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A theoretical framework for biological control of soil-borne plant pathogens: identifying effective strategies

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Abstract

We develop and analyse a flexible compartmental model of the interaction between a plant host, a soil-borne pathogen and a microbial antagonist, for use in optimising biological control. By extracting invasion and persistence thresholds of host, pathogen and biological control agent, performing an equilibrium analysis, and numerical investigation of sensitivity to parameters and initial conditions, we determine criteria for successful biological control. We identify conditions for biological control (i) to prevent a pathogen entering a system, (ii) to eradicate a pathogen that is already present and, if that is not possible, (iii) to reduce the density of the pathogen. Control depends upon the epidemiology of the pathogen and how efficiently the antagonist can colonise particular habitats (i.e. healthy tissue, infected tissue and/or soil-borne inoculum). A sharp transition between totally effective control (i.e. eradication of the pathogen) and totally ineffective control can follow slight changes in biologically-interpretable parameters or to the initial amounts of pathogen and biological control agent present. Effective biological control requires careful matching of antagonists to pathosystems. For preventative/eradicative control, antagonists must colonise susceptible hosts. However for reduction in disease prevalence, the range of habitat is less important than the antagonist's bulking-up efficiency.

Keywords: Epidemiological model, invasion, persistence, basic reproductive number R_0, biocontrol

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1. Introduction

Biological control uses a natural enemy (or antagonist) of a pathogen to effect a reduction in the level or prevalence of disease [15, 6]. There are obvious attractions. However, biological control has all too often either failed to work or proved too unreliable to be a realistic proposition [71, 66, 64, 33], despite successes in the controlled conditions of glasshouses and propagation systems [58]. With chemical control ever more unattractive because of increasingly stringent legislative constraints [34, 63] and the economic and operational challenges posed by rapid evolution of resistant pathogens [57, 7], attention naturally reverts to explaining the hitherto disappointing failure of biological control in the field.

The physiological basis of biological control has attracted significant attention, and there is good understanding of a number of small-scale antagonistic mechanisms, including mycoparasitism [19, 67], antibiosis [62], induced resistance [74] and hypovirulence [53]. However little is known at the population level, even though it is the coupled dynamics of the host, pathogen and antagonist at this larger scale that ultimately determine success. Disregarding purely statistical infection-dose responses that predict rather than explain [22, 42, 61, 55, 65, 68, 48, 13], mathematical models and simulations have often concentrated on low-level mechanistic representations of the physiological responses detailed above [46, 70, 43, 47].

Arguably a more illuminating approach, however, is to map these physiological responses to changes in one or more of a small set of epidemiologically-meaningful parameters, such as rates of infection and/or infectious periods, in a population-level model of disease [24, 26]. Extensive theoretical work of this broad type has examined interactions between parasitoids and their insect hosts [54], and the ecology of these systems is now well-understood. However with certain exceptions [76, 41, 77], few generic studies have focussed on biological control of plant disease, and instead models have typically concentrated on specific host-pathogen-antagonist combinations. Partic-

ularly well-studied are the interactions between *Rhizoctonia solani* and *Trichoderma viride* on radish [44, 1, 20, 2, 21, 45], and between *Sclerotina minor* and *Sporidesmium sclerotivorum* on lettuce [28, 29, 30, 31]. Unfortunately, this narrow focus means that relatively few general messages have emerged. Here we have a broader ambition, and consider how microbial antagonists affect the spread of pathogens through host populations of plants in general.

We concentrate on soil-borne plant pathogens, which exemplify economically-important systems for which biological control is considered to be a viable proposition [14, 37, 39]. Our underlying methodology of analysing the likely efficacy of control by investigating its effect on epidemiologically-meaningful parameters has typically been cast in terms of effects on pathogen invasion and persistence [25]. It has also been used to determine suitable controls for broad groups of pathogens, classified according to their epidemiology [35, 36, 16], an arguably more challenging objective. However previous work has not specifically targetted biological control. In particular the effect(s) of control either remained fixed, or pulsed and decayed according to a simple schedule of treatments [36], and the more complex temporal variation corresponding to the three species interaction in biological control has not been considered, except with reference to the *S. minor* and *S. sclerotivorum* interaction [28, 29, 30, 31].

Here we extend an existing compartmental model of the interaction between a plant host and a soil-borne fungal pathogen [16] to include a bacterial or fungal antagonist. The effect(s) of each species upon the other is controlled by tunable parameters. In particular the antagonist can bulk-up and increase in density on three distinct habitats (healthy plant tissue and/or infected plant tissue and/or soil-borne inoculum), and can deleteriously affect any or all of the pathogen's epidemiological rates (e.g. rates of primary and secondary infection, rates of decay of infectious material). Any alteration to these rates depends on the density of the biological control agent, and so varies over time. As the interactions between host, pathogen and antagonist are controlled by

parameters of the model, it retains sufficient flexibility to represent a range of systems.

We use the model to investigate how biological control is affected by (i) the properties of the host-pathogen interaction; (ii) the set of epidemiological rates the antagonist is capable of affecting; and (iii) the habitats the antagonist is capable of colonising. We examine:

1. preventative control, in which the antagonist prevents the pathogen from invading the system;
2. eradicative control, in which the antagonist eradicates the pathogen if it is already present;
3. reductive control, in which the antagonist reduces the density of the pathogen.

In the case of reductive control, we also characterise how the effectiveness of control (in terms of reduction in long-term pathogen density) depends on the antagonist's mode of action and population dynamics, and how suitable antagonists for particular pathogens are conditioned upon the pathogen's epidemiology. Finally we examine variations in the efficacy of control depending on the initial density of each species: host, pathogen and antagonist, and how under certain circumstances extreme changes in the efficacy of control can follow from only slight changes to either initial densities or to the parameters of the model.

2. Methods

2.1. Modelling

2.1.1. Host-pathogen interaction

The population of hosts is divided into two classes, susceptible (S) and infected (I). These variables may be defined in terms of the number or density of plants, or may be relative to smaller units such as roots, dependent upon the natural scale of the epidemic [24]. Additionally we track the density of primary inoculum (X), which for

fungal pathogens includes free-living infective stages such as spores and resting bodies including sclerotia and/or fragments of previously colonised host tissue:

$$\frac{dS}{dt} = \eta(\kappa - (S+I)) - (\beta_P X + \beta_S I) S, \quad (1)$$

$$\frac{dI}{dt} = (\beta_P X + \beta_S I) S - \mu I, \quad (2)$$

$$\frac{dX}{dt} = \nu I - \gamma X. \quad (3)$$

The model is a particular variant of a class of models introduced and analysed by Gubbins *et al.* [32]. It represents (at distinct rates β_P and β_S) the dual pathways of primary and secondary infection characteristic of soil-borne plant pathogens [10, 27, 49, 3]. Infected hosts decay at per capita rate μ, corresponding to disease-induced mortality (this parameter could also represent a combination of natural and disease-induced mortality, or a rate of loss of infectiousness of infected host tissue). External inoculum loses infectiousness at rate γ, and is replenished by release from infectious hosts with efficiency ν, corresponding to infected hosts either producing or becoming sources of inoculum [29, 25]. Replenishment of susceptible hosts is also included; without this the pathogen cannot persist in this class of model. Additionally for soil-borne plant pathogens, growth/creation of host tissue typically occurs over timescales comparable to the epidemiological dynamics [2, 5, 16], and so in contrast to models of aerial systems for which host demography is arguably less important [41, 77], a sub-model for host growth is required. Host growth is linear, where both susceptible and infected hosts contribute to the carrying capacity (κ), and in which the dynamics are governed by rate parameter η [23]. The particular host growth function we have taken has been used in a number of previous investigations of soil-borne plant pathogens [40, 23, 27, 73, 69], and additionally (when modelling at the scale with an individual plant as a single host) is applicable to the wide range of agricultural systems with continuous harvesting and replanting [51, 8]. As our preliminary investigations indicated that other

choices of the function, including logistic growth, appeared to have no effect on the qualitative results, we concentrated here on a relatively simple linear form in order to simplify both our analysis and the consequent presentation of our results.

2.1.2. Antagonist

Our extension to the model introduces the density of an antagonist species (A):

$$\frac{dS}{dt} = \eta(\kappa-(S+I)) - \left(\frac{\beta_P X}{1+\alpha_P A} + \frac{\beta_S I}{1+\alpha_S A}\right) S, \quad (4)$$

$$\frac{dI}{dt} = \left(\frac{\beta_P X}{1+\alpha_P A} + \frac{\beta_S I}{1+\alpha_S A}\right) S - \mu(1+\omega_\mu A) I, \quad (5)$$

$$\frac{dX}{dt} = \nu I - \gamma\left(1+\omega_\gamma A\right) X, \quad (6)$$

$$\frac{dA}{dt} = (\rho_S S + \rho_I I + \rho_X X - \sigma - \xi A) A. \quad (7)$$

The antagonist affects the pathogen and acts as an agent of biological control by (potentially) decreasing the rate(s) of infection and/or by increasing the rate(s) of decay of infectious material. The per capita parameters $\alpha_P, \alpha_S, \omega_\mu, \omega_\gamma$ characterise the pathogen-antagonist interaction. The antagonist is able to bulk-up upon susceptible hosts, infected hosts and/or soil-borne inoculum: we define each of these as a habitat. Antagonist bulking-up depends upon the habitat-specific parameters ρ_S, ρ_I and ρ_X, providing a mechanism to represent habitat-generalists ($\rho_S = \rho_I = \rho_X$), habitat-specialists (only one of ρ_S, ρ_I, ρ_X non-zero), or anywhere between these extremes. The antagonist density decays at per capita rate σ, corresponding to inter-specific competition from other soil-borne organisms and the natural death of the antagonist. There is density-dependence acting upon the antagonist population, controlled by the parameter ξ, and which prevents unbounded increase of antagonist density.

120 *2.2. Non-dimensionalisation*

To simplify the analysis we introduce the dimensionless variables

$$\hat{S} = S\kappa^{-1}, \quad \hat{I} = I\kappa^{-1}, \quad \hat{X} = \eta X \nu^{-1}\kappa^{-1}, \quad \hat{A} = \xi A \eta^{-1}, \quad \hat{t} = \eta t, \tag{8}$$

and parameters

$$\begin{aligned} &\hat{\beta}_P = \beta_P \nu\kappa\eta^{-2}, \quad \hat{\beta}_S = \beta_S \kappa\eta^{-1}, \quad \hat{\mu} = \mu\eta^{-1}, && \hat{\gamma} = \gamma\eta^{-1}, \\ &\hat{\alpha}_P = \alpha_P \eta\xi^{-1}, \quad \hat{\alpha}_S = \alpha_S \eta\xi^{-1}, \quad \hat{\omega}_\mu = \omega_P \eta\xi^{-1}, && \hat{\omega}_\gamma = \omega_S \eta\xi^{-1}, \\ &\hat{\rho}_S = \rho_S \kappa\eta^{-1}, \quad \hat{\rho}_I = \rho_I \kappa\eta^{-1}, \quad \hat{\rho}_X = \rho_X \nu\kappa\eta^{-2}, && \hat{\sigma} = \sigma\eta^{-1}. \end{aligned} \tag{9}$$

The model is transformed to (Table 1)

$$\frac{d\hat{S}}{d\hat{t}} = 1 - \left(\hat{S} + \hat{I}\right) - \left(\frac{\hat{\beta}_P \hat{X}}{1 + \hat{\alpha}_P \hat{A}} + \frac{\hat{\beta}_S \hat{I}}{1 + \hat{\alpha}_S \hat{A}}\right) \hat{S}, \tag{10}$$

$$\frac{d\hat{I}}{d\hat{t}} = \left(\frac{\hat{\beta}_P \hat{X}}{1 + \hat{\alpha}_P \hat{A}} + \frac{\hat{\beta}_S \hat{I}}{1 + \hat{\alpha}_S \hat{A}}\right) \hat{S} - \hat{\mu}\left(1 + \hat{\omega}_\mu \hat{A}\right) \hat{I}, \tag{11}$$

$$\frac{d\hat{X}}{d\hat{t}} = \hat{I} - \hat{\gamma}\left(1 + \hat{\omega}_\gamma \hat{A}\right) \hat{X}, \tag{12}$$

$$\frac{d\hat{A}}{d\hat{t}} = \left(\hat{\rho}_S \hat{S} + \hat{\rho}_I \hat{I} + \hat{\rho}_X \hat{X} - \hat{\sigma} - \hat{A}\right) \hat{A}. \tag{13}$$

121 Scaling according to Equations (8) and (9) leads to a dimensionless system parame-
122 terised in terms of the three key interactions which we focus upon: the effect of the
123 pathogen on its plant host; the effect of the antagonist on the pathogen; and the re-
124 sponse of the antagonist to its habitat.

125 *** INSERT TABLE ONE NEAR HERE ***

126 *2.3. Numerical methods*

Our analysis of Equations (10)-(13) is supplemented by numerical solution. We take as an example the control of a particular pathogen, with (unless otherwise stated)

$$\hat{\beta}_P = 0.5, \hat{\beta}_S = 0.375, \hat{\mu} = 0.25, \hat{\gamma} = 0.8, \tag{14}$$

and

$$\hat{S}_0 = 1.0, \hat{I}_0 = 0, \hat{X}_0 = 0.1, \hat{A}_0 = 0.1, \tag{15}$$

127 corresponding to the simultaneous introduction of a small density of inoculum and
128 antagonist to a host population at its carrying capacity. We focus upon three key nu-
129 merical scenarios (Table 2).

130 *** INSERT TABLE TWO NEAR HERE ***

131 **3. Results**

132 *3.1. Equilibrium analysis*

133 *3.1.1. Without antagonism*

The basic reproductive number of the pathogen in the absence of the antagonist (Appendix A.1) is

$$R_0 = R_0^P + R_0^S = \frac{1}{\hat{\mu}} \left(\frac{\hat{\beta}_P}{\hat{\gamma}} + \hat{\beta}_S \right), \tag{16}$$

where this key threshold may be partitioned into distinct components R_0^P and R_0^S corresponding to primary and secondary infection. If $R_0 < 1$ then the pathogen cannot invade, and the host density stabilises at its carrying capacity, with

$$\left(\hat{S}_\infty, \hat{I}_\infty, \hat{X}_\infty \right) = (1, 0, 0). \tag{17}$$

However if $R_0 > 1$ then the pathogen invades the host population, and

$$\left(\hat{S}_\infty, \hat{I}_\infty, \hat{X}_\infty\right) = \left(\frac{1}{R_0}, \frac{1}{1+\hat{\mu}}\left(1-\frac{1}{R_0}\right), \frac{1}{\hat{\gamma}(1+\hat{\mu})}\left(1-\frac{1}{R_0}\right)\right). \tag{18}$$

Furthermore it can be shown that the pathogen always persists at this level if $R_0 > 1$ (Appendix A.2).

3.1.2. Including antagonism

The full model with $\hat{A} \neq 0$ introduces two equilibria in addition to analogues of Equations (17) and (18) with $\hat{A}_\infty = 0$. The first corresponds to host and antagonist coexisting, with the pathogen absent:

$$\left(\hat{S}_\infty, \hat{I}_\infty, \hat{X}_\infty, \hat{A}_\infty\right) = (1, 0, 0, \hat{\rho}_S - \hat{\sigma}). \tag{19}$$

For Equation (19) to predict biologically plausible densities, the rate at which the antagonist bulks-up on susceptible hosts ($\hat{\rho}_S$) must be greater than its per capita rate of decay ($\hat{\sigma}$).

If we define

$$R(\hat{A}) = \frac{1}{\hat{\mu}\left(1+\hat{\omega}_\mu \hat{A}\right)}\left(\frac{\hat{\beta}_P}{\hat{\gamma}\left(1+\hat{\alpha}_P\hat{A}\right)\left(1+\hat{\omega}_\gamma\hat{A}\right)} + \frac{\hat{\beta}_S}{\left(1+\hat{\alpha}_S\hat{A}\right)}\right), \tag{20}$$

where $R(\hat{A})$ is a criterion for invasion, and $R(\hat{A}=0) = R(0) = R_0$ of the underlying model, the other additional equilibrium is given implicitly by

$$\hat{S}_\infty = \frac{1}{R(\hat{A}_\infty)}, \tag{21}$$

$$\hat{I}_\infty = \frac{1}{1+\hat{\mu}\left(1+\hat{\omega}_\mu\hat{A}_\infty\right)}\left(1-\frac{1}{R(\hat{A}_\infty)}\right), \tag{22}$$

$$\hat{X}_\infty = \frac{1}{\hat{\gamma}\left(1+\hat{\omega}_\gamma\hat{A}_\infty\right)\left(1+\hat{\mu}\left(1+\hat{\omega}_\mu\hat{A}_\infty\right)\right)}\left(1-\frac{1}{R(\hat{A}_\infty)}\right), \tag{23}$$

$$\hat{A}_\infty = \hat{\rho}_S\hat{S}_\infty + \hat{\rho}_I\hat{I}_\infty + \hat{\rho}_X\hat{X}_\infty - \hat{\sigma}. \tag{24}$$

The equilibrium specified by Equations (20)-(24) corresponds to all three species co-existing. For the densities of infected hosts and inoculum to be biologically plausible, $R(\hat{A}_\infty) > 1$ is required, and since $R(\cdot)$ is a decreasing function and $\hat{A}_\infty$ must be greater than zero, a precondition is that the pathogen can invade the antagonist-free system (i.e. $R(0) = R_0 > 1$). In principle the expressions in Equations (20)-(23) could be substituted into Equation (24) to give a sixth order polynomial fixing $\hat{A}_\infty$, but the complex expression that results adds little insight. The four equilibria of the full model, together with existence criteria, are summarised in Table 3.

*** INSERT TABLE THREE NEAR HERE ***

3.1.3. Invasion criteria

We examine invasion criteria for all three species: host, pathogen and antagonist. In particular we determine whether or not these species can invade, increasing in density when introduced to a system otherwise at equilibrium, and characterise how this depends upon the rates controlling infection and/or reproduction. The host can always invade (and in fact persist at non-zero density), as its birth rate at low densities is independent of its own population size, and so there is a constant influx of hosts into the system whenever the host density is small. We therefore focus upon invasion of pathogen and antagonist, firstly in the absence of the other, but thereafter when the other species is present (Table 4).

*** INSERT TABLE FOUR NEAR HERE ***

If the antagonist is absent (and so only the host is present), the pathogen can invade only if

$$R(0) = R_0 > 1, \tag{25}$$

using the results for the underlying model. When the pathogen is absent, the antagonist can invade the host population if

$$\frac{\hat{\rho}_S}{\hat{\sigma}} > 1, \tag{26}$$

i.e. if it is able to bulk-up more quickly on susceptible hosts than it decays.

Invasion of each species in the presence of the other is more complex. If the antagonist is present at equilibrium with the host, then the pathogen can only invade if (cf. Equation (20))

$$R(\hat{\rho}_S - \hat{\sigma}) > 1. \tag{27}$$

Note that since $R(\cdot)$ is decreasing, and because $\hat{\rho}_S - \hat{\sigma}$ must be greater than zero for the antagonist to be present in the absence of the pathogen (Equation (26)), $R_0 > 1$ is a necessary precondition for invasion of the pathogen when the antagonist is present (this is a consequence of the antagonist's deleterious effect on the pathogen). However, if the pathogen is present, the antagonist can only invade if

$$\frac{\hat{\rho}_S}{\hat{\sigma}}\hat{S}_\infty + \frac{\hat{\rho}_I}{\hat{\sigma}}\hat{I}_\infty + \frac{\hat{\rho}_X}{\hat{\sigma}}\hat{X}_\infty > 1, \tag{28}$$

where the values of $\hat{S}_\infty, \hat{I}_\infty$ and $\hat{X}_\infty$ follow from the antagonist-free equilibrium in Equation (18), i.e. when

$$\frac{\hat{\rho}_S}{\hat{\sigma}R_0} + \frac{\hat{\rho}_I}{\hat{\sigma}(1+\hat{\mu})}\left(1 - \frac{1}{R_0}\right) + \frac{\hat{\rho}_X}{\hat{\sigma}\hat{\gamma}(1+\hat{\mu})}\left(1 - \frac{1}{R_0}\right) > 1. \tag{29}$$

Depending on the preferred habitat of the antagonist (i.e. to what extent it can bulk-up on susceptible hosts, infected hosts and pathogen inoculum), invasion can become more or less likely. For example a habitat-specialist antagonist which can only bulk-up on susceptible hosts (i.e. $\hat{\rho}_S > 0, \hat{\rho}_I = \hat{\rho}_X = 0$) is less likely to invade in the presence of

the pathogen, whereas a similarly-specialised antagonist with a preference for infected hosts (i.e. $\hat{\rho}_I > 0, \hat{\rho}_S = \hat{\rho}_X = 0$) requires the pathogen to be present to have any chance of invading.

3.2. Control without antagonism

Biologically-plausible control strategies lead to reductions in the dimensionless rates of transmission ($\hat{\beta}_P$ and/or $\hat{\beta}_S$), and/or increases in the dimensionless rates of decay of infected hosts and inoculum ($\hat{\mu}$ and/or $\hat{\omega}$). Changes to these dimensionless parameters depend upon the intensity of control and the host-pathogen system in question. The efficacy of control may be conveniently characterised according to its effect on R_0, and in particular we distinguish: (i) eradication, in which the pathogen is excluded in the long term ($R_0 < 1$); and (ii) reduction, in which the pathogen persists at a smaller density ($R_0 > 1$). Certain control strategies can never lead to eradication in systems which have $R_0^P > 1$ or $R_0^S > 1$ in the absence of control, no matter how intensively applied (Table 5). This emphasises the need to match any control strategy with the host-pathogen interaction in question.

*** INSERT TABLE FIVE NEAR HERE ***

3.3. Control including antagonism

We initially assume that the antagonist is able to bulk-up very quickly, and so that it is able to persist in the system at a very large density, thereby identifying lower bounds for the endemic equilibrium pathogen density ($\hat{I}_\infty$) when the antagonist is present. Thereafter we extend this by numerical examination of several scenarios (Table 2), progressively investigating the effects upon $\hat{I}_\infty$ of smaller rates of antagonist bulking-up (and so lower antagonist density); the habitats that the antagonist is able to colonise; and the initial densities of antagonist, pathogen and host.

3.3.1. Maximum reductive control (i.e. minimum $\hat{I}_\infty$)

If the population dynamics of the antagonist allow it to persist in the system, the best that it can achieve in reducing $\hat{I}_\infty$ may be inferred directly from the antagonist-free behaviour. The maximum effect of a particular class of antagonist depends upon R_0^P and R_0^S for the host-pathogen system, and on the rate(s) that the antagonist is capable of affecting (Table 5). These lower bounds on $\hat{I}_\infty$ ignore the antagonist's per capita effect and/or its density, and therefore may not be attained in practice (however, see below). We note, however, that according to this analysis only single-mode antagonists able to affect the rate at which infected hosts decay (i.e. to shorten the infectious period of infected hosts, $\hat{\omega}_\mu > 0$) are capable of eradicating all classes of pathogen.

3.3.2. Antagonist density (Scenario A)

We first assume a habitat-generalist antagonist which bulks-up at equal rate $\hat{\lambda}$ on all habitats. Numerical analysis of the endemic level of infection (Figure 1), then shows the effect on $\hat{I}_\infty$ of any decrease in a per capita rate of antagonism may be compensated for by a suitably-sized increase in the antagonist's ability to bulk-up (as this leads to a larger equilibrium antagonist density and so an equal force of antagonism overall). Additionally whenever the antagonist has a large enough per capita effect on the pathogen and/or is able to bulk-up sufficiently, the limiting lower bounds upon the minimum infected density from Section 3.3.1 are attained.

*** INSERT FIGURE ONE NEAR HERE ***

3.3.3. Habitat-specificity (Scenario B)

We examine habitat-specificity by fixing the per capita effect of the antagonist while allowing a pair of habitat-specific bulking-up parameters (i.e. two of $\hat{\rho}_S, \hat{\rho}_I, \hat{\rho}_X$) to vary simultaneously (Figure 2). The contours of infected density are linear; this is because

$$\hat{A}_\infty = \hat{\rho}_S \hat{S}_\infty + \hat{\rho}_I \hat{I}_\infty + \hat{\rho}_X \hat{X}_\infty - \hat{\sigma}, \tag{30}$$

and so, all other things being equal, any increase in (say) $\hat{\rho}_S$ can be exactly offset by a suitably-sized decrease in (say) $\hat{\rho}_I$ to give an equally-sized antagonist population. We note there is no requirement for the antagonist to be able to bulk-up on all classes of habitat in order to attain the maximal control outlined in Section 3.3.1 (Figure 2b). However, if the antagonist is theoretically able to eradicate the pathogen, this is only actually possible when $\hat{\rho}_S > 0$, i.e. when the antagonist can bulk-up on susceptible hosts. Any antagonist that was not able to bulk-up upon healthy tissue but that eradicated the pathogen would destroy its own only habitat by exerting its antagonistic effect to the maximum possible extent.

*** INSERT FIGURE TWO NEAR HERE ***

3.3.4. Bistability, eradication and feedback (Scenario C)

It is possible that neither the pathogen nor the antagonist can invade when the other is present at equilibrium, when neither invasion criterion according to Equations (27) and (29) is satisfied. Accordingly the model is bistable for certain sets of parameters, with eradication of either pathogen or antagonist dependent on initial conditions. If the initial conditions are held fixed, bistability manifests itself with a sharp transition in the endemic infected density, as a small change in a parameter such as $\hat{\rho}_S$ leads to a sudden switch from no control to eradication (Figure 3b).

*** INSERT FIGURE THREE NEAR HERE ***

** INSERT FIGURE FOUR NEAR HERE ***

Examining the dynamics on either side of this transition illustrates the mechanism by which alternate equilibria are attained (Figure 4). For values of $\hat{\rho}_S$ (ability of the antagonist to bulk-up on healthy host tissue) either side of the transition point marked by a green dot in Figure 3b, the antagonist is able to invade initially and to bulk-up quickly to an intermediate plateau. Nevertheless for the smaller value of $\hat{\rho}_S$, the effective reproductive number of the pathogen remains above one, and the antagonist is eradicated as

the pathogen establishes itself and the antagonist's habitat is removed. For the slightly larger value of $\hat{\rho}_S$, however, the effective reproductive number drops below one at the intermediate plateau, and so the pathogen density begins to fall. Since any decrease in pathogen density leads to a corresponding increase in antagonist density as the latter has more habitat, and because this leads to a larger force of antagonism and so a further decrease in pathogen density, the pathogen is eradicated via a feedback mechanism.

The exact value of the per capita rate of antagonist bulking-up on susceptible habitat, $\hat{\rho}_S$, (with all other parameters fixed) at which there is a sharp transition depends on the initial conditions (Figures 3c and 3d). We note that, although this value depends upon the density of antagonist and pathogen at the initial plateau, the critical value of $\hat{\rho}_S$ is relatively irresponsive to $\hat{A}_0$ and $\hat{S}_0$ (since the dynamics of antagonist and host are fast, and the initial condition is soon "washed out" of the system). However the initial pathogen density (shown in Figures 3c and 3d via the proxy of initial inoculum density) has a large effect on the value of $\hat{\rho}_S$. This counter-intuitive result can be attributed to the following dynamics (Figure 4): the initial pathogen density exerts a large influence on the density of susceptible hosts that corresponds to the primary infection plateau, via the $\hat{S}+\hat{I}$ term in the host population's carrying capacity. This, in turn, leads to changes in the value of the bulk-up parameter required for the sharp transition, via the feedback described above.

4. Discussion

We have extended a well-studied and generic model of soil-borne plant pathogens to encompass biological control, by including the dynamics of an antagonist population. The antagonist can increase in density on a range of habitats, including susceptible hosts, infected hosts and soil-borne inoculum. The rate of increase on each habitat depends on a parameter, and so is configurable depending on the antagonist in question. The antagonist acts as an agent of biological control by affecting the epidemiologi-

cal processes that underpin the host-pathogen interaction; these effects are translated via effects on selected epidemiological parameters including rates of primary and secondary infection, and infectious periods of infected hosts and inoculum. Reduction(s) in these rates/periods depend(s) jointly on the antagonist's density and on a per capita parameter for the effectiveness of the antagonist. By allowing the control effect to depend on antagonist density, the complex temporal variation corresponding to the three species interaction in biological control is reflected. By decoupling the range of habitat(s) the antagonist is capable of colonising from its action(s) on the epidemiology of the pathogen, and by allowing both these aspects of its biology to be be controlled by tunable parameters, the model can target diverse pathogen-antagonist interactions. As the underlying epidemiological model is equally flexible, and can in principle represent any host-pathogen combination, the full model is therefore applicable to a wide range of host-pathogen-antagonist triplets.

It is instructive to show this flexibility in practice. Using take-all on wheat, caused by the fungus *Gaeumannomyces graminis* var. *tritici*, as an illustrative example, a number of studies have used a variant of our underlying model to investigate the host-pathogen dynamics [2, 4, 3, 5]. Both primary and secondary infection and host growth were shown to have an important role, and in particular it is necessary to take $\beta_P, \beta_S > 0$ in the epidemiological model. Turning to the biological control agent, a range of mechanisms for the antagonistic effect of *Pseudomonas* spp. bacteria have been proposed. However the current consensus [75] emphasises the role of antibiotic production (either 2,4-diacetylphloroglucinol [59] or phenazine-1-carboxylic acid [72, 60]). Antibiotics reduce the rates of both initial primary infection [12] and of the growth of lesions and secondary spread of the pathogen [14, 52]. This would correspond to the bacterium reducing the effective rates of primary (β_P), and secondary (β_S) infection, respectively, and so to $\alpha_P, \alpha_S > 0$ in the model. Finally, although the bacteria are acknowledged to colonise healthy roots [72], populations are much larger on diseased roots [52], and

so we would take $\rho_I > \rho_S > 0$. In principle a similar characterisation of a plausible set of non-zero parameters could easily be outlined for any host-pathogen-antagonist interaction.

Biological control can conveniently be divided into (i) preventative, in which pre-emptive application aims to stop the pathogen from entering the system; and (ii) reactive, with control applied after the pathogen has already invaded the population of plant hosts. Reactive control can be further subdivided into (a) eradicative, where the pathogen is driven out of the system by the antagonist; and (b) reductive, with the more modest aim of reducing the density of the pathogen. The model allows us to understand each of these types of control.

For preventative control, the pathogen's invasion criterion in the presence of the antagonist (Equations (20) and (27)) illustrates the importance of both the antagonist's density when the pathogen is absent, and its effect(s) on the epidemiology of the pathogen. Clearly to be able to prevent pathogen invasion, the antagonist must be able to bulk-up on susceptible host tissue (i.e. has $\hat{\rho}_S > 0$). However, depending on the division of the pathogen's basic reproductive number into distinct components corresponding to primary and secondary infection, $R_0 = R_0^P + R_0^S$, even a high density of antagonist may not be sufficient to stop invasion. In particular, a pathogen with $R_0^P > 1$ can only be prevented from invading by an antagonist that is able to alter at least one of the rates associated with primary infection (i.e. that affects the effective rate of primary infection, $\hat{\beta}_P$; of decay of inoculum, $\hat{\gamma}$; or of infected hosts, $\hat{\mu}$; and so has at least one of $\hat{\alpha}_P, \hat{\omega}_\gamma$ or $\hat{\omega}_\mu$ greater than zero). There is an analogous result for secondary infection. Note that an antagonist which affects the rate of decay of infectious hosts (i.e. has $\hat{\omega}_\mu > 0$) is, in principle at least, theoretically capable of preventing invasion irrespective of the pathogen's balance between primary and secondary infection. This is because the infectious period of infected hosts is implicated in both infection pathways. However, whether or not such an antagonist does indeed prevent the pathogen

316 from entering the system depends not only on the antagonist's value of $\hat{\omega}_\mu$, but also on
317 its density in the absence of the pathogen (i.e. on the balance between its bulk-up rate
318 on susceptible hosts, $\hat{\rho}_S$, and its natural decay rate, $\hat{\sigma}$).

319 The partitioning of R_0 is equally critical for eradicative reactive control. The max-
320 imum possible effect of any control which independently affects a single epidemio-
321 logical mechanism is shown in Table 5. Again the result is driven by the partitioning
322 $R_0 = R_0^P + R_0^S$. For example, if both $R_0^P, R_0^S > 1$, an antagonist is only able to eradicate
323 the pathogen (i.e. drive $\hat{I}_\infty$ to zero) if it is able to interfere with both infection pathways
324 simultaneously. This can either be because the antagonist is capable of affecting both
325 primary and secondary infection (eg. $\hat{\alpha}_P, \hat{\alpha}_S > 0$, although other combinations are pos-
326 sible), or because it can reduce the infectious period of infected hosts (i.e. $\hat{\omega}_\mu > 0$).
327 Even if the antagonist is able to bulk up to a large extent on the available habitat, it will
328 not be able to eradicate the pathogen unless a correct combination of epidemiological
329 mechanism(s) are targetted.

330 The significance of the antagonist's population dynamics for reactive control, how-
331 ever, is twofold. Firstly the antagonist must be able to invade when the pathogen is
332 present (cf. Equation (29)). This depends on a complex balance of the available den-
333 sity of susceptible and infected hosts and soil-borne inoculum, and which of these
334 habitats the antagonist is capable of colonising. Secondly, and arguably more impor-
335 tantly, useful reductive control is possible even if the pathogen is not eradicated. As
336 shown in Figure 1, broadly-speaking, the better the antagonist is at bulking-up on avail-
337 able habitat, the more effective it will be at controlling the pathogen, given a fixed per
338 capita efficiency of antagonism. This is unsurprising. However less obvious (Figure 2)
339 is that any increase in (say) the rate of increase on susceptible hosts, $\hat{\rho}_S$, can be exactly
340 offset by a suitably-sized decrease in (say) the rate of increase on infected hosts, $\hat{\rho}_I$.
341 This indicates that, if the antagonist is able to persist in the system, the range of habi-
342 tats that it is capable of colonising is less important than the rate at which it is able to

bulk-up on those habitats that it can use. In particular there is no requirement for the antagonist to be able to bulk-up on all classes of habitat in order to exert the maximal reductive control it is capable of as per Table 5, so long as it is sufficiently able to utilise those habitats it can colonise. Of course there is the important proviso in the limiting case of eradication that the antagonist must be able to bulk up on susceptible hosts (as otherwise it destroys its own habitat in exerting its antagonist effect). Finally we note that the maximum effect of reductive control again follows from a combination of R_0^P and R_0^S for the underlying host-pathogen interaction and the set of epidemiological mechanisms that the antagonist can affect.

We used the equilibrium density of infected hosts, $\hat{I}_\infty$, to assess the quality of biological control. This approach is fairly standard for models of this type [24, 16] and certainly has the dual advantages of simplicity and lack of ambiguity. However in certain circumstances it is possible that either (i) the equilibrium may not be reached within the timescale of interest for a particular application of the model (eg. within a single growing season); or (ii) the approach to equilibrium is oscillatory, and so the final density of infected hosts understates the impact of the pathogen on the quantity of practical interest (eg. the yield of a crop plant). Other approaches are possible, often based on some variant of the area under the disease progress curve (AUDPC) [50]. A particularly useful metric which concentrates on the yield within a single growing season of length T_{max} and which addresses both of these potential problems was proposed by Hall *et al.* [35]

$$y = \int_{t=0}^{T_{max}} w(t)S(t)dt, \tag{31}$$

where $w(t)$ gives an appropriate weighting to any growth stages that have a disproportionate effect on yield. However this approach (i) targets the particular case of within-season growth of a crop, and so is inappropriate for a generic framework such as that we present here; (ii) can only be calculated for any particular set of parameters using

simulation; and (iii) requires the weighting function $w(t)$ to be defined. Additionally, we note that this type of metric would be most useful if the approach to equilibrium were strongly oscillatory; this does not appear to be the case for our model, at least for the parameter sets we have examined. This is perhaps in part a consequence of the linear function we used to model host growth, which has recently been shown to be associated with a smooth approach to equilibrium in the underlying epidemiological model (in contrast to non-linear host growth functions such as logistic, which promote cycling of the state variables [16]). Finally we note that a rise then fall in the number of infected roots appears to be rare for the soil-borne systems we are most focussed upon [44, 20, 21, 2, 4, 3, 45, 5].

The above analyses of invasion have depended on either the antagonist or pathogen being well-established, and so one species or the other being initially present in the system at its equilibrium density. However this is not necessarily the case. While the above analyses remain broadly correct, it is possible that both the pathogen-free and antagonist-free equilibria are locally stable. In this bistable case, either pathogen or antagonist can eventually be eradicated. The final outcome of attempted control then depends critically on the initial conditions at the time of deployment. Interestingly for a fixed initial condition there is a sharp jump from totally effective eradicative control (i.e. eradication of the pathogen) to totally ineffective control (i.e. the pathogen persists at its antagonist-free equilibrium) as the parameters of the model are slightly altered. As changes in parameters can be driven by changes in environmental or other conditions [44], this mechanism arguably offers a plausible explanation for the wide-ranging outcomes of biological control in practice, and for spatial differences in the effectiveness of biological control in response to small-scale environmental changes. We have chosen not to explicitly model responses to environmental variables such as temperature and moisture levels, in the interests of parsimony and to avoid obscuring the messages of this introduction to the model framework. However we note that a

flexible technique based on rewriting the model as a stochastic differential equation and coupling it to a simple Markov-chain weather-generating model was presented by Truscott and Gilligan [73], and our result illustrating very large effects of small parameter changes indicates that this may be a fruitful area for our future work.

The generic nature of our work distinguishes it from previous models of biological control of soil-borne pathogens [28, 44, 1, 20, 29, 30, 31, 2, 21, 45]. However a flexible model of the biological control of airborne pathogens was recently introduced by Jeger *et al.* [41], and further investigated by Xu *et al.* [77]. Our model is more closely targetted to the soil-borne systems we consider, and in particular includes the distinct pathways of primary and secondary infection that have been shown to control epidemics of soil-borne disease [10, 27, 49, 3]. Furthermore our model includes the growth of the host, which is now well-acknowledged to be a crucial driver of the dynamics of soil-borne pathogens [2, 5]. Host growth was excluded from the models of Jeger *et al.* [41] and Xu *et al.* [77] on the grounds of expediency in simplifying analytic solution. Instead those authors allowed a proportion of tissue colonised by the biological control agent (their class H_b) to continuously become removed (R) or to revert to susceptible (H_s). The latter transition allows the pathogen to persist in the system. The former transition (i.e. $H_b \to R$) was removed in the updated version of the model due to Jeger *et al.* [77] to ameliorate the unrealistic immediate removal of a large proportion of host tissue following a large one-time application of biological control. As a consequence of our focus on soil-borne pathogens, it is the more extensive treatment of host growth and primary and secondary infection that distinguishes our work from the models of Jeger *et al.* [41] and Xu *et al.* [77].

In summary our results highlight the importance of both population dynamics and the mechanism(s) of antagonism for effective biological control of soil-borne plant pathogens. We illustrate how successful biological control depends crucially on the epidemiology of the host-pathogen interaction and the habitats that the antagonist is able

to colonise. While we acknowledge our underlying modelling framework is rather simple, by restricting ourselves to a non-spatial, autonomous, deterministic variant of the SIRX framework, we have avoided the proliferation of state variables and parameters which would have been associated with more complex models. Additionally models of this ostensibly simple type have been extensively and successfully confronted with data [27, 29, 30, 31, 2, 4, 3, 5]. However, our future work will concentrate on extending the framework to include stochasticity [21, 26]; spatial effects [56, 69]; environmental variation [73] and the periodic removal of hosts associated with commercial cropping in agricultural systems [30, 49].

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Variable or parameter	Definition	Description	Default value
$\hat{S}$	$S\kappa^{-1}$	Density of susceptible hosts	-
$\hat{I}$	$I\kappa^{-1}$	Density of infected hosts	-
$\hat{X}$	$\eta X \nu^{-1}\kappa^{-1}$	Density of soil-borne inoculum	-
$\hat{A}$	$\xi A \eta^{-1}$	Density of antagonist	-
$\hat{t}$	ηt	Time	-
$\hat{S}_0$	$S_0\kappa^{-1}$	Initial density of susceptible hosts	1.0
$\hat{I}_0$	$I_0\kappa^{-1}$	Initial density of infected hosts	0
$\hat{X}_0$	$\eta X_0 \nu^{-1}\kappa^{-1}$	Initial density of soil-borne inoculum	0.1
$\hat{A}_0$	$\xi A_0 \eta^{-1}$	Initial density of antagonist	0.1
$\hat{\beta}_P$	$\beta_P \nu\kappa\eta^{-2}$	Rate of primary infection	0.5
$\hat{\beta}_S$	$\beta_S \kappa\eta^{-1}$	Rate of secondary infection	0.375
$\hat{\mu}$	$\mu\eta^{-1}$	Death rate of infected hosts	0.25
$\hat{\gamma}$	$\gamma\eta^{-1}$	Decay rate of soil-borne inoculum	0.8
R_0	$\left(\hat{\beta}_P\hat{c}^{-1}+\hat{\beta}_S\right)\hat{\mu}^{-1}$	Pathogen's basic reproductive number (no $\hat{A}$)	4.0
R_0^P	$\hat{\beta}_P\hat{c}^{-1}\hat{\mu}^{-1}$	Component of R_0 due to primary infection	2.5
R_0^S	$\hat{\beta}_S\hat{\mu}^{-1}$	Component of R_0 due to secondary infection	1.5
$\hat{\alpha}_P$	$\alpha_P\eta\xi^{-1}$	Controls reduction in $\hat{\beta}_P$ by antagonist	0-5
$\hat{\alpha}_S$	$\alpha_S\eta\xi^{-1}$	Controls reduction in $\hat{\beta}_S$ by antagonist	0-5
$\hat{\omega}_\mu$	$\omega_P\eta\xi^{-1}$	Controls increase in $\hat{\mu}$ by antagonist	0-5
$\hat{\omega}_\gamma$	$\omega_S\eta\xi^{-1}$	Controls increase in $\hat{\gamma}$ by antagonist	0-5
$\hat{\rho}_S$	$\rho_S\kappa\eta^{-1}$	Bulk-up rate upon susceptible hosts	0-10
$\hat{\rho}_I$	$\rho_I\kappa\eta^{-1}$	Bulk-up rate upon infected hosts	0-10
$\hat{\rho}_X$	$\rho_X\nu\kappa\eta^{-2}$	Bulk-up rate upon soil-borne inoculum	0-10
$\hat{\sigma}$	$\sigma\eta^{-1}$	Rate of decay of antagonist	1 or 5

Table 1: Dimensionless variables and parameters (with illustrative parameter values and initial conditions, where appropriate).

Scenario	Description	Associated figures
A: Habitat-generalism	Antagonist bulks-up at equal rate $\hat{\lambda} = \hat{\rho}_S = \hat{\rho}_I = \hat{\rho}_X$ on all classes of habitat, with fixed death rate ($\hat{\sigma} = 1.0$). Examine endemic infected density as $\hat{\lambda}$ and any one per capita force of antagonism (i.e. $\hat{\alpha}_P, \hat{\alpha}_S, \hat{\omega}_\mu$ or $\hat{\omega}_\gamma$) co-vary, with all other parameters from that group set to zero.	Figure 1
B: Habitat-specialism	A pair of the habitat-specific bulking-up parameters $(\hat{\rho}_S, \hat{\rho}_I), (\hat{\rho}_S, \hat{\rho}_X)$ or $(\hat{\rho}_I, \hat{\rho}_X)$ co-vary, while the third parameter in this class is fixed at zero, with a fixed death rate (either $\hat{\sigma} = 1.0$ or $\hat{\sigma} = 5.0$). Examine endemic infected density as the bulking-up parameters are varied, when one of the per capita forces of antagonism (i.e. $\hat{\alpha}_P, \hat{\alpha}_S, \hat{\omega}_\mu$ or $\hat{\omega}_\gamma$) is fixed at 1.0, and all other parameters from that group are set to zero.	Figures 2 and 3a,b
C: Bistability and sharp transitions in control efficacy	Antagonist affects only the rate of decay of infected hosts ($\hat{\omega}_\mu = 1.0, \hat{\alpha}_P = \hat{\alpha}_S = \hat{\omega}_\gamma = 0$), is only able to bulk-up on susceptible hosts ($\hat{\rho}_S > 0$, $\hat{\rho}_I = \hat{\rho}_X = 0$), and has a large death rate in the absence of suitable habitat ($\hat{\sigma} = 5.0$). Examine variation of the value of $\hat{\rho}_S$ at which there is a phase transition in control efficacy with the initial conditions, focusing on changes with $(\hat{I}_0, \hat{A}_0)$ and $(\hat{S}_0, \hat{X}_0)$, and the mechanism by which this phase transition is attained.	Figures 3c,d and 4

Table 2: Summary of numerical scenarios (all numerical work considers an illustrative host-pathogen interaction with $\hat{\beta}_P = 0.5, \hat{\beta}_S = 0.375, \hat{\mu} = 0.25, \hat{\gamma} = 0.8$).

Equilibrium $(\hat{S}_\infty, \hat{I}_\infty, \hat{X}_\infty, \hat{A}_\infty)$	Interpretation	Existence criterion
(✓, ✗, ✗, ✗)	Only host persists	None
(✓, ✓, ✓, ✗)	Host and pathogen persist	$R(0) = R_0 > 1$
(✓, ✗, ✗, ✓)	Host and antagonist persist	$\hat{\rho}_S - \hat{\sigma} > 0$
(✓, ✓, ✓, ✓)	Coexistence of all three species	$\exists \hat{A}_\infty > 0$ in Equation (24) with $R_0 = R(\hat{A}_\infty) > 1$

Table 3: Equilibria and existence criteria.

Invasion of	Already present	Precondition	Invasion condition
$\hat{A}$	$\hat{S}$	None	$\frac{\hat{\rho}_S}{\hat{\sigma}} > 1$
	$\hat{S},\hat{I},\hat{X}$	$R(0) = R_0 > 1$	$\frac{\hat{\rho}_S}{\sigma}\hat{S}_\infty + \frac{\hat{\rho}_I}{\sigma}\hat{I}_\infty + \frac{\hat{\rho}_X}{\sigma}\hat{X}_\infty > 1$
$\hat{I}$	$\hat{S}$	None	$R(0) = R_0 > 1$
	$\hat{S},\hat{A}$	$\hat{\rho}_S - \hat{\sigma} > 0$	$R(\hat{\rho}_S - \hat{\sigma}) > 1$

Table 4: Invasion criteria.

Pathogen		Minimum long-term infected density $\hat{I}_\infty$ when control or antagonist reduces[1]			
$R_0^P > 1$	$R_0^S > 1$	primary infection rate $\hat{\beta}_P \to 0$ or $\hat{\alpha}_P \to \infty$	secondary infection rate $\hat{\beta}_S \to 0$ or $\hat{\alpha}_S \to \infty$	infected tissue infectious period $\hat{\mu} \to \infty$ or $\hat{\omega}_\mu \to \infty$	inoculum infectious period $\hat{\gamma} \to \infty$ or $\hat{\omega}_\gamma \to \infty$
✓	✓	$\frac{1}{1+\hat{\mu}}\left(1-\frac{1}{R_0^S}\right)$	$\frac{1}{1+\hat{\mu}}\left(1-\frac{1}{R_0^P}\right)$	0	$\frac{1}{1+\hat{\mu}}\left(1-\frac{1}{R_0^S}\right)$
✓	✗	0	$\frac{1}{1+\hat{\mu}}\left(1-\frac{1}{R_0^P}\right)$	0	0
✗	✓	$\frac{1}{1+\hat{\mu}}\left(1-\frac{1}{R_0^S}\right)$	0	0	$\frac{1}{1+\hat{\mu}}\left(1-\frac{1}{R_0^S}\right)$
✗	✗	0	0	0	0

Table 5: Dependence of the minimum long-term infected density, $\hat{I}_\infty$, on R_0^P, R_0^S and the epidemiological mechanism affected by control.

1. Note that lower bounds on infected density do not take into account the population dynamics of the antagonist, but are attained for reasonable values of the antagonist bulking-up parameters (see main text and Figures 1 and 2). Note also that here we restrict attention to single-mode controls/antagonists which are capable of affecting the effective size of a single epidemiological parameter.

Figure 1: Habitat-generalist antagonism. Figure (a) shows the dependence of the endemic density of infected hosts upon the per capita antagonistic effect on the rate of primary infection ($\hat{\alpha}_P$) and the rate at which the antagonist can bulk-up ($\hat{\lambda} = \hat{\rho}_S = \hat{\rho}_I = \hat{\rho}_X$). Figure (b) shows the dependence on antagonist bulking-up and the rate of decay of infected hosts ($\hat{\omega}_\mu$). The lower bounds in Table 5 are attained in practice, as $\hat{\lambda}$ and $\hat{\alpha}_P$ or $\hat{\omega}_\mu \to \infty$, but the actual density of infected hosts for particular parameters depends upon a combination of the bulk-up behaviour and the per capita effect of antagonism.

Figure 2: Habitat-specialist antagonism. All figures show the endemic density of infected hosts as individual components of bulking-up behaviour are altered. Figures (a) and (b) demonstrate the variation in $(\hat{\rho}_S, \hat{\rho}_I)$ space (with $\hat{\rho}_X = 0$), whereas Figures (c) and (d) demonstrate the variation in $(\hat{\rho}_I, \hat{\rho}_X)$ space (with $\hat{\rho}_S = 0$). The antagonist is able to affect only the rate of primary infection in Figures (a) and (c) ($\hat{\alpha}_P = 1.0, \hat{\alpha}_S = \hat{\omega}_\mu = \hat{\omega}_\gamma = 0$), whereas it affects only the rate of decay of infected hosts in Figures (b) and (d) ($\hat{\omega}_\mu = 1.0, \hat{\alpha}_P = \hat{\alpha}_S = \hat{\omega}_\gamma = 0$). Note the maximum reduction in infected density is achievable for antagonists that do not bulk-up on all classes of host, the linear contours of infected density, and the necessity for $\hat{\rho}_S > 0$ for the pathogen to be eradicated (i.e. the varying gradient of the contours in Figure (b)).

Figure 3: Sharp transitions: response to antagonist habitat, antagonist mode of action and the initial density of host, pathogen and antagonist. Bistability (here promoted by large antagonist death rate) leads to large changes in behaviour with small changes to the parameters. Figures 2(a) and 2(b) are replicated for an antagonist with large death rate ($\hat{\sigma} = 5.0$). When the antagonist is capable of eradicating the pathogen (i.e. Figure (b)) there can be a sharp transition on the $\hat{\rho}_S$ axis near the value $\hat{\rho}_S = 8.3$ (marked by a green dot), where the density of infected hosts abruptly decreases from its maximum value to zero (with initial conditions $\hat{S}_0 = 1.0, \hat{I}_0 = 0, \hat{X}_0 = 0.1, \hat{A}_0 = 0.1$). Figures (c) and (d) show the response of the location of the sharp transition in parameter space to the initial conditions. The value of $\hat{\rho}_S$ (the rate at which antagonist bulks-up on susceptible hosts) at which there is a phase transition between eradication and totally ineffective control is shown for different values of $(\hat{S}_0, \hat{X}_0)$ (c) and $(\hat{A}_0, \hat{X}_0)$ (d). Here $\hat{\rho}_I = \hat{\rho}_S = 0$, and so there is no bulking-up on infected hosts, although the qualitative behaviour generalises to antagonists that are also able to bulk-up on these habitats.

Figure 4: Sharp transitions: mechanism by which alternate equilibria are attained. The density of (a) susceptible hosts, (b) infected hosts, (c) inoculum and (d) antagonists for $\rho_S = 8.3$ (blue solid line) and $\hat{\rho}_S = 8.4$ (red dotted line). The extreme difference in behaviour for slightly different values of $\hat{\rho}_S$ is due to bistability in the model and the feedback described in the main text.

Appendix A. Stability analysis

Stability of the underlying epidemiological model (i.e. Equations (10)-(12) with $\hat{A}$ fixed at zero) is determined by the Eigenvalues of its Jacobian, which at a general point $(\hat{S},\hat{I},\hat{X})$ is

$$J = \begin{pmatrix} -1-\hat{\beta}_P\hat{X}-\hat{\beta}_S\hat{I} & -1-\hat{\beta}_S\hat{S} & -\hat{\beta}_P\hat{S} \\ \hat{\beta}_P\hat{X}+\hat{\beta}_S\hat{I} & \hat{\beta}_S\hat{S}-\hat{\mu} & \hat{\beta}_P\hat{S} \\ 0 & 1 & -\hat{c} \end{pmatrix}. \tag{A.1}$$

Appendix A.1. Pathogen-free equilibrium

At the pathogen-free equilibrium (Equation (17))

$$J = \begin{pmatrix} -1 & -1-\hat{\beta}_S & -\hat{\beta}_P \\ 0 & \hat{\beta}_S-\hat{\mu} & \hat{\beta}_P \\ 0 & 1 & -\hat{c} \end{pmatrix}. \tag{A.2}$$

The Eigenvalues λ satisfy

$$(1+\lambda)\left(\lambda^2+\left(\hat{\mu}-\hat{\beta}_S+\hat{c}\right)\lambda+\left(\hat{\mu}-\hat{\beta}_S\right)\hat{c}-\hat{\beta}_P\right)=0. \tag{A.3}$$

Clearly one Eigenvalue is always -1, and so the Routh-Hurwitz (R-H) criteria [11] applied to the inner quadratic factor indicates that all three Eigenvalues have negative real parts if and only if

$$\hat{\mu}-\hat{\beta}_S+\hat{c} > 0, \tag{A.4}$$

$$\left(\hat{\mu}-\hat{\beta}_S\right)\hat{c}-\hat{\beta}_P > 0, \tag{A.5}$$

which in combination form a condition for the pathogen-free equilibrium to be stable

$$\hat{\mu} - \hat{\beta}_S > \max\left(-\hat{c}, \frac{\hat{\beta}_P}{\hat{c}}\right). \tag{A.6}$$

Since all parameters are positive this may be reduced to

$$\frac{1}{\hat{\mu}}\left(\frac{\hat{\beta}_P}{\hat{c}} + \hat{\beta}_S\right) < 1, \tag{A.7}$$

which forms a final stability condition for the pathogen-free equilibrium of the underlying model. As the R-H criterion is a two-way implication, whenever Equation (A.7) is not satisfied the pathogen-free equilibrium is unstable, and the pathogen can invade a population of hosts at its carrying capacity in the absence of antagonism, allowing us to identify the basic reproductive number as

$$R_0 = \frac{1}{\hat{\mu}}\left(\frac{\hat{\beta}_P}{\hat{c}} + \hat{\beta}_S\right). \tag{A.8}$$

That the particular expression given in Equation (A.8) is the basic reproductive number of the pathogen (rather than for example a related quantity with similar threshold behaviour, such as its square root [38]) may be confirmed by either a retrospective biological interpretation of its components [9] or more formally by the Next Generation method [17, 18]. Full details for a similar model are given in [16].

Appendix A.2. Pathogen-present equilibrium

At the pathogen-present equilibrium of Equation (18), noting that

$$\hat{\beta}_P \hat{X} + \hat{\beta}_S \hat{I} = \frac{\hat{\mu}}{\hat{\mu}+1}\left(R_0 - 1\right), \tag{A.9}$$

the Jacobian reduces to

$$J = \begin{pmatrix} -1 - \frac{\hat{\mu}}{\hat{\mu}+1}(R_0 - 1) & -1 - \frac{\hat{\beta}_S}{R_0} & -\frac{\hat{\beta}_P}{R_0} \\ \frac{\hat{\mu}}{\hat{\mu}+1}(R_0 - 1) & \frac{\hat{\beta}_S}{R_0} - \hat{\mu} & \frac{\hat{\beta}_P}{R_0} \\ 0 & 1 & -\hat{c} \end{pmatrix}. \tag{A.10}$$

The characteristic equation is given by

$$\lambda^3 + a_1\lambda^2 + a_2\lambda + a_3 = 0, \tag{A.11}$$

where

$$a_1 = 1 + \hat{\mu} - \frac{\hat{\beta}_S}{R_0} + \frac{\hat{\mu}}{\hat{\mu}+1}(R_0 - 1) + \hat{c}, \tag{A.12}$$

$$a_2 = \hat{\mu} - \frac{\hat{\beta}_S}{R_0} + \hat{c} + \frac{\hat{c}\hat{\mu}}{\hat{\mu}+1}(R_0 - 1) + \hat{\mu}(R_0 - 1), \tag{A.13}$$

$$a_3 = \hat{\mu}\hat{c}(R_0 - 1). \tag{A.14}$$

The R-H criteria for cubic equations indicate that all three Eigenvalues have negative real part if and only if

$$a_3 > 0, \tag{A.15}$$

$$a_1 > 0, \tag{A.16}$$

$$a_1 a_2 - a_3 > 0. \tag{A.17}$$

Clearly (A.15) is satisfied only if $R_0 > 1$, and so the biological existence criterion $R_0 > 1$ is also necessary for the equilibrium to be stable. Rewriting

$$\hat{\mu} = \frac{1}{R_0}\left(\frac{\hat{\beta}_P}{\hat{c}} + \hat{\beta}_S\right) \tag{A.18}$$

indicates that

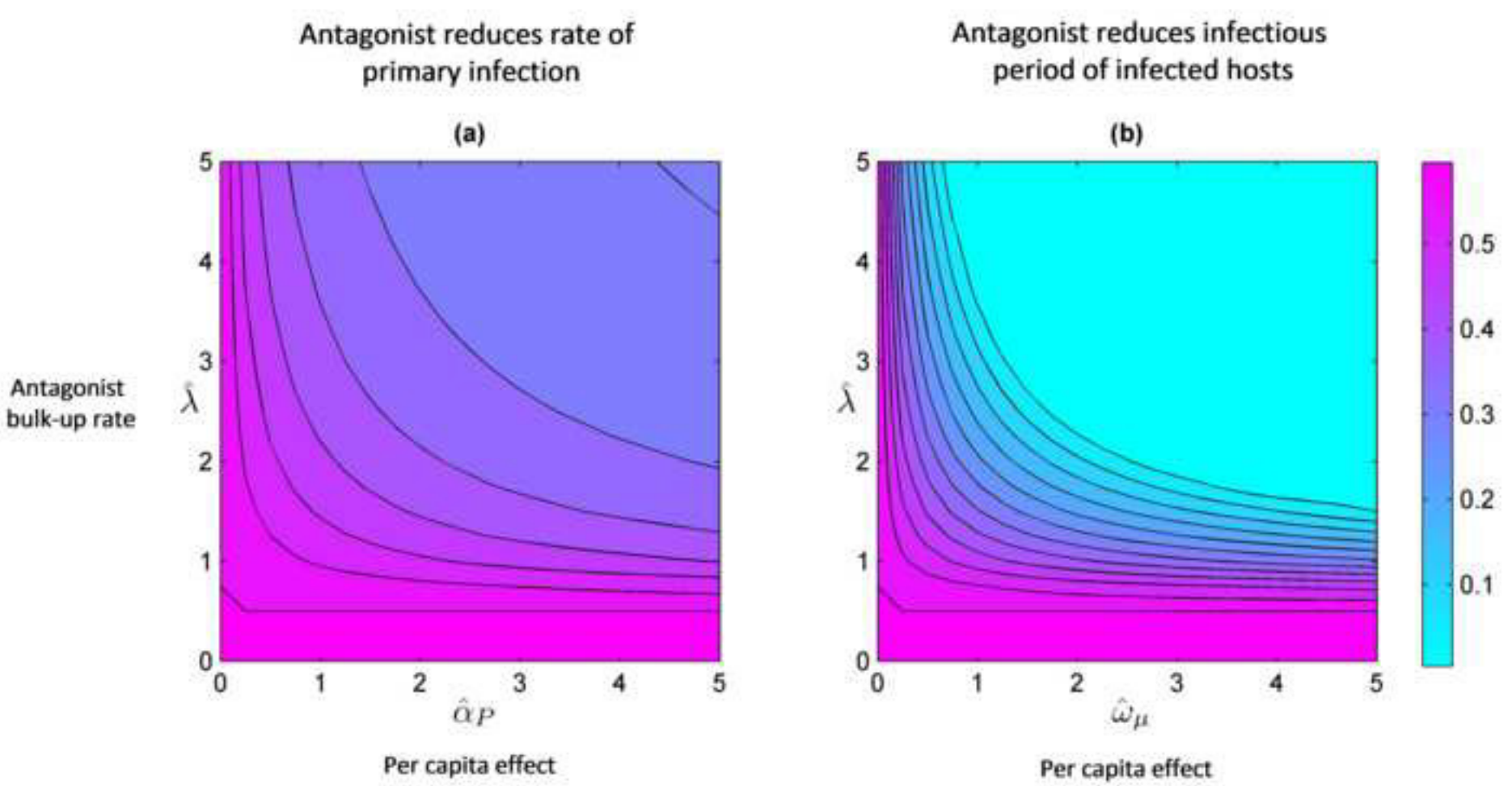
$$a_1 = 1 + \frac{\hat{\beta}_P}{\hat{c}R_0} + \frac{\hat{\mu}}{\hat{\mu}+1}(R_0 - 1) + \hat{c}, \tag{A.19}$$

and hence that (A.16) is true whenever $R_0 > 1$ (note that this is a sufficient rather than necessary condition for (A.16) to hold). The product in (A.17) can then be rearranged

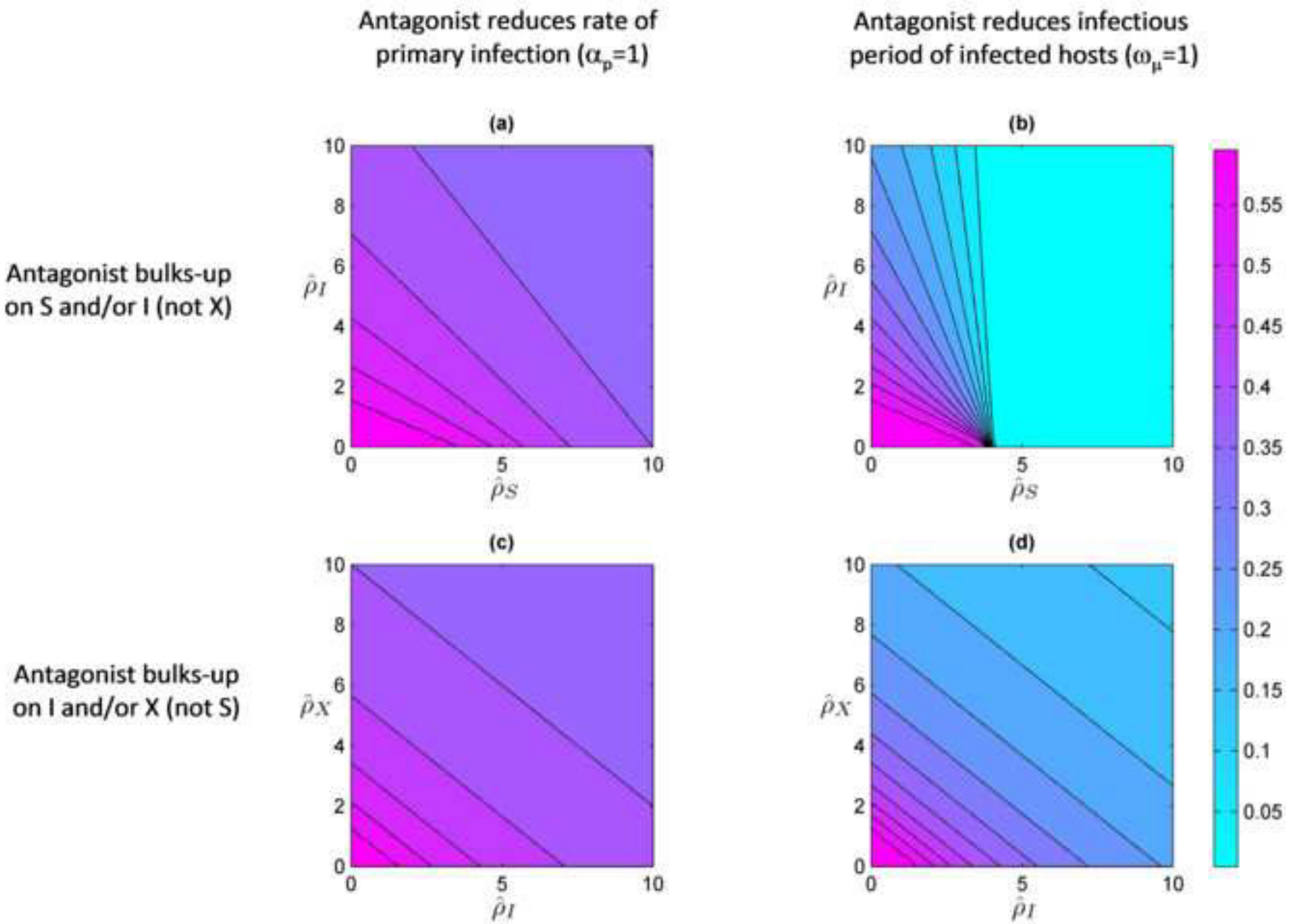
$$\begin{aligned} a_1 a_2 - a_3 \quad = \quad & \left(1 + \frac{\hat{\beta}_P}{\hat{c}R_0} + \frac{\hat{\mu}}{\hat{\mu}+1}(R_0 - 1)\right)\left(\hat{\mu}(R_0 - 1)\left(\frac{\hat{c}}{\hat{\mu}+1} + 1\right) + \frac{\hat{\beta}_P}{\hat{c}R_0} + \hat{c}\right) \\ & + \hat{c}\left(\frac{c\hat{\mu}}{\hat{\mu}+1}(R_0 - 1) + \frac{\hat{\beta}_P}{\hat{c}R_0} + \hat{c}\right), \end{aligned} \tag{A.20}$$

which is definitely positive if $R_0 > 1$ (again this is a sufficient rather than necessary condition). Overall a necessary and sufficient condition for all three R-H criteria to be satisfied, and therefore for the pathogen-present equilibrium of the underlying model to be stable, and for the pathogen to be able to persist at its non-zero equilibrium density in the host population in the absence of antagonism, is just $R_0 > 1$.

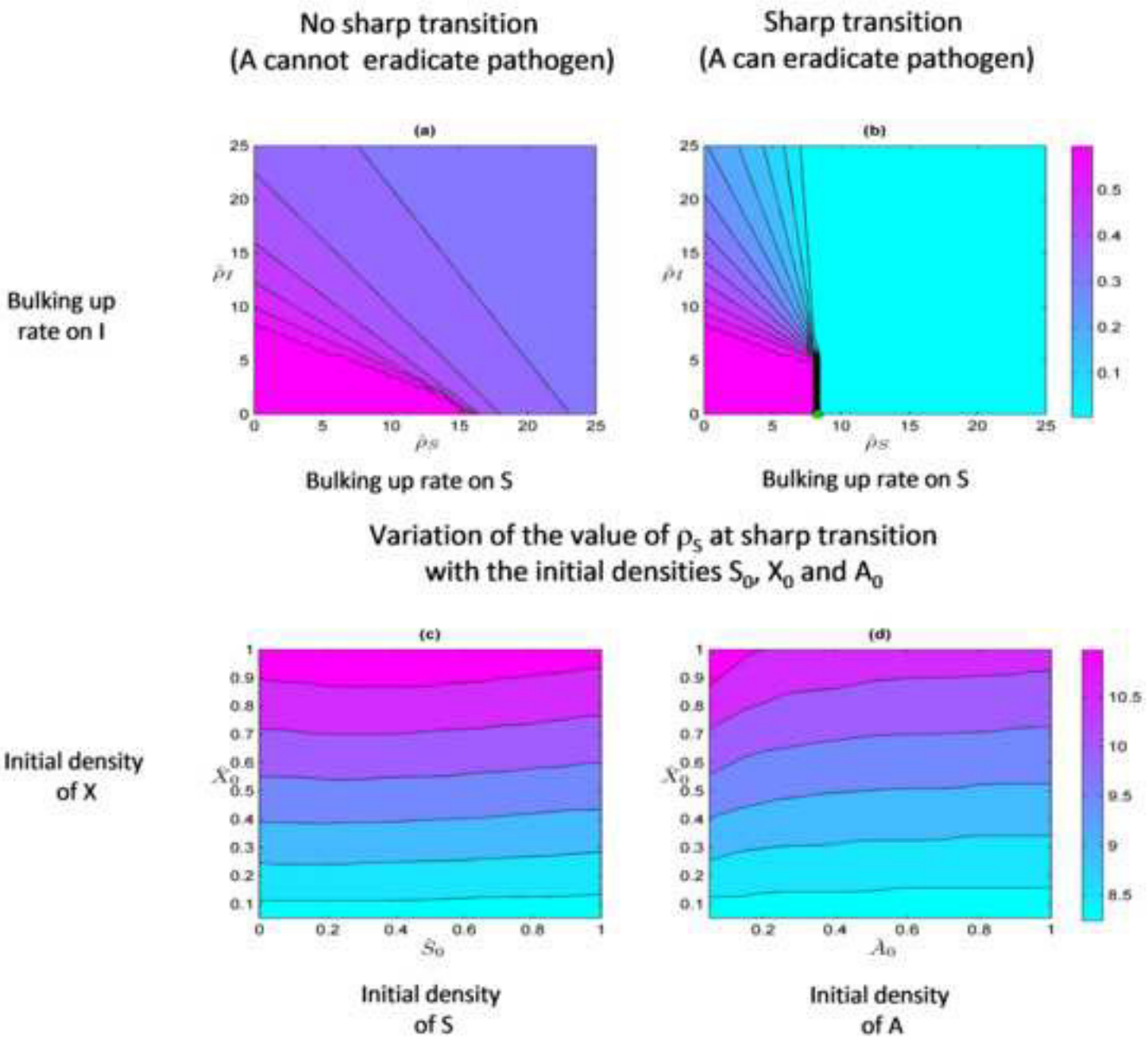
4. Figure



4. Figure



4. Figure



4. Figure