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Advisor: Julie Blackwood
Advisor is Co-author: None of the above
Second Advisor:
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# Modelling the spatial dynamics of White Nose Syndrome under various intervention scenarios

JACKSON BARBER

Advisor: Julie Blackwood

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# 1 Abstract

Since its recent introduction, White Nose Syndrome has infected bats throughout the North American continent, resulting in mass mortality across a wide geographic range. Because of the relative recency of the disease, the conservation community is largely uncertain about how to best address this chiropteran crisis. Insufficient research has been conducted to confidently inform ecologists how to prevent further bat mortality. This thesis implements a S-I-R type dynamical systems model to investigate and predict the efficacy of three proposed interventions: fungicidal treatment of hibernacula, microclimate engineering inside hibernacula, and implementation of a theoretical vaccine, under a number of epidemiological scenarios. My model indicates that, singularly among the three tested interventions, the theoretical vaccine promises to significantly reduce mortality among WNS-infected hibernacula in both single-hibernaculum and multi-hibernaculum scenarios; the fungicide and microclimate interventions, save in highly optimal conditions, fail to significantly reduce WNS-induced mortality, and in some cases actually exacerbate mortality.

# 2 Introduction

In the past decade, White Nose Syndrome (WNS) has escalated from a localized ecological problem to an international conservation crisis. In range spanning the Eastern seaboard of the United States and southern Canada, the U.S. midwest, and recently Washington state, bats are dying at unprecedented rates due to WNS[21][6]. The disease was first noted in during the winter of 2005-06, in a commercial cave near Albany, NY[11]. Since then, massive population decline across numerous species of North American bats has been documented. One of the most heavily impacted bat species is the Little Brown Bat (*Myotis lucifugus*), a prolific bat species in the United States[9]. Mortality up to 99% has been documented in colonies of M. Lucifugus subsequent to the invasion of WNS[11].

A number of distinctive features characterize WNS infection. Bats that develop WNS syndrome display notable, white lesions on their muzzles and wings as the infection develops[12]. The infection progresses during the winter months when bats are hibernating; it is during the winter season that most mortality due to WNS occurs[7]. The disease regresses during the summer sea-

son, when bats roost and swarm. Evidence suggests that infected bats that survive hibernation may partially clear the infection during the warmer summer months[17].

Since its introduction, considerable resources have been dedicated to the study of WNS and its causative agent, the fungal pathogen Pseudogymnoascus destructans (*Pd*). In consequence, a substantial amount of information has been gathered about the origin, pathology, and epidemiology of the disease. WNS likely originated in Europe, where *Pd* has been cultured from caves across the continent[19]. European bats have even been noted to display the characteristic white lesions that appear on infected North American bats; however, European bats do not appear to suffer mortality as a result of *Pd* infection[27]. It is likely that bat populations in Europe coevolved with the fungal pathogen, or have lived with *Pd* in their environment for a sufficient amount of time to develop tolerance[27].

Much has been learned about the pathology of WNS. *Pd* infection impacts bats during their hibernation season, when the preservation of body fat reserves is critical to survival. To preserve energy stores, bats enter torpor, a state of depressed metabolic activity. In winter, this means bats decrease their body temperatures to only a few degrees above freezing. This condition is characterized by massively decreased rates of energy consumption. By remaining in torpor for much of the winter season, bats are generally able to preserve fat stores until the warm summer months when food is plentifully available in the environment.[20] Typical bat hibernation is characterized by periods of torpor, interspersed with periodic arousals. Ecologists believe that these periodic arousals allow bats to rehydrate, among other possible purposes. It is therefore possible that arousal from torpor is initiated when bats body fluid levels fall below a critical threshold.[8]

WNS interferes with the normal pattern of arousal and torpor during the winter months. It has been shown that bats infected with *Pd* arouse more frequently during the winter season than non-infected bats, and their duration of winter arousals among infected bats is significantly longer than among non-infected bats[26]. Bats infected with *Pd* are frequently found flying outside or near the entrances of their hibernacula during the coldest months of the year[3]. Due to increased frequency and duration of arousal, it is thought that bats with WNS expend their crucial energy reserves before the end of the food-scarce season, and subsequently starve[26]. One leading hypothesis suggests that bats with fungal lesions dehydrate more quickly whilst in torpor, and must arouse more frequently to drink and replenish their body fluid content[8].

*Pd* is a psychrophilic fungus, meaning that it grows optimally in cold environments. Experiments have shown that the optimal temperature range for *Pd* growth is between 12-15°C[25]. Growth can occur above this temperature range, but growth is less robust, and growth below 5°C is substantially reduced[25]. *Pd* has been isolated and cultured not only from the skin and fur of infected bats, but also from the walls and floor sediment of hibernacula where infected bats are known to roost[13][24]. Strong evidence suggests that bats may become infected recurrently each hibernation season due to repeated contacted with an environmental reservoir of *Pd*, despite many bats successfully clearing the infection each season.[18]

Widespread bat mortality caused by WNS has triggered concern among conservation ecologists across the country. Bats provide important services in their native ecosystems, including helping to control insect populations [16]. Such services may become increasingly critical to public health in coming decades, as warming global temperatures increase the ranges of disease-carrying insects into previously disease-free latitudes. The U.S. Fish and WIldlife Service has provided over $17 million in grant funding to investigate solutions to WNS-caused bat mortality[10]. Effective response to WNS is a matter of national concern, and the time to respond is right now. The range of WNS expands each hibernation season; already, much of the North American continent is impacted by the disease. However, timely response could help prevent the spread of WNS into new territories, and potentially help already impacted bat populations persist or even recover.

One major barrier to effective response to WNS is an information gap: not enough is known about the potential impacts of various proposed interventions. Although many questions about WNS remain unanswered, ecologists have uncovered a wealth of information about *Pd* and the seasonal dynamics of WNS. Based on the known epidemiology of WNS, scientists have proposed interventions that could, in theory, help facilitate bat resistance to or tolerance of *Pd* infection. It is therefore the task for experimentalists and investigative researchers to test the relative efficacy of these interventions, and advise conservation biologists which approaches to combating WNS are most likely to yield significant results.

This document attempts to contribute to the effort of assessing the relative efficacy of various proposed interventions. The efficacy of interventions can be ascertained by several methods: via physical experimentation, as in a laboratory with test subjects, or via theoretical experimentation, as through a mathematical or statistical model. This thesis takes the latter approach. Here, I have

formulated an ordinary differential equation (ODE) and difference equation hybrid model based on known seasonal dynamics of WNS. The model investigated in this paper is derived from the model developed by my predecessors in this project, Alex Meyer '16 and David Stevens '14. In this thesis I have chosen to investigate the potential impact of three proposed interventions to WNS: vaccination of susceptible bats, fungicidal treatment of hibernacula, and microclimate engineering inside hibernacula[2].

Vaccination is likely the most intuitive approach to disease management. We are familiar with the benefits of vaccination with respect to human disease: effective vaccination programs have helped to control and/or eradicate in the U.S. many of the most virulent and debilitating diseases that plagued past generations: polio, influenza, smallpox, etc. As yet, no effective vaccine has been developed for bats to prevent against WNS, but some WNS experts are hopeful that a vaccine will emerge in the coming years.[14]

Fungicidal treatment of hibernacula aims at reducing or eliminating the environmental reservoir of *Pd*, which likely plays a major role in the rapid spread and multi-year persistence of WNS in hibernacula. Here, we understand fungicide to refer to any intervention that reduces the environmental *Pd* load, whether through a reduction of fungal-growth substrate (i.e. sediment on cave surfaces) or through chemical treatment.[2][5][23]

Microclimate is perhaps the most original and unexpected proposed intervention to have emerged in the last decade of research. One paper that gained wide circulation in the early stages of WNS research proposed that providing localized heating in infected hibernacula could reduce mortality by decreasing energy expenditures among WNS-aroused bats [3]. Since Boyles paper was published in 2010, researchers have grown increasingly interested in the idea of a localized climactic intervention to help reduce WNS-induced mortality among hibernating bats. The nature of the proposed intervention, however, has reversed: instead of warming caves, some conservationists are now proposing that cold air shafts be bored into hibernacula to reduce air temperatures around hibernating bats. Alternatively, artificial hibernacula could be constructed, the internal climates of which could be thermoregulated to maintain cool temperatures. Research since the publication of Boyles paper has revealed that *Pd* grows optimally at temperatures between 12-15°C, with decreasing rates of growth at lower temperatures and a zero-growth temperature threshhold of approximately 3°C[15][25]. This implies that if bats enter torpor in caves with lower ambient

temperatures, the progression of WNS may be greatly slowed or stopped altogether. This would translate to lower rates of disease-induced mortality.

This thesis first investigates the dynamics of WNS in a single model hibernaculum under the three proposed intervention conditions. Then, this thesis investigates the efficacy of the three interventions in a multi-hibernaculum scenario, where inter-hibernaculum migration of bats each summer season drives the spatial spread of WNS. This is the first academic effort, to my knowledge, that extends a dynamical-systems model to investigate the spatial dynamics of WNS in a multi-hibernaculum scenario. Understanding the spatial dynamics of WNS is crucial to informing conservation efforts to prevent the spread of the disease into naive populations.

# 3 The Model

The model used aims to incorporate key elements of the known epidemiology of WNS, as applied to a single ideal hibernaculum of bats. I utilize a variant of the dynamical system model introduced in Meyer et al. 2016 [22], with several parameters removed for the sake of simplification. Important features of the model include seasonality (components of the model corresponding to different times of year follow different dynamics) and a discrete-time summer season, which allows for the introduction of discontinuous dynamics such as a midsummer birth pulse and a vaccination pulse in the vaccine-intervention submodel.

This model is a variant of the canonical S-I-R disease model. My basic model includes three classes of individual, where each individual represents a bat in the model population. Bats are either susceptible (S), exposed (E), or infected (I). In the vaccine-intervention submodel, a fourth class of individual is introduced; vaccinated (V). The total population (N) of the model hibernaculum is equal to the sum individuals in each class: N = S + E + I ( + V ). Susceptible individuals are vulnerable to exposure to *Pd*, the fungal pathogen. In this event, they move from the S class to the E class. Individuals in the E class are said to be in the latency period of WNS infection: they have been exposed to the pathogen and will eventually develop symptoms, but they have not yet become infectious to susceptible individuals. After a latency period of set duration, individuals move from the E class to the I class. Individuals in the I class can either recover at the end of the hibernation season and return to the S class, or die off. Individuals in the V class are immune to

infection; they remain in the V class until they die due to natural mortality.

In addition to the four classes S, E, I, and V that model the population of bats in my model hibernaculum, we have a fifth population class, P. P models the size of the environmental *Pd* reservoir, which increases due to both natural fungal growth and shedding of spores from individuals in the I class.

My model consists of two seasons: a winter season ( 7 months) and a summer season ( 5 months.) This represents a simplification relative to the model presented by Meyer, which included three seasons (hibernation, swarming, and roosting). Recent literature [17] suggests that the swarming phase is not a time of significant disease progression, so I elected to simplify the dynamics of Meyers swarming phase to match roosting phase dynamics. This allowed for the elimination of two swarming season-specific parameters, which simplified the analyses necessary to evaluate this model. This simplification rendered the analysis of multi-hibernaculum dynamics more manageable, without compromising model fidelity to the known seasonal dynamics of WNS.

Every model hibernaculum begins with an initial bat population of 15,000, and a *Pd*-free environment (P = 0). Each simulation begins with a hibernation phase. In the single-hibernaculum simulations, a single infected bat is introduced to a population of 14,999 susceptibles.

## 3.1 Hibernation Phase

The hibernation phase of the basic model lasts 212 days. Hibernation-phase dynamics for S, E, and I are identical in this model to hibernation-phase dynamics in Meyer's model. I model all populations in continuous time during the hibernation, since infection and disease progression are assumed to be continuous processes. The hibernation season is known to be the annual period of greatest WNS-induced mortality. It is during this season that bats develop characteristic lesions, and during this season that bat carcasses are observed in and around hibernacula. Bat population

dynamics are governed by the following set of equations:

$$\frac{dS}{dt} = -(\beta I + \phi P)S - \mu S \tag{1a}$$
$$\frac{dE}{dt} = (\beta I + \phi P)S - (\tau + \mu)E \tag{1b}$$
$$\frac{dI}{dt} = \tau E - (\mu + \delta)I \tag{1c}$$
$$\frac{dV}{dt} = -\mu V \tag{1d}$$

Here, $\beta$ represents the rate of infection due to bat-to-bat contact; $\phi$ represents the rate of infection due to susceptible bats coming into contact with the environmental reservoir; $\tau$ represents the rate of disease progression from the latency period to the infectious period; $\mu$ represents the rate of natural mortality; and $\delta$ represents the rate of disease-induced mortality. In addition to the above equations which model bat population dynamics, we include the following equation to govern the dynamics of the environmental reservoir of *Pd*:

$$\frac{dP}{dt} = (\omega I + \eta P)(1 - \frac{P}{K_{Pd}}) \tag{2a}$$

Here, $\omega$ represents the rate of shedding of *Pd* spores from infected bats; $\eta$ represents the natural growth rate of *Pd*; and $K_{Pd}$ represents the carrying capacity of free-growing *Pd* in the environment. Note that the size of the environmental reservoir grows logistically.

## 3.2 Summer Phase

The summer phase of the model is a composite of Meyers roosting and swarming phases. While it is true that bats do engage in different patterns of behavior during the earlier and latter parts of the summer, evidence suggests that these differences in behavior are not significant in the context of WNS epidemiology. Research suggests that WNS infection prevalence does not increase during the summer season, and mass mortality due to WNS has been documented during the summer season, to the best of my knowledge[17]. This makes sense, given that *Pd* is known to be a psychrophilic, i.e. cold-loving, fungus[25]. In this model, we have chosen to express summertime bat dynamics through a system of difference equations, with a time step of one day. The reason for this is twofold: firstly, because the disease is assumed to not progress during the summer, and

there is generally no movement between the S, E, I, and V classes, we are left with a set of very simple, self-contained differential equations that may be expressed as difference equations to increase computational efficiency; and secondly, difference equations lend themselves to single-day variant dynamics, as in a midsummer birth pulse. Following Meyers model, the first day summer dynamics determines the fate of E and I class individuals:

$$S_t = e^{-\mu}(S_{t-1} + a_1 E_{t-1} + \varepsilon a_2 I_{t-1}) \tag{3a}$$

$$E_t = e^{-\mu}((1 - a_1)E_{t-1}) \tag{3b}$$

$$I_t = e^{-\mu}(\varepsilon(1 - a_2)I_{t-1}) \tag{3c}$$

$$V_t = e^{-\mu}V_{t-1} \tag{3d}$$

Note that this set of equations marks a transition from continuous time to discrete time. The 't-1' subscript indicates the populations at the end of the previous day—in this case, populations at the end of the last day of the hibernation season. Subscript 't' indicates the populations at the end of the current day. I will use this notation for all discrete-time equations in this pthesis.

All S and V class individuals are viable at the end of the hibernation season. E class individuals are also assumed to be viable, and recover (i.e. return to the S class) with probability $a_1$. E class individuals that do not recover stay in the E class for the rest of the summer season, but do not progress into the I class until the next hibernation season. I class individuals have probability $\varepsilon$ of being viable at the end of the hibernation season. Non-viable I class individuals die off the first day of summer. Viable I individuals recover with probability $a_2$. All classes of individual experience naturality mortality at rate $\mu$.

Ordinary summer phase population dynamics involve no movement of individuals between classes: E and I individuals do not recover, S individuals do not become infected, and no individuals enter or leave the V class. The only force acting on individuals is natural mortality. All summer phase

days are ordinary, except for the first day of summer, the birth-pulse day, and the vaccination day.

$$S_t = e^{-\mu} S_{t-1} \tag{4a}$$

$$E_t = e^{-\mu} E_{t-1} \tag{4b}$$

$$I_t = e^{-\mu} I_{t-1} \tag{4c}$$

$$V_t = e^{-\mu} V_{t-1} \tag{4d}$$

As in Meyers model, a logistical birth pulse occurs on the 47th day of the summer phase. The birth pulse is modelled as follows:

$$S_t = e^{-\mu}(S_{t-1} + \frac{1}{2} b N_{t-1}(1 - \frac{N_{t-1}}{K_{Ml}})) \tag{5a}$$

$$E_t = e^{-\mu} E_{t-1} \tag{5b}$$

$$I_t = e^{-\mu} I_{t-1} \tag{5c}$$

$$V_t = e^{-\mu} V_{t-1} \tag{5d}$$

All individuals, regardless of disease class, are assumed to be capable of reproduction. All new individuals enter the S class, and natural mortality still acts on all classes during the birth pulse day. $b$ represents the proportion of female bats that give birth annually. $K_{Ml}$ is the environmental carrying capacity of *M. lucifugus*.

Throughout the summer season, the environmental reservoir follows continuous-time growth dynamics. Because the disease does not progress in bats, it is assumed that bats do not shed spores that contribute to the environmental reservoir. As such, environmental reservoir dynamics are simpler in the summer phase than in the hibernation phase:

$$\frac{dP}{dt} = \eta P(1 - \frac{P}{K_{Pd}}) \tag{6a}$$

## 3.3 Modelling Interventions

This thesis investigates the efficacy of three proposed interventions: vaccination against WNS; microclimate modification of hibernacula; and fungicidal treatment of hibernacula. Each intervention was interpreted in the context of this relatively simple model with the known epidemiology of WNS in mind; as such, I believe the analyses conducted here provide useful insight into the real-life efficacy of these interventions, should they be implemented in the field.

In the single-hibernaculum model, each intervention was analyzed at a range of intensities $\alpha$, between 0 (no intervention applied to the hibernaculum) and 1 (maximum intervention intensity). It is difficult to predict at this stage exactly what level of intervention intensity is most true-to-life; however, it is likely somewhere in between 0 and 1. Consider as an example fungicidal treatment of hibernacula: it is unlikely that fungicidal treatment will eliminate all free-growing *Pd* (represented by an intervention intensity of 1), but neither will fungicidal treatment fail to eliminate any *Pd* (represented by an intervention intensity of 0). The real intensity of the intervention will depend on the quality of equipment used, environmental considerations like temperature and humidity, and the internal topography of the cave in question. These considerations lie outside the scope of this model, but merit the readers awareness.

### 3.3.1 Vaccine Intervention

The vaccine intervention model used here was inspired by an unpublished manuscript developed by Alex Capaldi and students at Valparaiso University[4]. I model the vaccine intervention by introducing a fourth class of individual, the V (vaccinated) class. I assume that immunity, once attained, lasts for life: individuals that enter the V class never return to the S class. The model could easily be modified to incorporate finite-length immunity; to acknowledege this potential, I include parameter $\lambda$ in the equations below. Individuals in the V class cannot move into the E or I classesthey are not affected by the environmental reservoir of *Pd*, nor by the presence of other infected bats. The only way an individual can leave the V class is by natural mortality. Bats enter the V class through an annual vaccination pulse, delivered each summer the day after the birth

pulse. Vaccination pulse dynamics are modelled as follows:

$$S_t = e^{-\mu}((1 - \nu e^{-\lambda})S_{t-1} + (1 - e^{-\lambda})V_{t-1}) \tag{7a}$$

$$E_t = e^{-\mu}E_{t-1} \tag{7b}$$

$$I_t = e^{-\mu}I_{t-1} \tag{7c}$$

$$V_t = e^{-\mu}(\nu e^{-\lambda}S_{t-1} + e^{-\lambda}V_{t-1}) \tag{7d}$$

$$\alpha * \nu \tag{8a}$$

Here, $\nu$ represents the proportion of S bats that are vaccinated each vaccination pulse, and can take on values between 0 and 1. This parameter determines the intensity of the intervention. $\lambda$ is the rate of immunity loss; for all analyses here, I have set $\lambda$ equal to zero, meaning that vaccinated bats retain immunity for life. I include $\lambda$ in this set of equations to demonstrate the potentiality of temporally finite vaccine scenarios; any implementation of this model with a nonzero $\lambda$ value would require all other dynamcis equations to account for immunity loss as well by appropriately including the paramter $\lambda$. I have omitted $\lambda$ from other dyamics equations for simplicity. Note that only bats from the S class may enter the vaccinated class. Bats in the E and I classes are assumed to have already developed an immune response to the disease, rendering a vaccine ineffectual.

### 3.3.2 Microclimate Intervention

I model the microclimate intervention by scaling the rate of disease-induced mortality, $\delta$. It is assumed that the primary impact of creating localized cool regions inside hibernacula will be to slow the growth of *Pd*. It is understood that this will primarily result in longer lifespans for infected bats, or, alternatively, in a smaller rate of disease-induced mortality. Note that the rate of disease-induced mortality is related to the probability of post-hibernation viability of infected bats, $\varepsilon$, by the following equation (the derivation of this relationship is outlined in the Electronic Supplementary Material for Meyer 2016):

$$\varepsilon = \frac{1}{600\ \delta + 1} \tag{9a}$$

Thus, an adjustment of $\delta$ necessitates an inverse shift in the value of $\varepsilon$. We model the intervention intensity as follows:

$$(1 - \alpha) * \delta \tag{10a}$$

$$\varepsilon = \frac{1}{600\ (1 - \alpha)\delta + 1} \tag{10b}$$

### 3.3.3 Fungicide Intervention

I model the fungicide intervention by scaling the environmental carrying capacity for free-living *Pd*, $K_{Pd}$. Initially, I presumed to include a fungicide treatment pulse during the summer time which would eliminate the current environmental *Pd* reservoir but leave $K_{Pd}$ unaffected. However, after observing the rapid rate at which free-growing *Pd* reached carrying capacity, I determined that the environmental reservoir would quickly recover following this type of fungicidal treatment, rendering this intervention ineffectual. Any fungicidal treatment that might significantly impact bat survival in a WNS-impacted hibernaculum would therefore need to have a persistent impact on the size of the free-growing *Pd* reservoir. This intervention could model a chemical treatment that persists in the hibernaculum environment to prevent the growth of *Pd*, or an intervention such as the removal of sediment which provides a growth medium for *Pd*. We model the intensity of the intervention with the following equation:

$$(1 - \alpha) * K_{Pd} \tag{11a}$$

Note that in the most intense version of the intervention I set $K_{Pd}$ = 0, indicating that there is no free-growing *Pd* in the hibernaculum. This eliminates a major avenue of disease transmission, leaving bat-to-bat transmission as the only avenue of disease spread.

## 3.4 Multi-Hibernaculum Modelling Strategies

In addition to modelling disease dynamics in a single hibernaculum, this thesis also addresses the spatial dynamics of WNS as it moves between hibernacula in a geographic region. One important consideration in developing a spatial model is determining the mechanism of disease movement through space. Previous publications (e.g. Maher et al 2012) have expressed disease spread through modified simple-diffusion models. Meteyer et al 2009 demonstrated that WNS can be spread through bat-to bat contact, but that airborne transmission did not appear to be a significant mechanism of disease spread. Others (Frick 2015) have suggested the importance of human activity in facilitating the rapid spread of *Pd* in the U.S.

The model employed here assumes that infected bats are the primary vector of disease transmission between hibernacula. At the end of the hibernation season, not all infected and exposed bats clear their WNS infection before entering the summer season. Although many gaps exist in our current understanding of M. Lucifugus ecology, it is thought that bats return each year to the same hibernacula with high fidelity. Here we assume that most, but not all, bats return to the same hibernaculum. Some will return to different hibernacula than the ones they departed from the previous hibernation season. One small subset of these migrant bats consists of those bats that have not fully cleared the infection. When an infected bat migrates to a naive hibernaculum, it effectively spreads the infection to the naive bat population.

Here I describe a geographic space consisting of a twenty hibernaculum by twenty hibernaculum square grid, including a total of 400 hibernacula. Each hibernaculum in this grid follows dynamics identical to those described above, with a few minor modifications (described below). Hibernacula in the grid are labelled according to a two-coordinate system; thus, hibernaculum (1,1) represents the hibernaculum in the lower left corner of the grid.

The populations of each hibernaculum in the hibernaculum grid exist in isolation of one another, save for the final day of the year. It is assumed that bat populations do not mix at all during the hibernation season. Bats from different hibernacula might well intermingle during the entirety of the summer roosting and swarming season, but since it is assumed that no disease transmission occurs during the summer phase, this intermingling is not epidemiologically significant. It becomes significant, however, if the intermingled bats do not return to their hibernacula of origin at

the beginning of the next hibernation season Thus, we model a single bat migration day as the final day of the summer phase. The proportion of bats that migrate between any two hibernacula in the grid is determined as a function of base migration ratio $\psi$ (here, 2%) and the distance between the two hibernacula in question:

Let $h_1(x_1, y_1)$ and $h_2(x_2, y_2)$ be hibernacula. Migration from $h_1$ to $h_2$ is managed by the following:

$$mig_{1,2} = X_1 * \frac{\psi}{\sqrt{(x_1 - x_2)^2 + (y_1 - y_2)^2}} \tag{12a}$$

$$\text{for } X_1 = S_1,\ E_1,\ I_1, \text{ and } V_1$$

2% of S, E, I, and V individuals in hibernaculum (1,1) will therefore migrate to hibernaculum (1,2) at the end of the summer season, but only 1% of each category of individual will migrate from hibernaculum (1,1) to hibernaculum (1,3).

All multi-hibernaculum scenarios were modeled across a period of five years. Every hibernaculum in the grid was given an initial population of 15,000, as in the single-hibernaculum scenarios, as well as an empty environmental reservoir of *Pd*. All populations began with 15,000 S individuals and zero E or I individuals, with the exception of hibernaculum (1,1), which began with a population of 14,999 S individuals and one I individual.

A simplifying assumption was applied to the summertime dynamics of the environmental reservoir for each hibernaculum: it was observed in the single-hibernaculum scenario that, once WNS was introduced to a hibernaculum at the beginning of the hibernation phase, the size of the environmental reservoir rapidly increased to carrying capacity, well before the end of the hibernation season. Thus, during the summer season, a hibernaculum would either have a saturated environmental reservoir or an empty environmental reservoir. I applied this observation and eliminated the dynamical system governing summertime P dynamics; I assumed that a hibernaculum had either an empty or saturated environmental reservoir.

## 3.5 Note on Paramter Values

The structure of this model is inspired almost totally by the model employed in Meyer et al 2016. With infrequent exceptions, parameter values in this model are taken directly from Meyer's

**Table 1: Values of parameters used in simulations of the model described in Section 3.**

| Parameter | | Value |
|---|---|---|
| $N_0$ | Initial bat population (Bats) | 15,000 |
| $\mu$ | Rate of natural mortality (Days$^{-1}$) | 1/(365*8.5) |
| $b$ | Proportion of female bats who give birth each year (Unitless) | 0.95 |
| $T_S$ | Duration of summer phase (Days) | 153 |
| $T_H$ | Duration of hibernation phase (Days) | 212 |
| $K_{Ml}$ | Carrying capacity of $M.lucifugus$ (Bats) | 18,082 |
| $\tau$ | Rate of progression from E to I (Days$^{-1}$) | 1/83 |
| $\delta$ | Rate of disease-induced mortality (Days$^{-1}$) | 1/60 |
| $\beta$ | Rate of infectious contact between bats (Bats$^{-1}$ Days$^{-1}$) | 0-2.25*10$^{-5}$ |
| $\phi$ | Rate of infection contact between bats and environment (CFUs$^{-1}$ Days$^{-1}$) | 0-1.2*10$^{-10}$ |
| $a1$ | P(post-hibernation recovery of E individuals) (Unitless) | 0.75 |
| $a2$ | P(post-hibernation recovery of viable I individuals) (Unitless) | 0.75 |
| $\varepsilon$ | P(post-hibernation viability of I individuals) (Unitless) | 1/11 |
| $K_{Pd}$ | Carrying capacity of $Pd$ in environmental reservoir (CFUs) | $10^{10}$ |
| $\eta$ | Natural growth rate of free-living $Pd$ (Days$^{-1}$) | 0.5 |
| $\omega$ | Rate of shedding of $Pd$ spores from I individuals (CFUs Bats$^{-1}$ Days$^{-1}$) | 50 |
| $\lambda$ | Rate of immunity loss (Days$^{-1}$) | 0 |
| $\nu$ | Proportion of susceptible bats vaccinated (Unitless) | 1 |
| $\psi$ | Basic migration ratio (Unitless) | 0.02 |

model, the derivation of which is outlined in the original paper's Electronic Supplementary Material. Parameter values are either informed by data, or reasonable approximations based on known epidemiology of WNS or standard disease-model assumptions.

This thesis introduces several new parameters in addition to the parameters dervied from Meyer's model; namely, this model includes parameters $\lambda$ (rate of immunity loss), $\nu$ (proportion of susceptible bats vaccinated), and $\psi$ (basic migration ratio), each of which is associated either with an intervention or the multi-hibernaculum model.

We adopt a standard assumption of infectious disease modelling with respect to the parameter $\lambda$ by assuming that immunity, once attained, is lifelong. Other literature explores vaccine-submodels with limited-length immunity.

The proportion of bats to be vaccinated each season, $\nu$, was selected to be 1. Namely, in the full-intensity vaccine intervention, all susceptible bats in a hibernating population are vaccinated. In practice, this paper explores the dynamics of the model under varying rates of vaccination; however, these various rates of vaccination are acheived by manipulating $\alpha$, the intervention intensity, not $\nu$.

The basic migration ratio $\psi$ was derived by reasonable approximation. No data exists, to my knowledge, that quantifies migration rates of *M lucifugus* between hibernacula. It is generally thought that bats return to the same hibernacula each hibernation season, which suggests a relatively low migration ratio. 2% was selected as a basic migration ratio so as to be small enough to reflect the real migration behavior of Little Brown Bats, but sufficiently large so as to serve as a susbtantive vector of disease transmission in my model.

# 4 Methods & Results

## 4.1 Establishment of 75% Mortality Curve

The first objective of this project was rigorous characterization of disease dynamics in a single hibernaculum. A defining feature of my single-hibernaculum analysis was the consideration of multiple possible parameter scenarios, where parameter uncertainty exists. Perhaps the two most significant parameters in my model for which significant uncertainty exists are $\phi$ and $\beta$, the rates of environment-to-bat and bat-to-bat disease transmission, respectively. Absence of clear disease transmission data means there is ambiguity whether bats primarily encounter *Pd* spores through to contact with infected compatriots or through contact with an spore-bearing surface in the hibernaculum. This suggests a wide array of possible combinations of $\phi$ and $\beta$ that characterize our model.

This analyses borrows a simplifying assumption from Meyer et al., who noted that population decline due to WNS is typically estimated to equal 75% two years after initial introduction of *Pd* [22][1]. I use this assumption to narrow the range of combinations of $\phi$ and $\beta$, selecting only those combinations which result in 75% mortality after two years of running the basic model, without interventions. To identify the combinations of values for which this condition was satisfied, I ran

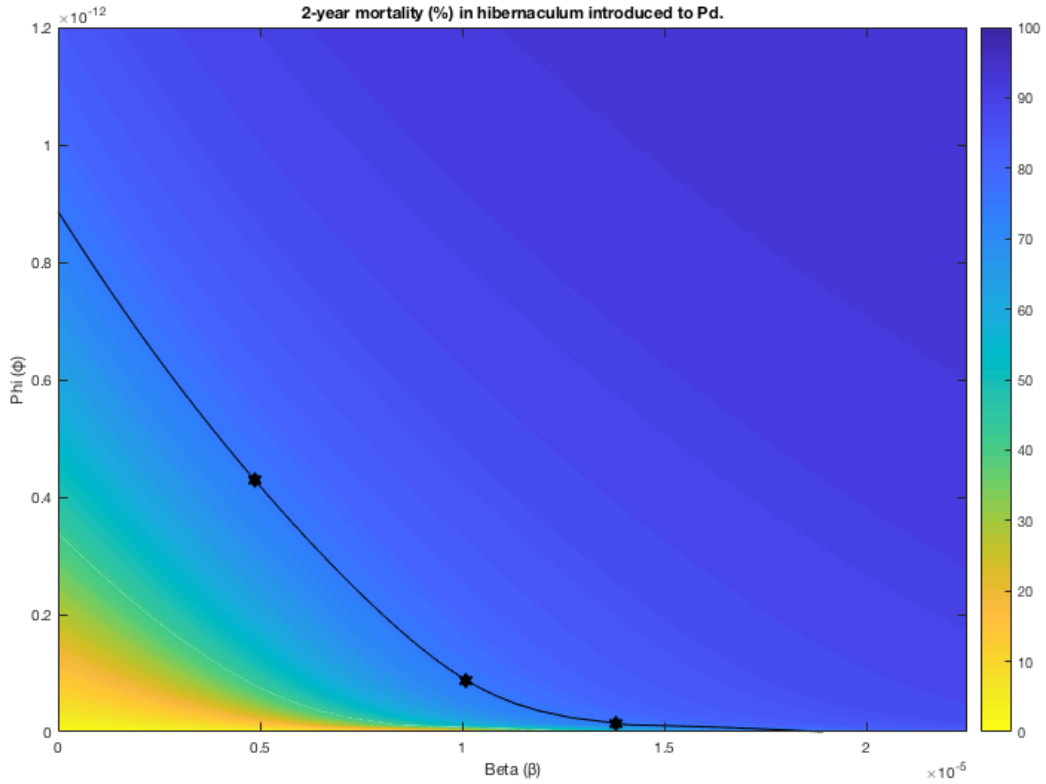


**Figure 1: Percent mortality after two simulated years for hibernacula with various $\phi$ and $\beta$ transmission rates. Contour highlights the combinations of $\phi$ and $\beta$ that resulted in 75% mortality; haxagrams mark the loci of Disease Cases 1-3, from left to right.**

the basic model for two years using $\beta$ values ranging from $0 - 2.25 * 10^{-}5$ and $\phi$ value ranging from $0 - 1.2 * 10^{-}12$.

I identified the pairs of parameters $\phi$ and $\beta$ which resulted in 75% mortality, which form a curve referred to here as the '75% mortality contour (Fig 1). In addition, I identified three particular pairs of parameters $\phi$ and $\beta$ along the 75% mortality contour that represented principle disease transmission scenarios, which I denoted as Case 1, Case 2, and Case 3. Transmission Case 1 represents transmission driven primarily by environment-to-bat contact; it is characterized by a relatively high value of $\phi$ and a relatively low value of $\beta$. Transmission Case 1 was identified by choosing a value of $\phi$ that caused 50% mortality after two years when $\beta$ was set at 0, and subsequently identifying a correspondent value of $\beta$ that located the case on the 75% mortality contour.

Transmission Case 2 represents transmission driven equally by environment-to-bat and bat-tobat contact; it is characterized by relatively moderate values of $\phi$ and $\beta$. Transmission Case 2 was iden-

tified by choosing values of $\phi$ and $\beta$ that caused equal percent mortality when the complementary parameter was set to 0, and which together cause 75% mortality.

Transmission Case 3 represents transmission driven primarily by bat-to-bat contact; it is characterized by a relatively high value of $\beta$ and a relatively low value of $\phi$. Transmission Case 3 was identified by choosing a value of $\beta$ that caused 50% mortality after two years when $\phi$ was set at 0, and subsequently identifying a correspondent value of $\phi$ that located the case on the 75% mortality contour.

**Table 2: Values of $\phi$ and $\beta$ that characterize disease cases 1-3.**

| Disease Case | $\phi$ | $\beta$ |
|---|---|---|
| Case 1 | $4.284 * 10^{-13}$ | $4.873 * 10^{-6}$ |
| Case 2 | $8.807 * 10^{-14}$ | $1.010 * 10^{-5}$ |
| Case 3 | $1.380 * 10^{-14}$ | $1.381 * 10^{-5}$ |

The entire 75% mortality contour was used to conduct critical analyses in the single-hibernaculum scenario; only Cases 1-3 were used to conduct analyses in the multi-hibernaculum scenario.

## 4.2 Single-Hibernaculum Scenario

Below are analysis results for all single-hibernaculum simualtions. The critical takeaway from this section is the much greater efficacy of the vaccine intervention relative to both the fungicide and microclimate interventions. Observe the 'blue box' phenomenon in Figs. 2 and 4, indicating massive mortality in most trials involving the fungicide and microclimate interventions. Contrast these plots with Fig. 6, which demonstrates a 'yellow box' phenomenon, indicative of widespread survival in a variety of infectiousness scenarios and intervention intensities.

### 4.2.1 Fungicide Intervention

To analyze each intervention in the single-hibernaculum scenario, I investigated the efficacy of each intervention across a range of infectiousness scenarios and time frames. The fungicide intervention is most effective in infectiousness scenarios that emphasize environment-to-bat trans-

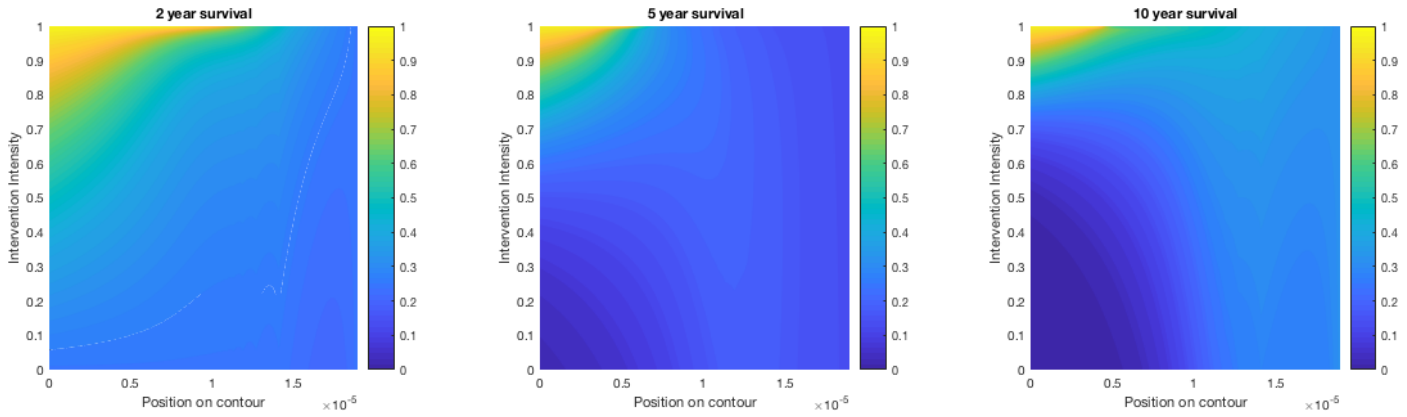


**Figure 2: Survival after 2, 5, and 10 years of simulated hibernacula under the fungicide intervention. Colorscale indicates survival as a percent of original colony size; y-axis is intervention intensity $\alpha$; x-axis is the $\beta$ value of the locus on the 75% mortality at which a particular simulation was run. Note high efficacy of the intervention only in upper left hand corner of plot, and deceasing efficacy over time.**

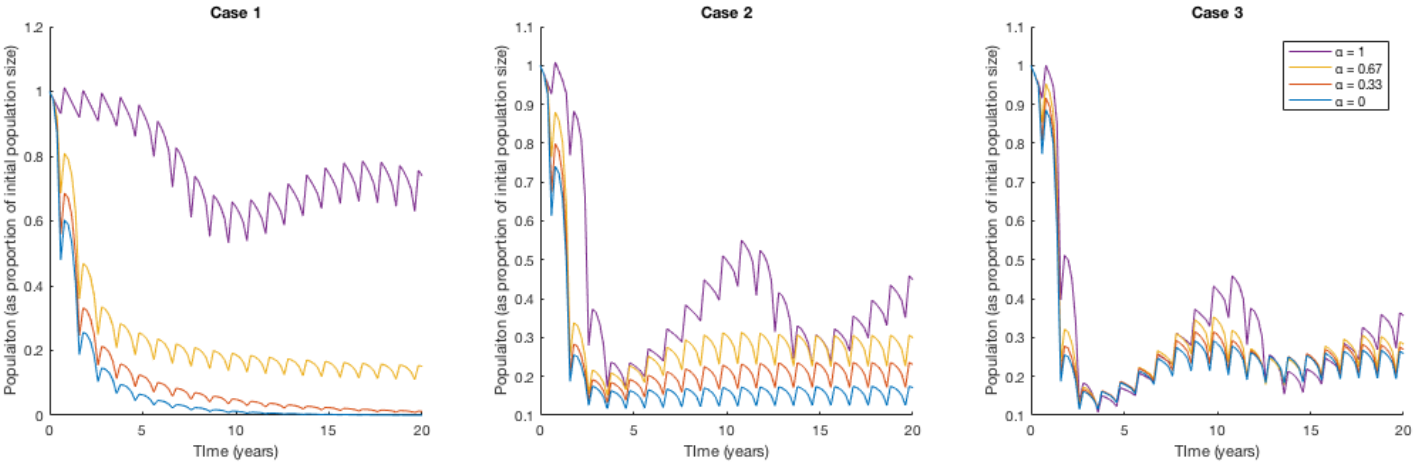


**Figure 3: Twenty-year population prediciton for a simulated hibernaculum under various fungicide intervention intensities $\alpha$ and various infectiousness scenarios.**

mission over bat-to-bat transmission, such as infectiousness Case 1. Even after twenty years, hibernacula assumed to follow infectiousness Case 1 treated with the full-intensity fungicide intervention exhibited approx. 75% survivalparticularly impressive when we consider that the non-intervention hibernaculum extirpated after twenty years in the same infectiousness scenario.

In hibernacula under infectiousness Cases 2 and 3, where bat-to-bat transmission plays a more central role in the propagation of the disease, the fungicide intervention is less effective, but still impactful. At maximal intensity, twenty-year survival was approx 50% for Case 2 and 35% for Case 3. These survival outcomes are significantly higher than non-intervention twenty-year survival outcomes in the same infectiousness scenarios, but clearly not as notably high as in infec-

tiousness Case 1.

### 4.2.2 Microclimate Intervention

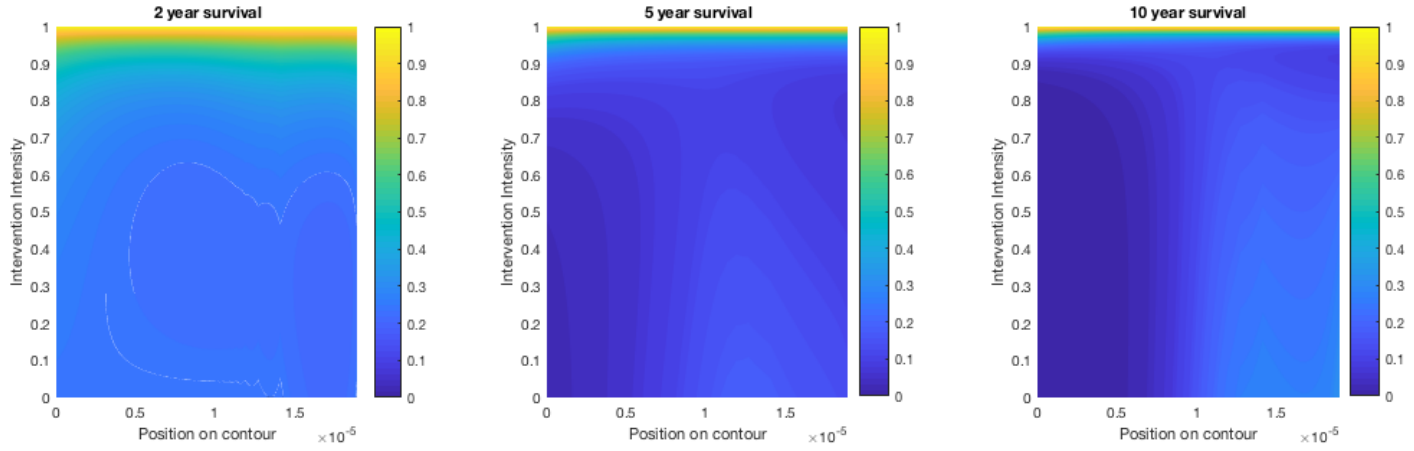


**Figure 4: Survival after 2, 5, and 10 years of simulated hibernacula under the microclimate intervention. Colorscale indicates survival as a percent of original colony size; y-axis is intervention intensity $\alpha$; x-axis is the $\beta$ value of the locus on the 75% mortality at which a particular simulation was run. Note high efficacy of intervention only along top rim of plot, and generally decreasing efficacy over time.**

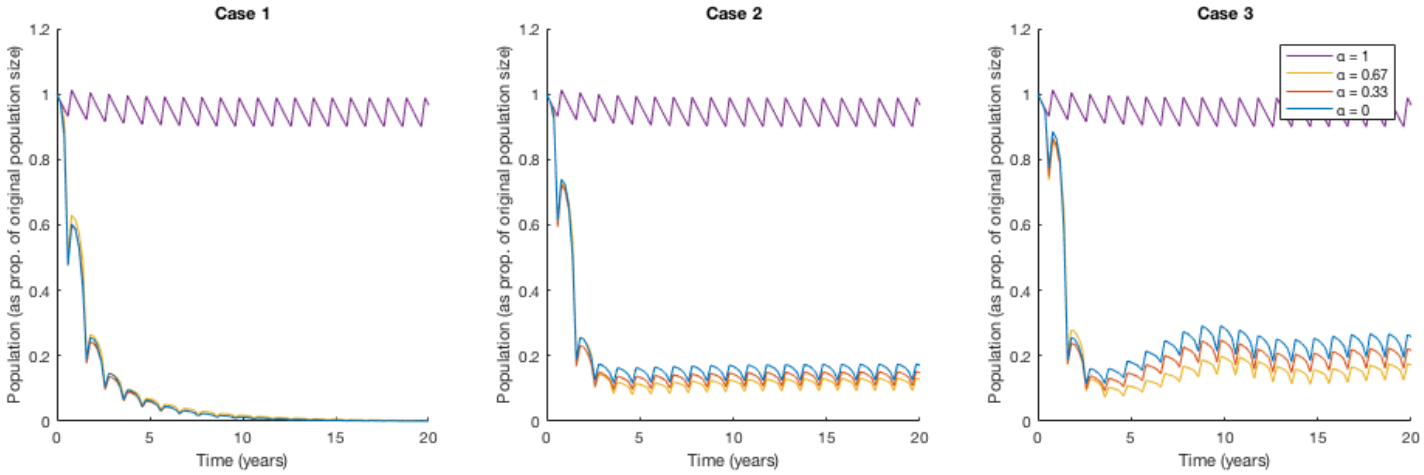


**Figure 5: Twenty-year population prediciton for a simulated hibernaculum under various microclimate intervention intensities $\alpha$ and various infectiousness scenarios.**

The microclimate intervention, according to this model, yielded little benefit to bat survival save for intervention intensities ranging approx. between $0.98 - 1.00$. For lower intervention intensities, populations subjected to WNS invasion experienced largely similar mortality to the non-intervention case. In high $\phi$, low $\beta$ scenarios, mortality was practically identical to the non-intervention case for intervention intensities between $0.00 - 0.90$. Conversely, in high bat-to-bat transmission scenarios, populations actually fared *worse* in higher-intervention intensity than in

lower-intervention intensity scenarios, up until about $\alpha = 0.95$. As in the non-intervention model, high bat-to-bat transmission scenarios established endemic equilibria; in general, higher intervention intensities translated to lower endemic equilibrium populations. Case 3 twenty-year survival for $\alpha = 0.67$ hibernacula was about 17.5% of initial population size, whereas Case 3 twenty-year survival for $\alpha = 0$ hibernacula was about 25% of initial population size.

### 4.2.3 Vaccine Intervention

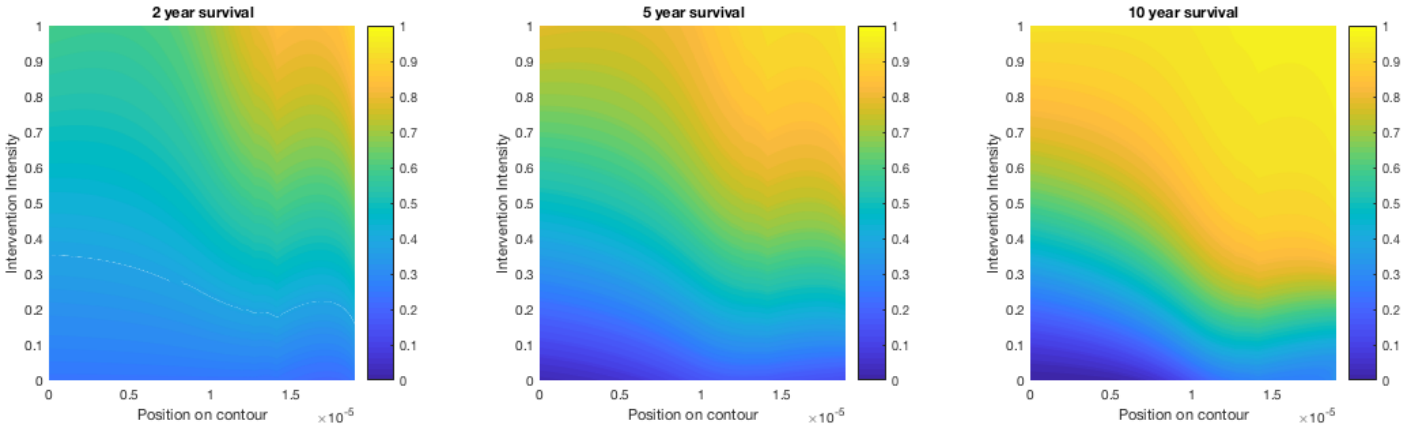


**Figure 6: Survival after 2, 5, and 10 years of simulated hibernacula under the vaccine intervention. Colorscale indicates survival as a percent of original colony size; y-axis is intervention intensity $\alpha$; x-axis is the $\beta$ value of the locus on the 75% mortality at which a particular simulation was run. Note 'yellow box' phenomenon which denotes widespread efficacy of intervention, that generally increases over time.**

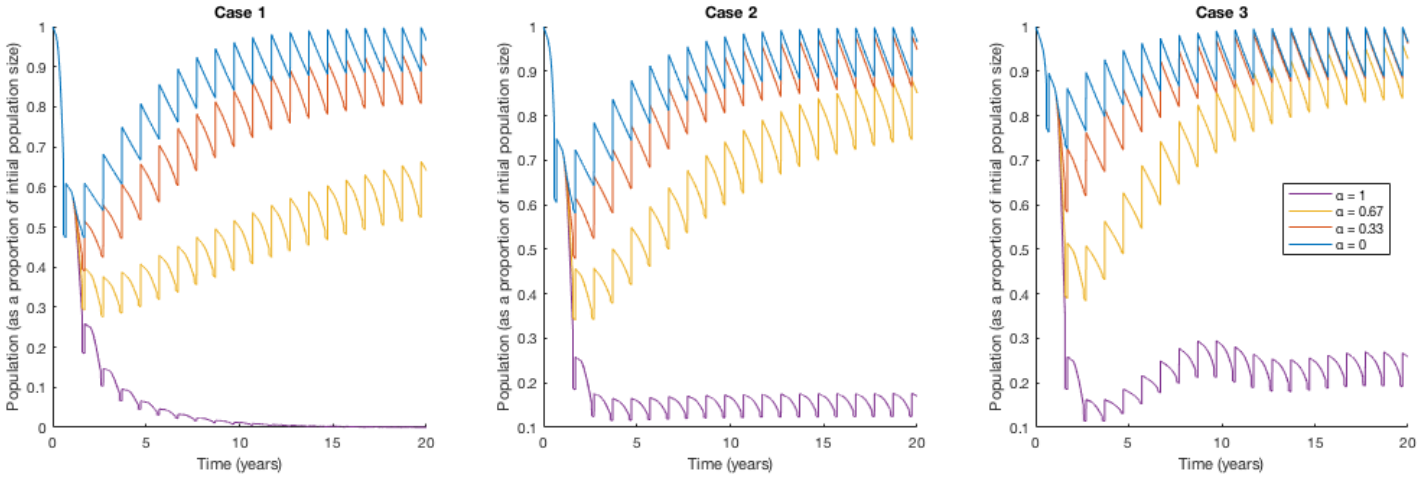


**Figure 7: Twenty-year population prediciton for a simulated hibernaculum under various vaccine intervention intensities $\alpha$ and various infectiousness scenarios.**

The vaccine intervention was, far-and-away, the most successful of the three interventions in

the single-hibernaculum scenario. Even for infectiousness scenarios at the leftmost extremity of the 75% mortality contourthat is, maximally environment-to-bat driven infectiousness scenarios, where populations quickly extirpate in the non-intervention scenariorelatively low intervention intensities between $0.20 - 0.25$ were sufficient to prevent extirpation. Success was even greater in bat-to-bat driven infectiousness scenarios like Case 3: for intervention intensities between $0.50 - 1.00$, populations were between 90%-100% of original population size after ten years; that is to say, these population were practically unaffected by WNS under even a moderately intense annual vaccination program. Populations only extirpated for primarily environment-to-bat driven infectiousness scenarios with intervention intensities below 0.20.

## 4.3 Multi-Hibernaculum Models

### 4.3.1 Setting Up the MHM Analysis

The analysis conducted for the multi-hibernaculum scenario was highly multi-dimensional. I sought to characterize WNS dynamics under a variety of intervention frequencies, infectiousness scenarios, and spatial distributions of applied interventions. Data was collected for the multi-hibernaculum scenarios in trials; for each unique combination of parameters, a single trial was conducted, amounting to 405 total trials.

Each trial consisted of 250 five-year simulations of the multi-hibernaculum model. In each simulation, a randomly identified subset of the 400 hibernacula in the hibernaculum grid were selected for application of intervention. The number of hibernacula chosen for intervention application was, variously: 20, 40, 60, 80, or 100. Thus, in the maximal intervention-frequency scenario, fully 25% of hibernacula in the grid were selected for intervention application.

Three varieties of spatial distribution of interventions were examined: random, corner-focused, and center-focused. This variation was intended to explore whether a particular spatial emphasis of intervention in the center or the periphery of a naive geographic region might positively impact regional population retention following the invasion of WNS. In the random scenario, hibernacula were selected for intervention indiscriminately across the grid. In the corner-focused, the first half of hibernacula were selected at random within the grid, and the second half were selected

randomly in corner regions defined by coordinates (x,y) in the following ranges:

$$x \leq 5 \cup 16 \leq x \tag{13a}$$

$$y \leq 5 \cup 16 \leq y \tag{13b}$$

In the center-focused scenario, the first half of hibernacula were selected at random within the grid, and the second half were selected randomly in a center region defined by coordinates on the following ranges:

$$6 \leq x \leq 15 \tag{14a}$$

$$6 \leq y \leq 15 \tag{14b}$$

Additionally, this thesis explores three different migration scenarios. Because relatively little is known about the migration behavior of Little Brown Bats, I sought to characterize several possible migration scenarios: nearest-neighbor migration, local migration, and global migration. In the nearest-neighbor migration scenario, bats migrate only between immediately adjacent hibernacula, not counting diagonally adjacent hibernacula. In the local migration scenario, bats migrate between hibernacula if the hibernacula lie within five grid-units of one another; otherwise, no migration occurs. In the global migration scenario, bats from each hibernaculum migrate to every other hibernaculum in the grid. In all migration scenarios, bats migrate according to equation 12. In each trial, only one intervention was applied: vaccine, microclimate, or fungicide. At no point

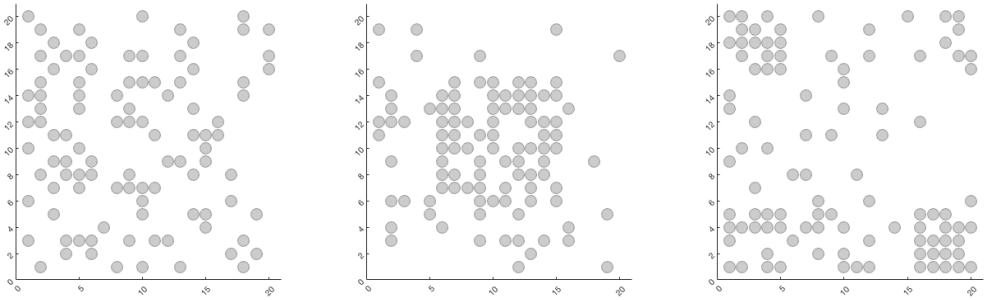

**Figure 8: Examples of the three different intervention distributions: random (left), center-focused (middle), and corner-focused (right).**

did I investigate the dynamics resulting from combined interventions; it is the primary goal of this thesis to characterize the relative efficacy of each individual intervention. Furthermore, each trial assumes that interventions are applied at maximal intensity ($\alpha = 1$).

The migration model was implemented with a minor simplifying assumption, such that natural mortality does not act on any population during the migration pulse day. The error introduced by this assumption should be small, since it only impacts the model on one out of every 365 simulated days.

To reiterate, the MHM analysis constitutes an exploration of: three infectiousness scenarios, three migration types, three intervention types, three intervention distributions, and five intervention frequencies. In the next section, I attempt to concisely summarize the generated data.

It is important to note a shortcoming of this migration model which emerges in particular in the global migration scenario. Because each hibernaculum sends portions of its population to each of the other 399 hibernacula in the grid during each migration pulse, highly interconnected hibernacula may send a large proportion of their population away during each migration pulse. This effect is most visible in the hibernacula at the center of the grid, which actually send a negative proportion of their population away during each migration pulse. There is no meaningful real-world interpretation of this dynamic. It is important to remember that mathematical models are only approximations of realitylimited in scope, not universally reflective of actual system dynamics, but still very informative if correctly interpreted.

### 4.3.2 MHM Analysis Results

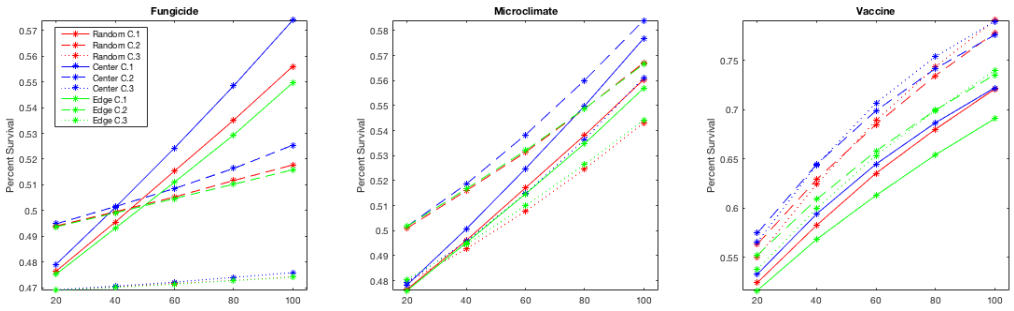


**Figure 9: Summary of data for all simulations involving local migration. All x-axes indicate the number of intervention hibernacula. Colors of lines/points indicate intervention distribution: red indicates random; blue indicates center-focused; green indicates edge or corner focused. Solid lines indicate infectiousness Case 1; dashed lines indicate Case 2; dotted lines indicate Case 3. In all cases, plotted points are averages of data from 250 simulations. Percent survival refers to the proportion of the total population across all hibernacula that remains after five simualted years.**

Here I will consider the MHM model results in three distinct sections: local migration scheme results, global migration scheme results, and a cross-comparison of results from all three migration

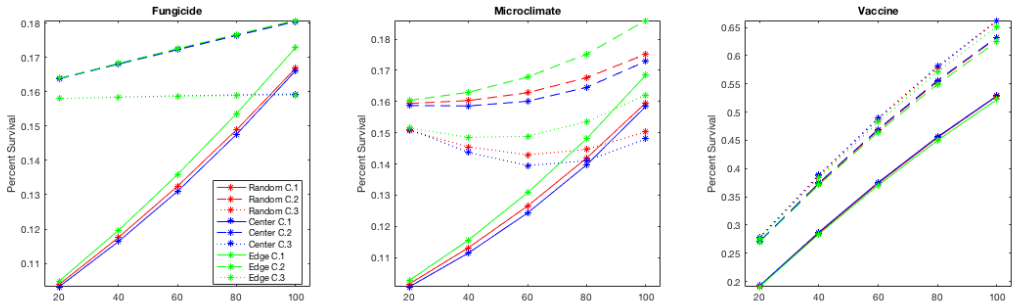


**Figure 10: Summary of data for all simulations involving global migration. All x-axes indicate the number of intervention hibernacula. Colors of lines/points indicate intervention distribution: red indicates random; blue indicates center-focused; green indicates edge or corner focused. Solid lines indicate infectiousness Case 1; dashed lines indicate Case 2; dotted lines indicate Case 3. In all cases, plotted points are averages of data from 250 simulations. Percent survival refers to the proportion of the total population across all hibernacula that remains after five simualted years.**

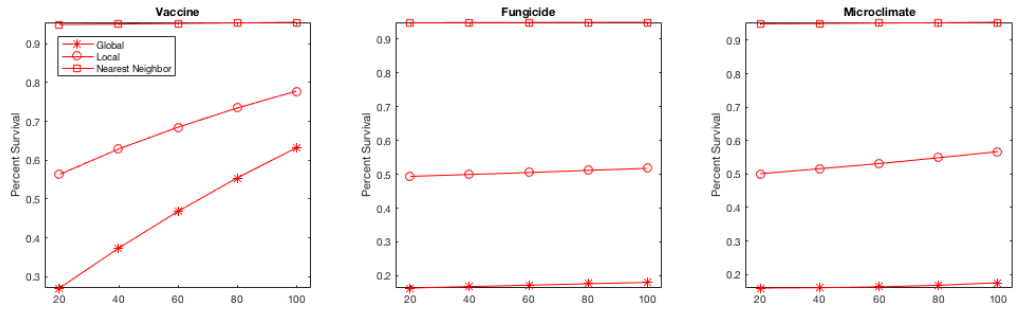


**Figure 11: Summary of data for simulations involving infectiousness Case 2 and random intervention distribution. All x-axes indicate the number of intervention hibernacula. Shape of marker indicates migration pattern: star indicates global migration, circle indicates local migration, and square indicates nearest-neighbor migration. In all cases, plotted points are averages of data from 250 simulations. Percent survival refers to the proportion of the total population across all hibernacula that remains after five simualted years.**

scenarios. I omit direct discussion of the nearest-neighbor migration scheme results, as the NN migration scheme did not allow for widespread progression of the disease during the five simulated years. At the end of the simulated period, the infection had only reached a small fraction of modelled hibernacula; a more robust portrait of NN dynamics would require a longer simulations, which transcend the computational and temporal resources available for this project.

In the local migration scheme trials, several trends emerge. Results are summarized in Fig. 9, which plots the data for all local migration scheme trials. Presented data averages results across the 250 simulations for each trial. Predictably, the greatest increases in net survival across the range of intervention hibernacula for the fungicide intervention occur for Case 3 trials, which emphasize environment-to-bat transmission. Microclimate and vaccine intervention trials do not demonstrate any difference in rate of survival increase among the three infectiousness scenarios,

nor among the three intervention schemes (that is, all lines are of equal slope in the microclimate and vaccine trials). Note that among trials with comparable infectiousness parameters, the center-focused trials consistently demonstrated higher rates of survival than edge-focused or random intervention distribution trials. Also note the difference in y-axis scales between the three plots: maximum survival among vaccine-intervention trials is, in fact, significantly greater than maximum survival among fungicide and microclimate interventions.

The global migration scheme trials reveal some similar trends to the local-scheme trials and some novel trends. Results are summarized in Fig. 10, which presents data for the global migration trials in similar fashion to FIg. 9. As with the local migration scheme, the vaccine intervention yields significantly higher rates of net population survival than do the fungicide or microclimate interventions. Note that the nature of the global migration scheme is such that the disease has been introduced to every simulated hibernaculum after the first migration pulse. Because of this high interconnectivity of hibernacula, mortality rates are much higher on average for global migration trials than for local migration trials. Despite this, maximum survival rates among vaccine intervention trials in the global migration scenario are only approximately 14% lower than in the local migration scenario. In contrast to the local migration scheme, center-focused intervention distributions do not consistently result in higher rates of survival than other intervention distributions. Note the initial decrease in survival rates as intervention frequency increases for the microclimate intervention. This dynamic is curiously reminiscent of the single-hibernaculum dynamics for the microclimate intervention, which demonstrated increased mortality as intervention intensity increased.

Shown in Fig. 11 are survival outcomes for trials with random intervention distribution and infectiousness Case 2. These results demonstrate intuitively the relative rates of survival for nearest-neighbor, local, and global migration trials: nearest-neighbor migration trials demonstrated the highest rates of survival, followed by local migration trials, followed finally by global migration trials.

# 5 Discussion

From the results presented here, it is apparent that the vaccine intervention is the most promising of the three tested interventions. Among the three tested interventions, only the vaccine intervention successfully sustained an infected bat population in a variety of parameter conditions and intervention intensities.

The single-hibernaculum dynamics for each of the three interventions makes sense according to the known dynamics of WNS. That is, a reasonable hypothesis can be developed to explain the efficacy outcomes of each of the three interventions.

The fungicide intervention was only effective for relatively high intervention intensities, and in parameter scenarios that emphasized environment-to-bat infection over bat-to-bat infection. It stands to reason that the fungicide intervention should only be effective in environment-to-bat transmission scenarios; the intervention only acts on the environmental reservoir of *Pd*, and would not be expected to increase survival if transmission is not primarily mediated by the environmental reservoir. It is surprising that fungicide intervention intensities as high as 0.7, even in highly environment-mediated infection scenarios, resulted in bat hibernaculum mortality as high as 80% after ten years. This suggests that the fungicide intervention will not facilitate significant increases in hibernaculum survival except if optimally implemented. In real-world scenarios it is often difficult to implement procedures perfectly (i.e. implement an intervention intensity of 1), which implies that it would be difficult to achieve significant increases in bat survival with the fungicide intervention.

The microclimate scenario is similarly limited in its effective implementability. For intervention intensities up to 0.95, survival outcomes in the single-hibernaculum scenario actually *worsened* as intervention intensities increased. This effect was most pronounced for predominantly bat-to-bat transmission scenarios. This stands to reason: a smaller $\delta$ Implies that bats will spend a longer time in the infectious class, which gives each infected bat a prolonged opportunity to infect susceptible bats. Although each individual infected bat lives longer, higher rates of infection translate to net increases in mortality for most intervention scenarios, relative to the non-intervention scenario. The conservation implications of this outcome are unmistakable: unless microclimates inside hibernacula can be perfectly maintained in the 0-5° range in which *Pd* growth is impossible

(perhaps achievable via climate-controlled artificial hibernacula, but likely quite difficult in naturally occuring caves), any attempted implementation of this intervention is likely to worsen the problem.

Only the vaccination intervention offered unwaveringly promising survival outcomes. In single-hibernaculum trials, populations generally declined during the first ten years of infection. Hibernacula treated with the vaccination intervention, however, uniquely demonstrated the inverse dynamic: populations actually *recovered* over time. Under many parameter and intervention intensity scenarios, populations treated with the vaccine intervention were actually more robust ten years after WNS introduction than two years after WNS introduction. These promising survival outcomes do not come without caveats: to begin, no successful vaccine for WNS has been developed to date, and we are likely several years away from an effective vaccine being introduced. Secondly, this model assumes an annual vaccination routine and lifelong immunity. Actual implementation of the intervention may not be feasible on an annual basis due to logistical constraints, and the vaccine (once developed) may not offer lifelong immunity. Further exploration of this intervention might involve biennial or triennial vaccination routines and non-lifelong immunity.

Results from the multi-hibernaculum model indicate similar efficacy profiles of the three interventions. Increases in the number of intervention hibernacula from 20 to 100 never yielded more than a 10% (of original population size) increase in net survival for the fungicide and microclimate interventions, whereas a similar increase in the number of intervention hibernacula for the vaccine intervention in some cases yielded net survival increases ¿30%. In the global migration scenario, the net survival values for highest-survival trial under the vaccine intervention exceeded those of the highest-survival trials under the fungicide and microclimate interventions by more than 40% of original population size. I conclude from these results that, of the three proposed interventions, the vaccine intervention alone demonstrates substantial capacity to preserve local and regional bat populations following the invasion of WNS.

The marked differences in survival outcomes between nearest-neighbor, local, and global migration trials (see Fig. 11) are attributable to rates of disease spread: more interconnected hibernacula transmit the disease between distinct populations more quickly, resulting in increased net mortality after five simulated years. We might characterize the chosen time frame of analysis as relatively short. In longer-run simulations, the distinct outcomes for the three migration schemes

would likely converge.

Although this research presents a compelling case for the development of a WNS vaccine, future iterations of this model could present a more nuanced profile of WNS dynamics under various intervention scenarios. In particular, future WNS models based on the present research might incorporate:

- A modified migration model. The current migration scheme incorporates some non-realistic dynamics, including negative self-migration values for the central hibernacula in the global migration scenario. Amendments to the migration scheme presented here might be limited to a simple reduction of $\psi$, the basic migration rate, or might go so far as to introduce stochastic and random dynamics so that migration rates fluctuate from season to season. Stochastic dynamics might present a more realistic portrait of WNS dynamics, as stochastic elements could account for random pathogen-spreading events such as human spelunkers translocating spores between caves. A maximally-accurate migration model might look like the local migration scheme presented here, with a reduced basic migration rate to and additional random pathogen-spreading events.

- Modifications to current migration schema to prevent fractions of bats from migrating. In its current form, migration of S,E, I, and V class bats is managed via constant rates. That is, if a hibernaculum contains a single I class bat during a particular migration pulse, then 0.02 bats will migrate to each of the adjacent hibernacula, thereby spreading WNS to each of these hibernacula. In this way, the current migration schema might overestimate the rate of disease spread between hibernacula. A more effective implementation of the model might correct for this error by setting a 1-lower-bound minimum for migration of bats from each infectiousness class.

- Variable time spans in the multi-hibernaculum model. Due to time and processor constraints, I ran each of my multi-hibernaculum models for five years. Both spatial and local disease dynamics are still far from a long-term steady-state after only five years of WNS infection. It would be informative to investigate this model across longer time intervals, such as ten or twenty years.

- A stochastic analog model. We can interpret the dynamical-system model presented here

instead as a system characterized by random encounters with probabilistic outcomes during each disease season. Reinterpreting this model as a probabilistic model that implements binomial distributions to determine survival outcomes of individual bats could provide valuable insight into the probable survival outcomes of regional populations in the years subsequent to WNS invasion. Specifically, the single-hibernaculum model indicates that populations often plunge very close to zero before rebounding towards an endemic equilibrium. If populations are highly likely to become extinct during these bottleneck events (a dynamic that would be revealed by stochastic models), conservations might be compelled to implement different interventions than if populations are assumed to persist through a dramatic bottleneck event.

- Investigation of combined interventions. This thesis does not investigate the possibility of emergent dynamics when two or more interventions are combined.

This work represents a preliminary effort to model the spatial dynamics of WNS, to the end of understanding how effectively different proposed interventions could prevent WNS-induced mortality. It is my sincere hope that this research will help inform the conservation biologists and volunteers who are working prevent regional extirpation or total extinction of bat species due to WNS. Moreover, I hope this work can serve as inspiration for future applied mathematical research into WNS and related diseases.

# 6 Acknowledgments

First and foremost, I would like to thank my thesis advisor, Prof. Julie Blackwood, for making this project possible. You have been a consistent source of positivity, kindness, inspiration, and energy. Many thanks.

Thanks to Prof. Stewart Johnson for acting as a second reader of this thesis, and for providing valuable criticism.

Thank you to Guy Randall and Adam Wang for helping me navigate the technical difficulties of implementing and analyzing my models on the Williams College computer system.

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Last but not least, thank you to all of my friends and family who helped and supported me through this project. You all know I couldnt have made it through an endeavor of this magnitude without your love.

Many thanks to all!

# A Source Code

## A.1 DeclareParametersMHM Function Code

This code describes the DeclareParametersMHM function.

```
% Code by JACKSON BARBER, Williams College '18|jdb3@williams.edu
% Written for his senior honors thesis
% Advisor: Julie Blackwood
% Last edited: 4/08/2018

% This function establishes the values of all parameters associated with
% the multi-hibernaculum model (MHM). It is designed for exclusive use
% with the MHM, not for the single hibernaculum model (SHM).

function r = DeclareParametersMHM(diseaseCase)

% LIST OF FIXED PARAMETERS
% add p. to parameters. Call 'p' in function to automatically load all
% parameters.

p = struct;

p.mu = 1/(8.5*365);          % Rate of natural mortality
p.b = 0.95;                  % Proportion of females who give birth
p.Kml = 18082;               % Carrying capcity of bats
p.tau = 1/83;                % Rate of passage from latency (E -> I)
p.delta = 1/60;              % Rate of disease-induced mortality
p.a1 = 0.75;                 % Prob. of recovery of E bat
p.a2 = 0.75;                 % Prob. of recovery of viable I bat
p.epsilon = 1/11;            % Prob. of viability of I bat
p.Kpd = 10^10;               % Carrying capacity of Pd in envi. res.
p.eta = 0.5;                 % Growth rate of Pd in envi. res.
p.omega = 50;                % Rate of Pd shedding by I bats.

p.lambda = 0;                % Rate of loss of immunity (V -> S)
p.nu = 0;                    % Proportion of S bats vaccinated each year

p.psi = 0.02;                % Mig. rate btwn. adjacent hibernacula

% SET DISEASE CASE
if diseaseCase == 1                % environment-to-bat
p.beta = 4.873 * 10^-6;
p.phi = 4.284 * 10^-13;

elseif diseaseCase == 2            % equal
p.beta = 1.010 * 10^-5;
p.phi = 8.807 * 10^-14;

elseif diseaseCase == 3            % bat-to-bat
```

```
p.beta = 1.381 * 10^-5;
p.phi = 1.380 * 10^-14;
end

% SET SIMULATION LENGTH
p.yearsSim = 5;

% Set function return value equal to the struct p.
r = p;

end
```

## A.2 Hibernaculum Class Code

This code described the hibernaculum class, an important component of my single-hibernaculum structure.

```
% Code by JACKSON BARBER, Williams College '18|jdb3@williams.edu
% Written for his senior honors thesis
% Advisor: Julie BLackwood
% Last edited: 4/08/2018

% This class describes a hibernaculum infected with WNS, according to the
% model developed for the author's 2018 senior thesis.

classdef Hibernaculum < handle

properties

% Organization of MasterVector: (t S E I V P N)
MasterVector;
currentDay = 1;
currentIndex = 1;
params;

end

methods

% Constructor method describes the creation of a hibernaculum
function this = Hibernaculum(p)
this.MasterVector = zeros(2000, 7);
this.params = p;

end

% Resets the time properties currentDay and currentIndex, and sets
% the inital population values S,E,I,and V.
function SetInitial(this,S,E,I,V)
```

```
this.currentDay = 1;
this.currentIndex = 1;

this.MasterVector = zeros(2000, 7);
this.MasterVector(1,:) = [1 S E I V 0 S+E+I+V];

end

% Simulates a single hibernation season
function Hibernate(this)
% Run ode45 for the hibernaiton season for S,E,I,V, and P
if this.params.Kpd ~= 0
[~,z] = ode45(@HFcnSimplifiedModel1MHM, (0:212),...
this.MasterVector(this.currentIndex,2:6), [], this.params);

else
[~,z] = ode45(@HFcnSimplifiedModel1MHMKpdZero, (0:212),...
this.MasterVector(this.currentIndex,2:6), [], this.params);
end

% Update currentDay & currentIndex
this.currentDay = this.currentDay + 212;

this.currentIndex = this.currentIndex + 1;

% Update MasterVector to include final calculated pop values
% after hibernation season
tMax = size(z,1);

this.MasterVector(this.currentIndex,2:6) = z(tMax,:);

this.MasterVector(this.currentIndex,1) = this.currentDay;

% Calculate the N values for the hibernation season UPDATE THIS
this.MasterVector(this.currentIndex,7) = ...
this.MasterVector(this.currentIndex,2) + ...
this.MasterVector(this.currentIndex,3) + ...
this.MasterVector(this.currentIndex,4) + ...
this.MasterVector(this.currentIndex,5);

end

% Simulates the first day of the summer phase
function SummerDay1(this)
% Bats
FirstDayS = exp(-this.params.mu) * [1 this.params.a1...
this.params.epsilon*this.params.a2...
(1 - exp(-this.params.lambda)) ; ...
0 1-this.params.a1 0 0; ...
0 0 this.params.epsilon*(1-this.params.a2) 0; ...
0 0 0 exp(-this.params.lambda)];

popVec = this.MasterVector(this.currentIndex,2:5);
```

```
popVec = (FirstDayS * popVec')';
this.MasterVector(this.currentIndex+1,2:5) = popVec;

% Pd
if this.MasterVector(this.currentIndex,6) == 0
this.MasterVector(this.currentIndex + 1,6) = 0;
else
this.MasterVector(this.currentIndex + 1,6) = this.params.Kpd;
end

% Update N
this.MasterVector(this.currentIndex + 1,7) = ...
this.MasterVector(this.currentIndex + 1,2) + ...
this.MasterVector(this.currentIndex + 1,3) + ...
this.MasterVector(this.currentIndex + 1,4) + ...
this.MasterVector(this.currentIndex + 1,5);

% Update currentDay & currentIndex
this.currentDay = this.currentDay + 1;

this.currentIndex = this.currentIndex + 1;

% Update time column
this.MasterVector(this.currentIndex,1) = this.currentDay;

end

% Simulates a regular summer day
function SummerRegularDay(this)
% Bats
OrdinaryDayS = exp(-this.params.mu) * [1 0 0  ...
(1-exp(-this.params.lambda)) ; ...
0 1 0 0 ; ...
0 0 1 0 ; ...
0 0 0 (exp(-this.params.lambda))];

popVec = this.MasterVector(this.currentIndex,2:5);

popVec = (OrdinaryDayS * popVec')';
this.MasterVector(this.currentIndex+1,2:5) = popVec;

% Pd
if this.MasterVector(this.currentIndex,6) == 0
this.MasterVector(this.currentIndex + 1,6) = 0;
else
this.MasterVector(this.currentIndex + 1,6) = this.params.Kpd;
end

% Update N
this.MasterVector(this.currentIndex + 1,7) = ...
this.MasterVector(this.currentIndex + 1,2) + ...
this.MasterVector(this.currentIndex + 1,3) + ...
```

```
this.MasterVector(this.currentIndex + 1,4) + ...
this.MasterVector(this.currentIndex + 1,5);

% Update currentDay & currentIndex
this.currentDay = this.currentDay + 1;

this.currentIndex = this.currentIndex + 1;

% Update time column
this.MasterVector(this.currentIndex,1) = this.currentDay;

end

% Simulates summer birth pulse day
function SummerBirthPulse(this)
% Bats
N = this.MasterVector(this.currentIndex,7);

BirthDay = [1 0 0 (1-exp(-this.params.lambda)) ; ...
0 1 0 0 ; ...
0 0 1 0 ; ...
0 0 0 (exp(-this.params.lambda))];

popVec = this.MasterVector(this.currentIndex,2:5);

% actually executing the critical calculation here
popVec = exp(-this.params.mu)*((BirthDay * popVec')' + ...
[0.5*this.params.b*N*(1-(N/this.params.Kml)) 0 0 0]);

this.MasterVector(this.currentIndex+1,2:5) = popVec;

% Pd
if this.MasterVector(this.currentIndex,6) == 0
this.MasterVector(this.currentIndex + 1,6) = 0;
else
this.MasterVector(this.currentIndex + 1,6) = this.params.Kpd;
end

% Update N
this.MasterVector(this.currentIndex + 1,7) = ...
this.MasterVector(this.currentIndex + 1,2) + ...
this.MasterVector(this.currentIndex + 1,3) + ...
this.MasterVector(this.currentIndex + 1,4) + ...
this.MasterVector(this.currentIndex + 1,5);

% Update currentDay & currentIndex
this.currentDay = this.currentDay + 1;

this.currentIndex = this.currentIndex + 1;

% Update time column
this.MasterVector(this.currentIndex,1) = this.currentDay;
```

```
end

% Simualtes the summer vaccination pulse day
function VaccinationDay(this)
% Bats
VaccineDay = exp(-this.params.mu) * ...
[1-(this.params.nu*exp(-this.params.lambda)) ...
0 ...
0 ...
1-exp(-this.params.lambda); ...
0 1 0 0; ...
0 0 1 0; ...
(this.params.nu*exp(-this.params.lambda)) ...
0 ...
0 ...
exp(-this.params.lambda)];

popVec = this.MasterVector(this.currentIndex,2:5);

% actually executing the calculation
popVec = (VaccineDay*popVec')';

% Update mastervector with new pop values
this.MasterVector(this.currentIndex+1,2:5) = popVec;

% Pd
if this.MasterVector(this.currentIndex,6) == 0
this.MasterVector(this.currentIndex + 1,6) = 0;
else
this.MasterVector(this.currentIndex + 1,6) = this.params.Kpd;
end

% Update N
this.MasterVector(this.currentIndex + 1,7) = ...
this.MasterVector(this.currentIndex + 1,2) + ...
this.MasterVector(this.currentIndex + 1,3) + ...
this.MasterVector(this.currentIndex + 1,4) + ...
this.MasterVector(this.currentIndex + 1,5);

% Update currentDay & currentIndex
this.currentDay = this.currentDay + 1;

this.currentIndex = this.currentIndex + 1;

% Update time column
this.MasterVector(this.currentIndex,1) = this.currentDay;

end

% Sets the values of the parameters associated with each
% intervention. Default values are set in DeclareParametersMHM
% class, and correspond to no intervention.
function SetIntervention(this,Kpd,delta,nu)
```

```
this.params.Kpd = Kpd;

this.params.nu = nu;

this.params.delta = delta;
this.params.epsilon = 1 / (600 * delta + 1);

end

% Resets the values of beta and phi, the values that control the
% infectiousness scenario.
function SetBetaPhi(this,beta,phi)
this.params.beta = beta;
this.params.phi = phi;

end

% Returns the proportion of the original colony size that survives
% at the current moment in the simulation.
function r = PercentSurvival(this)
r = this.MasterVector(this.currentIndex,7)/15000;
end

% Returns the population size at the current moment in the
% simulation.
function r = Population(this)
r = this.MasterVector(this.currentIndex,7);
end

end

end
```

## A.3 HibernaculumGrid Class Code

```
% Code by JACKSON BARBER, Williams College '18|jdb3@williams.edu
% Written for his senior honors thesis
% Advisor: Julie BLackwood
% Last edited: 4/08/2018

% This class establishes an m x n grid of Hibernaculum class objects. This
% is an important component of the multi-hibernaculum model (MHM).

classdef HibernaculumGrid

properties
Value
migMatrix

end
```

```
methods

% Constructor method creates the hibernaculum grid, and creates the
% migration matrix, an mn * mn matrix which is used to manage the
% migration day dynamics.
function this = HibernaculumGrid(m,n,p)
if nargin == 3
this = HibernaculumGrid(m,n);
for i = 1:m
for j = 1:n
this(i,j).Value = Hibernaculum(p);

end
end

% ~~~~Create mn x mn migration matrix~~~~

this(1,1).migMatrix = zeros(m*n,m*n);

for i = 1:1:m*n
for j = 1:1:m*n
if i ~= j
isource = ceil(j/n);
jsource = j - n*(ceil(j/n)-1);
idest = ceil(i/n);
jdest = i - n*(ceil(i/n)-1);

idiff = abs(isource - idest);
jdiff = abs(jsource - jdest);

% OPTION 1: Global Migration

%                             this(1,1).migMatrix(i,j) = ...
%                                 1/(sqrt(idiff^2 + jdiff^2));

% OPTION 2: Nearest-Neighbor Migration

%                             if (idiff + jdiff) == 1
%                                 this(1,1).migMatrix(i,j) = 1;
%                             end

% OPTION 3: Local Migration (if Euclidean distance is < 5,
% then migration occurs according to OPTION 1.
% Else, no migration occurs.

%                             if sqrt(idiff^2 + jdiff^2) <= 5
%                                 this(1,1).migMatrix(i,j) = ...
%                                     1/(sqrt(idiff^2 + jdiff^2));
%                             end

end
end
end
```

```
% Scale the migration matrix according to the migration
% coefficient psi
this(1,1).migMatrix = ...
p.psi * this(1,1).migMatrix;

% Set the diagonal values of the migration matrix
for x = 1:1:m*n
this(1,1).migMatrix(x,x) = -sum(this(1,1).migMatrix(x,:));
end

this(1,1).migMatrix = this(1,1).migMatrix + eye(m*n);

end

end

% Sets the initial values of all hibernacula in the grid to 15000
% susceptible bats except for hibernaculum(1,1), which has an
% initial S population of 14999 and an initial I populaiton of 1.
function InitializeAll(this)
% Save grid dimensions
m = size(this,1);
n = size(this,2);

% Initialize all hibernacula with purely susceptible population
% of 15000
for i = 1:1:m
for j = 1:1:n
this(i,j).Value.SetInitial(15000,0,0,0);
end
end

% Set hibernaculum(1,1) to have one infected bat to begin with.
this(1,1).Value.SetInitial(14999,0,1,0);

end

% Simulates the migration day, and employs the migration matrix.
function SummerLastDay(this)
% Save grid dimensions
m = size(this,1);
n = size(this,2);

% Store S,E,I, and V values for each hibernaculum in a huge
% mn x 4 vector
popMatrix = zeros(m*n,4);

iterator1 = 1;
for i = 1:1:m
for j = 1:1:n
popMatrix(iterator1,:) = ...
this(i,j).Value.MasterVector ...
```

```
(this(i,j).Value.currentIndex,2:5);

iterator1 = iterator1 + 1;
end
end

% Execute the multiplication of migMatrix by each of the column
% vectors of popMatrix
for x = 1:1:4
popMatrix(:,x) = this(1,1).migMatrix * popMatrix(:,x);
end

% Set the next day of each hibernaculum equal to the newly
% calculated values.
iterator2 = 1;
for i = 1:1:m
for j = 1:1:n
% Update currentIndex & currentDay
this(i,j).Value.currentIndex = ...
this(i,j).Value.currentIndex + 1;

this(i,j).Value.currentDay = ...
this(i,j).Value.currentDay + 1;

% Update S,E,I, and V
this(i,j).Value.MasterVector ...
(this(i,j).Value.currentIndex,2:5) = ...
popMatrix(iterator2,:);

% Update N
this(i,j).Value.MasterVector...
(this(i,j).Value.currentIndex,7) = ...
this(i,j).Value.MasterVector...
(this(i,j).Value.currentIndex,2) + ...
this(i,j).Value.MasterVector...
(this(i,j).Value.currentIndex,3) + ...
this(i,j).Value.MasterVector...
(this(i,j).Value.currentIndex,4) + ...
this(i,j).Value.MasterVector...
(this(i,j).Value.currentIndex,5);

% Update time column
this(i,j).Value.MasterVector...
(this(i,j).Value.currentIndex,1) = ...
this(i,j).Value.currentDay;

% Pd
if this(i,j).Value.MasterVector(...
this(i,j).Value.currentIndex-1,6) == 0

this(i,j).Value.MasterVector(...
this(i,j).Value.currentIndex,6) = 0;
else
```

```
this(i,j).Value.MasterVector(...
this(i,j).Value.currentIndex,6) = ...
this(i,j).Value.params.Kpd;
end

iterator2 = iterator2 + 1;
end
end
end

% Simulates a full year of the multi-hibernaculum model for every
% hibernaculum in the grid, where migration occurs on the last day.
function FullYear(this)
% Save grid dimensions
m = size(this,1);
n = size(this,2);

% Run every day of the year-long simulation, except for the
% last day of summer (migration day)
for i = 1:1:m
for j = 1:1:n
this(i,j).Value.Hibernate;
this(i,j).Value.SummerDay1;

for t = 1:45
this(i,j).Value.SummerRegularDay;
end

this(i,j).Value.SummerBirthPulse;
this(i,j).Value.VaccinationDay;

% Only 104 reg. summer days days b/c of migration day
for t = 1:104
this(i,j).Value.SummerRegularDay;
end
end
end

this.SummerLastDay;
end

end

end
```

## A.4 MHM Analysis Code

```
% Code by JACKSON BARBER, Williams College '18|jdb3@williams.edu
% Written for his senior honors thesis
% Advisor: Julie BLackwood
```

```
% Last edited: 4/08/2018

% This function establishes the values of all parameters associated with
% the multi-hibernaculum model (MHM). It is designed for exclusive use
% tiwht the MHM, not for the single hibernaculum model (SHM).

function MHMAnalysis2(run,intType,diseaseCase)
% Initialize the model by running DeclareParametersMHM
p = DeclareParametersMHM(diseaseCase);

%% ~~SET ANALYSIS PARAMETERS~~
n = 20;

% Intervention values
Kpd = 10^10;
delta = 1/60;
nu = 0;

if strcmp(intType,'fungicide')
Kpd = 0;
elseif strcmp(intType,'microclimate')
delta = 0;
elseif strcmp(intType,'vaccine')
nu = 1;
else

end


intVecSize = 20*run;              % Number of intervention hibernacula

Q = 250;                          % Number of model runs

% Stores the final population N numbers of every hibernaculum in every
% iteration of the analysis
masterSurvivalVec = zeros(n,n,Q);

% Stores the net population of all the hibernacula for each iteration of
% the analysis
msvNet = zeros(Q,1);

% Stores the cooredinates of the intervention hibernacula for iteration of
% the analysis
masterIntVec = zeros(intVecSize,2,Q);

%% ~~RUN ANALYSIS~~

for z = 1:1:Q

% ~~CREATE~~ an n x n hibernaculum grid
grid = HibernaculumGrid(n,n,p);

% ~~INITIALIZE~~ the grid
```

```
grid.InitializeAll;

% ~~SET INTERVENTIONS~~ by first creating a 2-column vector containing all of
% the (m,n) indices of the hibernacula to have an intervention. Then, use
% for loop to set the interventions for these hibernacula.

% RANDOM
% Create randomized int vector
intVector = randi(n,intVecSize,2);

% Make sure that none of the intervention vector entries are copies
for i = 1:intVecSize
X = 1;
while X < i
if intVector(X,:) == intVector(i,:)
intVector(i,:) = randi(n,1,2);
X = 0;
end

X = X + 1;
end
end

% % CENTER
% % Create randomized int vector--frist half are random, second half are all
% % in edge range ( x & y < 5 OR x & y > 16)
% intVector = randi(n,intVecSize,2);
% intVector((intVecSize/2 + 1):intVecSize,:) = ...
%                 randi([(n/4 + 1),(3*n/4)],intVecSize/2,2);
%
% % Make sure that none of the intervention vector entries are copies
% for i = 1:intVecSize
%     X = 1;
%     while X < i
%         if (intVector(X,:) == intVector(i,:))
%             if (i <= intVecSize/2)
%                 intVector(i,:) = randi(n,1,2);
%             elseif (i > intVecSize/2)
%                 intVector(i,:) = randi([(n/4 + 1),(3*n/4)],1,2);
%             end
%             X = 0;
%         end
%
%         X = X + 1;
%     end
% end

% % EDGE
% % Create randomized int vector--frist half are random, second half are all
% % in center range (5 < x & y < 16)
% intVector = randi(n,intVecSize,2);
% for x = (intVecSize/2 + 1):(intVecSize)
%     for y = 1:2
```

```
%         which = randi([0,1],1,1);
%         if which == 0
%             intVector(x,y) = randi([1,n/4],1,1);
%         else
%             intVector(x,y) = randi([(3*n/4)+1,n],1,1);
%         end
%     end
% end
%
% % Make sure that none of the intervention vector entries are copies
% for i = 1:intVecSize
%     X = 1;
%     while X < i
%         if (intVector(X,:) == intVector(i,:))
%             if (i <= (intVecSize/2))
%                 intVector(i,:) = randi(n,1,2);
%             elseif (i > intVecSize/2)
%                 for y = 1:2
%                     which = randi([0,1],1,1);
%                     if which == 0
%                         intVector(i,y) = randi([1,n/4],1,1);
%                     else
%                         intVector(i,y) = randi([(3*n/4)+1,n],1,1);
%                     end
%                 end
%             end
%             X = 0;
%         end
%
%         X = X + 1;
%     end
% end

% Set the intervention for the specified hibernacula
for x = 1:intVecSize
grid(intVector(x,1),intVector(x,2)).Value...
.SetIntervention(Kpd,delta,nu);
end


% ~~RUN THE MODEL FOR YEARSSIM YEARS~~
for x = 1:p.yearsSim
grid.FullYear;
end

% ~~STORE SURVIVAL OUTPUT AND INTERVENTION COORDINATES~~

% Store survival values
netPop = 0;
for i = 1:n
for j = 1:n
masterSurvivalVec(i,j,z) = grid(i,j).Value.Population;
```

```
netPop = netPop + grid(i,j).Value.Population;
end
end

msvNet(z) = netPop;


% Store intervention coordinates
masterIntVec(:,:,z) = intVector;

end

% ~~SET OUTPUT~~
save(strcat('masterSurvivalVec',int2str(run*20),intType,...
'Case',int2str(diseaseCase),'.mat'),'masterSurvivalVec');
save(strcat('msvNet',int2str(run*20),intType,...
'Case',int2str(diseaseCase),'.mat'),'msvNet');
save(strcat('masterIntVec',int2str(run*20),intType,...
'Case',int2str(diseaseCase),'.mat'),'masterIntVec');

end
```

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