A Mathematical Model for a *N. ceranae* Infection in an *A. mellifera* Colony

by

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ABSTRACT

A Mathematical Model for a *N. ceranae* Infection in an *A. mellifera* Colony

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The Western honey bee (*Apis mellifera*), a eusocial insect commonly kept to produce honey and pollinate crops, is affected by numerous stressors such as viruses, mites, pesticides, and weather. In recent years, colony losses have increased interest in the study of these stressors. Here, we present a model for the parasitic fungus *Nosema ceranae*, a spore-forming microsporidian which infects bees via a fecal-oral pathway and has been implicated in widespread colony failures in recent years. Insofar as possible, we analyze the stability of the system and present simulation results for the model. We further include in the model the effects of neonicotinoid pesticides on colony health. We conclude by studying the potential use of treatment strategies to mitigate the disease’s effects.
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Chapter 1

Introduction

1.1 Background

The Western honey bee (*Apis mellifera*) has been valued since antiquity for its use in the production of honey and beeswax. While honey bees have always played a natural role as a pollinator in food production, the agricultural sector has capitalized on this in modern times by placing honey bee hives around crop fields during blooming seasons, thereby maximizing pollination. This has allowed certain crops to be scaled upwards in production, but has also led to some agricultural sectors becoming dependent upon the use of honeybees. Indeed, a study of 107 globally traded crops found that the production of 75% of these crops were directly affected by pollinators such as honey bees. While most staple foods do not depend on pollinators for production, the absence of pollinators would restrict the variety and nutritional value of the current human diet [32].

Clearly, humanity has come to rely on the honey bee, and now has a vested interest in combatting threats to the honey bee. This fact was brought to the fore in the latter half of the first decade of the 2000s when numerous honey bee colonies in the United States showed unusual symptoms during Spring inspections [46]. In what became known as Colony Collapse Disorder

1
(CCD), bee colonies were found to be failing in large numbers, with few worker bees present to protect a peculiarly large amount of food and larval bees, the former of which normally would have been stolen by other intruder bees prior to inspection ([23]). In Canada and Germany, hives do not display CCD symptoms but have recorded higher-than-average losses over the winter months in recent years [23, 35].

The cause (or causes) of these phenomena remains unknown. However, many theories have been put forward, including (but not limited to) placing the blame on viruses, mites, pesticides, stress from transportation of hives, and habitat loss. It has been suggested that the true cause may lie in a confluence of a number of these factors [43].

One parasite in particular, Nosema ceranae, has been implicated in colony losses on a global scale, although its exact role in these losses is debated [20]. N. ceranae is a microsporidian which has traditionally been known to infect Asian honey bees (Apis cerana) but has also been observed in A. mellifera hives. Indeed, in Canadian hives, N. ceranae has been found to be more prevalent and more virulent than N. apis in recent years [15]. Its infective form is contained in a spore which contaminates the combs of a hive, where bees may ingest the spore while cleaning the combs [3, 13]. Upon ingestion, the spore germinates, multiplies in the midgut’s epithelial cells, and infects the bee, which defecates new spores onto the combs to be ingested by other bees. The infection itself has been shown to decrease the lifespans of bees once they leave the hive to forage for food [17].

Some have proposed that N. ceranae is the main cause of CCD in A. mel- lifera colonies [19], while others have suggested it as one of multiple stressors leading to hive failure [43]. In particular, another key stressor has been the recent introduction of a class of pesticides known as neonicotinoids. Sub-lethal doses of these pesticides have been found to compromise the immune systems of honey bees, and may make hives more susceptible to failure due to infections by pathogens such as N. ceranae [14].
1.2 Use of Mathematical Modelling

We propose employing mathematical modelling to studying the effects of *N. ceranae* on a honey bee colony. The scientific use of mathematical modelling has expanded greatly in recent years. While modelling was originally implemented in physical systems (e.g., [29]), it has also been applied in other scientific fields. Scientists have used mathematical modelling in areas such as ecology [34] and food science [4], and have even proposed its use in modelling social dynamics [47] and neurological systems [10].

The process involves identifying the aspects of the system that are believed to be the most relevant, and then translating these into a mathematical framework that can be studied more formally. Generally, this framework can be approached from an analytical standpoint to observe the most important aspects of the framework, or from a numerical perspective to confirm the analytical results or to hypothesize about those results when analytic techniques are unavailable. In many cases, this process requires simplifications of the original system, and these assumptions must inform the interpretation of the mathematical results.

Analytical and numerical analysis of mathematical systems have a number of uses in the sciences. They can serve as predictive tools after being fitted to past data and can be used to theorize about the underlying dynamics of a system based on the present knowledge of a system in the literature. In addition, they are often lower in cost than traditional field or lab experiments and can be used to guide the design of these larger experiments or to observe the potential outcome of experiments that are prevented for other reasons [33]. Further, models can reveal potential flaws in the understanding of a system when they do not yield similar results to those observed in other experiments [10].

In light of this, we propose that mathematical modelling can serve a purpose in analyzing the effects of many of the stressors that affect an *A. mellifera* colony. We aim to focus on the impacts of *N. ceranae* infections
and applications of neonicotinoids near colonies.

1.3 Review of Previous Literature

Bee colonies have been the subject of a variety of mathematical models to study a range of phenomena in apiculture. A recent summary of these models identifies three general categories: “varroa models,” used to study varroa mites, a particularly deadly pest; “forager models,” which include the effect of task division in the colony; and “colony models,” which focus on phenomena related to the development cycle of honey bees in greater detail [6]. There is, of course, overlap between these three categories.

While many disease-parasitic models have been put forward for varroa mites and the viruses they transmit (e.g., [44, 38]), a burgeoning area of research lies in disease models for other honey bee diseases and parasites. These models can also contain elements of the other model categories to include the effects of bee biology and ethology.

A model already exists for the transition of bees between the two largest classes in a colony: hive bees and forager bees [25]. The same group behind that model later developed it to include the effects of food stores on colony growth and to stratify the population into brood, hive bees, and forager bees [24]. The original model was also expanded into two generic disease models [26, 8]. Both are SIR-type models, with one modelling a forager-born disease and another modelling a disease spread by contact among healthy and infected bees and including food dynamics. While the authors propose that these models can potentially be applied to \textit{N. ceranae}, neither is focused on the particular dynamics of the disease and its spread within a colony via spores within the hive. In a similar vein, Bryden et al. (2013) proposed a model to study the effects of colony stress and individual bee impairment in social bee colonies, but this model focuses solely on generic stresses rather than particular diseases [12]. We have yet to see a mathematical model that
effectively portrays the effects of a *N. ceranae* infection, based on the known dynamics of the disease.

Regarding the pathology of *N. ceranae*, our understanding of the disease is lacking in some areas, in part because the microsporidian, and the distinction between *N. apis* and *N. ceranae*, are relatively recent discoveries. However, some studies have been conducted: one study made estimations for the effects of *N. ceranae* infections on the lifespans of bees [17], another compared the effects of *N. ceranae* on honey bee health to those of *N. apis* [16, 22], and a third found that antibiotics can be an effective treatment [48]. However, exact data on infection rates, mortality rates, and other factors have been difficult to obtain, due to the inherent structure of bee colonies and the nature of the disease.

Scientific understanding of neonicotinoids and their effects on honey bees is still developing. Henry et al. (2012) conducted a field study on the effects of neonicotinoids on the navigational abilities of foraging bees. They then applied their findings to the model in [25] to determine the impact of these pesticides on hive health and viability. Trials conducted by Di Prisco et al. (2013) also showed a compromised immune response in honey bees [14].

## 1.4 Objectives

In the following chapters, we will propose a model for the spread of *N. ceranae* within a colony of *A. mellifera*. This model will stratify bees into healthy and infected classes as well as hive and forager classes, and will add in the concept of an environmental potential or reservoir for the disease. We believe this to be a more accurate representation of the dynamics of a *N. ceranae* infection than those suggested in previous disease models. While the model can be applied to a general hive, we will, where necessary, focus our choices of parameters on a colony in southwestern Ontario.

We will then analyze this model using algebraic and computational tech-
niques with the aim of developing a better understanding of the dynamics of the disease within the colony. Further, we will introduce other terms in the model to simulate the potential impacts of pesticides and disease treatment strategies on the colony. We hope that these will give insight into how these different effects work in tandem to affect a colony. Finally, we will consider the economic implications of these treatment strategies for honey production and hive productivity and suggest possible future work in this area of study.
Chapter 2

Background, Model Assumptions, and Model Formulation

We wish to construct a model of ordinary differential equations to accurately reflect the population dynamics of an *A. mellifera* hive as well as the disease dynamics of *N. ceranae*. We first describe the known dynamics of honey bee colonies and the disease that are most salient.

2.1 *Apis mellifera* Biology

Below, “hive” refers to the physical structure in which bees store honey, raise brood, and avoid cold in Winter, whereas “colony” refers to the network of bees associated to a queen, including both the bees inside the physical hive and the foraging bees outside of the hive.

A colony of Western honey bees (*A. mellifera*) centres around the queen bee, which has the sole responsibility of laying eggs. The queen is tended to by female worker bees, whose population can grow in excess of 40,000 bees in Summer. Also present are hundreds of male drones which have the sole
task of mating with the queen [40].

The worker bees begin their lives as eggs laid by the queen in the hive’s combs. These eggs hatch into larvae which are fed by adult workers. The workers then seal the cells containing larvae with a wax cap, where they develop into pupae. When fully developed, the new worker bees emerge from the comb and cycle through various tasks including hive cleaning and protection, brood care, and tending to the queen [49, 41, 11]. Larger colonies correlate with higher brood production [30, 2].

Newly-emerged worker bees cycle through a number of tasks around the hive such as cell cleaning and brood rearing. The oldest workers leave the hive as foragers to collect nectar, pollen, and other hive materials, creating an overarching class division between hive bees and forager bees [41]. In a properly functioning colony, the rate at which bees become foragers depends on the distribution of labour within the colony and changes so that, at a given time during a foraging season, foragers compose approximately one third of the colony [7, 45]. Physiologically, it is believed that this transition is influenced by two hormones in hive bees, the juvenile hormone and vitellogenin, which are influenced by the presence of forager bees in the hive and serve to regulate the division of labour among worker bees [17].

Honey bee colonies exhibit an annual cycle of growth and decline, particularly in colder climates. A colony lies dormant in Winter as bees remain in the hive and vibrate to maintain an in-hive temperature above 10°C. In Spring, populations grow and, by late Spring, a larger colony is able to “swarm”, dividing into two colonies. Populations then remain high in Summer and decrease in Autumn toward their Winter lows [40].

The average age of a bee also depends on the season and can range from as low as a 15 days in the Summer to several months in the Winter [49].
2.2 *Nosema ceranae* Biology

As mentioned above, *N. ceranae* exists as a spore on the combs of the hive until ingested by a worker bee when cleaning cells to provide cells for the queen to lay eggs. Once inside a bee, the spore germinates and reproduces. During defecation, some spores exit the bee and can be deposited on the combs to be ingested by other bees [3, 13].

*N. ceranae* exhibits a cyclical nature where outbreaks often occur in the Spring and early Summer, apparently due to the hive’s behaviour. During Winter, bees cannot leave the hive and infected bees defecate on the combs, contaminating them with spores. Because the queen bee does not lay eggs for most of the Winter, the worker bees do not clean the combs, leading to a buildup of spores over Winter. As Spring approaches, the queen begins to lay eggs and so the workers clean combs, causing infections [3]. As the year progresses into Summer and Fall, the spores have been found to naturally decrease in infectivity and viability [27].

During Spring, Summer, and Fall, bees are able to defecate outside the hive in good weather, though inclement weather can force bees into the hive, leading to more spores being deposited in the hive [31].

Regarding the disease’s virulence, *N. ceranae* has been found to shorten the lifespan of bees, but the survival rates of healthy and infected bees were only seen to diverge after roughly 14 days [17].

2.3 Model Assumptions

Based on the biology of *A. Mellifera* and *N. Ceranae*, we make the following assumptions in our model:

1. While any events affecting the queen bee also affect the colony, we ignore events that compromise the health of the queen bee, viewing these as discrete events that are exceptions rather than rules. Thus,
we assume that the queen bee does not die or that the queen’s death
does not affect the colony’s performance. We also assume that the
queen bee is unaffected by the disease. This is similar to the approach
used in other studies [25, 38].

2. Similarly, since drones are not known to play a substantial role in the
colony’s ongoing dynamics, we ignore drones and focus our model solely
around adult worker bees. This also follows the precedent of previous
studies [25, 38].

3. Given the biological differences between hive bees and foragers and the
impact the class structure has on the colony, we distinguish between
hive bees and forager bees in our model.

4. We assume that bees simply emerge as adult worker bees, rather than
requiring that bees pass through larval and pupal stages. While this
reduces the faithfulness of our model, it circumvents the need to include
delays in our differential equations, which complicate mathematical
analysis.

5. To still include some of the effects of the brood stages on population
dynamics, we assume that the birth rate for hive bees is determined by
the product of the daily maximum potential birth rate and a measure of
the hive’s brood-rearing capacity, as in [25]. The former is determined
by the average number of eggs laid per day by the queen, while the
latter is a sigmoidal function of the total colony population that sharply
decreases when the population falls below a certain threshold value.
Thus, the birth rate can be hampered by low levels of hive bees (due
to lack of care) and forager bees (due to lack of food).

6. As the amount of spores on the hive combs directly impacts the rate
of infection, we also take as a model variable the “environmental po-
tential” or “environmental reservoir” of the disease, denoted $E$, which is analogous to the number of viable spores on the comb.

7. Hive bees are born healthy but can become infected by ingesting spores (i.e., through contact with the environmental potential) [13]. Thus, we distinguish between healthy hive bees ($H_0$) and infected hive bees ($H_1$).

8. We assume that no new infections occur among bees once they leave the hive to forage, based on our previous findings regarding the spread of the disease.

9. Since infection impacts the lifespan of bees in the later stages of development [17], we assume a pronounced effect on forager lifespans. Thus, we further distinguish between healthy foragers ($F_0$) and infected foragers ($F_1$), yielding four classes of bees.

10. The infection rate of hive bees increases with the number of healthy hive bees and with the strength of the environmental potential. This relationship is linear with respect to the bees, but it saturates with respect to the environmental potential when the potential is exceedingly large. The rationale for this is that, from a biological standpoint, once a large enough number of spores exist on the combs of the hive, having additional spores will not increase the chance of any bee becoming infected. However, the number of bees infected is, of course, directly proportional to the number of bees present.

11. The environmental potential of the disease increases due to the presence of infected hive bees and decreases due to natural decay (i.e., loss of viability of spores) and ingestion of spores by hive bees.

12. Hive bees leave the hive to become foragers at a specified maximum rate but the amount that transition is reduced depending on the ratio of foragers to the total colony population. We follow an approach similar to [25], which will be developed below.
13. When leaving the hive, healthy hive bees become healthy foragers, and infected hive bees become infected foragers. We assume that the ratios at which healthy and infected bees transition are equal.

## 2.4 Model Formulation

Based on our assumptions, we construct our model:

\[
\begin{align*}
\dot{H}_0 &= \beta(t) \frac{Z^2}{\kappa(t)^2 + Z^2} - \sigma_1(t)H_0 + \sigma_2(t) \frac{F}{Z} F_0 - \eta_0(t)H_0 - \alpha(t)H_0 \frac{E}{\lambda(t) + E} \quad (2.1) \\
\dot{H}_1 &= -\sigma_1(t)H_1 + \sigma_2(t) \frac{F}{Z} F_1 - \eta_1(t)H_1 + \alpha(t)H_0 \frac{E}{\lambda(t) + E} \quad (2.2) \\
\dot{F}_0 &= \sigma_1(t)H_0 - \sigma_2(t) \frac{F}{Z} F_0 - \phi_0(t)F_0 \quad (2.3) \\
\dot{F}_1 &= \sigma_1(t)H_1 - \sigma_2(t) \frac{F}{Z} F_1 - \phi_1(t)F_1 \quad (2.4) \\
\dot{E} &= \gamma(t)H_1 - \delta(t)E - \tilde{\alpha}(t)H_0 \frac{E}{\lambda(t) + E} \quad (2.5)
\end{align*}
\]

As shorthand, we set \( H = H_0 + H_1 \), \( F = F_0 + F_1 \), and \( Z = H + F \).

All coefficient parameters are time-dependent, and we take them to be periodic functions with periods of one year. Thus, we have seasonal changes in parameters which repeat each year.

Our model is based on the hive-forager model presented in [25], although we make some alterations and expansions.

New bees are introduced by a birth function, the first term in the equation for \( \dot{H}_0 \). \( \beta \) is the maximum birth/emergence rate of healthy hive bees, while \( \kappa \) is an estimate for the population threshold for brood maintenance. By choosing a Hill coefficient of 2, we impose an Allee effect on the colony: No new bees emerge when there are no bees already present to rear them; below \( \kappa \), few new bees can be reared by the relatively small colony population, but
above \( \kappa \), the emergence rate increases toward \( \beta \) as the colony population grows. This varies from the previous model and thus changes some dynamics of the system, but is more ecologically accurate. Bees are eusocial insects and colonies cannot exist in the long term with exceedingly low populations.

We include the terms containing \( \eta_0 \), \( \eta_1 \), \( \phi_0 \), and \( \phi_1 \) to model the deaths of their respective classes. Here as well, we vary from the original model in [25] by including death terms for hive bees, but this is a crucial addition, for analysis, for simulations, and for ecological modelling. While the natural death terms for hive bees may be near zero in active seasons, they must be clearly positive in Winter when all bees revert to being hive bees.

For new infections, we use the term \( \alpha \frac{E}{\lambda + E} H_0 \). This effectively models our understanding of the disease’s infection dynamics, as this term increases proportionally with respect to \( H_0 \) and increases to saturation with respect to \( E \). \( \alpha \) is the maximum infection rate, while \( \lambda \) is the half-saturation constant for the environmental potential.

For the remaining disease dynamics that are currently known, we take \( \gamma \) as the spore deposition rate, \( \delta \) as the decay rate of the disease, and \( \tilde{\alpha} \) as the removal rate of the potential due to ingestion of spores. We make the deposition and decay of spores to be proportional to the number of infected hive bees and the number of spores, respectively. We expect that the removal rate of the potential to correlate with the number of new infections, and therefore model this removal by \( \tilde{\alpha} \frac{E}{\lambda + E} H_0 \), a term with similar form to that of the infection term.

### 2.5 Comparison of Two Transition Terms

Lastly, the terms containing \( \sigma_1 \) and \( \sigma_2 \) determine the dynamics of class distribution within the colony. The model in [25], which is phrased in terms of \( H \) (hive bees) and \( F \) (forager bees), uses transition terms of the form \( \sigma_1 H - \sigma_2 \frac{F}{E} H \), which we denote the Khoury Transition Term, after the pa-
per’s author. This term cannot be expanded easily to an infectious disease model. Using the “natural” expansion of the transition term, $\sigma_1 H_0 - \sigma_2 \frac{F}{Z} H_0$ and $\sigma_1 H_1 - \sigma_2 \frac{F}{Z} H_1$, in the equations for $\dot{H}_0$ and $\dot{F}_0$ can result in negative values of $F_0$ when levels of $F_1$ are high and levels of $F_0$ are low. One solution to this positivity problem which has a form not unlike the original model is to use the terms $\sigma_1 H_0 - \sigma_2 \frac{F_0}{Z} H_0$ and $\sigma_1 H_1 - \sigma_2 \frac{F_1}{Z} H_1$. However, this is also undesirable as it allows transition rates between healthy and infected classes of bees to potentially vary widely.

Thus, in order to preserve positivity of solutions and equal transition ratios, we use the altered term $\sigma_1 H_0 - \sigma_2 \frac{F_0}{Z} F_0$ seen in the model formulation. We denote this term the Petric Transition Term. It should be noted, however, that the parameter $\sigma_2$ has slightly different interpretations between our model and the model in [25]. Whereas it previously acted as a measurement of maximum social inhibition (i.e., a reduction in transition of hive bees), it now refers to the maximum amount of foragers bees “fed back” into the hive component. However, in the context of our differential equations, we expect the results to be similar for carefully chosen parameters.

### 2.5.1 System Dynamics with Khoury Transition Term

Here we analyze the stability dynamics of the original system in [25] and of the system with our proposed alternate transition term. Phrased in our choice of parameters, the original system takes the form

$$
\dot{H} = \beta \frac{Z}{\kappa + Z} - \sigma_1 H + \sigma_2 \frac{F}{Z} H
$$

(2.6)

$$
\dot{F} = \sigma_1 H - \sigma_2 \frac{F}{Z} H - \phi F
$$

(2.7)
where $H$ represents hive bees and $F$ represents forager bees. This system has a positive steady-state $(H^*, F^*)$ of the form

$$F^* = \frac{\beta}{\phi} - \frac{\kappa J}{J + 1}, \quad H^* = \frac{1}{J} F^*$$

$$J = \frac{1}{2} \left[ \left( \frac{\sigma_1}{\phi} - \frac{\sigma_2}{\phi} - 1 \right) + \sqrt{\left( \frac{\sigma_1}{\phi} - \frac{\sigma_2}{\phi} - 1 \right)^2 + \frac{4 \sigma_1}{\phi}} \right]$$

which is stable when $\phi < \frac{\beta}{2 \kappa} \left( \frac{\sigma_1 + \sigma_2 + (\sigma_1 - \sigma_2)^2 + 4 \sigma_2 \sigma_1}{\sigma_1 - \frac{\phi}{\kappa}} \right)$ and $\sigma_1 - \frac{\beta}{\kappa} > 0$ [25].

### 2.5.2 System Dynamics with Petric Transition Term

We construct a similar system using the Petric Transition Term. Although above, we specified that the exponent in the birth term, $n$, would be greater than or equal to 2 in our system, here we set $n = 1$ to compare this to the system in [25]. Therefore, our alternate system takes the form

$$\dot{H} = \beta \frac{Z}{\kappa + Z} - \sigma_1 H + \sigma_2 \frac{F}{Z} F$$ \hspace{1cm} (2.8)$$

$$\dot{F} = \sigma_1 H - \sigma_2 \frac{F}{Z} F - \phi F$$ \hspace{1cm} (2.9)

We set the right-hand sides of both of these equations equal to zero, and add the second to the first to yield the following conditions for equilibria:

$$0 = \beta \frac{H^* + F^*}{\kappa + H^* + F^*} - \phi F^*$$ \hspace{1cm} (2.10)$$

$$0 = \sigma_1 H^* - \sigma_2 \frac{F^*}{H^* + F^*} F^* - \phi F^*$$ \hspace{1cm} (2.11)
Multiplying out the fractional parts of equation 2.11, we get a quadratic equation in $F$,

$$0 = -(\sigma_2 + \phi)F^*^2 + (\sigma_1 - \phi)H^*F^* + \sigma_1H^*^2$$

which has solutions

$$F^* = JH^*$$

where

$$J = \frac{\sigma_1 - \phi \pm \sqrt{(\sigma_1 + \phi)^2 + 4\sigma_1\sigma_2}}{2(\sigma_2 + \phi)} \quad (2.12)$$

This gives a pair of linear nullclines passing through the origin. We take the positive case as the negative case yields a nullcline through the second and fourth quadrants, which are of no ecological significance. Substituting $F^* = JH^*$ in equation 2.10, we then solve for $H^*$ to find an equilibrium of the form

$$H^* = \frac{\beta}{\phi J} - \frac{\kappa}{J + 1}, \quad F^* = \frac{\beta}{\phi} - \frac{\kappa J}{J + 1},$$

which is of the same form as the solutions to the system with the Khoury Transition Term. (Note, however, that the value of $J$, and hence the values of the solutions, differ in this case.)

Next, to study the stability of this equilibrium, we find the Jacobian matrix of the system in equations 2.8 and 2.9:

$$\mathcal{J}(H, F) = \begin{pmatrix}
\frac{\beta_\kappa}{(\kappa+Z)^2} - \sigma_1 - \sigma_2 \frac{F^2}{Z^2} & \frac{\beta_\kappa}{(\kappa+Z)^2} + \sigma_2 \frac{F(2H+F)}{Z^2} \\
\sigma_1 + \sigma_2 \frac{F^2}{Z^2} & -\sigma_2 \frac{F(2H+F)}{Z^2} - \phi
\end{pmatrix}$$

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At our equilibrium \((H^*, F^*) = (H^*, JH^*)\), the Jacobian matrix is

\[
J(H^*, F^*) = \begin{pmatrix}
\frac{\phi^2 J^2 \kappa}{\beta (J+1)^2} - \sigma_1 - \sigma_2 \frac{J^2}{(J+1)^2} & \frac{\phi^2 J^2 \kappa}{\beta (J+1)^2} + \sigma_2 \frac{J(J+2)}{(J+1)^2} \\
\sigma_1 + \sigma_2 \frac{J^2}{(J+1)^2} & -\sigma_2 \frac{J(J+2)}{(J+1)^2} - \phi
\end{pmatrix}
\]

For stability, we require the determinant of this matrix to be positive and the trace to be negative. The first condition is, therefore,

\[
\left(\frac{\phi^2 J^2 \kappa}{\beta (J+1)^2} - \sigma_1 - \sigma_2 \frac{J^2}{(J+1)^2}\right)\left(-\sigma_2 \frac{J(J+2)}{(J+1)^2} - \phi\right) > \left(\frac{\phi^2 J^2 \kappa}{\beta (J+1)^2} + \sigma_2 \frac{J(J+2)}{(J+1)^2}\right)\left(\sigma_1 + \sigma_2 \frac{J^2}{(J+1)^2}\right)
\]

By rearranging equation 2.12, we can isolate for \(\sigma_1 = \frac{\sigma_2 J^2}{J+1} + \phi J\). Making this substitution in the condition on the determinant and simplifying the inequality, we obtain the condition \(\frac{\beta}{\kappa} > \frac{\phi J}{J+1}\).

We also require that the trace of the Jacobian be negative. That is,

\[
\frac{\phi^2 J^2 \kappa}{\beta (J+1)^2} - \sigma_1 - 2\sigma_2 \frac{J}{J+1} - \phi < 0
\]

which, when making the same substitution as above for \(\sigma_1\), yields

\[
\frac{\phi^2 J^2 \kappa}{\beta (J+1)^2} < \sigma_2 \frac{J(J+2)}{J+1} + \phi (J+1)
\]

Assuming that the condition on the determinant holds, we can apply it to this inequality to obtain

\[
0 < \frac{\phi (J^2 + J + 1) + \sigma_2 J(J + 2)}{J+1}
\]

which, given our assumptions on our parameters, is always satisfied. Therefore, our only condition for stability for this equilibrium is \(\frac{\beta}{\kappa} > \frac{\phi J}{J+1}\) or, by
rearranging terms, \( \phi < \frac{\beta(J+1)}{\kappa J} \).

Since \( J \) depends on \( \phi \), this inequality must be resolved to find a clear upper bound on \( \phi \). We first substitute the expression for \( J \) in Equation 2.12 to yield

\[
\frac{\kappa \phi}{\beta} \left( \frac{\sigma_1 - \phi + \sqrt{(\sigma_1 + \phi)^2 + 4\sigma_1 \sigma_2}}{2(\sigma_2 + \phi)} \right) < \frac{\sigma_1 + \phi + 2\sigma_2 + \sqrt{(\sigma_1 + \phi)^2 + 4\sigma_1 \sigma_2}}{2(\sigma_2 + \phi)}
\]

which we multiply by \( 2(\sigma_2 + \phi) \neq 0 \) to obtain

\[
\frac{\kappa \phi}{\beta} \left( \sigma_1 - \phi + \sqrt{(\sigma_1 + \phi)^2 + 4\sigma_1 \sigma_2} \right) < \sigma_1 + \phi + 2\sigma_2 + \sqrt{(\sigma_1 + \phi)^2 + 4\sigma_1 \sigma_2}
\]

(2.13)

We change this to an equality and search for its roots. Rearranging the equation to isolate the root, we have

\[
\frac{\kappa \phi}{\beta} (\sigma_1 - \phi) - (\sigma_1 + \phi + 2\sigma_2) = \left( 1 - \frac{\kappa \phi}{\beta} \right) \sqrt{(\sigma_1 + \phi)^2 + 4\sigma_1 \sigma_2}
\]

Squaring both sides, we have

\[
\frac{\kappa^2 \phi^2}{\beta^2} (\sigma_1 - \phi)^2 + (\sigma_1 + \phi + 2\sigma_2)^2 - 2 \frac{\kappa \phi}{\beta} (\sigma_1 - \phi)(\sigma_1 + \phi + 2\sigma_2)
\]

\[= \left( 1 - \frac{\kappa \phi}{\beta} \right)^2 ((\sigma_1 + \phi)^2 + 4\sigma_1 \sigma_2)\]

We group terms by powers of \( \frac{\kappa \phi}{\beta} \):

\[
\frac{\kappa^2 \phi^2}{\beta^2} \left[ (\sigma_1 - \phi)^2 - (\sigma_1 + \phi)^2 - 4\sigma_1 \sigma_2 \right] - 2 \frac{\kappa \phi}{\beta} \left[ (\sigma_1 - \phi)(\sigma_1 + \phi + 2\sigma_2) - (\sigma_1 + \phi)^2 - 4\sigma_1 \sigma_2 \right]
\]

\[+ (\sigma_1 + \phi + 2\sigma_2)^2 - (\sigma_1 + \phi)^2 - 4\sigma_1 \sigma_2 = 0\]
The coefficients reduce as follows:

\begin{align*}
\sigma_1 - \phi - (\sigma_1 + \phi)^2 - 4\sigma_1\sigma_2 &= -4\sigma_1(\phi + \sigma_2) \\
(\sigma_1 - \phi)(\sigma_1 + \phi + 2\sigma_2) - (\sigma_1 + \phi)^2 - 4\sigma_1\sigma_2 &= -2(\phi + \sigma_2)(\phi + \sigma_1) \\
(\sigma_1 + \phi + 2\sigma_2)^2 - (\sigma_1 + \phi)^2 - 4\sigma_1\sigma_2 &= 4\sigma_2(\phi + \sigma_2)
\end{align*}

Therefore our equation is

\begin{equation*}
-4\frac{\kappa^2 \phi^2}{\beta^2} [\sigma_1(\phi + \sigma_2)] + 4\frac{\kappa \phi}{\beta} [(\phi + \sigma_2)(\phi + \sigma_1)] + 4\sigma_2(\phi + \sigma_2) = 0.
\end{equation*}

Dividing by $-4$ and factoring, we get

\begin{equation*}
\left[ \frac{\kappa^2 \phi^2}{\beta^2} \sigma_1 - \frac{\kappa \phi}{\beta}(\phi + \sigma_1) - \sigma_2 \right] (\phi + \sigma_2) = 0.
\end{equation*}

This is a cubic equation in $\phi$, with one root being $\phi = -\sigma_2$, an impossibility given our assumption of positive parameters. For the remaining roots, we must solve the quadratic equation in $\phi$,

\begin{equation*}
\frac{\kappa}{\beta} \left( \frac{\kappa \sigma_1}{\beta} - 1 \right) \phi^2 - \frac{\kappa \sigma_1}{\beta} \phi - \sigma_2 = 0
\end{equation*}

\begin{align*}
\Rightarrow (\kappa \sigma_1 - \beta) \phi^2 - \sigma_1 \beta \phi - \frac{\sigma_2 \beta^2}{\kappa} &= 0
\end{align*}

This has roots at

\begin{equation*}
\phi = \frac{\beta}{2} \left[ \frac{\sigma_1 \pm \sqrt{\sigma_1^2 + 4\sigma_2(\sigma_1 - \frac{\beta}{\kappa})}}{\kappa \sigma_1 - \beta} \right].
\end{equation*}

Inequality 2.13 thus depends on these roots, which in turn are determined by the sign of the denominator. If $\sigma_1 > \frac{\beta}{\kappa}$, as in [25], then both roots exist. Assuming this, we see that one root is positive and the other negative. We can then take $\phi = 0$ as a test value to determine whether values in between
the roots satisfy Inequality 2.13. This yields

\[ 0 < \sigma_1 + \phi + 2\sigma_2 + \sqrt{\sigma_1^2 + 4\sigma_1\sigma_2} \]

which is always true.

On the contrary, when \( \sigma_1 < \frac{\beta}{\kappa} \), neither of the roots exist, and the non-trivial equilibrium exists regardless of the value of \( \phi \).

Therefore, we require that \( \phi \) is between the two roots. \( i.e. \),

\[
\frac{\beta}{2k} \left[ \frac{\sigma_1 - \sqrt{\sigma_1^2 + 4\sigma_2(\sigma_1 - \frac{\phi}{\kappa})}}{\sigma_1 - \frac{\phi}{\kappa}} \right] < \phi < \frac{\beta}{2k} \left[ \frac{\sigma_1 + \sqrt{\sigma_1^2 + 4\sigma_2(\sigma_1 - \frac{\phi}{\kappa})}}{\sigma_1 - \frac{\phi}{\kappa}} \right].
\]

Since we have already assumed that \( \phi > 0 \) and the first root is negative, we must only require that \( \phi \) is less than the second root.

### 2.5.3 Numerical Comparison

Taking the same values for \( \sigma_1, \beta, \) and \( \kappa \) from [25], we then set \( \sigma_2 = 1.5 \) in the system with the Petric Transition Term to ensure that foragers begin to return to the hive when foragers make up more than two thirds of the colony population. (This is explained in greater detail below in Section 4.1.) With these parameters, the upper bound on \( \phi \) is approximately 27.5\%. It should be noted that this is 8\% lower than the upper bound for the model in [25], which is 35.5\%, but is still a positive value, meaning that our new model is qualitatively similar to the original model. This new bound implies that colonies will die out if stressors drive forager lifespans consistently below 3.63 days.
Figure 2.1: Phase Portrait of Equations 2.6 and 2.7, the System with Khoury Transition Term \((\sigma_1 H - \sigma_2 F_z H)\)
Figure 2.2: Phase Portrait of Equations 2.8 and 2.9, the System with Petric Transition Term ($\sigma_1H - \sigma_2\frac{F}{Z}F$)

Lastly, we present phase portraits for the original model from [25] in Figure 2.1, and for the model using the Petric Transition Term in Figure 2.2. In general, we use the parameters found in [25]: $\beta = 2000$, $\kappa = 27000$, $\sigma_1 = 0.25$, and $\phi = 0.24$. The one exception we make is for $\sigma_2$, which we set at 0.75 for the model with the Khoury Transition Term, and at 1.5 for
the model with the Petric Transition Term. The lines show the nullclines for both variables $H$ and $F$, with their intersection being the equilibrium for the system, marked by a black dot.

While these are not quantitatively identical, we believe their qualitative similarities are strong enough, particularly in the positive quadrant, to lend credence to this change in our model.
Chapter 3

Mathematical Analysis of the Model

In analyzing the model, we observe both the case where our coefficient functions are 1-year-periodic functions and the case where they are constant functions. We first verify that our solutions are bounded above and that solutions that begin in the positive orthant remain positive.

3.1 Boundedness and Positivity of Solutions

Proposition 1. Let \( Z = H + F = H_0 + H_1 + F_0 + F_1 \), and let \( \zeta(t) = \min\{\eta_0(t), \eta_1(t), \phi_0(t), \phi_1(t)\} \). Non-negative solutions to the system in Equations 2.1–2.5 are bounded by \( 0 \leq Z \leq X \) and \( 0 \leq E \leq W \) where

\[
X(t) = e^{-\int_{t_0}^t \zeta(s)ds} \int_{t_0}^t e^{\int_{t_0}^r \zeta(s)ds} \beta(s)ds + Z(t_0)
\]

and

\[
W(t) = e^{-\int_{t_0}^t \delta(s)ds} \int_{t_0}^t \gamma(s) e^{-\int_{t_0}^r \delta(r)\zeta(r)dr} \left[ \int_{t_0}^s e^{\int_{t_0}^r \zeta(q)dq} \beta(r)dr + Z(t_0) \right] ds + E(t_0)
\]
for some $t_0 \in \mathbb{R}$.

**Proof.** We first note that solutions which begin in the non-negative plane remain positive. Note that for $(H_0, H_1, F_0, F_1, E) = (0, H_1, F_0, F_1, E)$ with the four latter variables non-negative, we have

$$
\dot{H}_0 = \beta(t) \frac{(H_1 + F)^2}{\kappa(t)^2 + (H_1 + F)^2} + \sigma_2(t) \frac{F}{H_1 + F} F_0 \geq 0.
$$

Similar approaches for $H_1, F_0, F_1,$ and $E$ yield, respectively,

$$
\dot{H}_1 = \sigma_2(t) \frac{F}{H_0 + F} F_1 + \alpha(t) \frac{E}{\lambda(t) + E} H_0 \geq 0
$$

$$
\dot{F}_0 = \sigma_1(t) H_0 \geq 0
$$

$$
\dot{F}_1 = \sigma_1(t) H_1 \geq 0
$$

$$
\dot{E} = \gamma(t) H_1 \geq 0
$$

Solutions that begin in the non-negative plane can only become negative by having at least one of the variables pass through 0, yet for each variable, the derivative is non-negative at 0. Thus, non-negative solutions must remain non-negative.

Looking at the time derivative of $Z$,

$$
\dot{Z} = \dot{H}_0 + \dot{H}_1 + \dot{F}_0 + \dot{F}_1
$$

$$
= \beta(t) \frac{Z^2}{\kappa^2 + Z^2} - \eta_0(t) H_0 - \eta_1(t) H_1 - \phi_0(t) F_0 - \phi_1(t) F_1
$$

$$
\leq \beta(t) - \zeta(t) H_0 - \zeta(t) H_1 - \zeta(t) F_0 - \zeta(t) F_1
$$

$$
= \beta(t) - \zeta(t) Z
$$
Next, we then define $X$ by
\[
\dot{X} = \beta(t) - \zeta(t)X
\]
We see that for $Z(t_0) = X(t_0) \geq 0$, we have $\dot{Z} < \dot{X}$ for $t \in \mathbb{R}$, meaning that the solutions of the system in $Z$ are bounded above by the solutions to the system in $X$ which start with the same initial conditions.

Through the use of an integrating factor, we see that the solutions to the system in $X$ are of the form
\[
X(t) = e^{-\int_{t_0}^{t} \zeta(s) ds} \int_{t_0}^{t} e^{\int_{t_0}^{r} \zeta(s) ds} \beta(s) ds + C
\]
and these are, therefore, upper bounds for the solutions to the system in $Z$ with the same initial conditions. Setting $X(t_0) = Z(t_0)$, we get
\[
X(t) = e^{-\int_{t_0}^{t} \zeta(s) ds} \int_{t_0}^{t} e^{\int_{t_0}^{r} \zeta(s) ds} \beta(s) ds + Z(t_0)
\]

Next, we note that
\[
\dot{E} = \gamma(t)H_1 - \delta(t)E - \bar{\alpha}(t)H_0 \frac{E}{\lambda(t)} + E \\
\leq \gamma(t)Z - \delta(t)E
\]
We then define $W$ by
\[
\dot{W} = \gamma(t)Z - \delta(t)W
\]
and can solve this system to find
\[
W(t) = e^{-\int_{t_0}^{t} \delta(s) ds} \int_{t_0}^{t} \gamma(s) e^{-\int_{t_0}^{r} \delta(s) ds} \left[ \int_{t_0}^{r} e^{\int_{t_0}^{q} \zeta(q) dq} \beta(r) dr + Z(t_0) \right] ds + C
\]
which is an upper bound on $E$ when $E$ and $W$ have identical initial condi-
tions. Setting $W(t_0) = E(t_0)$, we solve to find

$$W(t) = e^{-\int_{t_0}^{t} \delta(s) ds} \int_{t_0}^{t} \gamma(s) e^{-\int_{t_0}^{s} \delta(r) \zeta(r) dr} \left[ \int_{t_0}^{s} e^{\int_{t_0}^{r} \zeta(q) dq} \beta(r) dr + Z(t_0) \right] ds + E(t_0)$$

\[\Box\]

For the remaining analysis, we consider the case of constant coefficient functions. While these functions change in the natural context, this analysis will both confirm certain desired qualities of our mathematical model and shed light on the fundamental dynamics of the system. As well, it will better inform our later numerical simulations and our interpretations of numerical results.

### 3.2 Existence and Stability of the Trivial Equilibrium in the Constant Coefficient Case

**Proposition 2.** Consider the system with constant parameters,

$$\begin{align*}
\dot{H}_0 &= \beta \frac{Z^2}{\kappa^2 + Z^2} - \sigma_1 H_0 + \sigma_2 \frac{F}{Z} F_0 - \eta_0 H_0 - \alpha H_0 \frac{E}{\lambda + E} \\
\dot{H}_1 &= -\sigma_1 H_1 + \sigma_2 \frac{F}{Z} F_1 - \eta_1 H_1 + \alpha H_0 \frac{E}{\lambda + E} \\
\dot{F}_0 &= \sigma_1 H_0 - \sigma_2 \frac{F}{Z} F_0 - \phi_0 F_0 \\
\dot{F}_1 &= \sigma_1 H_1 - \sigma_2 \frac{F}{Z} F_1 - \phi_1 F_1 \\
\dot{E} &= \gamma H_1 - \delta E - \tilde{\alpha} H_0 \frac{E}{\lambda + E}
\end{align*}$$

$(H_0^*, H_1^*, F_0^*, F_1^*, E^*) = (0, 0, 0, 0, 0)$, the “empty hive” equilibrium, is locally asymptotically stable in the non-negative orthant.
Proof. Again, we consider the time-derivative of \( Z \):

\[
\dot{Z} = \beta \frac{Z^2}{\kappa^2 + Z^2} - \eta_0 H_0 - \eta_1 H_1 - \phi_0 F_0 - \phi_1 F_1
\]

and note that \( Z = 0 \) is an equilibrium of this single differential equation.

We then define \( Y \) by

\[
\dot{Y} = \beta \frac{Y^2}{\kappa^2 + Y^2} - \zeta Y
\]

where \( \zeta = \min\{\eta_0, \eta_1, \phi_0, \phi_1\} > 0 \), and we note that for \( Y(t_0) = Z(t_0) \geq 0 \), we have \( \dot{Y} \geq \dot{Z} \) for \( t \in \mathbb{R} \). Now, in searching for equilibria of this differential equation, we have

\[
0 = \dot{Y}
\]

\[
\implies 0 = \beta \frac{Y^2}{\kappa^2 + Y^2} - \zeta Y
\]

\[
\implies 0 = \beta Y^2 - \zeta \kappa^2 Y - \zeta Y^3
\]

\[
\implies 0 = Y(-\zeta Y^2 + \beta Y - \zeta \kappa^2)
\]

The equilibria points are thus \( Y = 0, R_1, R_2 \), where \( R_1 \) and \( R_2 \) are the roots of the quadratic equation \( 0 = -\zeta Y^2 + \beta Y - \zeta \kappa^2 \). By the quadratic formula, these are

\[
R_1 = \frac{\beta + \sqrt{\beta^2 - 4\zeta^2 \kappa^2}}{2\zeta} \quad \text{and} \quad R_2 = \frac{\beta - \sqrt{\beta^2 - 4\zeta^2 \kappa^2}}{2\zeta}
\]

Since \( \sqrt{\beta^2 - 4\zeta^2 \kappa^2} < \beta \), both of these roots must be positive when they exist on the real line. Now,

\[
\frac{d\dot{Y}}{dt} = \frac{2\beta \kappa^2 Y}{(\kappa^2 + Y^2)^2} - \zeta,
\]

(3.6)
so by evaluating at $Y = 0$, we have

$$\frac{d\dot{Y}}{dt} = -\zeta \kappa^2 < 0$$

when, as assumed, $\zeta > 0$. Thus, $Y = 0$ is an asymptotically stable equilibrium.

For $R_1$ and $R_2$, we note that after simplification,

$$R_1^2 = \frac{\beta^2 - 2\zeta^2 \kappa^2 + \beta \sqrt{\beta^2 - 4\zeta^2 \kappa^2}}{2\zeta^2}$$

and

$$(\kappa^2 + R_1^2)^2 = \frac{\beta^2(\beta^2 - 2\zeta^2 \kappa^2 + \beta \sqrt{\beta^2 - 4\zeta^2 \kappa^2})}{2\zeta^4} = \frac{\beta^2}{\zeta^2} R_1.$$ 

Thus, evaluating the second derivative in Equation 3.6 at $R_1$, we have

$$\frac{d\dot{Y}}{dt}(R_1) = \frac{2\beta \kappa^2 R_1}{\beta^2 R_1} - \zeta$$

$$= \frac{2\zeta^2 \kappa^2}{\beta R_1} - \zeta$$

$$= \zeta \left( \frac{2\zeta \kappa^2}{\beta R_1} - 1 \right)$$

Given that our parameters are positive and that $R_1 > 0$, this is negative when

$$\frac{2\zeta \kappa^2}{\beta R_1} < 1$$

$$\Rightarrow 2\zeta \kappa^2 < \frac{\beta^2 + \beta \sqrt{\beta^2 - 4\zeta^2 \kappa^2}}{2\zeta}$$

$$\Rightarrow 4\zeta^2 \kappa^2 < \beta^2 + \beta \sqrt{\beta^2 - 4\zeta^2 \kappa^2}$$

Since $R_1$ only exists for $\beta^2 > 4\zeta^2 \kappa^2$, this condition is always satisfied. Therefore, $R_1$ is always a stable equilibrium when it exists on the real line.
Similarly for $R_2$, we have $(\kappa^2 + R_2^2)^2 = \frac{\beta^2}{\xi}R_2$, and so the second derivative evaluated at $R_2$ is

$$
\frac{d\dot{Y}}{dt}(R_1) = \zeta \left( \frac{2\zeta \kappa^2}{\beta R_2} - 1 \right) = \zeta \left( \frac{4\zeta^2 \kappa^2}{\beta^2 - \beta \beta \sqrt{\beta^2 - 4\zeta^2 \kappa^2}} - 1 \right)
$$

This is positive when

$$
\frac{4\zeta^2 \kappa^2}{\beta^2 - \beta \beta \sqrt{\beta^2 - 4\zeta^2 \kappa^2}} > 1
\implies 4\zeta^2 \kappa^2 - \beta^2 > -\beta \sqrt{\beta^2 - 4\zeta^2 \kappa^2}
\implies \beta^2 - 4\zeta^2 \kappa^2 < \beta \sqrt{\beta^2 - 4\zeta^2 \kappa^2}
$$

In the last inequality, both sides are positive, so the inequality holds when both sides of the equation are squared. That is,

$$
\beta^4 + 16\zeta^4 \kappa^4 - 8\beta^2 \zeta^2 \kappa^2 < \beta^4 - 4\beta^2 \zeta^2 \kappa^2
\implies 16\zeta^4 \kappa^4 - 4\beta^2 \zeta^2 \kappa^2 < 0
\implies 4\zeta^2 \kappa^2 (4\zeta^2 \kappa^2 - \beta^2) < 0
$$

This is always satisfied when $R_2$ exists, which requires that $\beta^2 > 4\zeta^2 \kappa^2$. Therefore, $R_2$ is an unstable equilibrium between 0 and $R_1$. From this, it follows that trajectories starting in the interval $[0, R_2)$ will asymptotically tend toward the origin.

As noted above, when $Y(t_0) = Z(t_0) \geq 0$, we have $\dot{Y} \geq \dot{Z}$ for $t \in \mathbb{R}$. Therefore, we have $\dot{Z} \leq \dot{Y} < 0$ for $Z(t_0) = Y(t_0) \in (0, R_2)$, so $Z = 0$ is an asymptotically stable equilibrium point of the system $\dot{Z}$.

Lastly, as $Z \to 0$, $\dot{E} \to -\delta E$, meaning that $E \to 0$. Thus, the “empty-hive” equilibrium is seen to be asymptotically stable for $0 \leq Z < R_2$, $E \in \mathbb{R}$. □
3.3 Existence and Stability of Disease-Free Equilibria in the Constant Coefficient Case

**Proposition 3.** Consider the system with constant parameters in Equations 3.1–3.5. The disease-free equilibrium, \((H_0^*, H_1^*, F^*, F_1^*, E^*) = (H_0^*, 0, F^*, 0, 0)\) (where \(H_0^* > 0\) and \(F^* > 0\)), exists when \(G = \frac{(\phi_0 - \sigma_1)\pm\sqrt{(\sigma_1 + \phi_0)^2 - 4\sigma_1\sigma_2}}{2\sigma_1} > 0\) and \(\beta^2 > 4\frac{(\eta_0 + \phi_0 G)^2\kappa^2}{(G+1)^2}\).

**Proof.** If this equilibrium exists, then at such a point, we immediately have \(\dot{H}_1 = \dot{F}_1 = \dot{E} = 0\). For the other two derivatives, we require the following conditions:

\[
\dot{H}_0 = \beta \frac{(H_0^* + F_0^*)^2}{\kappa^2 + (H_0^* + F_0^*)^2} - \eta_0 H_0^* - \sigma_1 H_0^* + \sigma_2 \frac{F_0^{*2}}{(H_0^* + F_0^*)} \tag{3.7}
\]

\[
\dot{F}_0 = \sigma_1 H_0^* - \sigma_2 \frac{F_0^{*2}}{(H_0^* + F_0^*)} - \phi_0 F_0^* \tag{3.8}
\]

Setting the right-hand sides of Equations 3.7 and 3.8 equal to 0, we then have

\[
0 = \beta \frac{(H_0^* + F_0^*)^2}{\kappa^2 + (H_0^* + F_0^*)^2} - \eta_0 H_0^* - \sigma_1 H_0^* + \sigma_2 \frac{F_0^{*2}}{(H_0^* + F_0^*)} \tag{3.9}
\]

\[
0 = \sigma_1 H_0^* - \sigma_2 \frac{F_0^{*2}}{H_0^* + F_0^*} - \phi_0 F_0^* \tag{3.10}
\]

Adding the second equation to the first, we form the system:

\[
0 = \beta \frac{(H_0^* + F_0^*)^2}{\kappa^2 + (H_0^* + F_0^*)^2} - \eta_0 H_0^* - \sigma_1 H_0^* - \sigma_2 \frac{F_0^{*2}}{H_0^* + F_0^*} - \phi_0 F_0^* \tag{3.9}
\]

From Equation 3.10, we require:

\[
0 = \sigma_1 H_0^{*2} + \sigma_1 H_0^* F_0^* - \sigma_2 F_0^{*2} - \phi_0 F_0^{*2} - \phi_0 H_0^* F_0^*
\]
Solving for \( F_0^* \) using the quadratic formula, we have

\[
F_0^* = \frac{(\phi_0 - \sigma_1)H_0^* \pm \sqrt{(\sigma_1 - \phi_0)^2H_0^{*2} + 4\sigma_1(\sigma_2 + \phi_0)H_0^{*2}}}{-2(\sigma_2 + \phi_0)}
\]

\[
= \frac{(\sigma_1 - \phi_0) \pm \sqrt{(\sigma_1 - \phi_0)^2 + 4\sigma_1(\sigma_2 + \phi_0)}}{2(\sigma_1 + \phi_0)} H_0^*
\]

\[
= \frac{(\sigma_1 - \phi_0) \pm \sqrt{(\sigma_1 + \phi_0)^2 + 4\sigma_1\sigma_2}}{2(\sigma_1 + \phi_0)} H_0^*
\]

\[
: = GH_0^*
\]

We take the positive case of \( G \) as the negative case yields a linear function in the second and fourth quadrants. Substituting this into Equation (3.1), we have

\[
0 = \beta \frac{((G + 1)H_0^*)^2}{\kappa^2 + ((G + 1)H_0^*)^2} - \eta_0 H_0^* - \phi_0 G H_0^*
\]

\[
0 = \beta(G + 1)^2H_0^{*2} - (\eta_0 + \phi_0 G)\kappa^2 H_0^* - (\eta_0 + \phi_0 G)(G + 1)^2 H_0^{*3}
\]

\[
0 = -(\eta_0 + \phi_0 G)(G + 1)^2 H_0^{*2} + \beta(G + 1)^2 H_0^* - (\eta_0 G + \phi_0)\kappa^2 \text{ or } H_0^* = 0
\]

Solving for \( H_0^* \) by the quadratic formula, we have

\[
H_0^* = \frac{-\beta(G + 1)^2 \pm \sqrt{(\beta(G + 1)^2)^2 - 4(\eta_0 + \phi_0 G)^2(G + 1)^2\kappa^2}}{-2(\eta_0 + \phi_0 G)(G + 1)^2}
\]

\[
= \frac{[\beta(G + 1) \pm \sqrt{\beta^2(G + 1)^2 - 4(\eta_0 + \phi_0 G)^2\kappa^2}](G + 1)}{2(\eta_0 + \phi_0 G)(G + 1)^2}
\]

\[
= \frac{1}{2(\eta_0 + \phi_0 G)} \left( \beta \pm \sqrt{\beta^2 - 4\frac{(\eta_0 + \phi_0 G)^2\kappa^2}{(G + 1)^2}} \right)
\]

This yields two solutions which are positive when \( G > 0 \) and \( \beta^2 > 4\frac{(\eta_0 + \phi_0 G)^2\kappa^2}{(G + 1)^2} \). Thus, when this is satisfied, two disease-free equilibria exist. □

**Proposition 4.** Let all coefficient parameter functions be constant for all \( t \). Then, when it exists, the disease-free equilibrium, \((H_0^*, H_1^*, F_0^*, F_1^*, E^*) = \)
\((H^*_0, 0, F^*_0, 0, 0)\) (where \(H^*_0 > 0\) and \(F^*_0 > 0\), is stable when \(\frac{2\beta\kappa^2 Z^*_0}{(\kappa^2 + Z^*_0)^2} < \eta_0, \frac{2\beta\kappa^2 Z^*_0}{(\kappa^2 + Z^*_0)^2} < \phi_0, \gamma < \eta_1\) and \(\alpha < \delta \frac{\lambda}{H^*_0} + \bar{\alpha}\).

**Proof.** We first rearrange the system by swapping the second and third equations, and for shorthand, set \(Z = H + F\):

\[
\dot{H}_0 = \beta \frac{Z^n}{\kappa^n + Z^n} - \sigma_1 H_0 + \sigma_2 \frac{F}{Z} F_0 - \eta_0 H_0 - \alpha H_0 \frac{E}{\lambda + E},
\]

\[
\dot{F}_0 = + \sigma_1 H_0 - \sigma_2 \frac{F}{Z} F_0 - \phi_0 F_0,
\]

\[
\dot{H}_1 = - \sigma_1 H_1 + \sigma_2 \frac{F}{Z} F_1 - \eta_1 H_1 + \alpha H_0 \frac{E}{\lambda + E},
\]

\[
\dot{F}_1 = + \sigma_1 H_1 - \sigma_2 \frac{F}{Z} F_1 - \phi_1 F_1,
\]

\[
\dot{E} = \gamma H_1 - \delta E - \bar{\alpha} H_0 \frac{E}{\lambda + E}.
\]

This does not affect the values of the disease-free equilibrium, now written \((H^*_0, F^*_0, H^*_1, F^*_1, E^*) = (H^*_0, F^*_0, 0, 0, 0)\).
Next, we linearize the system around this equilibrium. The Jacobian matrix for this rearranged system is

\[
J = \begin{bmatrix}
\frac{2 \beta \kappa^2 Z_0}{(\kappa^2 + Z_0^2)^2} - \sigma_1 - \sigma_2 \frac{F_0^*}{Z_0^*} - \eta_0 - \alpha \frac{E}{\lambda + E} & \frac{2 \beta \kappa^2 Z_0}{(\kappa^2 + Z_0^2)^2} + \sigma_2 \frac{F^2 + H(2F_0 + F_1)}{Z_0^2} & \frac{2 \beta \kappa^2 Z_0}{(\kappa^2 + Z_0^2)^2} - \sigma_2 \frac{F_0^*}{Z_0^*} & \frac{2 \beta \kappa^2 Z_0}{(\kappa^2 + Z_0^2)^2} + \sigma_2 \frac{H F_0^*}{Z_0^*} & -\alpha H_0 \frac{\lambda}{(\lambda + E)^2} \\
\sigma_1 + \sigma_2 \frac{F_0^*}{Z_0^*} & -\sigma_2 \frac{F^2 + H(2F_0 + F_1)}{Z_0^2} - \phi_0 & \sigma_2 \frac{F_0^*}{Z_0^*} & -\sigma_2 \frac{H F_0^*}{Z_0^*} & 0 \\
-\sigma_2 \frac{F_0^*}{Z_0^*} + \alpha \frac{E}{\lambda + E} & \sigma_2 \frac{F_0^*}{Z_0^*} & -\sigma_1 - \sigma_2 \frac{F_0^*}{Z_0^*} - \eta_1 & \sigma_2 \frac{F^2 + H(2F_0 + F_1)}{Z_0^2} & \alpha H_0 \frac{\lambda}{(\lambda + E)^2} \\
\sigma_2 \frac{F_0^*}{Z_0^*} & -\sigma_2 \frac{H F_0^*}{Z_0^*} & \sigma_1 + \sigma_2 \frac{F_0^*}{Z_0^*} & -\sigma_2 \frac{F^2 + H(2F_0 + F_1)}{Z_0^2} - \phi_1 & 0 \\
-\tilde{\alpha} \frac{E}{\lambda + E} & 0 & \gamma & 0 & -\delta - \tilde{\alpha} H_0 \frac{\lambda}{(\lambda + E)^2}
\end{bmatrix}
\]

Evaluating this at the disease-free equilibrium, we obtain the following matrix:

\[
J = \begin{bmatrix}
\frac{2 \beta \kappa^2 Z_0^*}{(\kappa^2 + Z_0^* F_0^*)} - \sigma_1 - \sigma_2 \frac{F_0^*}{Z_0^*} - \eta_0 - \alpha \frac{E}{\lambda + E} & \frac{2 \beta \kappa^2 Z_0^*}{(\kappa^2 + Z_0^* F_0^*)} + \sigma_2 \frac{F^2 + 2H_0 F_0^*}{Z_0^*} & \frac{2 \beta \kappa^2 Z_0^*}{(\kappa^2 + Z_0^* F_0^*)} - \sigma_2 \frac{H_0 F_0^*}{Z_0^*} & -\alpha H_0 \frac{\lambda}{\lambda} \\
\sigma_1 + \sigma_2 \frac{F_0^*}{Z_0^*} & -\sigma_2 \frac{F^2 + 2H_0 F_0^*}{Z_0^*} - \phi_0 & \sigma_2 \frac{F_0^*}{Z_0^*} & 0 \\
0 & 0 & -\sigma_1 - \eta_1 & \sigma_2 \frac{F_0^*}{Z_0^*} & \alpha H_0 \frac{\lambda}{\lambda} \\
0 & 0 & \sigma_1 & -\sigma_2 \frac{F_0^*}{Z_0^*} - \phi_1 & 0 \\
0 & 0 & \gamma & 0 & -\delta - \tilde{\alpha} H_0 \frac{\lambda}{(\lambda + E)^2}
\end{bmatrix}
\]

where \( Z_0^* = H_0^* + F_0^* = (G + 1)F_0^* \).
We note that this is a block upper triangular matrix of the form
\[ J = \begin{vmatrix} A & B \\ 0 & C \end{vmatrix}. \]
Since \( \sigma(J) = \sigma(A) \cup \sigma(C) \) [21], we need only guarantee that the

eigenvalues of \( A \) and \( C \) are negative to ensure stability of the system around
the disease-free equilibrium.

We apply Gershgorin’s theorem of disks [28] to these two submatrices:
the eigenvalues of a general square matrix \( (a_{ij}) \) must lie in the union of disks
in the complex plane defined by \( D(a_{ii}, \sum_{j \neq i} |a_{ji}|) \) (i.e., disks centred at the
diagonal elements of the matrix with radii of lengths equal to the sums of
the absolute values of the non-diagonal elements each respective column).

Applying this to our submatrices, we find that the eigenvalues of \( C \) are

guaranteed to be negative when \( \gamma < \eta_1, 0 < \phi_1 \) (which is always true, given
our parameter assumptions), and \( \alpha < \frac{\delta \lambda}{\beta_0} + \tilde{\alpha} \). Similarly, the eigenvalues of
\( A \) are negative when \( \frac{2\beta \kappa^2 Z_0^*}{(\kappa^2 + Z_0^2)^2} < \eta_0 \) and
\( \frac{2\beta \kappa^2 Z_0^*}{(\kappa^2 + Z_0^2)^2} < \phi_0 \). Thus, when these
conditions are satisfied, the disease-free equilibrium in the constant coefficient

case (if it exists) is stable.

Ecologically, this implies that the death rates of the different classes of
bees must be sufficiently high and the infection and natural spore decay rates
sufficiently low for the disease-free equilibrium to be stable.

Further analysis of the model has been attempted, particularly in the

case of periodic coefficients using Floquet Theory. However, the results have
proven too algebraically complex for current analytic approaches and are
unlikely to have any real ecological significance.
Chapter 4

Parameter Estimation, Simulations, and Numerical Analysis

We turn now to numerical simulations to better understand the dynamics of the system. These simulations were executed using the software $R$ [36] and the associated package $deSolve$ [42].

4.1 Parameter Estimation

For each of our time-dependent parameter functions, we construct smooth functions based on seasonal averages. We use the $pchip$ function found in R’s $pracma$ package [9], which constructs a piecewise-smooth Hermite interpolating Polynomial function through a specified collection of points over a collection of x-values.

We list the seasonal average values in Table 4.1. Based on simple rounded calculations, we assume that there are 91 days in each season.

For birth rates, we refer to [44] for seasonal averages, and we follow [37] in choosing 8000, 12000, 8000, and 6000 as seasonal averages for $\kappa$ in Spring,
Table 4.1: Seasonal Parameter Values

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Symbol</th>
<th>Unit</th>
<th>Spring</th>
<th>Summer</th>
<th>Fall</th>
<th>Winter</th>
</tr>
</thead>
<tbody>
<tr>
<td>Max. Birth Rate</td>
<td>$\beta$</td>
<td>Bees/Day</td>
<td>500</td>
<td>1500</td>
<td>500</td>
<td>0</td>
</tr>
<tr>
<td>Half-Sat. Birth Constant</td>
<td>$\kappa$</td>
<td>Bees</td>
<td>8000</td>
<td>12000</td>
<td>8000</td>
<td>6000</td>
</tr>
<tr>
<td>Base Transition Rate</td>
<td>$\sigma_1$</td>
<td>Bees/Day</td>
<td>0.25</td>
<td>0.25</td>
<td>0.25</td>
<td>0</td>
</tr>
<tr>
<td>Max. Feedback Rate</td>
<td>$\sigma_2$</td>
<td>Bees/Day</td>
<td>1.5</td>
<td>1.5</td>
<td>1.5</td>
<td>1.5</td>
</tr>
<tr>
<td>$H_0$ Death Rate</td>
<td>$\eta_0$</td>
<td>Bees/Day</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0.00649</td>
</tr>
<tr>
<td>$H_1$ Death Rate</td>
<td>$\eta_1$</td>
<td>Bees/Day</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0.00649</td>
</tr>
<tr>
<td>$F_0$ Death Rate</td>
<td>$\phi_0$</td>
<td>Bees/Day</td>
<td>0.08511</td>
<td>0.08511</td>
<td>0.08511</td>
<td>0.00649</td>
</tr>
<tr>
<td>$F_1$ Death Rate</td>
<td>$\phi_1$</td>
<td>Bees/Day</td>
<td>0.16936</td>
<td>0.16936</td>
<td>0.16936</td>
<td>0</td>
</tr>
<tr>
<td>Infection Rate</td>
<td>$\alpha$</td>
<td>Bees/Day</td>
<td>0.55</td>
<td>0.12</td>
<td>0.24</td>
<td>0</td>
</tr>
<tr>
<td>Deposition Rate</td>
<td>$\gamma$</td>
<td>Env.Pot./Day</td>
<td>0.2061</td>
<td>0.2835</td>
<td>0.2527</td>
<td>0.2835</td>
</tr>
<tr>
<td>Decay Rate</td>
<td>$\delta$</td>
<td>Env.Pot./Day</td>
<td>0.006570</td>
<td>0.023300</td>
<td>0.015683</td>
<td>0.023300</td>
</tr>
<tr>
<td>Uptake Rate</td>
<td>$\tilde{\alpha}$</td>
<td>Env.Pot./Day</td>
<td>$\tilde{\alpha}$</td>
<td>$\tilde{\alpha}$</td>
<td>$\tilde{\alpha}$</td>
<td>0</td>
</tr>
</tbody>
</table>

Summer, Fall, and Winter (respectively). We also set $n = 2$ as a constant to impose an Allee Effect on the colony.

Based on [5], we estimate that healthy adult foragers have average lifespans of $\frac{11.6 + 11.9}{2} = 11.75$ days, and from [17], we assume that N. ceranae infection increases the death rate of foragers by a factor of 1.99. Thus, we set $\phi_0 = \frac{1}{1 \text{1.75}} \approx 0.08511$ and $\phi_1 = 1.99 \cdot \phi_0 \approx 0.16936$. We assume that these are constant throughout Spring, Summer, and Fall, but change in Winter [39]. In the Winter, we assume that bees cease foraging and revert to being hive bees, so we take $\phi_0 = \phi_1 = 0$ during Winter. We handle this reversion below through the transition rates $\sigma_1$ and $\sigma_2$.

We take hive bee deaths to be negligible during the active seasons, so for Spring, Summer, and Winter, we set $\eta_0 = \eta_1 = 0$. Based on [39], we assume a Winter lifespan of 154.095 days for hive bees. Given that the disease’s impacts are most notable in forager bees, we assume that even in Winter, $\eta_1 = \eta_0$.

In general, hive bees leave the hive to become foragers after no less than
4 days \[25\], so we take \( \sigma_1 \) (the maximum transition rate) to be \( \frac{1}{4} = 0.25 \) in Spring, Summer, and Winter. We wish to select \( \sigma_2 \) so that in the absence of disease, forager bees begin to revert to hive bees when their population exceeds one-third of the total colony population. This requires that the transition terms sum to zero when \( H = 2F \). (The result will be equivalent for the healthy and infected classes.) Therefore,

\[
0 = 2(0.25)F - \sigma_2 \frac{F}{3F}F
\]

\[
\Rightarrow 0 = 0.5 - \frac{\sigma_2}{3}
\]

\[
\Rightarrow \sigma_2 = 1.5
\]

and we use this value for Spring, Summer, and Fall. In Winter, we assume that all forager bees quickly revert to hive bees, and we therefore set \( \sigma_1 = 0 \) and we maintain \( \sigma_2 \) at 1.5, as this will result in all foragers reverting to the hive classes.

### 4.1.1 Disease Parameters

For disease parameters, we first assume that infections drop to zero in the Winter, given that infections are caused by spore exposure during comb cleaning, which is driven by a need for combs for new brood. Since births and honey production are minimal in Winter, we expect very little cell cleaning during Winter, and we therefore set \( \alpha = \tilde{\alpha} = 0 \).

In Spring, Summer, and Fall, we take the number of infections to be a percentage of the number of spore-bee interactions depending on the infectivity of the disease. Based on infectivity levels in \[27\], we take \( \alpha = 0.55, 0.12, \) and 0.24 in the Spring, Summer, and Fall, respectively. We let \( \tilde{\alpha} \) be variable, but constant across seasons, since spore removal is unaffected by the infectivity of the disease.

Many aspects of the dynamics of *N. ceranae* remain poorly understood,
including how spores lose viability and whether spores can regain viability. In our model and simulations, we assume that spores cannot regain viability after losing it, and that therefore, over the course of a season, the reduction due to decay in the environmental potential can be approximated by $\alpha$, the level of infectivity. Therefore, in solving the initial value problem

$$\dot{E} = -\delta E, \quad E(l) = \alpha E(0)$$

where $l$ is the length of each season, we calculate $\delta = -\frac{\ln(\alpha)}{l}$ in Spring, Summer, and Fall. In the absence of data in the literature, we assume that spores do not exhibit substantial decay in Winter and thus, we set $\delta = 0$ during the Winter.

Concerning $\gamma$, we note that because bees remain in the hive over Winter, infected bees will continually deposit new spores on the comb. During active seasons, bees must remain in the hive on days with poor weather (i.e., precipitation), and infected bees can again deposit spores on the comb during these days. We therefore assume that the deposition rate outside of Winter is a percentage of the Winter rate. To calculate this percentage, we refer to climate data listed in [1] for the Waterloo Wellington Weather Station, the closest station to the University of Guelph. Summing the days with over 5mm of precipitation from March to May, from June to August, and from September to November, and then dividing by the number of days in those months, we estimate that the deposition rates in Spring, Summer, and Fall are respectively 20.61%, 28.35%, and 25.27% of the Winter rate, $\gamma_W$, which we leave as variable.

We observe that $\lambda$ (the half-saturation disease threshold), $\gamma$ (the deposition rate), and $\alpha$ (the removal rate of potential due to ingestion by bees) are the only parameters directly related to the scale of $E$, which is simply measured in units of “environmental potential.” Indeed, we can rescale $E$ with respect to $\lambda$. By making the substitution $e = \frac{E}{\lambda}$, the equation for $\dot{E}$ can
be rewritten as

\[ \dot{e} = \frac{\gamma}{\lambda} H_1 - \delta e - \frac{\tilde{\alpha}}{\lambda} \frac{e}{1 + e} H_0 \]

This implies that for simulation results, the values of these parameters do not matter nearly as much as the relative value sizes between the three parameters. Little precise data exists to estimate any of these three values, so we fix \( \lambda = 10^4 \) in all seasons and allow the values of \( \gamma_W \) and \( \tilde{\alpha} \) to vary with the restrictions described above.

### 4.2 Formation of Parameter Functions

For each parameter that varies by season, we create a smoothened parameter function using R’s `pchip` function. We note that the parameters fall into three main classes.

The first class includes parameters such as \( \beta \) and \( \kappa \) and exhibits a low value in Winter, and high value in Summer, and intermediate values in Spring and Fall. The second class features constant values from Spring through Fall, with a change in Winter. This class includes parameters that increase in Winter, such as \( \eta_0 \), and those that decrease in Winter, such as \( \phi_0 \). Finally, the third class, which includes \( \alpha \) and \( \gamma \), continuously switches between increases and decreases between seasons. We smoothen each of these classes differently.

For the first class, we set the function equal to the average from \( \frac{1}{4} l \) to \( \frac{3}{4} l \) in Summer and Winter (where \( l \) is the length of the season). Then, we set the function equal to the seasonal averages at the midpoints of Spring and Fall, and we interpolate the values between these midpoints and the endpoints of the constant portions from Summer and Winter.

For the second class, we apply a similar technique, interpolating in the last \( \frac{1}{4} l \) days of Fall, the first and last \( \frac{1}{4} l \) days of Winter, and the first \( \frac{1}{4} l \) days of Spring. We set the functions equal to the seasonal averages in the remaining portions of the seasons (including the entirety of Summer). For \( \sigma_1 \), we only reduce the season lengths by \( \frac{1}{32} l \), since the migration back to the
hive occurs on a relatively small time scale.

We use a similar approach to that of the second class for the third class, although here we interpolate between all seasons.

As a visual aid, we provide graphs below showing single periods of $\beta(t)$, $\phi_0(t)$, and $\alpha(t)$. Respectively, these variables are in the first, second, and third classes listed above. Plots for the remaining functions are shown in Appendix A.

![Graph of $\beta(t)$ function](image)

Figure 4.1: A Single Period of the Formed $\beta(t)$ Function
Figure 4.2: A Single Period of the Formed $\phi_0(t)$ Function
4.3 Simulation Criteria and a Base Simulation

We proceed to examine results of numerically integrating the system. We begin each simulation with initial values $H_0(0) = 10^4$, $H_1(0) = 0$, $F_0(0) = 10^4$, $F_1(0) = 0$, and $E(0) = 0$ where $t = 0$ is the beginning of the first day of Spring. We numerically integrate the system over Spring, Summer, Fall, and Winter, saving the population values at which the integration ends. To integrate, we used the $ode$ function in R’s $deSolve$ package, using the $lsoda$ method with absolute and relative tolerances of $10^{-6}$. After this, we continue to integrate the system, and at the beginning of each year, we compare
population values for $H_0$, $H_1$, $F_0$, $F_1$, and $E$ to those at the beginning of the previous year. If these values are sufficiently close, we assume that the simulation is sufficiently close to a limit cycle (or, if the colony dies out, to a steady state) and so we end the simulation. Otherwise, we integrate for another year and check population levels again, continuing this process until we are sufficiently close to a limit cycle.

Our stopping criterion was

$$\frac{||x_i - x_{i-1}||}{||x_i|| + ||x_{i-1}|| + \tau} < \epsilon$$

where $\tau = 0.001$ (to prevent division by zero), $\epsilon = 0.01$, and $x_i$ is the value of the variable $x$ on the first day of the $i^{th}$ year. In our use of the $ode$ function, we calculated values with time differences of 0.01 days. The integration time step is determined internally by the function.
We first examine a base case in which no disease is present in the system, shown in Figure 4.4. This will serve as a benchmark to which to compare later cases involving colony stressors.

In the absence of *N. ceranae*, the colony very quickly reaches a healthy limit cycle, as shown in Figure 4.4. Since no disease is introduced, the colony only contains healthy hive bees and healthy forager bees, the populations of which fluctuate with the seasons as expected. The colony population peaks toward the end of Summer and reaches a minimum near the end of Winter. As well, foragers return to the hive in Winter, increasing hive bee populations. This effect is reversed at the beginning of Spring.
4.4 \textit{N. ceranae} Infection as a Sublethal and Lethal Effect

We now study the effect of varying the parameter values $\gamma_W$ and $\tilde{\alpha}$ when the disease is present in the colony. We proceed with the method described above, but to simulate the onset of the disease, we manually increase the level of $H_1$ to 10 on the first day of Winter of the first year to simulate a small number of infected individuals returning to the hive for Winter.

Based on preliminary tests, we first set $\gamma_W = 0.1$ and observe the behaviour of our system as it is integrated to a limit cycle for levels of $\tilde{\alpha}$ increasing from 0.1 to 0.2 in increments of 0.005.

Our results show that the removal rate $\tilde{\alpha}$ has a notable impact on bee populations. Below, we present the simulation results for $\tilde{\alpha} = 0.15, 0.165,$ and $0.2$, in Figures 4.5, 4.6, and 4.7, respectively.
Figure 4.5: Colony Failure Due to Low Spore Uptake ($\tilde{\alpha} = 0.15, \gamma_W = 0.1$)

When $\tilde{\alpha} = 0.15$, the disease potential grows steadily over several years. In Spring of the second year, a small percentage of hive bees are infected, and this percentage increases in the third, fourth, and fifth years as well, although the colony is able to survive with decreasing populations. In the fourth and fifth years, we also observe that the infected hive bee population exceeds the healthy hive bee population slightly. In the sixth year, the colony population plummets immediately after foragers begin to leave the hive, and the colony is effectively dead by the end of Summer.

We also see that the environmental potential grows larger in each Winter when the hive has sufficient numbers of bees. In the sixth Winter, the potential peaks at a lower value than in the prior year, before being depleted due to natural decay following the colony’s failure.
Figure 4.6: Endemic Colony Due to Moderate Spore Uptake ($\tilde{\alpha} = 0.165, \gamma_W = 0.1$)

In Figure 4.6, the disease is reined in by a higher removal term ($\tilde{\alpha}=0.165$) to the extent that the hive does not die but instead reaches an endemic limit cycle. The amount of the hive bees being infected remains low, although it is large enough to replenish the disease reservoir each year.

Increases are seen each year in the environmental potential until the system grows sufficiently close to a limit cycle. In Figure 4.5, this reservoir reached approximately 1400 units at its maximum, whereas in the endemic scenario, the potential approaches roughly 550 units at its peak.
When the removal term grows large enough, as in Figure 4.7 where \( \tilde{\alpha} = 0.2 \), the spores are eliminated quickly enough that the disease cannot take root in the hive. In this scenario, we do not see significant levels of infection, even in the first few years when the disease potential is largest. The colony approaches a disease-free cycle, although it takes several years for our program to reach its stopping criterion.

With regard to the environmental potential, we see a peak in the first Winter around 150 units. This is quite low in comparison to the previous simulations. Each year, the level of the reservoir peaks at a lower value until the disease is effectively eradicated.

We now present plots showing the limit cycle values of \( H_0 \), \( H_1 \), and \( E \).
at the beginning of Spring for values of $\tilde{\alpha}$ between 0.1 and 0.2. The graphs of $F_0$ and $F_1$ exhibit similar behaviour to those of $H_0$ and $H_1$, respectively, and so we omit them here. However, we include these graphs, along with the graph for the colony size as a function of $\tilde{\alpha}$, in Appendix A.

Figure 4.8: Healthy Hive Bees on the First Day of Spring in Limit Cycle for Variable Levels of $\tilde{\alpha}$ ($\gamma_W = 0.1$)
Figure 4.9: Infected Hive Bees on the First Day of Spring in Limit Cycle for Variable Levels of $\hat{\alpha}$ ($\gamma_W = 0.1$)
As we saw in the individual simulations, low levels of \( \bar{\alpha} \) lead to an absence of healthy and infected bees and environmental potential, implying a hive failure. Moderate values of \( \bar{\alpha} \) yield endemic limit cycles where all three exist, and high levels remove all potential and infected bees, leaving a healthy hive. Here, we see the empty-hive limit cycle being stable for \( \bar{\alpha} \leq 0.15 \), the endemic limit cycle being stable for \( 0.155 \leq \bar{\alpha} \leq 0.17 \), and the healthy hive being stable for \( 0.175 \leq \bar{\alpha} \). Our analytical results support these findings, as they require that \( \alpha < \frac{\delta \lambda}{\beta_0} + \bar{\alpha} \) for the stability of the disease-free limit cycle. It is not unexpected, then, that this limit cycle reaches stability as \( \bar{\alpha} \) grows.

Although one may be tempted to infer from this that \( N. \ ceranae \) rarely results in an endemic limit cycle when it affects a hive, the above simulations
assume that $\gamma_W = 0.1$. In reality, $\gamma_W$ could have a different value which could change these bounds. It is also difficult, based on the current literature, to determine an exact value for $\tilde{\alpha}$ or for $\lambda$ in the ecological context. Ultimately, we infer from these simulations a direct relationship between the spore uptake rate and the strength of the colony. We also note the possibility for all three potential outcomes: colony failure, endemic colony infection, and disease eradication.

Thus far, we have held $\gamma_W$ (the spore deposition rate) constant and let $\tilde{\alpha}$ vary. Now, we fix $\tilde{\alpha} = 0.17$ in Spring, Summer, and Fall and $\tilde{\alpha} = 0.0$ in Winter. We allow $\gamma_W$ to vary from 0.1 to 0.2 in increments of 0.005, as we have with $\tilde{\alpha}$. We show the numerical solutions to the system of differential equations for $\gamma_W = 0.1$, 0.12, and 0.125.
Figure 4.11: Disease-Free Colony Due to Low Spore Deposition ($\gamma_W = 0.1, \bar{\alpha} = 0.17$)

We see a similar, though mirrored, effect as $\gamma_W$ increases. Low levels, as in Figure 4.11 where $\gamma_W = 0.1$, prevent the disease from taking root and maintain a disease-free colony. Indeed, this result is incredibly similar to that in Figure 4.7. Infection levels remain low throughout all years, and the environmental potential peaks (in this case, around 140 units) in the first year before decreasing in each subsequent year.
Figure 4.12: Endemic Colony Due to Moderate Spore Deposition ($\gamma_W = 0.12, \tilde{\alpha} = 0.17$)

Moderate levels, as in Figure 4.12 where $\gamma_W = 0.12$, yield an endemic limit cycle in the hive. Infection levels are initially low and increase over time, although they do not grow large enough to cause colony death. This does result, however, in reduced colony populations (with greater reductions than in Figure 4.6), which we will explore below in conjunction with other effects.
High levels of $\gamma_W$ overwhelm the colony and lead to colony failure, as shown in Figure 4.13 where $\gamma_W = 0.125$. This result occurs in the Spring of the fourth year, which is earlier than the colony death seen in Figure 4.5. Here, the infected hive bee population overtakes that of the healthy hive bees in Spring of the fourth year, and the colony dies early in that year. In this case, we also see high levels of infected forager bees prior to colony death. Increasing $\gamma_W$ further only results in a faster colony death.

Regarding the disease, we see the environmental potential reaching previously unseen levels, peaking in the third year around 2000 units. This quickly leads to colony failure as the infection rates skyrocket.

As above, we also present the general trends of limit cycle values for $H_0$, $H_1$, $F_0$, and $F_1$. 

Figure 4.13: Colony Failure Due to High Spore Deposition ($\gamma_W = 0.125, \tilde{\alpha} = 0.17$)
$H_1$, and $E$ on the first day of Spring at the limit cycle, in Figures 4.14, 4.15, and 4.16. (We also provide this data for $F_0$, $F_1$, and the colony population in Appendix A.)

Figure 4.14: Healthy Hive Bees on the First Day of Spring in Limit Cycle for Variable Levels of $\gamma_W$ ($\tilde{\alpha} = 0.17$)
Figure 4.15: Infected Hive Bees on the First Day of Spring in Limit Cycle for Variable Levels of $\gamma_W$ ($\tilde{\alpha} = 0.17$)
Figure 4.16: Environmental Potential on the First Day of Spring in Limit Cycle for Variable Levels of $\gamma W (\tilde{\alpha} = 0.17)$

The trend we find is, again, a mirrored trend to that of $\tilde{\alpha}$. The healthy hive limit cycle is stable for $\gamma W \leq 0.105$, as seen in the presence of healthy hive bees and the absence of infected bees and environmental potential. The endemic limit cycle is stable for $0.11 \leq \gamma W \leq 0.12$, where all populations are present, and the empty hive limit cycle is stable for $0.125 \leq \gamma W$, where all populations fall to zero. Again, this aligns with our analysis, which suggested that high values of $\gamma W$ would destabilize the disease-free limit cycle, as they required $\gamma < \eta_l$ in the constant coefficient case.

Again, we must note that, in the absence of confident estimations of either parameter, the quantitative impact of these simulations should not be overstated. Instead, we focus on the qualitative implications of these results.
on the existence of the three limit cycles and on the relationship between these parameters and colony strength.

Also to be noted from these graphs, and from those demonstrating the effect of $\tilde{\alpha}$ on these populations, is the impact on the colony of the Allee effect imposed on the birth function. Rather than having the colony populations slowly decrease to an empty hive, there is a sudden drop when, above, $\tilde{\alpha} \approx 0.1525$ and $\gamma_W = 0.1$, as well as when $\tilde{\alpha} = 0.17$ and $\gamma_W \approx 0.1225$. 
4.5 Homing Failure Caused by Neonicotinoids as a Sublethal and Lethal Effect

Next, we turn our attention to the impact of neonicotinoid pesticides, such as thiamethoxam and clothianidin, on colony health. While claims exist for a variety of effects from these pesticides, we focus on their ability to cause homing failure in foraging bees, which has been demonstrated in [18]. These pesticides interfere with a bee’s memory and navigational capacity, which can prevent a forager bee from successfully returning to the hive. This quickly leads to death for the individual bee, which cannot survive on its own.

To incorporate this into our model, we augment the death rates of foraging bees at selected times throughout the year. Our modified model is then

\[
\begin{align*}
\dot{H}_0 &= \beta(t) \frac{Z^2}{\kappa(t)^2 + Z^2} - \sigma_1(t)H_0 + \sigma_2(t)\frac{F}{Z}F_0 - \eta_0(t)H_0 - \alpha(t)H_0 \frac{E}{\lambda(t) + E} \\
\dot{H}_1 &= -\sigma_1(t)H_1 + \sigma_2(t)\frac{F}{Z}F_1 - \eta_1(t)H_1 + \alpha(t)H_0 \frac{E}{\lambda(t) + E} \\
\dot{F}_0 &= +\sigma_1(t)H_0 - \sigma_2(t)\frac{F}{Z}F_0 - (\phi_0(t) + \xi(t))F_0 \\
\dot{F}_1 &= +\sigma_1(t)H_1 - \sigma_2(t)\frac{F}{Z}F_1 - (\phi_1(t) + \xi(t))F_1 \\
\dot{E} &= \gamma(t)H_1 - \delta(t)E - \tilde{\alpha}(t)H_0 \frac{E}{\lambda + E}
\end{align*}
\]

where \(\xi(t)\) is the increase (due to homing failure) in forager deaths.

We observe this in simulation with low, medium, and high estimates of homing failure rates of 0.102, 0.209, and 0.316, respectively [18], and compare these to the case where no homing failure occurs, shown above in Figure 4.4. We include these increases for a 21-day period at the beginning of Spring in Years 4 through 6, to simulate the spray application of neonicotinoid pesticides on crops near the colony.

As with our other time-dependent parameters, we form a smooth function that gradually shifts between 0 and the specified homing failure rate. In the
Spring seasons when we apply homing failure, we use the last $\frac{1}{64}$ days of the previous Winter and the first $\frac{1}{64}$ days of Spring to gradually increase the homing failure rate. We also decrease it to 0 over a similar period at the end of the 21 days, which begins at $21 - \frac{1}{64}$ days into Spring and ends at $21 + \frac{1}{64}$ days into Spring.

Figure 4.17: Colony Survives a Low Level of Homing Failure ($\xi = 0.102$)

In Figure 4.17, we observe the case where homing failure occurs at a low level in the absence of disease. We see a marked hollowing in colony populations during the weeks when homing failure is imposed on the colony. Here, forager death rates are augmented by 10.2% in the aforementioned weeks, but the colony is able to survive this added stress, and indeed, following the application of homing failure, the colony quickly returns in the following year to its previous strength.
Figure 4.18 shows a similar simulation using a moderate level of homing failure, where $\xi = 0.209$. Already, we see the impact of this increase in forager deaths, as the colony quickly dies in Spring of the fourth year, despite having appeared healthy up until this point. The heightened forager death rate draws hive bees out at a faster rate, and the colony is unable to sustain itself through new births, which leads to hive failure.

Given that this moderate level can already wipe out a colony, we omit results for a high level of homing failure ($\xi = 0.316$).
4.6  \textit{N. ceranae} and Homing Failure as a Lethal Joint Effect

We now present a simulation combining the joint effects of neonicotinoids and \textit{N. ceranae}. We use a homing failure rate of $\xi = 0.102$ for 21 days at the beginning of Spring, as above. In doing so, we demonstrate the lethality of multiple stressors in a colony. For infection parameters, we take $\gamma_W = 0.12$ and $\tilde{\alpha} = 0.17$, which, as shown above in Figure 4.12, will (in the absence of homing failure) result in an endemic limit cycle with a small reduction in colony size. This limit cycle is reached after 13 years, so we first allow the system to near this limit cycle and then apply homing failure in years 13, 14, and 15.
As depicted in Figure 4.19, the colony, after initial inoculation, survives several seasons of infection. While infected bees are present, their population remains relatively low, and the environmental potential stays well below the level at which mass outbreaks and/or hive failure occur. When homing failure rates increase, the increased death toll for foragers draws higher numbers of hive bees out precociously, and the colony cannot sustain itself through new births. Populations plummet and the colony dies due to the joint effect of *N. ceranae* and homing failure caused by neonicotinoids.

We propose that this result, in which two sublethal effects combine to destroy a colony, should be considered in studying the effects of these stressors in a lab. For example, while experiments may determine a particular dose
of pesticide as being safe for bee colonies, this level may need to be adjusted if experiments were performed in a closed environment, to account for the absence of other stressors.
Chapter 5

Hive Cleaning by Comb Replacement

5.1 Comb Replacement as a Useful Means of Disease Treatment

We turn our attention now to the potential use of hive cleaning to treat an *N. ceranae* infection in a colony. Since the spores of the disease rest on the combs of the hive, some beekeepers replace a fraction of the comb frames with spore-free frames in an attempt to mitigate the infection. To investigate this with our model, we make certain assumptions about frame replacement:

1. Based on discussions with biologists and apiarists, we assume that frames can be replaced at two points of the year: in early Spring before brood combs are used to rear bees, and in late Spring when one hive is split into two and new combs can be placed into the split hive.

2. We assume that this frame replacement can be done instantaneously (i.e., in one time step in simulations).

3. Apiarists usually replace two to three of the ten frames in a hive. With
equal distribution of spores among frames, this would remove around 20% to 30% of the environmental potential. Since distribution may be uneven, we allow for the percentage of spores removed to vary between 0% and 98% in our simulations. However, we keep this rate constant in each simulation to see the overall effect of average cleaning levels being more thorough or less thorough.

In our model, we implement this by adding a removal term, \(-C(t)E\), to the equation for \(\dot{E}\).

\[
\dot{H}_0 = \beta(t) \frac{Z^2}{\kappa(t)^2 + Z^2} - \sigma_1(t)H_0 + \sigma_2(t)\frac{F}{Z}F_0 - \eta_0(t)H_0 - \alpha(t)H_0 \frac{E}{\lambda(t) + E}
\]
\[
\dot{H}_1 = -\sigma_1(t)H_1 + \sigma_2(t)\frac{F}{Z}F_1 - \eta_1(t)H_1 + \alpha(t)H_0 \frac{E}{\lambda(t) + E}
\]
\[
\dot{F}_0 = \sigma_1(t)H_0 - \sigma_2(t)\frac{F}{Z}F_0 - \phi_0(t)F_0
\]
\[
\dot{F}_1 = \sigma_1(t)H_1 - \sigma_2(t)\frac{F}{Z}F_1 - \phi_1(t)F_1
\]
\[
\dot{E} = \gamma(t)H_1 - \delta(t)E - C(t)E - \tilde{\alpha}(t)H_0 \frac{E}{\lambda + E}
\]

\(C(t)\) is a step function which is zero at all times other than those specified for cleaning. Since each comb replacement is instantaneous, the function is non-zero over a single time-step, and so we do not smoothen the function, unlike with our other parameters.

To derive values for \(C(t)\), we use a similar approach to that used to estimate values for \(\delta\) in Section 4.1.1. We specify \(r\), the percentage of spores to remain after cleaning, and then calculate \(C(t_{\text{clean}}) = -\frac{\log(r)}{\Delta t}\), where \(t_{\text{clean}}\) is any time at which cleaning occurs. We then construct our step function with this height at the start of the desired days of of each year.

We wish to minimize the replacement of frames, which is a labour cost for beekeepers, and the shortfall in colony health due to disease, which decreases the productivity of the colony. Thus, we first calculate the optimal population level by running a simulation in the absence of disease. Since population
levels peak in Summer in each year, and this can be an indicator of the amount of honey a hive will produce, we take the population at the beginning of the final day of Summer for a disease-free colony as the optimal colony population.

Based on our simulations in Section 4.4, we select $\tilde{\alpha} = 0.18$ and $\gamma_W = 0.12$ for our disease parameters. As we noted previously, these are within the range where the hive tends toward an endemic limit cycle. In particular, this choice of parameters results in a noticeably weakened hive when no treatment is applied.

We begin with $r = 1.0$ (when 0% of spores are removed) and as before, we integrate until sufficiently close to a limit cycle, noting the colony shortfall at the end of Summer in this limit cycle. We proceed to decrease $r$ in increments of 0.02 until $r = 0.02$, and we run a simulation for each value of $r$.

We hypothesize that more frequent cleaning will better contain the disease, and that comb replacement is most effective when done earlier in the year. Early comb replacement should remove spores before they are able to infect the hive and propagate. To examine this, we run three experiments: one in which we clean the hive on the 7th and 84th days of Spring, one in which we clean only on the 7th day of Spring, and one in which we clean only on the 84th day of Spring.
Figure 5.1: Effect of Frame Replacement on Days 7 and 84 on Percent Colony Population Shortfall ($\tilde{\alpha} = 0.17, \gamma_W = 0.12$)

The plot in Figure 5.1 comes from the first experiment. The graph shows the percent shortfall of the colony’s population at the end of Summer (in the limit cycle) as a function of the percentage of the disease reservoir removed in each instance of cleaning. As the amount removed increases from 0% to 98%, the shortfall decreases in an sublinear fashion from roughly 21% to roughly 2%. While the largest decreases in colony losses are likely unattainable, these results do suggest that comb replacement is, in theory, a powerful treatment.

On a more practical note, if we assume that a beekeeper, by changing 2 to 3 frames per cleaning, can remove 20% to 30% of the environmental potential, the colony losses can still be roughly halved, a reduction that is not insignificant. Given the low cost to the beekeeper of changing frames, this could be a helpful method of disease containment that would strengthen colonies and may increase honey production by increasing colony populations.
Figure 5.2: Effect of Frame Replacement on Day 7 on Percent Colony Population Shortfall ($\tilde{\alpha} = 0.17, \gamma_W = 0.12$)

Figure 5.2 shows the results of the second experiment, where frames are replaced only on the 7th day of each year. Here we see less of an impact than the previous experiment: colony losses can theoretically be reduced from 20% of the colony to around 4%, but a realistic approach would likely see them reduced to around 14%. This suggests that the frequency with which one cleans has a notable effect on the containment of the disease.
In Figure 5.3, we see the impact of only replacing frames in late Spring. Under the strongest cleaning regimen, colony losses are reduced to around 7.5%, and in the 20% to 30% range of spore removal, they are only reduced to around 15%. Both of these levels are higher than those seen in the second experiment, lending credence to our hypothesis that earlier cleaning is more effective. However, the actual benefit of cleaning earlier appears relatively small at lower cleaning levels.

Ultimately, we infer from these results that hive cleaning can be used to decrease colony losses at low cost to an apiary, although it is unlikely to cure a hive. It appears most effective when done often during times of high *N. ceranae* levels, such as in early Spring.
5.2 Comb Replacement as a Poor Means of Combatting Multiple Stressors

In light of the results from our experiments involving homing failure, we wish to see whether periodic comb replacement can be used to strengthen a colony to the point that it overcomes a bout of homing failure. To this end, we run a simulation like the previous cleaning simulations, where the cleaning levels on days 7 and 84 increase together from 0% to 98%. However, we now allow for a low homing failure force ($\xi = 0.102$) active for the first 21 days of years 13, 14, and 15. As seen in Section 4.6, this disease set-up normally leads to an endemic limit cycle. We present the results in Figure 5.4.

![Figure 5.4: Effect of Frame Replacement on Days 7 and 84 on Percent Colony Population Shortfall with Homing Failure Applied in Years 13 through 15 ($\tilde{\alpha} = 0.17$, $\gamma_W = 0.12$, $\xi = 0.102$)](image)

Here, we see that the colony dies in most comb replacement applications, exhibited by a 100% colony loss. We observe that for disease removal levels
upwards of 90%, the colony is able to survive the application of homing failure, though it still experiences a small population reduction. To clean to this extent on a regular basis is largely unattainable in reality, making frame replacement a poor response in this case. However, we note that these results would likely vary depending on the virulence of the disease (controlled by $\gamma_W$, $\bar{\alpha}$, and $\lambda$), the length of the homing failure period, and the rate at which it affects bees.
Chapter 6

Conclusion and Future Work

In this work, we have proposed a model for a *N. ceranae* infection within an *A. mellifera* colony. This model includes division of labour between hive and forager bees and proposes the use of an environmental potential as the route of infection. Admittedly, our model is not perfect, in part due to some uncertainties regarding the spread of the disease within the hive. In these areas, we have attempted to include what we believe are the most salient known aspects of the disease’s pathology.

Our results confirm much of the present understanding of the disease: colonies can fight off infection, coexist with the disease, or be overtaken by the disease. In some cases of colony failure, we see a gradual decrease in population each year until the entire colony is wiped out, showing the effect of seasonally variant parameters. Hive failure occurs in early Spring when infection rates are high.

As well, through our simulations including the effect of homing failure from pesticide use, we see that two sublethal effects can weaken a hive to the point of failure when applied together. Since this colony failure occurs in early Spring, this provides a potential explanation of Colony Collapse Disorder as a multi-causal phenomenon created by the confluence of pesticide and disease stresses in a colony.
We also used our model to investigate the usefulness of comb replacement as a way of mitigating a *N. Ceranae* infection. Our results indicate that comb replacement is unlikely to eradicate the disease, given that it is unlikely to remove all spores and that it does not remove infected bees which can regenerate the disease reservoir. However, comb replacement, even at the levels commonly applied, can have positive effects on colony strength, particularly when done earlier in the season. Given the low cost of the procedure, we do not see great drawbacks of applying this strategy to a small number of hives in which *N. ceranae* is the main health concern.

Lastly, we considered the case of a colony affected by *N. ceranae* and homing failure to see whether comb replacement could mitigate the stress on the colony. Unfortunately, our model predicts that only the most stringent cleaning would prevent hive death, suggesting that such an approach would not be effective at lower, more attainable cleaning levels. Therefore, in general, we infer that other methods of treatment such as antibiotics and natural chemical remedies should be included in disease management when other stressors are known to be present.

Many questions remain regarding *N. ceranae*, and much work is still to be done. In part, the work above would benefit from better estimation of parameters and a better understanding of the disease’s pathology from the biological sciences. Admittedly, a colony of bees is not a co-operative study subject, and some knowledge may remain unknown well into the future.

As well, while we obtained some analytical results, we do not have a full mathematical understanding of the system’s dynamics and eventually had to resort to numerical simulations. While, in theory, our problems have solutions, we currently lack advanced techniques for handling systems of this size and algebraic complexity.

There is still work to be done with this model in particular. While we have studied comb replacement as a potential treatment regimen, other strategies
do exist, including the use of the antibiotic fumagillin. Time constraints prevented a proper study of this approach. Additionally, much of our work included events that were heavily time-dependent. Forces such as homing failure, comb replacement, and even the onset of the disease occur at specific times of the year, and there may be benefits in observing the impact of these forces at different times of the year.

We must note that other variables exist in our approach that we fixed arbitrarily. The application of homing failure over 21 days in 3 consecutive years is simply one of many possible applications of the phenomenon. Due to time constraints, we were unable to investigate other cases. Further, homing failure is only one of the suggested effects of neonicotinoids on honey bees and their colonies, and our model could be further developed to include and investigate other effects.

Finally, our work could also be extended with the same structures used in other models to include other effects on the colony. These could include the effects of food stores, brood and larval stages, and a more stratified task distribution among hive bees. These would complicate the analysis further (likely well beyond the point of feasibility) but could provide insight via simulations into the interaction of these effects in a colony.
Bibliography


[22] **Huang, W.-F., Solter, L., Aronstein, K., and Huang, Z.** Infectivity and Virulence of *Nosema ceranae* and *Nosema apis* in Commem-


Appendix A

Supplementary Graphs

A.1 Population Graphs

Below, we provide the additional population graphs from the simulations in Chapter 4. These show the populations of healthy forager bees, infected forager bees, and the entire colony, as functions of changing levels of the uptake rate and the deposition rate.
Figure A.1: Limit Cycle Values for Healthy Forager Bees on the First Day of Spring for Variable Levels of $\alpha$ ($\gamma_W = 0.11$)
Figure A.2: Limit Cycle Values for Infected Forager Bees on the First Day of Spring for Variable Levels of $\tilde{\alpha}$ ($\gamma_w = 0.11$)
Figure A.3: Limit Cycle Values for Total Colony Population on the First Day of Spring for Variable Levels of $\bar{\alpha}$ ($\gamma_W = 0.11$)
Figure A.4: Limit Cycle Values for Healthy Forager Bees on the First Day of Spring for Variable Levels of $\gamma_W$ ($\tilde{\alpha} = 0.18$)
Figure A.5: Limit Cycle Values for Infected Forager Bees on the First Day of Spring for Variable Levels of $\gamma_W$ ($\tilde{\alpha} = 0.18$)
Figure A.6: Limit Cycle Values for Total Colony Population on the First Day of Spring for Variable Levels of $\gamma_W$ ($\tilde{\alpha} = 0.18$)

A.2 Function Graphs

Below, we provide plots showing single cycles of the functions $\tilde{\alpha}(t)$, $\kappa(t)$, $\gamma(t)$, $\delta(t)$, $\eta_0(t)$, $\eta_1(t)$, $\phi_1(t)$, and $\sigma_1(t)$.
Figure A.7: A Single Period of the Formed $\tilde{\alpha}(t)$ Function with $\tilde{\alpha} = 0.17$ in Spring, Summer, and Fall
Figure A.8: A Single Period of the Formed $\kappa(t)$ Function
Figure A.9: A Single Period of the Formed $\gamma(t)$ Function with $\gamma_W = 0.12$
Figure A.10: A Single Period of the Formed $\delta(t)$ Function
Figure A.11: A Single Period of the Formed $\eta_0(t)$ Function
Figure A.12: A Single Period of the Formed $\eta_1(t)$ Function
Figure A.13: A Single Period of the Formed $\phi_1(t)$ Function
Figure A.14: A Single Period of the Formed $\sigma_1(t)$ Function
Appendix B

Source Code for

\textit{nosemaContModelLC.R}

Below is the source code for the general routine used in the simulations in Chapter 4. For some work, this code was modified to be continuously run with parameter values that changed after each iteration, but the script remained faithful to what follows.
# SCRIPT solves ODE system for a honeybee colony affected by Nosema Ceranae using the R package deSolve. This is iterated over each year, with populations at the beginning of each year compared to those of the previous year until the system is determined to be sufficiently close to the limit cycle.

# Created by Alexander Petric, Dept. of Math/Stats, Univ. of Guelph, 7 August 2015
# Current version created 22 March 2016

# Variables:  
# y1: Healthy Hive Bees  
# y2: Infected Hive Bees  
# y3: Healthy Forager Bees  
# y4: Infected Forager Bees  
# y5: Environmental Potential of Disease

# Basic Parameters:  
# beta: maximum birth rate in bees/day  
# kappa: critical threshold of bees needed for births  
# n: degree of dependence of birth rate on base hive population  
# sigma1: base recruitment from hive bees to forager bees as a percent  
# sigma2: "feedback" ratio from forager bees to hive bees as a percent  
# eta0,1: healthy and sick hive death rates as a percentage  
# phi0,1: healthy and sick forager death rates as a percentage  
# gamma: rate of increase in environmental potential from infected hive bees as a percentage  
# delta: rate of loss of viability in disease as a percentage  
# alpha_tilde: uptake rate of disease by hive bees  
# lambda: half-saturation constant for environmental potential

# Disease Parameters:  
# diseaseOnsetYear, diseaseOnsetSeason, diseaseOnsetDay: determine time of disease introduction  
# initialDisease: initial number of sick bees introduced at specified time

# Cleaning Parameters:  
# reduction: percentage of disease REMAINING after each instance of cleaning  
# cleaningDays: days on which cleaning occurs

# Input: A csv file formatted for input  
# Output: Two plots: one showing class populations and environmental potential over time, one showing hive, forager, and colony populations over time
t1 =Sys.time()  # Start time
print(t1)

library(deSolve)
library(abind)
library(pracma)

flag=1  # set to 0 for manual parameter entry, 1 to read from .csv file

# Manual input of variables if desired
if(flag==0){
  # Build parameter sets for season-dependent parameters.
  # Vectors have the form (Spring, Summer, Autumn, Winter).
  betavals=c(500.0,1500.0,500.0,0.0)
  kappa=c(5000,8000,5000,4000)
  sigma1vals=c(0.25,0.25,0.25,0.0)
  sigma2vals=c(1.24468,1.24468,1.24468,100.0)
  eta0vals=c(0.0,0.0,0.0,0.00649)
  eta1vals=c(0.0,0.0,0.0,0.01291)
  phi0vals=c(0.08511,0.08511,0.08511,0.00649)
  phi1vals=c(0.16936,0.16936,0.16936,0.01291)
  # Constant parameters
  n=2
  lambda=10000.0
  # Homing Failure parameters:
  HFRate=0.0
  HFStartYear=3
  HFEndYear=4
  HFDelay=0  # Homing Failure begins this many days into Spring
  HFDuration=28
  # Time parameters:
  years=5.0  # number of years
  daysPerSeason=c(91,91,91,91)
  dt=0.01  # step size; if this is too large, R cannot successfully integrate for
            # certain values of alpha
  # Set initial conditions
  yini = c(y1=4000, y2=0, y3=2000, y4=0, y5=0)
# Disease onset parameters:
```r
diseaseOnsetYear = 1
diseaseOnsetSeason = 4
diseaseOnsetDay = 1
initialDisease = 10
```

# Cleaning parameters:
```r
cleanFrequency = 91 # Colony is cleaned every cleanFrequency days
reduction = 1.0 # Percentage of disease remaining after cleaning
```

# Read from .csv file if desired
```r
if(flag==1){
p=read.csv("SeasonalParametersLC.csv",header=TRUE,sep=";")
# Seasonal parameters are taken directly from a file of vectors.
# Each vector has the form (Spring, Summer, Autumn, Winter).
betavals=p[,1]
kappavals=p[,2]
alphavals=p[,3]
sigma1vals=p[,4]
sigma2vals=p[,5]
etavals=p[,6]
etavals=p[,7]
phival=p[,8]
phival=p[,9]
gammavals=p[,10]
deltavals=p[,11]
alphatildevals=p[,12]
# Constant parameters
n=p[1,13]
lambda=p[2,13]
# Time parameters:
dt=p[1,14] # Step size; if this is too large, R cannot successfully integrate for
# certain values of alpha
daysPerSeason=p[,15]
```

# Set initial conditions
```r
yini=c(p[1,16],p[2,16],p[3,16],p[4,16],p[1,17])
# Disease onset parameters:
```
diseaseOnsetYear = p[1,18]
diseaseOnsetSeason = p[2,18]
diseaseOnsetDay = p[3,18]
initialDisease = p[4,18]

# Homing Failure parameters:
HFRate=p[1,19]
HFStartYear=p[2,19]
HFEndYear=p[3,19]
HFDelay=p[4,19]  # Homing Failure begins this many days into Spring
HFDuration=p[1,20]

# Cleaning parameters:
cleaningDays = p[,21]  # Colony is cleaned at these days each year
reduction = p[,22]  # Percentage of disease REMAINING after cleaning

# Create parameter functions which change with seasons.
# This uses the pchip (piecewise cubic hermite interpolating polynomial) function found in the
# pracma package

daysperyear=sum(daysPerSeason)

deltavals[1]=log(alphavals[1])/(daysPerSeason[1])
deltavals[2]=log(alphavals[2])/(daysPerSeason[2])
deltavals[3]=log(alphavals[3])/(daysPerSeason[3])

# Create nodes for the cubic polynomials. Each xtype is used for a group of parameters which
# follow a common form.
xtype1=c(-3.0*daysPerSeason[4]/4.0,-daysPerSeason[4]/4.0,daysPerSeason[1]/2.0,daysPerSeason[1]
   +daysPerSeason[2]/4.0,daysPerSeason[1]+3.0*daysPerSeason[2]/4.0,sum(daysPerSeason[1:2])
   +daysPerSeason[3]/2.0,sum(daysPerSeason[1:3])+daysPerSeason[4]/4.0,sum(daysPerSeason[1:3])
   +3.0*daysPerSeason[4]/4.0,daysperyear+daysPerSeason[1]/2.0,daysperyear+daysPerSeason[1]
   +daysPerSeason[2]/4.0,daysperyear+daysPerSeason[1]+3.0*daysPerSeason[2]/4.0)

xtype2=c(-3.0*daysPerSeason[4]/4.0,-daysPerSeason[4]/4.0,daysPerSeason[1]/4.0,sum(daysPerSeason[1:2]
   +3.0*daysPerSeason[3]/4.0,sum(daysPerSeason[1:3])+daysPerSeason[4]/4.0,daysperyear
   -daysPerSeason[4]/4.0,daysperyear+daysPerSeason[1]/4.0,daysperyear+sum(daysPerSeason[1:2])
   +3.0*daysPerSeason[3]/4.0,daysperyear+sum(daysPerSeason[1:3])+daysPerSeason[4]/4.0,
   2.0*daysPeryear-daysPerSeason[4]/4.0)
xtype3 = c(-3.0*daysPerSeason[4]/4.0, -daysPerSeason[4]/4.0, daysPerSeason[1]/4.0, 3.0*daysPerSeason[1]/4.0, daysPerSeason[1]+daysPerSeason[2]/4.0, daysPerSeason[1] +3.0*daysPerSeason[2]/4.0, sum(daysPerSeason[1:2])+daysPerSeason[3]/4.0, sum(daysPerSeason[1:2]+3.0*daysPerSeason[3]/4.0, sum(daysPerSeason[1:3])+daysPerSeason[4]/4.0, sum(daysPerSeason[1:3]+3.0*daysPerSeason[4]/4.0, daysperyear+daysPerSeason[1]/4.0, daysperyear+3.0*daysPerSeason[1])/

xs1 = c(-63.0*daysPerSeason[4]/64.0, -daysPerSeason[4]/64.0, daysPerSeason[1]/64.0, sum(daysPerSeason[1:2]+3.0*daysPerSeason[3]/64.0, sum(daysPerSeason[1:3])+daysPerSeason[4]/64.0, sum(daysPerSeason[1:3]+3.0*daysPerSeason[4]/64.0, daysperyear+sum(daysPerSeason[1:3])+daysPerSeason[4]/64.0, daysperyear+sum(daysPerSeason[1:3]+3.0*daysPerSeason[4]/64.0)

# Create a list of data points over which to estimate the cubic polynomial.
# These run over one year and use a step-size of dt.
xi = seq(0, daysperyear, by=dt)

# Make an array of values over one year for each parameter based on the cubic polynomial made
# from the above x values and the seasonal averages of the parameters. Then reorder the array
# to begin at t=0.
betaFunc = pchip(xtype1, c(betavals[4], betavals[4], betavals[1], betavals[2], betavals[2], betavals[3], betavals[4], betavals[4], betavals[1], betavals[2], betavals[2]), xi)

alhatildeFunc = pchip(xtype2, c(alphatildevals[4], alphatildevals[4], alphatildevals[1], alphatildevals[3], alphatildevals[4], alphatildevals[4], alphatildevals[1], alphatildevals[3], alphatildevals[4], alphatildevals[4], xi)

sigma1Func = pchip(xs1, c(sigma1vals[4], sigma1vals[4], sigma1vals[1], sigma1vals[3], sigma1vals[4], sigma1vals[4], sigma1vals[1], sigma1vals[3], sigma1vals[4], sigma1vals[4], xi)

sigma2Func = pchip(xs1, c(sigma2vals[4], sigma2vals[4], sigma2vals[1], sigma2vals[3], sigma2vals[4], sigma2vals[3], sigma2vals[1], sigma2vals[3], sigma2vals[4], sigma2vals[4], xi)

eta0Func = pchip(xtype2, c(eta0vals[4], eta0vals[4], eta0vals[1], eta0vals[3], eta0vals[4], eta0vals[4], eta0vals[1], eta0vals[3], eta0vals[4], eta0vals[4], xi)

eta1Func = pchip(xtype2, c(eta1vals[4], eta1vals[4], eta1vals[1], eta1vals[3], eta1vals[4], eta1vals[4], eta1vals[4], eta1vals[4], eta1vals[4], eta1vals[4], xi)
eta1vals[1], eta1vals[3], eta1vals[4], eta1vals[4], xi)

phi0Func=pchip(xtype2, c(eta1vals[4], eta1vals[4], phi0vals[1], phi0vals[3], phi0vals[4], phi0vals[4], phi0vals[1], phi0vals[3], phi0vals[4], phi0vals[4]), xi)

phi1Func=pchip(xtype2, c(eta1vals[4], eta1vals[4], phi1vals[1], phi1vals[3], phi1vals[4], phi1vals[4], phi1vals[1], phi1vals[3], phi1vals[4], phi1vals[4]), xi)

alphaFunc=pchip(xtype3, c(alphavals[4], alphavals[4], alphavals[1], alphavals[2], alphavals[2], alphavals[2], alphavals[3], alphavals[3], alphavals[3], alphavals[3]), xi)

gammaFunc=pchip(xtype3, c(gammavals[4], gammavals[4], gammavals[1], gammavals[1], gammavals[2], gammavals[2], gammavals[1], gammavals[1], gammavals[1], gammavals[1]), xi)

deltaFunc=pchip(xtype1, c(deltavals[4], deltavals[4], deltavals[1], deltavals[2], deltavals[2], deltavals[2], deltavals[4], deltavals[4], deltavals[1], deltavals[2], deltavals[2], deltavals[2]), xi)

kappaFunc=pchip(xtype1, c(kappavals[4], kappavals[4], kappavals[1], kappavals[2], kappavals[2], kappavals[2], kappavals[4], kappavals[4], kappavals[1], kappavals[2], kappavals[2], kappavals[2]), xi)

# For Homing Failure, the same process is done for the number of years specified.
xHF=g(round(daysperyear*(HFStartYear-1)-daysPerSeason[1]/64.0, 2), round(daysperyear*(HFStartYear-1)+HFDuration-daysPerSeason[1]/64.0, 2), round(daysperyear*(HFStartYear-1)+HFDuration+daysPerSeason[2]/64.0, 2))

yHF=g(yHF, HFRate, HFRate, 0)

for(i in HFStartYear:(HFEndYear-1)){
xHF=g(xHF, round(daysperyear*i-daysPerSeason[1]/64.0, 2), round(daysperyear*i-daysPerSeason[2]/64.0, 2), round(daysperyear*i-HFDuration-daysPerSeason[1]/64.0, 2), round(daysperyear*i+HFDuration+daysPerSeason[2]/64.0, 2))

yHF=g(yHF, 0, HFRate, HFRate, 0)
}

HF=pchip(xHF, yHF, xiHF)
# Create a function that returns the proper HF value for any time from the first application
# to the last and returns 0 outside of this range.

```r
homingFailure <- function(t){
  if((t<xHF[1]) || (t>xHF[length(xHF)]))
    return (0)
  else
    return (HF[1+(t-xHF[1])/dt])
}
```

# Decrease the diseaseOnset parameters by 1 for use in calculations

diseaseOnsetYear=diseaseOnsetYear-1
diseaseOnsetSeason=diseaseOnsetSeason-1
diseaseOnsetDay=diseaseOnsetDay-1

# Create impulse step function to add disease at time specified in the input file

```r
impulseTimes = c(diseaseOnsetDay+sum(daysPerSeason[1:diseaseOnsetSeason])+diseaseOnsetYear*daysperyear,diseaseOnsetDay+sum(daysPerSeason[1:diseaseOnsetSeason])+diseaseOnsetYear*daysperyear+dt)
impulseAmount = c(0.0,initialDisease/dt,0.0)
impulse = stepfun(impulseTimes,impulseAmount)
```

# Create clean step function to clean colony at times specified in the input file

```r
intensity = -log(reduction)/dt
cleanTimes = c(cleaningDays[1],cleaningDays[1]+dt)
# Only include positive cleaning times
for(i in 2:4) {
  if(cleaningDays[i]>0)
    cleanTimes = c(cleanTimes,cleaningDays[i],cleaningDays[i]+dt)
}
cleanLevel = c(0.0,intensity)
for(i in 2:(length(cleanTimes)/2)){
  cleanLevel=c(cleanLevel,c(0.0,intensity))
}
cleanLevel=abind(cleanLevel,0.0)
```
clean = \texttt{stepfun}(cleanTimes, cleanLevel)

# Set computational variables and tolerances. These are used below for stopping criteria.
err1 = 1e-3
tau = 1e-2
maxit=100

# A function that takes the modulus of the day with respect to the year length and returns
# the value shifted for use in the cubic polynomials from above.
day <- function(t){
  return (((t%%daysperyear)/(dt))+1)
}

# Set up the ODE:
nosemaTimeSeasonal = \texttt{function}(t,y,parms) {
  \texttt{with(as.list(c(y,parms)),{
    dy1 = (((betaFunc[day(t)]*(((y[1]+y[2])+y[3]+y[4]))^n)/(kappaFunc[day(t)])^n
    -alphaFunc[day(t)]*y[1]*y[5]/(lambda+y[5]))
    dy2 = (- sigma1Func[day(t)]*y[2]+sigma2Func[day(t)])*y[4]
    +alphaFunc[day(t)]*y[1]*y[5]/(lambda+y[5])+impulse(t))
    *y[3] - (phi0Func[day(t)]+homingFailure(t))*y[3])
    *y[4] - (phi0Func[day(t)]+homingFailure(t))*y[4])
    dy5 = (gammaFunc[day(t)]*y[2] - (deltaFunc[day(t)]+alphatildeFunc[day(t)]
    )*y[1]/(lambda+y[5])+clean(t))*y[5])
  }\})
}

cntr=0

# (Re)Set finalPopn values to ensure entry into while loop.
finalH0Popn1=-1
finalH0Popn2=-10

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while (stop == 1) {
    par = c(kappa = kappa, n = n)
    # On the first iteration, integrate system for one year and record populations.
    if (cntr == 0) {
        times = seq(cntr * daysperyear, (cntr + 1) * daysperyear, by = dt)
        out = ode(y = yini, times = times, func = nosemaTimeSeasonal, parms = par, method = "lsoda",
                  atol = 1e-6, rtol = 1e-6)
        finalH0Popn1 = out[length(out[, 1]), 2]
        finalH1Popn1 = out[length(out[, 1]), 3]
        finalF0Popn1 = out[length(out[, 1]), 4]
        finalF1Popn1 = out[length(out[, 1]), 5]
        finalEPopn1 = out[length(out[, 1]), 6]
    } else {
        times = seq(cntr * daysperyear, (cntr + 1) * daysperyear, by = dt)
        yini2 = c(out[length(out[, 1]), 2], out[length(out[, 1]), 3], out[length(out[, 1]), 4],
                  out[length(out[, 1]), 5], out[length(out[, 1]), 6])
        out = abind(out[1:length(out[, 1])], 1, ode(y = yini2, times = times,
                         func = nosemaTimeSeasonal, parms = par, method = "lsoda",
                         atol = 1e-6, rtol = 1e-6), along = 1)
        finalH0Popn2 = finalH0Popn1
        finalH1Popn2 = finalH1Popn1
        finalF0Popn2 = finalF0Popn1
        finalF1Popn2 = finalF1Popn1
        finalEPopn2 = finalEPopn1
    }
}
finalH0Popn1 = out[length(out[,1]), 2]
finalH1Popn1 = out[length(out[,1]), 3]
finalF0Popn1 = out[length(out[,1]), 4]
finalF1Popn1 = out[length(out[,1]), 5]
finalEPopn1 = out[length(out[,1]), 6]

# Check stopping criteria
if(((abs(finalH0Popn1-finalH0Popn2)/(abs(finalH0Popn1)+abs(finalH0Popn2)+tau)<err1)
    &((abs(finalH1Popn1-finalH1Popn2)/(abs(finalH1Popn1)+abs(finalH1Popn2)+tau)<err1)
    &((abs(finalF0Popn1-finalF0Popn2)/(abs(finalF0Popn1)+abs(finalF0Popn2)+tau)<err1)
    &((abs(finalF1Popn1-finalF1Popn2)/(abs(finalF1Popn1)+abs(finalF1Popn2)+tau)<err1)
    &((abs(finalEPopn1-finalEPopn2)/(abs(finalEPopn1)+abs(finalEPopn2)+tau)<err1))
    {stop = 0}
}
if(cntr==0)
    cntr=cntr+1
else
    cntr=cntr+1
}

# Rescale times
out[1] = out[1]*dt

# The remainder of the script graphs the results
graphics.off()

pdf('nosemaContinuousModel1.eps', width=10, height=7)

# If graphchoice=0, plot bee populations together. Otherwise, plot each class separately.
graphchoice = 0
if(graphchoice==0){
    par(mfrow=c(2,1))

    # Plot bee populations against time on one plot
}

ticklabels=c("Sp", "Su", "F", "W")
for(i in seq(daysperyear, out[length(out[,1]), 1]-daysperyear, daysperyear)){
  ticklabels=c(ticklabels, c("Sp", "Su", "F", "W"))
}
ticklabels=c(ticklabels, "Sp")
plot(out[,1], out[,2], ylab="Bees", xlab="Time (Days)", type="l", ylim=c(0, 1), xaxt='n'
axis(1, at=seq(0, out[length(out[,1]),1], 91), labels=ticklabels)
lines(out[,1], out[,4], lty=2)
lines(out[,1], out[,3], lty=3)
lines(out[,1], out[,5], lty=4)
legend(x="topright", legend=c("H0", "H1", "F0", "F1"), cex=.8, lwd=2.5, lty=c(1, 2, 3, 4))

# Plot Environmental Potential over time on second plot
plot(out[,1], out[,6], ylab="Environmental Potential", xlab="Time (Days)", type="l", xaxt='n'
axis(1, at=seq(0, out[length(out[,1]),1], 91), labels=ticklabels)
}
par(mfrow=c(2,3))

# Plot each variable against time
plot(out[,1], out[,2], ylab="Healthy Hive Bees", xlab="Time (Days)", type="l",
main="Healthy Hive Pop'n/Time")
plot(out[,1], out[,4], ylab="Healthy Forager Bees", xlab="Time (Days)", type="l",
main="Healthy Forager Pop'n/Time")
plot(out[,1], out[,6], ylab="Disease Environmental Potential",
  xlab="Time (Days)", type="l", main="Disease Env. Potential/Time")
plot(out[,1], out[,3], ylab="Infected Hive Bees", xlab="Time (Days)", type="l",
main="Infected Hive Pop'n/Time")
plot(out[,1], out[,5], ylab="Infected Forager Bees", xlab="Time (Days)", type="l",
main="Infected Forager Pop'n/Time")
}
dev.off()

pdf('nosemaContinuousModel2.eps')
par(mfrow=c(2,2))
# Plot population of hive bees over time
```
plot(out[,1],out[,2]+out[,3],ylab="Total Hive Population",xlab="Time (Days)",type="l",
     main="Total Hive Pop'n/Time")
```

# Plot population of forager bees over time
```
plot(out[,1],out[,4]+out[,5],ylab="Total Forager Population",
     xlab="Time (Days)",type="l",main="Total Forager Pop'n/Time")
```

# Plot population of entire colony over time
```
plot(out[,1],out[,2]+out[,3]+out[,4]+out[,5],ylab="Total Colony Population",
     xlab="Time (Days)",type="l",main="Total Colony Pop'n/Time")
```

```
dev.off()
```

```
t2=Sys.time(); # End time
```

# Print total computation time
```
print(difftime(t2,t1))
```