equilibrium under the Fixed k Model and the Feasible Aggregation Model with different values of parasite reproduction λ and varying levels of parasite pathogenicity α. **B.** Parasite efficiency, defined as the negative log percentage of unparasitized hosts divided by equilibrium parasite abundance, under the Fixed k and Feasible Aggregation Models. **C.** The equilibrium mean parasite intensity under the Fixed k and Feasible Aggregation Models. Both models have an equilibrium mean parasite intensity of $x^* = \frac{b-d}{\alpha}$. **D.** The equilibrium variance to mean ratio under the Fixed k and Feasible Aggregation Models. As λ does not affect the mean parasite load under the Fixed k Model, the variance to mean ratio is the same for both Fixed k Models. The other parameters are $\mu = 0.1$ time^{-1}, $H_0 = 40$, $b = 3$ time^{-1}, $d = 1$ time^{-1}, and $\xi = 0$.

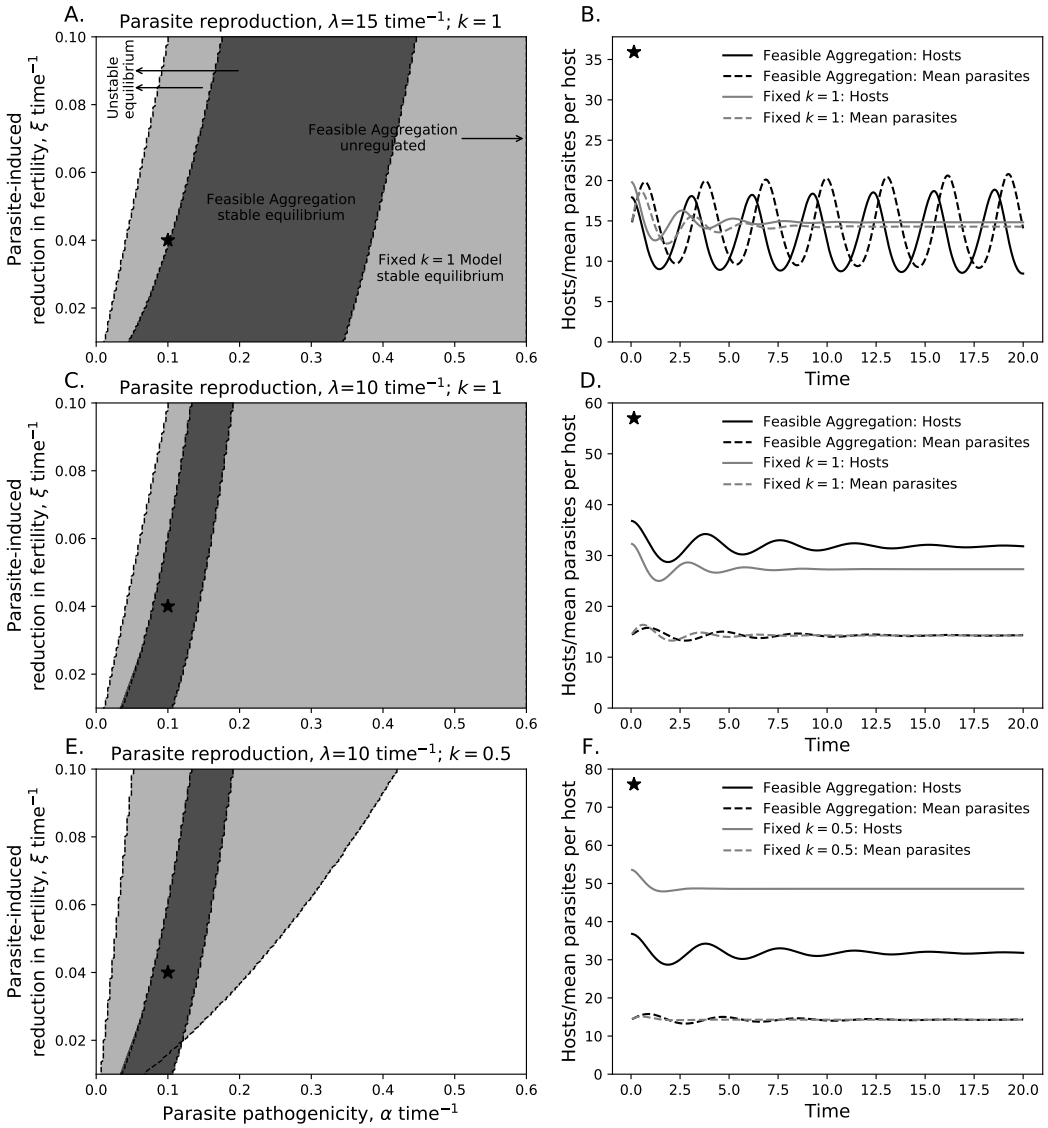

Figure 5: Stability properties and dynamics of the Fixed k and Feasible Aggregation Models when parasites cause a linear, load-dependent reduction in host fecundity. **A., C., E.** The parameter space in which the host-parasite equilibrium is stable for varying parasite pathogenicity α, parasite reduction in fecundity ξ, parasite reproduction λ, and aggregation parameter k for the Fixed k Model. The dark gray regions show where the Feasible Aggregation Model has a stable equilibrium and the light gray regions show where the Fixed k Model has a stable equilibrium. To the right of the shaded regions the parasite fails to regulate the host population. To the left of the shaded regions the parasite can regulate the host, but the resulting equilibrium is unstable. The dynamics from these different regions are shown in **B., D.**, which correspond to the black stars shown in **A., C., E.**. All other parameters are $\mu = 0.1$ time^{-1}, $H_0 = 40$, $b = 3$ time^{-1}, and $d = 1$ time^{-1}.