ABSTRACT

PREDICTIVE MODELING OF THE DISEASE DYNAMICS OF THE
HONEYBEE-VARROA MITE-VIRUS SYSTEMS

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Western honeybees, *Apis mellifera*, are currently affected by abrupt depopulation worldwide which affects the economy as bees are the most valuable pollinators of agricultural crops. Many factors are suspected to be involved, either alone or in combination. Parasites and pathogens are considered as principal causes, in particular the ectoparasitic mite *Varroa destructor* and associated viruses. In this dissertation, we present SIR-type mathematical models of honeybee-varroa mite-Acute Bee Paralysis Virus (ABPV) systems. In particular, we (1) study the model by taking into account the seasonal variations, (2) investigate the effect of homing failure on a honeybee colony infested with mites and virus and, (3) formulate the model in terms of discrete-continuous system in order to apply it to the process of swarming as a preliminary step. A combination of analytical techniques and computational methods were employed to study the problem. Our model simulations suggest that in particular the transition from winter to spring is critical for the survival of honeybee colonies. If the bee population is not strong enough in winter to survive in the spring, the colony collapses in the winter. This pattern is also observed in natural honeybee colonies. Our model implies that a mite and ABPV infested colony can sometimes function properly for several years but then fail suddenly. It is also observed that increased forager loss due to external causes may trigger the colony die off if the colony is infested with the varroa mite and ABPV. Overall, we find that the use of the infectious disease modeling framework is extremely valuable in
understanding the long term dynamics of honeybee colonies infested with varroa mites and viruses.
To him who knew me before I knew myself...
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Contents

List of Tables .......................................................... viii
List of Figures ........................................................... ix

1 Introduction ............................................................ 1
   1.1 Thesis outline .................................................. 8

2 A mathematical model for population dynamics in honeybee colonies
   infested with Varroa destructor and the Acute Bee Paralysis Virus 17
   2.1 Introduction .................................................... 18
   2.2 Governing equations ........................................... 23
   2.3 Analysis in the autonomous case ............................. 27
   2.4 Computational investigation of the periodic coefficient case . . 40
   2.5 Summary and Conclusion ..................................... 49

3 A Mathematical Model of the Honeybee- Varroa destructor-Acute Bee
   Paralysis Virus System with Seasonal Effects 57
   3.1 Introduction .................................................... 58
   3.2 Mathematical model ............................................ 64
   3.3 Stability of periodic solutions ............................... 70
   3.4 Computer Simulations ......................................... 77
   3.5 Conclusions .................................................... 87
   3.6 Construction of continuous parameters from seasonal averages . . 94
4 The interplay between Varroa destructor-Acute Bee Paralysis Virus infestation and division of labour in a honeybee colony 102

4.1 Introduction ......................................................... 103
4.2 Mathematical model .............................................. 110
4.3 Model with constant parameters ............................... 118
4.4 Model with seasonally varying parameters .................... 128
4.5 Summary and Conclusion ........................................ 135

5 A discrete-continuous modeling framework to study the role of swarming in a honeybee colony infested with Varroa destructor and Acute Bee Paralysis Virus 145

5.1 Introduction ......................................................... 146
5.2 Model Equations .................................................... 148
5.3 Mathematical Formulation of Discrete Interventions .......... 151
5.4 Computer Simulations .............................................. 152
5.5 Conclusion .......................................................... 158

6 Conclusion and Future Work 163

6.1 Research Findings .................................................. 163
6.2 Future Work ........................................................ 165
List of Tables

2.1 Seasonal averages of model parameters, derived from the data presented in [31]. .................................................. 26

3.1 Seasonal averages of model parameters, derived from the data in [29, 30, 36, 40]. The parameters included here are kept constant for all simulations; the values of the parameters that are varied are given in the text. .................................................. 69

3.2 Comparison between the average values of the parameters obtained from literature and their approximate forms shown in Figure 3.6 . . 99

4.1 Seasonal averages of some of the model parameters, derived from the data in [26, 33, 34, 41, 49]. .................................................. 116

5.1 Seasonal averages of model parameters, derived from the data presented in the literature[5, 6, 11, 13]. The parameters included here are kept constant for all simulations; the values of the parameters that are varied are given in the text. .................................................. 150
List of Figures

1.1 Conceptualisation of the SIR modeling framework: After infection, susceptible individuals leave the S compartment and enter the I compartment. After recovery/removal, they leave the I compartment and enter the R compartment. The infection rate can depend on both, the number of already infected and susceptible individuals. 4

1.2 Combined representation of the SIR modeling framework and the role of mites in a honeybee colony. Virus carrying mites affect the transmission rate from susceptible to infected bees. All mites, virus carrying or not, affect mortality of susceptible and infected bees. . . 5

2.1 Direction field for the system (2.8), (2.9) for $0 < x < \tilde{x}$, $0 < M < \alpha < \tilde{x}$ with $\tilde{x} < x^*_2$, the unstable equilibrium of (2.6). We have used the summer parameter values with $K = 8000$ and $\alpha = 0.2$. The initial values used are $x(0) = 30$ and $M(0) = 20$ . . . . . . . . 32

2.2 Nullclines and equilibria of the bee-mite model: (a) the trivial equilibrium A is the only equilibrium; (b) only the mite free equilibria A,B,C exist; (c), (d) two additional equilibria $D$, $E$ with $M^* = \alpha x^* > 0$ exist, in (c) $x^*_E < \tilde{x}$, in (d) $x^*_E > \tilde{x} = \sqrt{n - 1}K$ . . . . . . . . 33
2.3 Simulation of bee-mite population dynamics: periodic solutions for varying brood maintenance coefficients $K$: low [top row, (a), (b)] versus high [bottom row (c),(d)] values, without mites [left column (a), (c)] and with mites [right column (b), (d)]. Time is given in days; the symbol Y on the y-axes represents population. See text for details of parameter values. ............................................. 43

2.4 Simulation of bee-mite dynamics: disappearing bee colonies for brood maintenance coefficients $K$ varying over the range $K = 11600$ and $K = 14000$ in spring, summer, winter. Time is given in days; the symbol Y on the y-axes represents population. See text for details on model parameters. ............................................. 47

2.5 Simulation of the bee-mite-virus complex: Panel (a) bees and mites co-exist in the absence of disease. In panel (b) the simulation is repeated with mites carrying the virus, leading to collapse during the 6th summer after introduction of the disease. In panel(c) the relative carrying capacity $\alpha$ is decreased in summer and spring compared to panel (b); the disease is fought off, the number of parasites is lower than in panel (a). Time is in days; the symbol Y on the y-axes represents population. See text for details on model parameters. ... 48
3.1 Illustration of potential model outcomes, tracked over several years:
(a) periodic solution describing a healthy honeybee colony in the absence of mites and virus with high $K$ values, (b) the same simulation scenario as in (a) but with mites present and with enough varroa treatment to fight off the mites, (c) the same simulation scenario as in (b) but with insufficient varroa treatment leading to bee-mite co-existence, (d) failure of the bee population caused by mites only (absence of ABPV) due to insufficient varroacide treatment, (e) presence of ABPV leading to the failure of the colony after more than 10 years with low $K$ values, (f) same scenario as in (e) but a rapid failure of the colony after 4 years due to milder varroa treatment application as compared to (e), (g) same scenario as in (f) but with the extent of treatment sufficient to fight off virus but not mites, (h) same simulation scenario as in (g) but with enough varroa treatment to eradicate the disease (mites as well as virus).

3.2 Effect of initial disease infestation ($m_0$ and $M_0$) on the time at which the colony collapses (where different lines represent different $M_0$ values).

3.3 (a) System without varroacide treatment. (b) System with treatment. Varroacides are applied three times in spring and fall each, with an interval of one month (with $\delta_2 = 1.2$). (c) System with treatment. Varroacides are applied three times in spring and fall each, with an interval of one month (with $\delta_2 = 1.3$).

3.4 Magnified version of Figure 3.3(b). Vertically downwards arrows show the times when treatment is applied and how the mite population decreases.
3.5 Effect of death rate of mites due to treatment (i.e., $\delta_2$) on the average mite population (scale shown on the colour bar) ... 86

3.6 Three different profiles observed in the parameters ($\mu$ and $K$ in (a), $\beta_1, \beta_2, \beta_3, d_1$ in (b), and $r$ and $d_2$ in (c)) by interpolating the piecewise constant seasonal averages using two methods. ... 97

3.7 Comparison of the bee-mite dynamics using two different methods for interpolation of the piecewise constant parameters. ... 98

3.8 Comparison of the bee-mite-virus dynamics using two different methods for interpolation of the piecewise constant parameters. ... 98

3.9 Dynamics of the bee-mite-virus system by varying the reduction of the intervals in Method 1. ... 101

4.1 Trace-determinant plot of the Jacobian (4.12) for steady states $A(0, 0)$, $B(x_{h1}^*, Fx_{h1}^*)$ and $C(x_{h2}^*, Fx_{h2}^*)$ of the two dimensional disease free model. Red, blue and cyan curves are obtained by varying the parameters $p, \sigma_1$ and $\sigma_2$ respectively over the range from 0 to 2. The solid black curve represents $\Delta = \tau^2/4$. Summer parameters from Table 4.1 are used for this Figure. ... 121

4.2 Comparison of the dynamics of a mite-virus infested honeybee population between simulated colonies with no homing failure (i.e., $p = 0$), a low rate of homing failure (i.e., $p = 0.1$) and a high rate of homing failure (i.e., $p = 0.7$). Shaded areas delineate the time period of increased homing failure (i.e. when the colonies are exposed to a treated crop). These results are obtained with parameters fixed at the spring values. ... 128
4.3 Comparison of the dynamics of honeybee population between an exposed colony that is disease free and an exposed colony \((p = 0.1)\) that is infested with mites and virus. **Note that** the curve for the disease-infested case lies below the curve for the disease-free case but it is difficult to distinguish them as they are very close to each other. 

4.4 **(a)** Comparison of average total bee population between a disease-free colony, a colony infested with mites, a colony infested with mites but treated with varroacides and a colony infested with mites and virus but treated with varroacides by varying the forager mortality due to homing failure i.e., \(p\) from 0 to 1.5. The average total bee population is calculated at the final time (i.e., after \(t = 20\) years). **Note that** the curve for the mite-infested but treated and the mite-virus infested but treated case overlap with each other. **(b)** Temporal dynamics of a colony infested with mites and virus where the virus is fought off due to the varroacide treatment when the forager mortality rate \(p\) is 0.89. **(c)** Temporal dynamics of a colony infested with mites and virus where the virus is fought off due to the varroacide treatment and the forager mortality rate \(p\) is 0.9. 

5.1 **(a)** Bee-mite-virus system in the absence of swarming. **(b)** Bee-mite-virus system in the presence of swarming due to congestion. Threshold bee population at which swarming takes place is 31342 and we assume \(a_1 = 0.65, b_1 = 0.5\).
5.2 When swarming takes place due to overcrowding: (a) Effect of the percentage of the healthy bees leaving the parent colony on the average healthy bee population of the (i) disease free colony, (ii) mite infested colony with \(a_1 = 0.05\), and (iii) mite infested colony with \(a_1 = 0.7\). (b) The colony fights off the virus when \(b_1 = 0.5\) and \(a_1 = 0.65\). (c) The colony dies off after 7000 days when \(b_1 = 0.6\) and \(a_1 = 0.65\). (d) The colony dies off after 6600 days when \(a_1 = 0.64\) and \(b_1 = 0.5\). (e) The colony fights off the virus when \(a_1 = 0.65\) and \(b_1 = 0.5\).

5.3 When swarming takes place every two years: (a) Effect of the percentage of the healthy bees leaving the parent colony on the average healthy bee population of the colony that is (i) disease free, (ii) mite infested with \(a_1 = 0.05\), and (iii) mite infested with \(a_1 = 0.7\) (b) The colony fights off the virus when \(b_1 = 0.76\) and \(a_1 = 0.7\) (c) The colony dies off after 1000 days when \(b_1 = 0.77\) and \(a_1 = 0.7\) (d) The colony dies off after 6000 days when \(a_1 = 0.91\) and \(b_1 = 0.5\) (e) The colony fights off the virus when \(a_1 = 0.92\) and \(b_1 = 0.5\).
Chapter 1

Introduction

Honeybees play a vital role in agriculture. Besides their ecological importance [14], honeybee populations have a huge economical impact on agriculture in North America, Europe, Japan and the Middle East [8, 35, 43]. Honeybees pollinate one third of Canadian food crops. In the United States, 80% of the human diet that comes from insect-pollinated plants. Their value to Canadian crop pollination amounts to over $2 billion and to the US crop production is $14 billion annually [7, 36].

Since 2006, an alarming decline in the number of honeybee colonies has been reported worldwide [23, 47]. The Canadian Honey Council reports a loss of 25% of Canadian honeybee colonies for the Winter of 2013/14 [6]. Similar hive loss has been a concern in the U.S, throughout Europe, and in Japan. The symptoms of colony losses are different in different parts of the world and hence losses are designated by different names. For instance, in U.S this syndrome is known as Colony Collapse Disorder (CCD) and the symptoms are the absence of adult bees and their dead bodies inspite of the food and brood remain present in the hive. In other countries like Canada and Germany, the colonies are observed to be too weak in Winter to emerge as healthy colonies in the Spring. This is known as Win-
tering Losses. Several possible causes have been suggested to be responsible for these colony losses e.g., varroa (*Varroa destructor* Anderson and Trueman) mites [29, 42], pathogens (i.e. bee viruses and *Nosema spp.*; [12, 19, 22]), pesticides residues [1, 21, 24, 45] and beekeeping practices [36]. However, there is a growing consensus that the decline in honeybee health is not caused by a single factor but a combination of factors (e.g. [38, 46]).

One of the greatest threats to honeybee populations worldwide is the invasive mite *Varroa destructor* and the deadly viruses it carries and transmits among bees. A combination of varroa and viruses are now frequently implicated in colony failures [9, 18, 32]. Varroa mites are serious and devastating ectoparasites of the honeybee which live either attached to the adult bees, known as the phoretic phase, or within a sealed brood cell where it reproduces. The mites not only feed on the bees by piercing their inter-segmental membrane but also act as a vector for the fatal viruses. There has been around 20 known honeybee viruses, of which 12 are transmitted by varroa mites [25, 37]. The virus that is frequently implicated in the colony losses (mostly Wintering losses), especially when the colony is infested with varroa mites, is Acute Bee Paralysis Virus (ABPV) [20, 25, 49]. This globally distributed virus appears to be the most common bee virus in Europe and South America [2, 3]. Bees affected by this virus suffer from paralysis, loss of body hair, trembling, inability to fly and the gradual skin darkening. Infected pupae suffer rapid death and do not usually develop into adult bees. Varroa mites act as a mechanical vector for the transmission of ABPV i.e., the virus replication does not take place inside the body of varroa mites; they solely serve as virus carriers. The virus is transmitted to the bees when mites feed on them. When a virus-carrying mite feeds on an uninfected bee, it might release the virus into the bee’s haemolymph. Similarly when a virus-free mite feeds on an already infected bee, it can acquire the virus.
The other main stressor (either alone or at least in interaction with other stressors) that is suspected to hold a central place in colony-weakening processes is the loss of foragers. There could be various causes behind the forager loss e.g., precocious foraging, use of environmental pesticides, viral infections, nosema etc.[1, 13, 30, 36, 48]. Honey bees are readily exposed to pesticides because they rely heavily on common blooming crops, such as oilseed rape, maize, or sunflower, that are now routinely treated against insect pests [11]. These pesticides contaminate nectar and pollen [41]. Foraging honeybees are therefore directly exposed which may affect their memory, learning ability and navigational skills; they fail to return to the hive which is known as homing failure. The rest of the colony is also affected as the returning foragers store or exchange contaminated material with hive individuals [10, 41].

The dynamics of infectious diseases can be studied using mathematical models, which have been developed over many years and have experienced a huge surge in activity in the last decade [5, 15, 31]. While most of these research efforts are driven by diseases of human populations, the underlying concepts can be adapted to diseases of animals as well. We have adapted the traditional modeling framework, the so-called SIR models. For viruses in honeybees, several of the simplifying assumptions often made in infectious disease models for humans are not possible. For example, because the bee population size fluctuates greatly with the seasons and because viral diseases can reduce the population considerably, to the point of extinction, the usual assumption that the overall population size remains relatively unaffected by the virus and can be considered a constant is not possible. This leads to algebraically more involved models. Moreover, because the characteristic time scale of the disease is comparable to or even bigger than the characteristic time scale of bee biology, birth and natural death of bees cannot be neglected. Therefore, models must be developed in a way that they account for the particularities of bee
reproduction. Furthermore, varroa mite and ABPV are to be modeled as vector borne-diseases by using Ross-Macdonald models which are an extension of the SIR modeling framework.

The basic, traditional SIR model divides the host population into susceptible (S), infected (I), and removed or recovered (R) individuals. The susceptibles are the individuals that are not currently, but may become, infected and the infected group consists of the individuals that are currently infected. Depending on the disease, the R group can indicate those individuals who were infected but are now recovered from the disease, or those who were removed, e.g. by death. The SIR model is conceptualized in Figure 1.1.

![Figure 1.1: Conceptualisation of the SIR modeling framework: After infection, susceptible individuals leave the S compartment and enter the I compartment. After recovery/removal, they leave the I compartment and enter the R compartment. The infection rate can depend on both, the number of already infected and susceptible individuals.](image)

Each compartment in this model is described by an ordinary differential equation which is governed by the basic approach of mass action, i.e. a balance of gain and loss in the compartment. The rate at which susceptible individuals become infected, i.e. the rate of transfer from the S into the I compartment, depends on the number of already infected individuals but can also depend on the number of susceptible individuals. In the literature the SIR model has been adapted to describe a variety of diseases. For example, it can be considered that recovered individuals become susceptible again, etc. An extension of the model to vector borne diseases can be achieved by making the infection rate dependent also on the number of vectors that carry the virus. In many instances, this requires to include additional differential
equations that described how the vector population evolves and how vectors acquire the virus, see for example Figure 1.2.

In our SIR framework, the susceptible individuals are the healthy bees, infected individuals are the sick bees and the vector is the varroa mite. The virus is transmitted to the bees via mites which feed on their haemolymph by piercing the inter-segmental membrane. The model for honeybees is with demography i.e. the birth and the death of the bees taken into consideration. In our case, the removed compartment is the deceased bees. A schematic of the virus transmission is given in Figure 1.2: The mites that carry the virus affect the transmission of the disease. All mites, vector carrying or not, affect the mortality of susceptible and the infected bees.

Figure 1.2: Combined representation of the SIR modeling framework and the role of mites in a honeybee colony. Virus carrying mites affect the transmission rate from susceptible to infected bees. All mites, virus carrying or not, affect mortality of susceptible and infected bees.

Extensive research has been dedicated to study the effect of the causes behind colony failures individually and also as a combination using mathematical models [4, 16, 21, 26, 27, 28, 44]. The first published model for honeybee-mite-virus systems is [44] which is an SIR model. They studied two viruses: Deformed Wing Virus (DWV) and Acute Bee Paralysis Virus (ABPV). The authors considered the autonomous case and studied the model behavior for each season separately, based
on seasonal averages for the parameters. The critical mite load, that the colony can tolerate before it dies off, was calculated. The model assumed the bee birth rate and the total mite infestation to be a constant. [16] extended the model in [44] for ABPV by introducing the brood maintenance terms that reflect that a certain number of worker bees is always required to care for the brood in order for new bees to be born. However, the total mite load was still assumed to be a constant. To study the effect of forager loss, [26] developed a compartmental model of honeybee colony population dynamics to explore the impact of different death rates of forager bees on colony growth and development. The authors in [27] extended the model in [26] to include food and brood explicitly; they explored how food availability and bee death rates interact to determine colony growth and development. The model in [4] combined the dynamics of the spread of a hypothetical disease within a bee colony with the underlying demographic dynamics of the colony to determine the ultimate fate of the colony. [28] presented a model that accounts for the transmissible infection brought into the hive by foragers. Both [4] and [28] discusses the model in the context of a general infection that is brought into the hive by foragers.

The main objective of this thesis is to develop a better understanding of the complex interaction between honeybees, mites and the viruses they carry. To understand the long term dynamics of the colony, we present mathematical models of the honeybee-varroa mite-virus systems by taking into account the seasonal fluctuations which has not been studied yet. All the mathematical models discussed above assume the parameters to be constant over a season. It is assumed that the seasonal averages are a good description of the environmental dynamics and that the time scale of the the dynamics is sufficiently fast, so that the system equilibrates quickly, in significantly less time than the duration of a season. However, the models with these assumptions cannot be used to study the long term fate of the colony which is an acute limitation because the time period for which disease progresses may vary
from several seasons to several years. For instance, these models are not capable of studying the process of Wintering losses which occur when a bee population is too low at the end of Fall to make it through Winter and emerge as a healthy colony in Spring. This is the because the model is not able to cover an entire year by spanning the transitions between seasons.

In this dissertation,

- We develop and study a mathematical model for honeybee-mite-ABPV system for the constant coefficient case and perform ad hoc simulation experiments by assuming the parameters to be seasonally constant i.e., jump functions.

- We incorporate the effect of seasonal fluctuations and extend the model by explicitly including the option to account for mite control, e.g. by varroacide application.

- The SIR type models of honeybee-mite-virus systems are combined with the already existing bee models in which bee population is divided into hive bees and forager bees. This facilitates us to study the interplay of forager loss and varroa-virus infestation in a colony.

- A general discrete-continuous model is formulated to study the discrete events occurring in the colony. In particular, this model is applied to the process of swarming in a colony infested with varroa mite and virus.

We use a combination of analytical techniques and numerical simulations to study the behavior of the models. In particular, the models will be studied using invariance theorems, comparison principles, linear stability analysis, nonlinear Floquet theory, and computational methods.
1.1 Thesis outline

The thesis is arranged as follows:

Chapter 2, A mathematical model for population dynamics in honeybee colonies infested with Varroa destructor and the Acute Bee Paralysis Virus, presents a mathematical model of the honeybee colony infested with varroa mites and Acute Bee Paralysis Virus. It is a non linear and non autonomous system of four ordinary differential equations for the dependent variables: uninfected bees, infected bees, virus carrying mites and total mites that infest the colony. A qualitative description of the autonomous model solution is given, based on analytical techniques. The model is quantitatively studied using numerical simulations and it is verified whether or not the qualitative features of the autonomous case can be observed in the non-autonomous case. The model parameters are assumed to be varying with time but constant over a season. This chapter was published in the Canadian Applied Mathematics Quarterly [39]:


Another version of this chapter was published as a book chapter in the book titled as In Silico bees [17]:

Eberl H.J.; Kevan, P.G.; Ratti, V.; Infectious disease modeling for honey bee colonies, in :J. devillers (ed)., In Silico Bees, p.87-134, CRC, Press Boca Raton, 2014

Some minor corrections and clarifications have been made in this chapter as compared to the original paper.
Chapter 3, A mathematical model for population dynamics in honeybee colonies infested with Varroa destructor and the Acute Bee Paralysis Virus with seasonal effects, extends upon the modeling framework of the previous chapter and studies the behavior of the model with seasonally varying parameters over several years. Some ad hoc simulations are included in Chapter 2. In these exploratory simulations, seasonally constant parameters are used, which we extend here to depend continuously in time. The stability of disease-free periodic solutions is studied which is not studied in the previous chapter. To account for mite control, explicit death terms are included in the model. The conditions on the parameters have been determined under which vector control is a viable remedial strategy for the virus infestation. This chapter is accepted for publication by the Bulletin of Mathematical Biology [40]:

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Chapter 4, The interplay between Varroa destructor-Acute Bee Paralysis Virus infestation and division of labour in a honeybee colony, focusses on the role of homing failure in the dynamics of a honeybee colony infested with varroa mite and virus. To study this, division of labor in honeybees must be introduced in the mathematical model presented in the previous chapter. The stability of the disease free solution is studied using analytical techniques. Numerically, we investigate the role of forager mortality due to homing failure on the dynamics of the honeybee colony. This manuscript is currently under revision with collaborative authors and is near submission.

Chapter 5, Swarming in a honeybee colony infested with Varroa destructor and Acute Bee Paralysis Virus, incorporates the discrete time interventions in the mod-
eling framework presented in Chapter 2. The discrete interventions are formulated with the intention of applying the framework to the process of swarming. The model is studied numerically and the parameters are assumed to be piecewise constant as in Chapter 2. We focus on two major causes of swarming: congestion in the hive and natural death of the queen bee. We investigate numerically if swarming prevents the build up of detrimental levels of varroa populations. This chapter is submitted to the proceedings of The 2015 AMMCS-CAIMS Congress.

Chapter 6, *Conclusions and Future Work*, presents the key findings of this dissertation and gives suggestions for future work.
Bibliography


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Chapter 2

A mathematical model for population dynamics in honeybee colonies infested with *Varroa destructor* and the Acute Bee Paralysis Virus

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Abstract

We present a simple SIR model of Ross-MacDonald type for the infestation of a honeybee (*Apis mellifera*) colony by the Acute Bee Paralysis Virus (ABPV), which is transmitted by parasitic varroa mites (*Varroa destructor*) as vector. The model is a four dimensional system of nonlinear ordinary differential equations for the dependent variables, healthy and virus infected bees, number of mites in the colony overall, and number of mites that carry the virus. In the autonomous case we study the model with analytical techniques deriving conditions under which the bee colony can fight off an ABPV epidemic. These results are then used to design and discuss numerical simulations of the more realistic case with periodic coefficient functions that mimic seasonal changes in bee colonies.
Keywords: Honeybees, *Varroa destructor*, Acute Bee Paralysis Virus, Mathematical Model, Infectious Disease Model

2.1 Introduction

Western honeybees (*Apis mellifera*) are very important for sustaining life on Earth by contribution to pollination of crops and and other plants. Humans, in particular, rely heavily on honeybee services. The estimated value of honeybees for crop pollination is over $2 billion annually [8]. Honeybees have been estimated to account for at least 80% of all pollinators [7]. In addition to pollination, bees play an important, age-old role as producers of honey and wax, which in turn have various nutritional and industrial uses. According to Tautz [32], honeybees are, in economical terms, the third most important domestic animal after cattle and pigs, and before poultry.

A honeybee colony usually consists of a single reproductive queen and, depending on the season, up to around 60 000 adult female worker bees, 10, 000-30, 000 individuals at the brood stage (egg, larvae and pupae) and up to hundreds of male drones [20]. The only fertile individual in the colony is the queen with an average life span of 2-3 years [30]. She lays fertilized eggs that produce worker bees or, much more rarely, queens, while drones develop from non-fertilized eggs. A large population of workers is needed to carry out the tasks of the bee colony, including foraging, pollination, honey production and, in particular, caring for the brood and rearing the next generation of bees. In northern temperate locales, the queen bee usually begins laying eggs in February at a rate that increases until about mid-summer. From August until mid-October the rate of egg laying declines. It comes to a halt in the middle of October [24]. Therefore, during the winter, honeybee colonies decline in size as bees die off [3]. The life span of an adult worker bee
depends on the season. The average life span of worker honeybees in June is 28.3 days and in July is 32.4 days. In winter, honeybees live for almost 154.1 days and the longevity of post wintering bees is 23.4 days [13]. The adult drone life span is around 59 days under optimal colony conditions [13].

A rapid decrease in the number of honeybee colonies has been observed since 2006 in North America [16, 23]. The syndrome, which is characterized by the disappearance of adult bees while the capped brood and honey remains in the hive, is known as Colony Collapse Disorder (CCD). It was first diagnosed in the U.S. Symptoms include an insufficient workforce present in the collapsing colony to care for the brood present. This workforce consists primarily of young adult bees. The bees that are present in the colony are reluctant to consume the stored honey and pollen. The queen may or may not be present in a collapsing colony. Throughout U.S, CCD is spreading rapidly. In other parts of the world, the symptoms are not exactly the same as in CCD but huge losses, in particular wintering losses in Canada, have been reported [16]. The exact reasons and the triggering factors for CCD have not been understood yet. Several possible stressors causing the decline of bee colonies have been proposed, including pesticides, intensive agriculture, harsh winter conditions, and the parasitic mites *Varroa destructor*, which are also vectors of viral diseases.

In Canada, varroa mites have been found to be the main reason behind wintering losses of bee colonies [14]. In the years subsequent to the introduction of *Varroa destructor* into Canada, normal long-term overwintering mortality is regarded as being 15%. In 2008-2009, the mortality from wintering losses and spring dwindling was 33.9%, or 2.3 times the normal rate [9]. This loss is similar to the 2007-08 winter mortality figure of 35.0 % and exceeded the 2006-07 rate of 29.0%. In recent years, much scientific research in this area has focused on infestation of honeybee colonies by the mite *V. destructor*. These parasites not only ectoparasitically feed
on bees, but also vertically transmit a number of deadly viruses to the bees [16]. Many beekeepers have reported that honeybee colonies die if the mite population is not controlled, see also [29]. Thus, varroa mites have a marked economic impact on the beekeeping industry. *Varroa destructor*’s natural host is the Asiatic honeybee *Apis cerana*. In the late 1950s and 1960s it shifted host to the Western honeybee *A.mellifera* [2]. Subsequently *V. destructor* has spread quickly all over the Western world. Mite reproduction can occur only if honeybee brood is available. The female mite reproduces within the honeybee sealed brood cell. It enters the cell just prior to it being capped. After the capping of the cell, the mite feeds on the developing bee. It lays a single male egg and several female eggs at 30-hour intervals [18]. The mother mite prepares a site on the host bee so that the offspring can feed [11], mature and mate within the cell. When the host bee leaves the cell, the mature female mites leave the cell with male and immature female mites, if present. Immature female mites die as they come out of the cell; they cannot survive outside the sealed cell. The adult female mite becomes attached to the adult bee. This is known as the phoretic phase. It feeds on the bee’s haemolymph by piercing the intersegmental membrane of the bees [1, 5], harming the host. Thus, mites affect the life span of honeybees directly.

Indirectly, they also affect honeybees as vectors of viral diseases. There have been at least 14 viruses found in honeybee colonies [4, 16], which can differ in intensity of impact, virulence, etc. for their host. For example, the Acute Bee Paralysis Virus (ABPV) affects the larvae and pupae which fail to metamorphose into the adult stage, while in contrast the Deformed Wing Virus (DWV) also affects larvae and pupae, but in this case they can survive to the adult stage [31]. As the mites are the main cause for transmission of viruses between bees, these viruses are transmitted to the bees when mites feed on bees. When a virus-carrying mite attaches to a healthy bee during its phoretic phase, it can transmit the virus to the bee [5, 20, 26].
Thus, the previously uninfected bee becomes infected. A virus free phoretic mite can begin carrying a virus when it moves from an uninfected to an infected bee [26, 21].

In this study we focus on one honeybee virus: the Acute Bee Paralysis Virus. ABPV belongs to the family Dicistroviridae, like the Kashmir Bee Virus, Black Queen Cell Virus and the Israeli Acute Paralysis Virus, to name but a few members of this group. These viruses share a number of biological characteristics, such as principal transmission routes, and primary host life stages [25]. ABPV is a common infective agent of honeybees that is frequently detected in apparently healthy colonies. Bees affected by this virus are unable to fly, lose the hair from their bodies and tremble uncontrollably. The virus has been suggested as a primary cause of bee mortality. Infected pupae and adults suffer rapid death. ABPV is associated with Varroa mites and has been implicated in Colony Collapse Disorder (CCD); it is highly relevant for the beekeeping industry. Because mites and virus appear simultaneously under field conditions it is difficult to separate the effects of both pathogens [16]. Therefore, they should be studied together and mathematical models of the disease dynamics should include both pathogens simultaneously.

The course of many infectious diseases can be predicted using mathematical models. Infectious disease modeling have been developed over many years and has experienced a huge surge in activity in the last decade [6, 10, 17]. Although most of these research efforts are driven by diseases of human populations, the underlying concepts can be adapted to diseases of animals as well. However, not many predictive models for honeybee and varroa mite population dynamics have been published in the literature. The most relevant for our study are [19, 20, 31]. In particular, [31] presents a first model of the honeybee-mite-virus system using a traditional SIR-like modeling approach. In this model the number of mites infesting the colony overall
is a given parameter while the number of mites carrying the virus is a dependent variable. Those authors consider the constant coefficient case and give a stability analysis of the infestation equilibrium, using the number of mites in the colony as the bifurcation parameter. The main result is an explicit formula for the dependence of the critical mite load on model parameters, for which the colony is able to survive the disease. The result sheds light on the interplay between bee biology and infection dynamics, and on the effect on the fate of the colony if this balance tips. In [12], that model was modified for ABPV by including brood maintenance terms that reflect that a certain number of worker bees is always required to care for the brood in order for new bees to eclose. Because the model of [31] assumed a constant rate of birth of bees, it does not permit a trivial equilibrium and allows one to study only whether or not a virus epidemic can be fought off. The extended model of [12], on the other hand permits a trivial (collapse) equilibrium, which is shown to be locally unconditionally, but not globally, stable. Thus, our extended model also enables to study under which circumstances the colony vanishes. That happens once the healthy population size drops below a certain threshold (which depends on the brood maintenance terms), which explains e.g., wintering losses. On the other hand, the stability of the infestation equilibrium is qualitatively the same as in [31], but including brood maintenance terms shows that the maximum mite load for which the disease can be fought off, as computed by [31] is an overestimation.

Both, [31] and [12] assumed the mite load to be a given model parameter. In the current study we omit this restriction and couple the disease model with a simple logistic population growth model for the varroa mites. This extension not only requires us to add another equation to the system but also to modify the equations describing the growth of the bee population, by adding mite induced death terms.

The model that we obtained after this modification is a system of four nonlinear
ordinary differential equations. Because essential features of bee population dynamics, such as birth rates and death rates, vary drastically with the seasons, our model is a non autonomous system, which is difficult to analyze. We first use well established methods for autonomous systems to study the special case of constant coefficients and then investigate in computer simulations whether or not these findings carry over to the more general transient case. In particular we are interested in the question, and if so, under which conditions a proper working, stable bee colony that becomes infested with varroa mites can fight off an epidemic of the Acute Bee Paralysis Virus.

2.2 Governing equations

We formulate a mathematical model for the honeybee-varroa mite-ABPV complex in terms of the dependent variables

\[ x: \] number of honeybees that are virus free,

\[ y: \] number of honeybees that are infected with the virus,

\[ M: \] number of mites that infest the colony,

\[ m: \] number of mites that carry the virus.

Given that bee and mite populations are large, consisting of thousands of individuals, we can consider these variables as continuous variables which allow us to use traditional SIR-like Ross-MacDonald differential equations to describe the progression of the vector borne disease. Our proposed mathematical model is based on [12] and extends this model by adding for the mite population an additional simple
logistic equation with bee population size dependent carrying capacity, whereas in the previous studies the mite population strength was treated as a given parameter. Thus the modified model reads

\[
\frac{dm}{dt} = \beta_1(M - m)\frac{y}{x + y} - \beta_2m\frac{x}{x + y}, \quad (2.1)
\]

\[
\frac{dx}{dt} = \mu g(x)h(m) - \beta_3m\frac{x}{x + y} - d_1x - \gamma_1Mx, \quad (2.2)
\]

\[
\frac{dy}{dt} = \beta_3m\frac{x}{x + y} - d_2y - \gamma_2My, \quad (2.3)
\]

\[
\frac{dM}{dt} = rM \left(1 - \frac{M}{\alpha(x + y)}\right). \quad (2.4)
\]

The parameter \( \mu \) in (2.2) is the maximum birth rate, specified as the number of worker bees eclose per day.

The function \( g(x) \) expresses that a sufficiently large number of healthy worker bees is required to care for the brood. We think of \( g(x) \) as a switch function. If \( x \) falls below a critical value, which may seasonally depend on time, essential work in the maintenance of the brood can no longer be carried out and no new bees are born. If \( x \) is above this value, the birth of bees is not hampered. Thus \( g(0, \cdot) = 0, \frac{dg(0)}{dx} \geq 0, \lim_{x \to \infty} g(x) = 1 \). A convenient formulation for such switch like behavior is given by the sigmoidal Hill function

\[
g(x) = \frac{x^n}{K^n + x^n}, \quad (2.5)
\]

where the parameter \( K \) is the size of the bee colony at which the birth rate is half of the maximum possible rate and the integer exponent \( n > 1 \). If \( K = 0 \) is chosen, then the bee birth terms of the original model of [31] is recovered. The brood is then always reared at maximum capacity, independent of the actual bee population size, because \( g(x) \equiv 1 \).

The function \( h(m) \) in (2.2) indicates that the eclosion rate is affected by the presence of mites that carry the virus. This dependence is particularly important for viruses
like ABPV that kill infected pupae before they develop into bees. The function \( h(m) \) is assumed to decrease as \( m \) increases. We use \( h(0) = 1, \frac{dh}{dm}(m) < 0 \) and \( \lim_{m \to \infty} h(m) = 0 \); [31] suggests that an appropriate choice for \( h(m) \) is an exponential function \( h(m) \approx e^{-mk} \), where \( k \) is non-negative. We will use this expression in the computer simulations later on.

The parameter \( \beta_1 \) in (2.1) is the rate at which mites that do not carry the virus acquire it. The rate at which infected mites lose their virus to an uninfected host is \( \beta_2 \). The rate at which uninfected bees become infected is \( \beta_3 \), in bees per virus carrying mite and time.

Finally, \( d_1 \) and \( d_2 \) are the death rates for uninfected and infected honeybees, respectively. We can assume that infected bees live have shorter lifespan than healthy bees, thus \( d_2 > d_1 \).

The newly added equation (2.4) is a logistic growth model for varroa mites. By \( r \) we denote the maximum mite birth rate. The carrying capacity for the mites changes with the host population site, \( x + y \), and is characterized by the parameter \( \alpha \) which indicates how many mites can be sustained per bee on average. This assumption is in agreement with [13].

Mites contribute to an increased mortality of bees. This effect is included in (2.2) and (2.3) by including death terms that depend on \( M \); the parameters \( \gamma_{1,2} \) are the rates at which mites kill bees.

The parameters \( \mu, k, \alpha, \beta_i, d_i, \gamma_i, g(x), h(m), r \) are assumed to be non-negative. They can change with time. In particular, major differences may be observed between seasons. For example, the life span of a worker bee in summer is much shorter than in winter [1, 27]; the birth rate for bees is higher in summer than in spring and autumn, and it drops down to 0 in winter [32]. Seasonal averages for the
model parameters $\beta_{1,2,3}, \mu, d_{1,2}$ and $k$ can be derived from the data in [31]. These values are summarized in Table 2.1 and will be used in the simulations below.

In order to investigate the fate of a honeybee colony after mite/virus infestation over several years, the complete non-autonomous model with time dependent coefficients must be studied. This is not easily possible with purely analytical techniques and so we will resort to numerical simulations for this purpose below. In preparation for our simulation study, it is useful to study the governing equations in the autonomous case, i.e. assuming constant parameters and using qualitative analytical methods. For one, this approach will provide insight into the disease dynamics that will be helpful later when we discuss simulation results. Secondly, the analysis of the autonomous case will allow us to determine critical parameters and estimates for their numerical values which can be used to design the numerical simulation study.

### Table 2.1: Seasonal averages of model parameters, derived from the data presented in [31].

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Spring</th>
<th>Summer</th>
<th>Autumn</th>
<th>Winter</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\beta_1$</td>
<td>0.1593</td>
<td>0.1460</td>
<td>0.1489</td>
<td>0.04226</td>
</tr>
<tr>
<td>$\beta_2$</td>
<td>0.04959</td>
<td>0.03721</td>
<td>0.04750</td>
<td>0.008460</td>
</tr>
<tr>
<td>$\beta_3$</td>
<td>0.1984</td>
<td>0.1460</td>
<td>0.1900</td>
<td>0.03384</td>
</tr>
<tr>
<td>$d_1$</td>
<td>0.02272</td>
<td>0.04</td>
<td>0.02272</td>
<td>0.005263</td>
</tr>
<tr>
<td>$d_2$</td>
<td>0.2</td>
<td>0.2</td>
<td>0.2</td>
<td>0.005300</td>
</tr>
<tr>
<td>$\mu$</td>
<td>500</td>
<td>1500</td>
<td>500</td>
<td>0</td>
</tr>
<tr>
<td>$k$</td>
<td>0.000075</td>
<td>0.00003125</td>
<td>0.000075</td>
<td>N/A</td>
</tr>
<tr>
<td>$r$</td>
<td>0.0165</td>
<td>0.0165</td>
<td>0.0045</td>
<td>0.0045</td>
</tr>
</tbody>
</table>
2.3 Analysis in the autonomous case

In order to prepare for the analysis of the complete four dimensional model (2.1)-(2.4), we began our investigation by studying smaller, more easily accessible sub-models. We begin by discussing the model for a healthy bee colony without mites and virus. In a second preliminary step we will introduce mites but not the virus. The analysis of the complete model builds on the results of these simpler special cases.

2.3.1 The one-dimensional healthy bee sub-model

In the absence of parasites and viruses, the model becomes

\[
\frac{dx}{dt} = \mu g(x) - d_1 x. \tag{2.6}
\]

It is easily verified that the solutions of this equation also give parasite and virus free solutions of (2.1)-(2.4) for initial data \(m(0) = y(0) = M(0)\).

This system satisfies a Lipschitz condition for all \(x \geq 0\), i.e. the initial value problem with \(x(0) \geq 0\) has a unique solution. It follows by comparison with the trivial solution \(x \equiv 0\), that the solution is non-negative.

The dynamics of one-dimensional autonomous systems is simple: Either the solutions converge to an asymptotically stable equilibrium or, they diverge to \(\pm \infty\). Because \(g(0) = 0\), we always find the trivial equilibrium \(x_0^* = 0\), and because \(g'(0) = 0\) the trivial equilibrium is asymptotically stable for all positive parameter values. The intersections of the line \(y = \frac{d_1}{\mu} x\) with the function \(g(x)\) gives further non-trivial equilibria. Since \(g\) is a sigmoidal function, it is easily verified that no such intersection for positive \(x\) exists for large \(d_1/\mu\), and two such intersections exist if \(d_1/\mu\) is small enough. We denote these the two intersections by \(x_1^*\) and \(x_2^*\).
with $x_1^* > x_2^*$. From geometrical arguments it follows that in the latter case, $x_2^*$ is unstable while $x_1^*$ is stable. Assuming $g(x)$ to be the Hill function (2.5) we make this statement more precise:

**Lemma 2.3.1.** The differential equation (2.6) with (2.5) has an asymptotically stable equilibrium at $x_0^* = 0$. If $\frac{d_1}{\mu} > \frac{n-1}{n} \frac{1}{K\sqrt{n-1}}$ then this equilibrium is the only steady state. If $\frac{d_1}{\mu} < \frac{n-1}{n} \frac{1}{K\sqrt{n-1}}$ then two positive steady states $x_1^*, x_2^*$ exist with $x_1^* > x_2^*$. Equilibrium $x_1^*$ is asymptotically stable, and $x_2^*$ is unstable.

**Proof.** The non-trivial equilibria of (2.6) with (2.5) are obtained as roots of the polynomial

$$G(x) = x^n - \frac{\mu}{d_1} x^{n-1} + K^n.$$ 

Descarte’s Rule of Signs immediately implies that there are either two or no positive roots. No such equilibrium exists if the line $f(x) = \frac{d_1}{\mu} x$ lies above $g(x)$ for all $x > 0$. We denote by $\Delta$ the critical value of $d_1/\mu$ for which $f(x)$ is tangential to $g(x)$ in a point $\hat{x}$. Then

$$\Delta = \frac{g(\hat{x})}{\hat{x}} = \frac{\hat{x}^{n-1}}{K^n + \hat{x}^n}, \quad \text{and} \quad \Delta = g'(\hat{x}) = \frac{nKx^{n-1}}{(K^n + \hat{x}^n)^2},$$

whence

$$\hat{x} = K\sqrt[n-1]{-1}.$$ 

Thus we calculate the critical value for $\Delta$ as

$$\Delta = \frac{n-1}{n} \frac{1}{K\sqrt[n-1]{-1}}.$$ 

If $d_1/\mu > \Delta$, then $f(x)$ and $g(x)$ have no intersection, i.e. no non-trivial equilibrium of (2.6) exists. If $d_1/\mu < \Delta$, then $f(x)$ intersects with $g(x)$ twice, in points $x_1^*, x_2^*$, where w.l.o.g. we assume $x_1^* > x_2^*$. The stability of these equilibria is determined from the signs of $g'(x_1^*) - f'(x_1^*)$. Since both functions satisfy $f(0) = g(0) = 0$ and $g'(0) < f'(0)$, the line $f(x)$ intersects with $g(x)$ in $x_2^*$ from above, i.e. $f'(x_2^*) < g'(x_2^*)$ and in $x_1^*$ from below, i.e. $f'(x_1^*) > g'(x_1^*)$. □
Remark 1. The solutions of the initial value problem (2.6) with (2.5) and \( x(0) \geq 0 \) are bounded from above by \( \max\{x(0), x^*_2\} \), thus they exist globally. If \( x^*_2 \) does not exist they are monotonously decreasing and thus bounded by \( x(0) \).

Remark 2. In the special case \( n = 2 \), we can explicitly calculate the two positive equilibria as
\[
x^*_{1,2} = \frac{1}{2} \left( \frac{\mu}{d_1} \pm \sqrt{\frac{\mu^2}{d_1^2} - 4K^2} \right),
\]
(2.7)

The unconditional stability of the trivial equilibrium reflects that a certain number of honeybees is required to care for the brood. If the initial value \( x(0) < x^*_2 \) the colony dies out, if \( x(0) > x^*_2 \), a healthy colony can establish itself attaining equilibrium \( x^*_1 \).

For the data in Table 2.1, the non-trivial equilibria \( x^*_{1,2} \) exist in spring, summer, and fall, but not in winter, when no new bees are born. Thus in winter all solutions converge to the trivial one, however, as this is not reached in finite time.

2.3.2 The two-dimensional bee-mite sub-model

We investigate now how the stability of the equilibria \( x^*_{0,1,2} \) changes when parasitic mites are considered in the colony that does not carry the virus. To this end we study the bee-mite subsystem of (2.1)-(2.4),
\[
\begin{align*}
\frac{dx}{dt} &= \mu g(x) - d_1 x - \gamma_1 Mx, \\
\frac{dM}{dt} &= rM \left( 1 - \frac{M}{\alpha x} \right),
\end{align*}
\]
(2.8) \hspace{1cm} (2.9)

where we again assume a sigmoidal Hill function as in (2.5) for the brood maintenance function \( g(x) \).

It suffices to consider the case of strictly positive initial data. If initially \( M = 0 \) then \( M = 0 \) for all \( t \) and the model reduces to (2.6). Because bees are required as hosts for mites, the case of initial data \( M(0) \geq 0 \) and \( x(0) = 0 \) is irrelevant.
Proposition 2.3.1. The initial value problem of (2.8), (2.9) with \( x(0) = x_0, M(0) = M_0 \) and \( (x_0, M_0) \in D := \{(x, M) : x > 0, M > 0\} \) possesses a unique solution in \( D \), which is non-negative. Moreover, the set \( \tilde{D}_x = \{(x, M) : 0 \leq x \leq \tilde{x}, 0 \leq M \leq \alpha \tilde{x}\} \) is positively invariant for all \( \tilde{x} > \frac{\mu}{d_1}. \)

Proof. Local existence and uniqueness follow from standard arguments, since (2.8), (2.9) satisfy a Lipschitz condition in \( D \). The result that positive initial data lead to positive solutions follows from the tangent criterion in the usual form.

To show the boundedness of \( x \), we note that from equation (2.8), it follows that

\[
\frac{dx}{dt} = \mu g(x) - d_1 x - \gamma_1 M x < \mu - d_1 x.
\]

This means that

\[
x(t) < \frac{\mu}{d_1} - \left( \frac{\mu}{d_1} - x_0 \right) e^{-d_1 t},
\]

whence, \( x(t) < \max\{x_0, \frac{\mu}{d_1}\} \). In order to show the boundedness of \( M \), we pick a \( \tilde{x} \geq x \). We have

\[
\frac{dM}{dt} = r M \left( 1 - \frac{M}{\alpha \tilde{x}} \right) \leq r M \left( 1 - \frac{M}{\alpha \tilde{x}} \right).
\]

Hence, \( M(t) \) is bounded from above by the solution of the logistic equation

\[
\frac{d\tilde{M}}{dt} = r \tilde{M} \left( 1 - \frac{\tilde{M}}{\alpha \tilde{x}} \right)
\]

with carrying capacity \( \alpha \tilde{x} \). Thus, if \( M_0 \leq \alpha \tilde{x}, \) then \( M(t) \leq \alpha \tilde{x} \) for all \( t > 0 \).

To study the longtime behavior and stability of system (2.8), (2.9), we investigate its equilibria. The system admits, under some conditions on parameters, the following equilibria:

A: the trivial equilibrium \((x^*, M^*) = (0, 0)\) exists for all choices of parameters
B: the mite-free equilibrium \((x^*, M^*) = (x^*_2, 0)\), where \(x^*_2\) is the unstable equilibrium of (2.6), according to Lemma 2.3.1; this equilibrium exists under the conditions discussed there.

C: the mite-free equilibrium \((x^*, M^*) = (x^*_1, 0)\), where \(x^*_1\) is the stable equilibrium of (2.6), according to Lemma 2.3.1; this equilibrium exists under the conditions discussed there.

D,E: mite infested equilibria of the form \((x^*, M^*) = (x^*, \alpha x^*)\) with \(x^* > 0\), the existence of these equilibria.

**Proposition 2.3.2.** The set \(D_\bar{x} = \{(x, M) : 0 < x < \bar{x}, 0 < M < \alpha \bar{x}\}\) is positively invariant for all \(\bar{x} < x^*_2\) according to Lemma 2.3.1. All solutions entering such a \(D_\bar{x}\) converge to the trivial equilibrium \(A\).

**Proof.** From (2.8) it follows that for all \(x < \bar{x} < x^*_2\)

\[
\frac{dx}{dt} = \mu g(x) - (d_1 + \delta_1(M))x \leq \mu g(x) - d_1 x < 0.
\]

Moreover, for all \(M > \alpha x\) we have

\[
\frac{dM}{dt} = rM \left(1 - \frac{M}{\alpha x}\right) < 0.
\]

Furthermore, with standard arguments, the \(M\)- and \(x\)-axis are positively invariant (and all solutions on the axes converge to \(A\)). Thus, \(D_\bar{x}\) is positively invariant with inward pointing flux along the boundaries \(x = \bar{x}\) and \(M = \alpha \bar{x}\).

In \(D_\bar{x}\), \(\frac{dx}{dt} < 0\) for all solutions. On the other hand, in the lower triangle \(M < \alpha x\), \(M\) is increasing, and in the upper triangle \(M > \alpha x\) it is decreasing; see Figure 2.1 for an illustration. Because the trivial equilibrium \(A\) is the only equilibrium in the closure of \(D_\bar{x}\), all solutions entering the upper triangle therefore converge to \(A\). Solutions in the lower triangle increase in \(M\) until they enter the upper triangle. \(\square\)
Figure 2.1: Direction field for the system (2.8), (2.9) for \(0 < x < \tilde{x}, 0 < M < \alpha < \tilde{x}\) with \(\tilde{x} < x^*_2\), the unstable equilibrium of (2.6). We have used the summer parameter values with \(K = 8000\) and \(\alpha = 0.2\). The initial values used are \(x(0) = 30\) and \(M(0) = 20\).

**Proposition 2.3.3.** If they exist, the equilibrium \(B = (x^*, 0) = (x^*_1, 0)\) of (2.8), (2.9) is an unstable node, while the equilibrium \(C = (x^*, 0) = (x^*_2, 0)\) is an unstable saddle.

**Proof.** The Jacobian of the right hand side of the differential equation is

\[
J(x, M) = \begin{bmatrix} 
\mu g'(x) - (d_1 + \gamma_1 M) & -\gamma_1 x \\
\frac{rM^2}{\alpha x^2} & r \left(1 - \frac{2M}{\alpha x}\right)
\end{bmatrix}. \tag{2.10}
\]

Equilibria \(B, C\) exist if the equilibria \(x^*_{1,2}\) of the one-dimensional model (2.6) exist. In this case we have for \(B, C\) that

\[
J(x^*_1, 0) = \begin{bmatrix} 
\mu g'(x^*_1) - d_1 & -\gamma_1 x^*_1 \\
0 & r
\end{bmatrix}
\]

The eigenvalues are \(\lambda_1 = \mu g'(x^*_1) - d_1\) and \(\lambda_2 = r\). Eigenvalue \(\lambda_2\) is positive for all parameter sets and both equilibria \(B, C\). With Lemma 2.3.1, we have \(\lambda_1 > 0\) for \(x^*_2\), and \(\lambda_1 < 0\) for \(x^*_1\). Thus, \(C\) is a saddle and \(B\) is an unstable node. \(\square\)
Figure 2.2: Nullclines and equilibria of the bee-mite model: (a) the trivial equilibrium A is the only equilibrium; (b) only the mite free equilibria A, B, C exist; (c), (d) two additional equilibria D, E with $M^* = \alpha x^* > 0$ exist, in (c) $x^*_E < \hat{x}$, in (d) $x^*_E > \hat{x} = \sqrt{n - 1}K$.

Remark 3. In the special case $n = 2$, the eigenvalues $\lambda_1$ of B and C are obtained as

$$\lambda_1 = \pm d_1 \sqrt{1 - 4K^2 \left( \frac{d_1}{\mu} \right)^2}.$$ 

Proposition 2.3.4. There are at most two mite-infested equilibria D, E, with $x^* > 0$, $M^* = \alpha x^* > 0$. We denote the one with the smaller $x^*$ by D, the other by E. The point D is always unstable. If $x^* > \sqrt{n - 1}K$ for E, then E is stable; if $x^* < \sqrt{n - 1}K$ for E, then E is stable for small enough $r$, otherwise it is unstable.

Proof. The points D and E are the intersections of the $x$-nullcline

$$\hat{M}(x) = \alpha x$$

with the $M$-nullcline

$$\tilde{M}(x) = \frac{\mu}{\gamma_1} \frac{g(x)}{x} - \frac{d_1}{\gamma_1}.$$
Whether or not these intersections exist depends on the values of the model parameters. Using \( \hat{M}(x^*) = \tilde{M}(x^*) \) and (2.5), we find \( x^* \) as the roots of the polynomial

\[
-\gamma \alpha x^{n+1} - d_1 x^n + \mu x^{n-1} - \gamma \alpha x K^n - d_1 K^n = 0.
\]

Descartes’ Rule of Signs implies that this polynomial has at most two positive roots. For \( n = 2 \), \( \mu > \gamma \alpha K^2 \) must also be satisfied, i.e. the birth rate must be sufficiently high or the maximum sustainable mite load and brood maintenance coefficient sufficiently low.

For \( x > 0 \), the function \( \tilde{M}(x) \) is a continuous, differentiable function with

\[
\tilde{M}(0) = -\frac{d_1}{\gamma_1}, \quad \text{and} \quad \lim_{x \to \infty} \tilde{M}(x) = -\frac{d_1}{\gamma_1}.
\]

With the usual calculus arguments we find that it has a single extremum, namely a maximum at

\[
\hat{x} = \sqrt[n]{n - 1} K.
\]

The function is strictly monotonically increasing for \( x < \hat{x} \) and strictly decreasing for \( x > \hat{x} \). We consider now the case where \( D \) and \( E \) exist. The stability of these equilibria is investigated with the help of the Jacobian (2.10). Substituting \( M = \hat{M} = \alpha x \) into the second row and the equivalent \( M = \tilde{M} = \frac{\mu g(x)}{x} - \frac{d}{\gamma_1} \) into the first row, we find

\[
J(x^*, \alpha x^*) = \begin{bmatrix}
\mu \left( g'(x^*) - \frac{g(x^*)}{x^*} \right) & -\gamma_1 x^* \\
r \alpha & -r
\end{bmatrix}.
\]

We introduce the notation

\[
z(x) = \mu \left( g'(x) - \frac{g(x)}{x} \right)
\]

and note that

\[
\tilde{M}'(x) = \frac{z(x)}{\gamma_1 x}.
\]
The stability of the equilibria is assessed from the trace and determinant of $J(x^*, \alpha x^*)$. We have
\[ \text{det} = -r(z^* - \alpha \gamma_1 x^*), \quad \text{tr} = z^* - r, \]
where we used the shorthand notation $z^* = z(x^*)$. In equilibrium point $D$, the $x$-nullcline $\tilde{M}(x)$ intersects with the $M$-nullcline $\hat{M}(x)$ from below, thus
\[ \tilde{M}'(x^*) = \frac{z^*}{\gamma_1 x^*} > \alpha = \hat{M}'(x^*), \]
whence $z^* > \gamma_1 \alpha x^*$ and, therefore, $\text{det} < 0$. Thus, the equilibrium $D$ is unstable.

In equilibrium point $E$, the $x$-nullcline $\tilde{M}(x)$ intersects with the $M$-nullcline $\hat{M}(x)$ from above, thus
\[ \tilde{M}'(x^*) = \frac{z^*}{\gamma_1 x^*} < \alpha = \hat{M}'(x^*), \]
whence $z^* < \gamma_1 \alpha x^*$. Thus $\text{det} = -r(z^* - \alpha \gamma_1 x^*) > 0$. To analyse the stability of equilibrium $E$ further, we have to distinguish between two possibilities:

If $x^*_E < \hat{x} = K \sqrt{n - 1}$, then $z^* > 0$. In this case $\text{tr} = z^* - r < 0$ for all $r < z^*$. Thus $E$ is stable for small enough $r$ but unstable if $r > z$.

If $x^*_E > \hat{x} = K \sqrt{n - 1}$, then $z^* < 0$. In this case $\text{tr} = z^* - r < 0$ for all $r$. Thus $E$ is stable.

\[ \square \]

Remark 4. The value of $z$ in the proof of the above proposition depends only on the parameters of the birth term, $\mu$ and $K$. It does not depend on bee death or mite parameters.

Remark 5. If $\alpha$ is sufficiently small or $\mu$ is sufficiently large the two intersections of $\tilde{M}(x)$ and $\hat{M}(x)$ exist. The possible cases are illustrated in Figure 2.2.
Note that in the proposed model, a mite infestation can never be fought off by the bee colony. This is an immediate consequence of the logistic growth function but agrees with observations reported by beekeepers.

2.3.3 The complete bee-mite-virus model

We investigate now the question whether a stable, mite infested honeybee colony can fight off the virus. To this end we consider the complete four-dimensional model (2.1)-(2.4) with (2.5).

**Proposition 2.3.5.** The initial value problem of (2.1)-(2.4) with \((m_0, x_0, y_0, M_0) \in D := \{(m, x, y, M) : m > 0, x > 0, y > 0, M > 0\}\) possesses a unique solution, which is non-negative. Moreover, the set

\[
Z_\tilde{x} = \{(m, x, y, M) : 0 \leq m \leq \alpha \tilde{x}, 0 \leq x, 0 \leq y, (x + y) \leq \tilde{x}, 0 \leq M \leq \alpha \tilde{x}\}
\]

is positively invariant for all \(\tilde{x} > \frac{\mu}{d_1}\).

**Proof.** Existence, uniqueness and non-negativity of the solution follow with standard arguments that can be found in [33]. For boundedness of \(x + y\), we note that from equations (2.2) and (2.3),

\[
\frac{dx}{dt} + \frac{dy}{dt} = \mu g(x) - d_1 x - d_2 y - \gamma_1 M x - \gamma_2 M y \\
\leq \mu g(x) - d_1 x - d_2 y \\
\leq \mu g(x + y) - d(x + y) =: G(x + y)
\]

where \(d = \min\{d_1, d_2\}\). Here we used that \(g(x)\) is a monotonously increasing function. Therefore, we have

\[
G(x + y) \leq 0 \quad \forall \quad (x + y) \geq \tilde{x} > \frac{\mu}{d_1}.
\]
In order to show the boundedness of $M$, we assume that $x + y \leq \tilde{x}$, and so
\[ \frac{dM}{dt} = rM \left( 1 - \frac{M}{\alpha(x + y)} \right) \leq rM \left( 1 - \frac{M}{\alpha \tilde{x}} \right) \]
Thus, if $M(0) < \alpha \tilde{x}$, $M(t)$ is bounded from above by the solution of the logistic equation
\[ \frac{dz}{dt} = rz \left( 1 - \frac{z}{\alpha \tilde{x}} \right) \]
with carrying capacity $\alpha \tilde{x}$, in particular it is bounded by $\alpha \tilde{x}$. In order to show the boundedness of $m$, we have
\[ \frac{dm}{dt} = \frac{\beta_1(M - m)y}{x + y} - \frac{\beta_2mx}{x + y} \leq \beta_1(M - m) \leq \beta_1(\alpha \tilde{x} - m). \]
Therefore, $m$ is bounded from above by the solution of the linear equation
\[ \frac{d\tilde{m}}{dt} = \beta_1(\alpha \tilde{x} - z), \]
i.e. in particular by the constant $\alpha \tilde{x}$, if $m(0) < \alpha \tilde{x}$. \qed

It is easy to verify from (2.1) and (2.3) that equilibria with $m^* = 0$ imply $y^* = 0$ and vice versa. Moreover, we find that to every equilibrium $A, ..., E : (x^*, M^*)$ of the two-dimensional bee-mite model, there corresponds a disease free equilibrium $A_4, ..., E_4 : (0, x^*, 0, M^*)$ of the complete four-dimensional bee-mite-virus model.
The question of whether or not a virus free colony at equilibrium can fight off a virus infection is primarily of interest for the only non-trivial stable equilibrium of the two-dimensional model, namely $E$. The equilibrium $E$ can occur in two distinctively different types, either $x^* < K \sqrt[n]{n - 1}$ or $x^* > K \sqrt[n]{n - 1}$. In the former the bee colony is small, and while its population may be stable under the conditions outlined above, it is not a properly working bee colony, i.e. it might be able to maintain itself but is not able to produce sufficient honey, etc. More interesting is the other case. It depends on the specific parameters, such as $\alpha$ or $\gamma_1$ how strong the colony is. In many cases it might be very strong, i.e. closer to the
disease and mite free equilibrium $x_1^*$ than to $\dot{x} = K \sqrt{n-1}$. We investigate the stability of the equilibrium $E_4 : (0, x^*, 0, \alpha x^*)$ under (2.1)-(2.4).

**Proposition 2.3.6.** Let $E : (x^*, \alpha x^*)$, $x^* > 0$, be an asymptotically stable equilibrium of (2.8),(2.9). Then $E_4 : (0, x^*, 0, \alpha x^*)$ is an asymptotically stable equilibrium of (2.1)-(2.4) if

$$
\beta_3 \beta_1 \alpha < \beta_2 (d_2 + \gamma_2 \alpha x^*). 
$$

(2.11)

**Proof.** We analyse the Jacobian in $E_4$,

$$
J(0, x^*, 0, \alpha x^*) = 
\begin{bmatrix}
-\beta_2 & 0 & \beta_1 \alpha & 0 \\
\mu g(x^*)h'(0) - \beta_3 & \mu g'(x^*) - d_1 - \gamma_1 \alpha x^* & 0 & -\gamma_1 x^* \\
\beta_3 & 0 & -d_2 - \gamma_2 \alpha x^* & 0 \\
0 & r \alpha & r \alpha & -r
\end{bmatrix}.
$$

Its eigenvalues are

$$
\lambda_1 = -\frac{1}{2} \left[ (d_2 + \gamma_2 \alpha x^* + \beta_2) - \sqrt{(d_2 + \gamma_2 \alpha x^* - \beta_2)^2 + 4 \beta_3 \beta_1 \alpha} \right],
$$

$$
\lambda_2 = -\frac{1}{2} \left[ (d_2 + \gamma_2 \alpha x^* + \beta_2) + \sqrt{(d_2 + \gamma_2 \alpha x^* - \beta_2)^2 + 4 \beta_3 \beta_1 \alpha} \right],
$$

$$
\lambda_3 = \frac{1}{2} (\mu g'(x^*) - d_1 - \gamma_1 \alpha x^* - r) + \frac{1}{2} \sqrt{(\mu g'(x^*) - d_1 - \gamma_1 \alpha x^* + r)^2 - 4 r \gamma_1 \alpha x^*},
$$

$$
\lambda_4 = \frac{1}{2} (\mu g'(x^*) - d_1 - \gamma_1 \alpha x^* - r) - \frac{1}{2} \sqrt{(\mu g'(x^*) - d_1 - \gamma_1 \alpha x^* + r)^2 - 4 r \gamma_1 \alpha x^*}.
$$

Since all parameters are non-negative, it follows immediately that $\lambda_1$ and $\lambda_2$ are real. The eigenvalue $\lambda_2$ is always negative.

For $\lambda_1$ to be negative we require

$$(d_2 + \gamma_2 \alpha x^* + \beta_2) > \sqrt{(d_2 + \gamma_2 \alpha x^* - \beta_2)^2 + 4 \beta_3 \beta_1 \alpha},$$

or, equivalently

$$4 \beta_3 \beta_1 \alpha < (d_2 + \gamma_2 \alpha x^* + \beta_2)^2 - (d_2 + \gamma_2 \alpha x^* - \beta_2)^2,$$

38
which is the same as
\[ \beta_3 \beta_1 \alpha < \beta_2 (d_2 + \gamma_2 \alpha x^*). \] (2.12)

We will use the results of the two-dimensional model to investigate \( \lambda_3 \) and \( \lambda_4 \). At equilibrium, we have
\[ \mu \frac{g(x^*)}{x^*} = d_1 + \gamma_1 \alpha x^*. \]

This allows us to rewrite \( \lambda_3 \) in terms of the function \( z(x) = \mu \left( g'(x) - \frac{g(x)}{x} \right) \) which was introduced above in the proof of Proposition 2.3.4. This gives
\[ \lambda_3 = \frac{1}{2} \left[ (z^* - r) + \sqrt{(z^* + r)^2 - 4\gamma_1 \alpha x^* r} \right]. \]

Defining
\[ c := -4r(z^* - \gamma_1 \alpha x^*), \]

We can rewrite \( \lambda_3 \) as
\[ \lambda_3 = \frac{1}{2} \left[ (z^* - r) + \sqrt{(z^* - r)^2 - c} \right]. \]

Recall from the proof of Proposition 2.3.4 that \( z^* - r < 0 \) (this is the trace of the stability matrix of \( E \) in the 2D case) and \( c > 0 \) (this is four times the determinant of the stability matrix of \( E \) in the 2D case), because \( E \) is stable for \( x^* > K \sqrt{n-1} \). If \( c > (z^* - r)^2 \), then \( \lambda_3 \) is complex with negative real part \( z^* - \lambda \). Otherwise, \( |z^* - r| > \sqrt{(z^* - r)^2 - c} \), implying that \( \lambda_3 \) is negative.

The last eigenvalue \( \lambda_4 \) is rewritten as
\[ \lambda_4 = \frac{1}{2} \left[ (z^* - r) - \sqrt{(z^* - r)^2 - c} \right]. \]

Again, if \( c > (z^* - r)^2 \) then \( \lambda_4 \) is complex with negative real part \( z^* - \lambda \). Otherwise, \( \lambda_4 \) is negative.

\textbf{Remark 6.} Keeping in mind that at equilibrium \( E \) the number of mites is \( M^* = \alpha x^* \), the stability criterion (2.12) is a straightforward extension of the criterion for
the model of [12], which treated the mite load as a known constant, to the model
(2.1)-(2.4) in which the mites are a dependent variable.

2.4 Computational investigation of the periodic coefficient case

2.4.1 Computational setup and parameters

The study of the nonlinear non-autonomous model is more complicated than the
autonomous case and an analytical treatment is not easily done. Therefore, we
study the model in computer simulations. The focus of this numerical study is to
verify whether or not the various types of system behaviour that were found with
analytical techniques for the autonomous case can also be observed in the non-
autonomous case with seasonally fluctuating coefficients (periodic over the year).
The results of the autonomous analysis are thereby used to design the computations
that we execute numerically.

For the computer simulations we use the software package MATLAB. The ordinary
differential equations are integrated by the built in routine ode15s, a variable order
solver based on numerical differentiation formulas. In all cases, we run the com-
puter simulations for a period of 7000 days (approx 20 years), or until the colony
vanishes, whichever comes first.

Numerical values for the seasonal averages of the parameters $\beta_i, d_i, \mu, k$ are ob-
tained from [31], see Table 2.1. Lacking more detailed information, we use these
values to construct piecewise constant time varying parameter functions, assuming
four equally long seasons of 91.25 days. For simplicity, we fix the Hill coefficient
in the growth maintenance terms as $n = 2$, in accordance with [12]. The values of
\( \gamma_1 \) and \( \gamma_2 \) are estimated to be \( 10^{-7} \) for every season, based on order of magnitude considerations. The parameter \( r \) is obtained from [19, 22].

We assume the above parameters to be given and investigate the behaviour of the model with respect to the remaining parameters, \( K \) and \( \alpha \). The former affects the bee birth rate, the latter the size of the mite population that can be established. There is no fixed value of the parameter \( \alpha \) available in the literature. In [31], it has been found that for a summer colony with 37,500 bees, 12,289 mites are required to start an epidemic, while an autumn population of 22,000 bees requires 6,830 mites for an epidemic. From this we conclude \( \alpha \approx 0.3 \). On the other hand, in [5], the values 0.1321 (Oct-Dec) and 0.4785 (Jan-Feb) are reported, while an average value of 0.5 is found in [28]. In our simulations, we vary \( \alpha \) over the range that covers these values.

In order to estimate values for the brood maintenance constant \( K \), we look at the bee-model (2.6). The number of bees in an established colony, \( x^* = \frac{I}{d_1} \), is greater than the brood maintenance constant \( K \). The value of \( \frac{I}{d_1} \) for spring and fall is computed as 22,007, and for summer 37,500. This calculation gives upper bounds on the values that we will choose for \( K \).

### 2.4.2 The bee-mite sub-model

We start our investigation by considering the sub-model that is comprised of bees and mites only, without taking the virus into account, i.e., model (2.8), (2.9). In the autonomous case, we found that bee colonies infested with mites either collapse (equilibrium A is attained) or that an endemic equilibrium, in which mites and bees co-exists is attained (equilibrium E). The latter was the case if \( x^* < K^n \sqrt{n - 1} \) or if the mite birth rate \( r \) is small enough. In a first simulation experiment, we
investigate whether or not this result carries over to the transient, non-autonomous case with seasonally changing coefficients.

In the two-dimensional case, a bee population can vanish either because the initial population are too small for a colony to establish itself even in the absence of mites, or because the equilibrium \( E \) is unstable, or although \( E \) might be stable the solution can be attracted by the stable trivial equilibrium. In our experiment, we vary the brood maintenance coefficient \( K \) and the mite carrying capacity \( \alpha \). Both parameters affect the steady state population size \( x^* \) and thus the stability criterion for \( E \). Moreover, we will compare the fate of the bee population in these cases in the absence and presence of parasitic mites.

We start with the following simulations, the results of which are plotted in the corresponding Figures. In this first set of simulations, the mite carrying capacity \( \alpha \) was set to 0.4784, 0.5, 0.5, 0.4784 for spring, summer, fall, and winter, respectively. See Table 2.1 for the remaining parameters. Four simulation experiments were conducted and the results are presented in the following figures:

Figure 2.3(a): low brood maintenance coefficient for \( K \) for spring, summer, fall, and winter as 6,000, 8,000, 6,000, 6,000, respectively; and initial data \( x(0) = 20,000 \) and \( M(0) = 0 \) (no mites)

Figure 2.3(b): brood maintenance coefficient \( K \) as in 2.3(a), but with initial data \( x(0) = 20,000 \) and \( M(0) = 100 \) (mite infestation)

Figure 2.3(c): high brood maintenance coefficient for \( K \) for spring, summer, fall, and winter as 11,800, 12,000, 11,800, 6,000, respectively; and initial data \( x(0) = 20,000 \) and \( M(0) = 0 \) (no mites)
Figure 2.3(d): brood maintenance coefficient $K$ as in 2.3(c), but with initial data $x(0) = 20,000$ and $M(0) = 100$ (mite infestation)

Figure 2.3: Simulation of bee-mite population dynamics: periodic solutions for varying brood maintenance coefficients $K$: low [top row, (a), (b)] versus high [bottom row (c),(d)] values, without mites [left column (a), (c)] and with mites [right column (b), (d)]. Time is given in days; the symbol $Y$ on the y-axes represents population. See text for details of parameter values.

*Comparison between 2.3(a) and 2.3(b).* Figures 2.3(a) and 2.3(b) show the development of a honeybee colony with and without mites. In Figure 2.3(a), in the absence of mites, the bee population increases in spring and in summer, it reaches a level of approximately 35,000. It decreases in fall and winter to approximately 14,000. This pattern repeats annually. In Figure 2.3(b), in the presence of mites, the bee population behaves similarly. However, after mites are established, in our
simulations from year two on, the bee population will attain lower values. The mite population starts at a very small value, increasing steadily until the end of the second summer. Then it declines as the bee population declines, and thus the number of hosts. In this stage, the mite population size is above the seasonal carrying capacity. From then on the mite population shows the same oscillatory behaviour as the bee population. From the third year on, it reaches in summer a maximum value approximately 12,000. On the other hand, in winter the mite population drops to minimum values around 8,000. Thus, the behaviour of the mite population is determined essentially by the development of the host population. The seasonally varying simulation of Figure 2.3(a) corresponds to the stable equilibrium $x_1^*$ of the autonomous one-dimensional bee population model. The seasonally varying simulation in Figure 2.3(b) corresponds to the stable equilibrium $E$ of the autonomous two-dimensional model.

Comparison between 2.3(a) and 2.3(c). Figures 2.3(a) and 2.3(c) show honeybee colonies in the absence of mites. The simulations differ with respect to the brood maintenance coefficient $K$ that was used, which is lower in Figure 2.3(a) than in Figure 2.3(c). In both cases a periodic solution for the bee population is attained approximately from the second year on. In case 2.3(c) more bees are required to rear the brood at full capacity. Therefore, the bee population reaches a lower size, fluctuating over the seasons between 10,000 and 30,000, compared to 14,000 $\sim$ 35,000 in case 2.3(a).

Comparison between 2.3(c) and 2.3(d). Figure 2.3(c) shows a properly working honeybee colony in the absence of mites for higher values of $K$. It has been described in the previous paragraph. In Figure 2.3(d), the colony is infested by mites. After an initial transient period of three complete cycles during which the bee population decreases, compared to the data in Figure 2.3(c), a stable periodic solution
is attained after the mite population establishes itself. The bee population size in the mite infested case Fig 2.3(d), however, is smaller than in the mite free case of Figure 2.3(c). The summer maximum decreased from around 31,000 to 28,000, the winter minimum from around 10,000 to around 8,000. The periodic solution in Figure 2.3(d) corresponds to the equilibrium of type E of the two-dimensional model in the autonomous case.

Comparison between 2.3(b) and 2.3(d). We compare the stable mite infested colonies for two different sets of brood maintenance coefficient $K$. Both figures have been explained above in detail. The maximum value of honeybees in summer is much more in 2.3(b) as compared to 2.3(d). The reason is that fewer worker bees are required to obtain bee birth at maximum capacity. A similar effect is also observed in the mite population as well. The difference in bee population values are also reflected in the differences of the sizes of the mite populations.

In the first simulation experiment we noticed that drastic changes in $K$ can affect the fate of the bee population, but for relatively low values, the effect of mites on the bee population was less pronounced than for higher values.

In a second simulation experiment, we investigate whether or not mite infestation can lead to the extinction of 11,600 and 12,200 in spring and fall and between 12,000 and 14,000 in summer. The relative carrying capacity parameter $\alpha$ is fixed as 0.4784, 0.1321, 0.1321, 0.4784 in spring, summer, fall, and winter. That is, we assume a smaller tolerance of bees for mites in summer and spring compared to the previous simulations. The initial data used in the experiment is $x(0) = 20,000$ and $M(0) = 100$. Four simulation experiments were conducted and the results are presented in the following figures:

Figure 2.4(a): brood maintenance coefficient for $K$ for spring, summer, fall, and
winter as 11600, 12000, 11600, and 6000, respectively

Figure 2.4(b): brood maintenance coefficient $K$ for spring, summer, fall, winter as 11700, 14000, 11700, 6000, respectively

Figure 2.4(c): brood maintenance coefficient for $K$ for spring, summer, fall, winter as 11900, 14000, 11900, 6000, respectively

Figure 2.4(d): brood maintenance coefficient for $K$ for spring, summer, fall, winter as 12200, 14000, 12200, 6000, respectively

In the first case, Figure 2.4(a), as in the previous case we find a periodic co-existence solution that corresponds to the equilibrium $E$ of the autonomous case, as in the simulations before. In the three other simulations, the bee colony vanishes after four [Fig. 2.4(b)], three [Fig. 2.4(c), or two [Fig. 2.4(d)] years. In all three cases the collapse happens at the onset of spring, when the bee population comes out of winter too weak to care for the brood, i.e. the bee population falls during winter below the brood maintenance coefficient. However, the decline in the bee population is visible from year one on as the maximum and minimum values clearly decrease from year to year.

2.4.3 The complete bee-mite-virus model

In our final simulation experiment we investigate the effect of the virus on bee populations that are infested by mites but attain a stable co-existence equilibrium. The analysis of the autonomous case showed that the disease can be fought off if inequality (2.11) is satisfied. In our simulations we keep the disease transmission parameters $\beta_{1,2,3}$ at the given value and investigate whether result of the autonomous
Figure 2.4: Simulation of bee-mite dynamics: disappearing bee colonies for brood maintenance coefficients $K$ varying over the range $K = 11600$ and $K = 14000$ in spring, summer, winter. Time is given in days; the symbol $Y$ on the $y$-axes represents population. See text for details on model parameters.

Case carries over to the non-autonomous case by varying parameter $\alpha$. This also has an effect on $x^*$ that enters (2.11). The values for the brood maintenance coefficient $K$ used in all simulations are $[8000, 12000, 8000, 6000]$ for spring, summer, fall and winter respectively. Four simulation experiments were conducted and the results are presented in the following figures:

Figure 2.5(a): high value of $\alpha$ for spring, summer, fall, winter as 0.4784, 0.5, 0.5, 0.4784, respectively; and initial data $x(0) = 20,000$, $M(0) = 100$ and $m(0) = 0$ (no virus)
Figure 2.5: Simulation of the bee-mite-virus complex: Panel (a) bees and mites co-exist in the absence of disease. In panel (b) the simulation is repeated with mites carrying the virus, leading to collapse during the 6th summer after introduction of the disease. In panel (c) the relative carrying capacity $\alpha$ is decreased in summer and spring compared to panel (b); the disease is fought off, the number of parasites is lower than in panel (a). Time is in days; the symbol Y on the y-axes represents population. See text for details on model parameters.

Figure 2.5(b): high value of $\alpha$ as in 2.5(a), but with initial data $x(0) = 20,000$, $M(0) = 100$ and $m(0) = 80$ (virus present)

Figure 2.5(c): low value of $\alpha$ for spring, summer, fall, winter as 0.1, 0.1, 0.1, 0.1, respectively; and initial data $x(0) = 20,000$, $M(0) = 100$ and $m(0) = 80$ (virus present)
Comparison between Figures 2.5(a), 2.5(b) and 2.5(c). The mite infested colony can be seen in the figure 2.5(a). Figure 2.5(b) shows that the colony collapses after 4 years due to virus and mites. It is interesting to see that the colony is working properly for the first 4 years and the mites are also in equilibrium with the bees. The virus is present in the colony for several years without being noticeable. After almost 6 years, the virus starts growing slowly. Due to this the bee population decreases in spring but it again starts increasing in summer. Now the virus grows rapidly, therefore the colony is not able survive the winter in the next year and it vanishes. This simulation experiment shows the collapse equilibrium of the four dimensional bee-mite-virus model. This kind of behaviour was also observed in [11]. Therefore it is observed that the honeybee colony (with virus) vanishes for high values of the parameter $\alpha$. This result is in agreement with [13].

For lower values of $\alpha$, we observe in Figure 2.5(c) that the disease is fought off and that a mite infested but stable honeybee colony survives. The parameter $\alpha$ is only reduced in two of the four seasons, compared to the previous simulations. Nevertheless the number of mites remains at much lower levels than in Figure 2.5(a) throughout.

2.5 Summary and Conclusion

In spring, summer, and fall, in the absence of parasitic mites honeybee colonies can attain a healthy stable population size, which results from a balance between growth and natural death. Because workers are not produced in winter born, the colony decreases in size. The lifespan of winter bees is much longer than that of summer bees, so this decline in population size is small. However, if at the end of the winter season the bee colony is too small to care for the new brood, the
colony will not recover in spring and will die off. This phenomenon is know as Wintering Losses and has been described as a major contributor to the decline of honeybee colonies in colder climates. This phenomenon is well represented by the bee growth model that underlies the more complex model of the honeybee-varroa-ABPV complex presented here.

In our model that describes mite growth by a simple logistic equation with host population dependent carrying capacity, parasitic varroa mites that infest a bee colony cannot be fought off. Depending on the severity of the original infestation and on seasonal parameters such as bee birth and date rates, mite birth rates, tolerance of bees for mites (as expressed by the relative carrying capacity $\alpha$), mites might lead to a complete decline and die off of the bee colony, or an endemic equilibrium might be established, in which a stable bee and and stable mite population co-exist. In which case the bee colony often would be slightly weaker but still function well. However, depending on parameters, also the possibility was observed that a mite infested bee population co-exists with the parasite at a population strength that is far from that of stable healthy, uninfested population. When a bee population vanishes as a consequence of a mite infestation, this can be a process of declining over several years (in our simulations we observed periods of 2-4 years), however, from year to year the bee population will be remarkably smaller.

The picture can change when the parasitic varroa mites become vectors for bee diseases, such as the Acute Bee Paralysis Virus. Even if in the absence of the disease the bees can co-exist with their parasite in healthy, strong numbers, this balance might tip as a consequence of the virus epidemic, and an eventual die out of the bee colony might be observed. This process can stretch over several years that it takes until the virus infestation has grown strong enough. During this transient period, virtually no sick bees are observed and it can appear as if bees and mites
co-exist in a stable endemic equilibrium. The decline in the bee population from year to year can be very small and difficult to detect. The eventual collapse is then sudden.

Whether or not the bee population can fight off of a virus epidemic depends on model parameters describing the disease transmission rates and death rates of infected bees, as well as the size of the mite population in the stable bee-mite co-existence equilibrium. The latter depends on the growth and death rates of bees as well as on the tolerance level of the bees for the parasite (expressed in terms of the parameter $\alpha$), though appears to be independent of the birth rate of the mites. For given disease transmission rates (expressed in terms of $\beta_{1,2,3}$) and tolerance toward mites, faster death of infected bees helps the colony.

Although the model we present here yields qualitative insight into the progression of the bee disease, one has to realize that this is a simple, bare-bones model that neglects certain effects that can be of relevance. Therefore, its primary value has to be seen in the context of qualitative understanding rather than quantitative prediction.

For example, it is assumed here that the queen bee is always unaffected by mites and virus and that an old queen bees is replaced in the hive without swarming, i.e. loss of worker bees. We also assume that one year is identical to the next, i.e. that the parameters are periodic without accounting for random modifications, e.g. due to weather, or for systematic changes of the environment (e.g. due to human development activities). Also, we conducted our simulation using seasonally averaged parameter values and so it remains to be investigated whether the qualitative results remain the same if we consider continuously changing parameters instead. Nevertheless, despite this simplicity the model presented here might be a good starting point, for investigation of the efficacy of various varroa treatment strategies.
The results here were obtained using analytical techniques for the constant coefficient case and then verifying numerically whether or not the qualitative features of the autonomous case can also be observed in the non-autonomous case. We did not yet investigate whether or not the non-autonomous case can show additional behaviour that is not observable in the autonomous case. This question needs to be explored computationally. Considering the high dimensionality of the parameter space and that the parameters are time dependent functions, computational investigation of the model is an ambitious undertaking that warrants a dedicated study in its own right.

Acknowledgement

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Bibliography


Chapter 3

A Mathematical Model of the Honeybee- Varroa destructor-Acute Bee Paralysis Virus System with Seasonal Effects

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Abstract

A mathematical model for the honeybee-varroa mite-ABPV system is proposed in terms of four differential equations for the: infected and uninfected bees in the colony, number of mites overall, and of mites carrying the virus. To account for seasonal variability, all parameters are time periodic. We obtain linearized stability conditions for the disease free periodic solutions. Numerically we illustrate that, for appropriate parameters, mites can establish themselves in colonies that are not treated with varroacides, leading to colonies with slightly reduced number of bees. If some of these mites carry the virus, however, the colony might fail suddenly after several years without a noticeable sign of stress leading up to the failure. The immediate cause of failure is that at the end of fall colonies are not strong enough
to survive the winter in viable numbers. We investigate the effect of the initial disease infestation on collapse time, and how varroacide treatment affects longterm behavior. We find that to control the virus epidemic, the mites as disease vector should be controlled.

**Keywords:** Honeybees, *Varroa destructor*, Acute Bee Paralysis Virus, varroacides, mathematical model, seasonal effects **MSC:** 92D30, 34C60

### 3.1 Introduction

The Western honeybee, *Apis melifera*, is responsible for pollinating one-third of Canadian food crops [7], corresponding to an economic value to Canadian agriculture of over $2 billion annually [8]. The key factor in the effectiveness of honeybees is their colony size and the life span, which varies with the seasons. A honeybee colony usually consists of a single reproductive queen, 20,000-60,000 adult female worker bees, 10,000-30,000 worker brood (in the form of egg, larvae and pupae) and hundreds of male drones [40]. A sufficient number of adult worker bees are required to perform the tasks of brood rearing, guarding, foraging and honey production. The size of a honeybee colony and the average life span of individuals varies greatly over the year from season to season. The egg laying rate of the queen bee is slow in spring, increases into summer and then decreases in fall. The queen bee stops laying eggs before winter [31].

The number of honeybee colony losses worldwide has been increasing rapidly since 2006 [22, 35, 41]. The symptoms of colony failure are different in different parts of the world and hence losses are designated by different names. The losses first observed in the U.S are called Colony Collapse Disorder (CCD). The syndrome is characterized by the disappearance of mature adult bees. The capped brood still
remains in the hive. There are no dead bodies in the colony, but only an insufficient number of young adult worker bees remain to care for the hive. There is nectar, pollen and honey present in the colony, indicating that the young bees are reluctant to consume the food. In other countries, e.g. Canada and Germany, it has been observed that the colonies become so weak in the winter that they cannot emerge as healthy colonies in the spring. This is known as Wintering losses [15, 17]. No single factor is believed to be responsible for these colony losses; various possible factors could involve weather conditions, poor diet, transportation of bees for agricultural practices, pesticides and parasites [4]. One main cause is thought to be the parasitic mite *Varroa destructor* and the viruses it carries [15, 27, 38].

*Varroa destructor* is an ectoparasitic mite that infests honeybee colonies. It is one of the haplotypes of *Varroa jacobsoni*, a parasite that infests the Eastern honeybee *Apis cerana* [1]. *Varroa destructor* is the species that parasitized *Apis melifera* and spread rapidly in Western countries thereafter. Varroa mites not only feed on brood and adult bees, but also carry and transmit deadly viruses from bee to bee [6, 37]. Mites reproduce inside a honeybee brood cell. Female mites enter into the brood cell before the cell is capped. After the capping of the cell, the mite not only feeds on the developing bee but also reproduce in the cell. When the host bee leaves the cell, the mother mite leaves the cell with its progeny. The adult female mite becomes attached to the adult bee and feeds on it by squeezing between the overlapping segments on the ventral side of bee’s abdomen.

Viral infections may get injected into the bee’s body during this feeding process. When a virus-carrying mite feeds on an uninfected bee, it might release the virus into the bee’s haemolymph. Similarly when a virus-free mite feeds on an already infected bee, it can acquire the virus. There have been around 20 known honeybee viruses, of which 12 are transmitted by varroa mites [21, 34]. These viruses differ
in their transmission routes, virulence and impact on the host.

Our focus is on the Acute Bee Paralysis Virus (ABPV). This virus belongs to the family of Dicistroviridae along with some other viruses such as Kashmir Bee Virus (KBV) and Israeli Acute Paralysis Virus (IAPV). ABPV is frequently implicated in honeybee colony failure, especially when the colonies are infested with the parasitic mite *Varroa destructor* [21]. It has often been associated with wintering losses [15, 42]. This virus is distributed worldwide and appears to be the most common bee virus in Europe and South America [2, 3]. Adult bees infected with this virus suffer from paralysis, trembling, inability to fly and the gradual darkening and loss of hair from the thorax and abdomen before they die. Pupae that are infected with ABPV die quickly and normally do not develop into adult bees [28, 33]. Varroa mites are a mechanical vector for the transmission of ABPV, i.e. unlike other honeybee viruses such as the Deformed Wing Virus (DWV) or the Israeli Acute Paralysis Virus (IAPV), ABPV does not replicate in the mites [14, 32, 42]. Other transmission routes of ABPV have been suggested, but the literature is inconclusive and quantitative data that would allow a parameterization of a mathematical model are scarce. For example, [9] investigated the question of vertical transmission for six viruses. While they found for five of them, including DWV, that infection of the queen implied infection of her offspring, this was not found for ABPV. Another study [10] found ABPV in pollen but not in the bees and their glandular secretion, suggesting that the ingestion of food which contains virus might not lead to infection. Moreover, they report that in colonies without varroa mites ABPV, if it is present, is latent, whereas the presence of varroa triggers the disease, suggesting ABPV virulence is directly related to varroa infestation, cf also [14, 33, 42].

A recent summary of many honeybee mathematical models [4], based on a keyword database search, divides the models into three categories: colony models,
varroa models and foraging models. The level of sophistication and detail of these models and, accordingly, the level of input data required, varies widely from very simple models that can be expressed in algebraic relationships to computer simulation models consisting of several dozens of differential equations. While some of these models are very detailed with respect to honeybee biology, and while some of these models include aspects of varroa population dynamics, only very few models can be found that include mites and the diseases for which they are a vector. In particular, there are few existing papers that study models for ABPV [11, 36, 40].

The first published model for the honeybee-mite-virus system in the literature was [40]. This is an SIR-type model, in which the overall number of mites infesting the colony is a fixed parameter but the number of mites carrying the virus is a dependent variable. The model is formulated for two viruses, ABPV and DWV separately. The authors consider the autonomous case and study the model behavior for each season separately, based on seasonal averages for the parameters. The data requirement for this model, in terms of number of parameters is moderate; the authors present a complete model parameter set for each season obtained from the observational and experimental literature. For ABPV, this model was modified in [11], to include brood maintenance terms reflecting that a minimum number of worker bees is always required to care for the brood in order for new bees to be born. This modification introduces an Allee effect with an unconditionally stable trivial equilibrium. On the other hand, the original model [40] assumes that the birth rate is independent of colony strength and does not permit a trivial equilibrium, unless the death rate is higher than the birth rate, which naturally leads to collapse.

In [36] (see also [12]), the model of [11] was extended, adding a simple growth model for the mite population dispensing with the assumption that the mite load in the colony is constant. The mite dynamics are described by a logistic equation with
a carrying capacity that depends on bee colony strength which is used here as an approximate indicator of brood size. Also, while in [11, 40] the direct detrimental effect of mites on bee colony size was subsumed in the bee death rate, the dynamic model for the mite population [36] distinguished between natural death of bees and death caused by the parasite.

A current and parallel bee colony model without disease is developed in [23], where the colony is compartmentalized into hive and forager bees. This compartmentalization leads to a two-dimensional system of ODEs that can be discussed completely in the phase plane. The original purpose of the model was to investigate the effect of the loss of forager bees on the adaptive early recruitment of hive bees to foraging, and how this adaptation affects overall colony strength and survival. This model was used to investigate the effect of environmental pesticides on survival of strength of colonies in [18], see also [19, 20]. In [25], it was extended to account for an unspecified disease that is brought into the colony by the foragers. This extended model was studied in much detail analytically and numerically. The description of disease in this model is rather general and it is left open to what extent the results apply to specific diseases such as ABPV and DWV, which require both a vector and a causative agent. Another current extension of [23], although less relevant for our particular study but important in modeling work on the colony collapse phenomenon is [24], where brood size and food stores and their role in colony dynamics were explicitly considered. A generic disease model similar to [25] is presented in [5]. This model explicitly accounts for food storage as does the model [24] and assumes that in addition to worker population size food availability can limit the birth rate. The resulting system of five ODEs is numerically studied through a sensitivity analysis, including an investigation of Wintering effects, by adjusting growth rate, forager recruitment rate and food production rate to zero. Consistent with [25], the model in [5] assumes direct transmission of virus between
bees, without a vector.

The models discussed above all are formulated under the assumption of constant model parameters. Consequently, these models are, strictly speaking, only valid for at most a single season under the assumption that seasonal averages give a good description of environmental dynamics and under the assumption that the time scale of the dynamics is sufficiently fast, so that the system equilibrates quickly, in significantly less time than the duration of a season. However, these assumptions precludes the model from being used to study the fate of a mite, and possibly virus, infested colony over a period of several years. This constraint is a severe limitation of these models as the disease process appears to be, in many cases, fundamentally a multi-season or even multi-year process. For example, Wintering Losses occur when a bee population is too weak at the end of fall to make it through winter in numbers that allow the colony to rebound and function properly in spring. To investigate these phenomena, a model must be able to cover the transition between seasons and span an entire year.

In this study we build on and extend our previous work: (i) We will first study the behavior of the model with seasonally varying parameters over several years. Some preliminary ad hoc simulations were included in [36]. In these exploratory simulations, seasonally constant parameters were used, i.e jump functions, which we extend here to parameters that depend continuously in time. The exploratory simulations in [36] focused on the role of two parameters, one of the honeybee population submodel, the other one of the varroa mite population submodel. In the current study we will fix these parameters based on the earlier results and focus on the quantitative role of the initial levels of mite and virus infestations. (ii) Secondly, in [36], the important theoretical question about the stability of disease free periodic solutions remained open. We will give an answer in this paper. (iii) Thirdly,
we will extend the model by explicitly including the option to account for mite control through, for example, varroacide application. This extension will allow us to investigate the question under which conditions (on parameters) vector control is a viable remedial strategy for the virus infestation.

### 3.2 Mathematical model

#### 3.2.1 Model assumptions

Our model is based on the earlier studies discussed above [11, 36, 40]. Accordingly, many of the assumptions made there will be adopted here as well. Our model will also include features not accounted for in these earlier models, which will lead to additional model assumptions. A brief list of key model assumptions is provided here:

1. Following [40], the model will be formulated in terms of the dependent variables (i) healthy and (ii) virus infected bees, and (iii) number of mites that carry the virus. Following [36], we also include (iv) the total number of mites, virus carrying and virus free, as a dependent variable, which allows us to account for the dependency of the virus and its effect on the population dynamics of the vector.

2. The queen bee is not affected by the disease. This is an implicit assumption, which allows us to assume that the egg laying rate of the queen is independent of mites and virus. This assumption follows [5, 11, 24, 25, 36, 40].

3. The only route of virus transmission that we account for is horizontal transmission vectored by varroa mites. In accordance with [14, 32, 42], the mites
are assumed to be a mechanical vector only. In particular, no virus replication takes place inside the mites.

4. In accordance with [28, 33] we assume that infected pupae die quickly before they develop into adult bees, and that all newly born bees are uninfected. In [3] it is suggested that mortality of brood in mite infested colonies is associated with secondary infections by pathogenic agents. Therefore, following [40] we assume that only virus carrying mites affect the rate at which brood emerge as adult bees.

5. Since mite reproduction depends on brood availability, we assume a carrying capacity for the mite population that depends on colony strength, as in [36]. Colony strength is used here as an approximate measure of brood size. For simplicity we use a logistic model to describe the development of the mite population.

6. Since worker bees are needed to allow the brood to develop to the adult stage, the birth rate is dependent on the number of bees in the colony. Since bees infected with ABPV suffer from paralysis and die quickly, we assume that only healthy bees take part in brood rearing. As in [11] we use a Hill function to describe the brood rearing term, which introduces an Allee effect.

7. It is assumed that healthy and sick bees both die naturally, and also due to mites feeding on them and/or infecting them with virus. Therefore, as in [36], the death rate has two components, one that depends on the mite population and one that does not. In [11, 40], where the number of mites was a given parameter this assumption was not necessary, as both effects could be compounded into one term. We further assume that the death rates of infected bees are higher than the death rates of uninfected bees.
8. In contrast to [23, 40], we assume that all model parameters are functions of time. This allows us to account for seasonal differences in bee biology. We assume that these functions are periodic with a period of one year to reflect seasonal patterns.

9. We account for varroacide treatment by introducing additional sink terms for the vectoring mites. We also include additional sink terms for the bees depending on varroacide treatment. However, we assume that the varroacide effect on the mites is stronger than its effect on the bees.

To describe the transmission of the diseases according to the assumptions 2, 3, 4 above, we follow the ABPV model originally worked out in [40], where also a complete set of parameters for disease dynamics is given that was inferred from observational data.

### 3.2.2 Model Equations

Our model extends [11, 36, 40] by introducing the model assumptions 8 and 9 above. It reads:

\[
\begin{align*}
\frac{dm}{dt} & = \beta_1(t)(M - m) \frac{y}{x + y} - \beta_2(t)m \frac{x}{x + y} - \delta_2 m, \\
\frac{dx}{dt} & = \mu(t)g(x, t)h(m, t) - \beta_3(t)m \frac{x}{x + y} - d_1(t)x - \gamma_1 Mx - \delta_1 x, \\
\frac{dy}{dt} & = \beta_3(t)m \frac{x}{x + y} - d_2(t)y - \gamma_2 My - \delta_3 y, \\
\frac{dM}{dt} & = r(t)\left(1 - \frac{M}{\alpha(t)(x + y)}\right) - \delta_2 M,
\end{align*}
\]  

(3.1) \hspace{1cm} (3.2) \hspace{1cm} (3.3) \hspace{1cm} (3.4)

where the dependent variables are:

\[m: \text{number of mites that carry the virus,}\]
\( x \): number of honeybees that are virus free,

\( y \): number of honeybees that are infected with the virus,

\( M \): number of mites that infest the colony.

The parameter \( \mu(t) \) in (3.2) is the maximum birth rate, specified as the number of worker bees born per day.

The function \( g(x, t) \) in (3.2) expresses that due to nursing the birth rate depends on the number of worker bees. If \( x \) becomes small, essential work in the maintenance of the brood cannot be carried out anymore and no new bees are born. If \( x \) is large, bee rearing is not severely slowed down. Thus \( g(0, \cdot) = 0 \), \( \frac{dg(0)}{dx} = 0 \), \( \frac{dg(x)}{dx} > 0 \), \( x > 0 \), \( \lim_{x \to \infty} g(x, t) = 1 \). A convenient formulation for such switch like behavior is given by the sigmoidal Hill function

\[
g(x, t) = \frac{x^n}{K(t)^n + x^n}, \tag{3.5}
\]

where the parameter \( K(t) \) is the size of the bee colony at which the birth rate is half of the maximum possible rate and \( n > 1 \) is an integer exponent. For \( n = 1 \), the same birth term as in [23] is obtained. We will use instead \( n > 1 \) because we assume that a sufficient number of healthy worker bees is required to rear the brood, which induces an Allee effect as in [11]. If \( K = 0 \), then the bee birth terms of the original model in [40] is recovered, i.e. the brood is always reared at maximum capacity, independent of the actual bee population size. In this case no trivial solution can be expected. Since the parameter \( K \) represents a sufficient number of healthy adult bees required to care for the brood and the brood population varies with the seasons, the parameter \( K \) also varies seasonally.

The function \( h(m, t) \) in (3.2) indicates that the birth rate of bees is affected by the presence of mites that carry the virus. This behavior is particularly important
for viruses like ABPV that kill infected pupae before they develop into bees. The function $h(m, t)$ is assumed to decrease as $m$ increases, $h(0, t) = 1$, $\frac{dh}{dm}(m, t) < 0$ and $\lim_{m \to \infty} h(m, t) = 0$; [40] suggests that $h(m, t)$ is an exponential function, $h(m, t) \approx e^{-mk(t)}$, where $k(t)$ is non-negative.

The transmission of disease is described by the terms with coefficients $\beta_i$, as originally proposed in [40]. Parameter $\beta_1$ in (3.1) is the rate at which mites that do not carry the virus acquire it. The rate at which infected mites lose their virus to an uninfected host bee is $\beta_2$. The rate at which uninfected bees become infected is $\beta_3$, in bees per virus carrying mite and time.

The parameters $d_1$ and $d_2$ are the natural death rates for uninfected and infected honeybees, respectively. We can assume that infected bees have a shorter lifespan than healthy bees, thus $d_2 > d_1$.

The last equation, (3.4), is a logistic growth model for varroa mites. By $r(t)$ we denote the maximum mite birth rate. The carrying capacity for the mites changes with the host population size, $x + y$, and is characterized by the parameter $\alpha(t)$ which indicates how many mites can be ”sustained per bee” on average.

Mites contribute to increased bee mortality. This is considered in (3.2) and (3.3) by including death terms that depend on $M$; the parameters $\gamma_{1,2}$ give the rates at which mites directly kill healthy and virus-infected bees.

The potential effects of externally applied varroacides is described by three new parameters: $\delta_1$, $\delta_2$ and $\delta_3$. The parameters $\delta_1$ and $\delta_3$ respectively represent the death rates of uninfected and infected bees due to varroacides. We assume that, $\delta_2$, the effect of varroacides on the mites that carry the virus and on the total number of mites is the same.
Table 3.1: Seasonal averages of model parameters, derived from the data in [29, 30, 36, 40]. The parameters included here are kept constant for all simulations; the values of the parameters that are varied are given in the text.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Spring</th>
<th>Summer</th>
<th>Autumn</th>
<th>Winter</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\beta_1$</td>
<td>0.1593</td>
<td>0.1460</td>
<td>0.1489</td>
<td>0.04226</td>
</tr>
<tr>
<td>$\beta_2$</td>
<td>0.04959</td>
<td>0.03721</td>
<td>0.04750</td>
<td>0.008460</td>
</tr>
<tr>
<td>$\beta_3$</td>
<td>0.1984</td>
<td>0.1460</td>
<td>0.1900</td>
<td>0.03384</td>
</tr>
<tr>
<td>$d_1$</td>
<td>0.02272</td>
<td>0.04</td>
<td>0.02272</td>
<td>0.005263</td>
</tr>
<tr>
<td>$d_2$</td>
<td>0.2</td>
<td>0.2</td>
<td>0.2</td>
<td>0.005300</td>
</tr>
<tr>
<td>$\mu$</td>
<td>500</td>
<td>1500</td>
<td>500</td>
<td>0</td>
</tr>
<tr>
<td>$k$</td>
<td>0.000075</td>
<td>0.00003125</td>
<td>0.000075</td>
<td>N/A</td>
</tr>
<tr>
<td>$r$</td>
<td>0.0165</td>
<td>0.0165</td>
<td>0.0045</td>
<td>0.0045</td>
</tr>
<tr>
<td>$\alpha$</td>
<td>0.4784</td>
<td>0.5</td>
<td>0.5</td>
<td>0.4784</td>
</tr>
</tbody>
</table>

The parameters $\mu$, $k$, $K$, $\alpha$, $\beta_i$, $d_i$, $\delta_i$, $\gamma_i$ and $r$ are assumed to be non-negative and periodic functions of time with a period $T$; in practice $T = 1$ year. Seasonal averages of the parameters $\mu$, $\beta_i$, $d_i$ and $k$ can be computed from the observational data given in [40] and for $r$ from the data in [29, 30]. A fixed set of seasonal averages for the parameter $K$ is not available in the literature. However, we have high and low ranges of $K$ based on [36] and we use these sets of values in this paper. The data are summarized in Table 3.1.

The values of $\gamma_1$ and $\gamma_2$ are estimated to be of the order of $10^{-7}$ for every season, based on order of magnitude considerations. For the numerical simulations presented below we will use these seasonal averages to construct continuous, smooth coefficient functions. The construction of such functions is not unique. While the particular choice of construction affects the solutions quantitatively, it is not a priori
clear whether and to what extent this construction will also affect the qualitative behavior, such as the stability of solutions. The effect of function construction on the solutions is discussed and investigated in more detail in the Appendix, where two strategies based on Piecewise Cubic Hermite Interpolating Polynomials (PCHIP) are described and compared.

### 3.3 Stability of periodic solutions

Numerical simulations suggest the existence of periodic solutions to (3.1)-(3.4), see below. A formal proof of the existence of such solution hinges on additional properties, which the coefficient functions must have. Since we only have at most *a priori* information about piecewise monotonicity of the coefficients as the seasons change, a general proof of the existence appears out of reach at this point, without introducing additional conditions on the parameters. Therefore, we conjecture the existence of periodic solutions, as observed in simulations, and aim to give conditions for their stability, particularly in the disease free case. Although our objective is an analysis of the complete four-dimensional model (3.1)-(3.4) it is instructive to study simpler sub-models first. We begin with the mite and virus free model, and then analyse the model where bees and mites are considered but the virus is absent.

In the absence of mites and virus, model (3.1)-(3.4) reduces to the single differential equation

$$\dot{x} = \mu g(x, t) - dx - \delta x$$

(3.6)

where $d$ is the natural death rate of the bees and $\delta$ is the death rate at which bees die due to varroacides.

**Proposition 3.3.1.** Suppose $x(t) = x^*(t)$ is a periodic solution of the bee-only model (3.6). Then $x = x^*$ is asymptotically stable if $\int_0^1 (\mu g'(x^*) - d - \delta)d\rho \leq 0$. 

70
Proof. Linearizing equation (3.6) about \( x = x^* \) gives,
\[
\dot{u} = (\mu g'(x^*) - d - \delta)u,
\]
where \( u = x - x^* \). This is a linear differential equation that can be solved with the method of integrating factors. We find
\[
u(t) = c_0 e^{\int_0^t (\mu g'(x^*) - d - \delta) \, d\rho}.
\]
In order for the periodic solution \( x = x^* \) to be asymptotically stable, the solution of the perturbed system, \( u(t) \), should go to zero. This means that the periodic solution \( x = x^* \) is stable if \( \int_0^t (\mu g'(x^*) - d - \delta) \, d\rho \leq 0 \).

This result shows, as intuitively expected, that in the absence of parasites and virus, a healthy bee colony will be maintained over multiple years only if the death rate is greater than or equal to the birth rate per bee over a period of time. Otherwise, the colony will grow without bound. On the other hand, since \( x^* \equiv 0 \) is a periodic solution for which the integral in the exponent is always negative, this result also shows that this trivial equilibrium is unconditionally stable, i.e. that the Allee effect of the autonomous model in [11, 36] carries over to the nonautonomous model.

Next we consider (3.1)-(3.4) in the absence of the viral disease but potential presence of mites. The model reduces then to the two differential equations for bees and mites.
\[
\begin{align*}
\frac{dx}{dt} &= \mu g(x) - \delta x - \gamma_1 M x, \\
\frac{dM}{dt} &= (r - \delta_2) M \left( 1 - \frac{r M}{(r - \delta_2) \alpha x} \right),
\end{align*}
\]
where \( \delta = d_1 + \delta_1 \). Here \( d_1 \) represents the natural death rate of the bees and \( \delta_1 \) is the death rate of the bees due to varroacides. The parameter \( \delta_2 \) is the death rate of mites because of varroacid application.
**Proposition 3.3.2.** Suppose \( x^*(t) \) is a periodic positive solution of (3.6). Then \((x^*, 0)\) is a periodic solution of (3.7)-(3.8). It is is stable if \( \int_0^T (r - \delta_2) dt \leq 0 \) and \( \int_0^T (\mu g'(x^*) - \delta) dt \leq 0 \).

**Proof.** That a positive periodic solution of (3.6) defines a disease free solution of (3.7)-(3.8) is immediate from the model equations. In order to analyse its stability, we use linearization and Floquet theory. We linearize the system about the periodic solution \((x^*, 0)\), i.e. we investigate the longterm behaviour of the perturbation \( u := x - x^* \), \( v := M - 0 \).

The Jacobian of the system is

\[
J(x, M) = \begin{pmatrix}
\mu g'(x) - \delta - \gamma_1 M & -\gamma_1 x \\
-\gamma_1 Mx^2 & (r - \delta_2) - \frac{2\gamma_1 M}{Mx^2}
\end{pmatrix},
\]

and at \((x^*, 0)\), we find

\[
J(x^*, 0) = \begin{pmatrix}
\mu g'(x^*) - \delta - \gamma_1 x^* \\
0 & (r - \delta_2)
\end{pmatrix}.
\]

Thus, the system linearized about \((x^*, 0)\) is

\[
\begin{pmatrix}
\dot{u} \\
\dot{v}
\end{pmatrix} = \begin{pmatrix}
\mu g'(x^*) - \delta - \gamma_1 x^* \\
0 & (r - \delta_2)
\end{pmatrix} \begin{pmatrix}
u \\
v
\end{pmatrix}.
\]

We choose the linearly independent set of initial conditions

\[
u_1(0) = 1, \quad \nu_2(0) = 0,
\]

\[
\nu_1(0) = 0, \quad \nu_2(0) = 1.
\]
to find linearly independent solutions \((u_1(t), v_1(t))\) and \((u_2(t), v_2(t))\) of the linearized system.

\[
\begin{align*}
  u_1(t) &= e^{\int_0^t (\mu g'(x^*)(\rho) - \delta) \, d\rho}, \\
  v_1(t) &= 0, \\
  u_2(t) &= e^{\int_0^t (\mu g'(x^*)(\rho) - \delta) \, d\rho} \int_0^t -\gamma_1 x^* e^{\int_0^\rho (r - \delta_2 + \delta - \mu g'(x^*(\tau))) \, d\tau} \, d\rho, \\
  v_2(t) &= e^{\int_0^t (r - \delta_2) \, d\rho}.
\end{align*}
\]

The next step is to construct the fundamental matrix \(A(t)\) of the linearized system over the interval \(0 \leq t \leq T\), where \(T\) is the period, and to determine the eigenvalues of the transition matrix

\[
C = A(T) = \begin{bmatrix} u_1(T) & u_2(T) \\ v_1(T) & v_2(T) \end{bmatrix},
\]

which are found as

\[
\lambda_1 = e^{\int_0^T (\mu g'(x^*) - \delta) \, dt}, \quad \lambda_2 = e^{\int_0^T (r - \delta_2) \, dt}.
\]

Stability of \((x^*, 0)\) is then obtained if \(\int_0^T (r - \delta_2) \, dt \leq 0\) and \(\int_0^T (\mu g'(x^*) - \delta) \, dt \leq 0\), whereas instability is implied if one of the inequalities is reversed.

This result indicates that the mite infestation in a colony can be fought off if (i) the cumulative death rate of mites due to treatment is greater than or equal to their birth rate and (ii) the cumulative death rate of healthy bees is greater than or equal to their birth rate. The mite-free equilibrium is always unstable in the absence of varroacide treatment, when \(\delta_2 = 0\), i.e. a mite invasion cannot be fought off by the bees alone as a consequence of the logistic growth assumption for mites. This generalizes the findings in [36] for the autonomous systems. If \((x^*, 0)\) is unstable, it is not clear whether the system will converge to the trivial state or whether, for
example, an endemic periodic solution will be obtained in which the bee colony persists in the presence of mites. The simulations in [12, 36] suggest the possibility of such an endemic periodic bee-mite solution for certain parameters. While in principle Floquet theory could be used to derive a stability condition for such a periodic solution, algebraic complexity prevented this.

Finally, we turn to the full bee-mite-virus model

$$\frac{dm}{dt} = \beta_1 (M - m) \frac{y}{x + y} - \beta_2 m \frac{x}{x + y} - \delta_2 m,$$  \hspace{1cm} (3.9)

$$\frac{dx}{dt} = \mu g(x) h(m) - \beta_3 m \frac{x}{x + y} - \delta x - \gamma_1 M x,$$ \hspace{1cm} (3.10)

$$\frac{dy}{dt} = \beta_3 m \frac{x}{x + y} - \delta' y - \gamma_2 M y,$$ \hspace{1cm} (3.11)

$$\frac{dM}{dt} = (r - \delta_2) M \left( 1 - \frac{r M}{(r - \delta_2) \alpha (x + y)} \right),$$ \hspace{1cm} (3.12)

where $\delta = d_1 + \delta_1$ and $\delta' = d_2 + \delta_3$.

**Proposition 3.3.3.** Suppose $(0, x^*, 0, 0)$ is a periodic nonnegative disease free solution of (3.9)-(3.12), where $x^*$ is a periodic solution of the bee-only model (3.6). Then $(0, x^*, 0, 0)$ is linearly stable if $\int_0^T (\mu g'(x^*) - \delta) dt \leq 0$ and $\int_0^T (r - \delta_2) dt \leq 0$.

**Proof.** Suppose that there exists a periodic mite free solution $(0, x^*, 0, 0)$ of the bee-mite-virus model. We will again use Floquet theory to examine the stability of the linearised system.

We find the Jacobian matrix of the system as

$$J(m, x, y, M) = \begin{bmatrix}
-\beta_1 y - \beta_2 x & -\beta_1 (M - m)y - \beta_3 my & \beta_1 (M - m)x + \beta_2 mx & \beta_1 y \\
\mu g(x) h'(m) - \beta_3 x & \mu g'(x) h(m) - \beta_3 mx \frac{x + y}{(x + y)^2} - \delta - \gamma_1 M & \beta_3 mx \frac{x + y}{(x + y)^2} - \gamma_1 M & 0 \\
\beta_3 x \frac{x + y}{(x + y)^2} & \beta_3 mx \frac{x + y}{(x + y)^2} - \delta - \gamma_2 M & -\gamma_2 y & \frac{r M^2}{\alpha (x + y)^2} \\
0 & \frac{r M^2}{\alpha (x + y)^2} & \frac{r M^2}{\alpha (x + y)^2} & (r - \delta_2) - \frac{2r M}{\alpha (x + y)}
\end{bmatrix},$$
which at \((0, x^*, 0, 0)\) reduces to

\[
J(0, x^*, 0, 0) = \begin{bmatrix} -\beta_2 - \delta_2 & 0 & 0 & 0 \\ -\beta_3 & \mu g'(x^*) - \delta & 0 & -\gamma_1 x^* \\ \beta_3 & 0 & -\delta' & 0 \\ 0 & 0 & 0 & r - \delta_2 \end{bmatrix}.
\]

The system linearized about \((0, x^*, 0, 0)\) is then

\[
\begin{bmatrix} \dot{u} \\ \dot{v} \\ \dot{w} \\ \dot{p} \end{bmatrix} = \begin{bmatrix} -\beta_2 - \delta_2 & 0 & 0 & 0 \\ -\beta_3 & \mu g'(x^*) - \delta & 0 & -\gamma_1 x^* \\ \beta_3 & 0 & -\delta' & 0 \\ 0 & 0 & 0 & r - \delta_2 \end{bmatrix} \begin{bmatrix} u \\ v \\ w \\ p \end{bmatrix}.
\]

where \(u = m - 0, v = x - x^*, w = y - 0\) and \(p = M - 0\). Let \((u_1(t), v_1(t), w_1(t), p_1(t)), (u_2(t), v_2(t), w_2(t), p_2(t)), (u_3(t), v_3(t), w_3(t), p_3(t))\) and \((u_4(t), v_4(t), w_4(t), p_4(t))\) denote linearly independent solutions of the linearized system, with linearly independent initial conditions

\[
\begin{aligned}
u_1(0) &= 1, & u_2(0) &= 0, & u_3(0) &= 0, & u_4(0) &= 0, \\
v_1(0) &= 0, & v_2(0) &= 1, & v_3(0) &= 0, & v_4(0) &= 0, \\
w_1(0) &= 0, & w_2(0) &= 0, & w_3(0) &= 1, & w_4(0) &= 0, \\
p_1(0) &= 0, & p_2(0) &= 0, & p_3(0) &= 0, & p_4(0) &= 1.
\end{aligned}
\]

The fundamental matrix \(A(t)\) of the linearized system over the interval \(0 \leq t \leq T\),
where $T$ is the period, is obtained as

$$A(t) = \begin{bmatrix} u_1(t) & u_2(t) & u_3(t) & u_4(t) \\ v_1(t) & v_2(t) & v_3(t) & v_4(t) \\ w_1(t) & w_2(t) & w_3(t) & w_4(t) \\ p_1(t) & p_2(t) & p_3(t) & p_4(t) \end{bmatrix} =$$

$$\begin{bmatrix} e^{\int_0^t (\beta_2 + \delta_2) d\rho} & 0 & 0 & 0 \\ 0 & e^{\int_0^t (\mu g' (x^*) - \delta) d\rho} & 0 & e^{\int_0^t (\mu g' (x^*) - \delta) d\rho} \\ e^{\int_0^t \delta' d\rho} \int_0^t \beta_3 e^{\int_0^t \delta' d\rho} d\tau d\rho & 0 & e^{-\int_0^t \delta' d\rho} & 0 \\ 0 & 0 & 0 & e^{\int_0^t (r - \delta_2) d\rho} \end{bmatrix}.$$ 

The transition matrix $C = A(T)$

$$C = \begin{bmatrix} u_1(T) & u_2(T) & u_3(T) & u_4(T) \\ v_1(T) & v_2(T) & v_3(T) & v_4(T) \\ w_1(T) & w_2(T) & w_3(T) & w_4(T) \\ p_1(T) & p_2(T) & p_3(T) & p_4(T) \end{bmatrix},$$

has eigenvalues

$$\lambda_1 = e^{-\int_0^T (\beta_2 + \delta_2) dt},$$

$$\lambda_2 = e^{\int_0^T (\mu g' (x^*) - \delta) dt},$$

$$\lambda_3 = e^{-\int_0^T \delta' dt},$$

$$\lambda_4 = e^{\int_0^T (r - \delta_2) dt}.$$ 

It is observed that $| \lambda_1 |$ and $| \lambda_3 |$ are always less than 1. Therefore $(0, x^*, 0, 0)$ of the linearized model is stable if $\int_0^T (\mu g' (x^*) - \delta) dt \leq 0$ and $\int_0^T (r - \delta_2) dt \leq 0$. 

\(\square\)
Hence, the conditions for the virus infestation to be fought off are the same as the conditions for the eradication of mites. This indicates that in order for the honeybee colony to become disease-free, it is sufficient to fight off the mites. An important observation is that the stability of the periodic disease-free equilibrium depends on the annual average values of the parameters not the seasonal average values. As in the simpler bee-mite case above, algebraic complexity does not allow an analytical investigation of the behavior of the system if the disease free solution \((0, x^*, 0, 0)\) becomes unstable, i.e under which condition the colony will converge to collapse or reach a stable endemic solution. To investigate the system further we will, therefore, resort to numerical experimentation.

### 3.4 Computer Simulations

#### 3.4.1 Sample simulations illustrating model behavior

Before we conduct systematic numerical experiments to investigate the model in detail, we present some selected simulations for illustration of potential model outcomes, see Figure 3.1. These are guided by the analysis carried out in the previous section.

The seasonal averages of parameters \(\beta_i, d_i, \mu, k, r\) used in Figure 3.1 are given in Table 1; these have been used to determine continuous time varying parameters as described in the Appendix. The seasonal averages of the parameter \(\alpha\) are chosen to be 0.4784, 0.5, 0.5, 0.4784 for spring, summer, fall and winter respectively (see [36] for the choice of these values). Since there are various varroa treatment strategies available in the literature, there cannot be a general profile for the death rates of bees and mites due to treatment [16, 26]. Often varroa treatment is applied in spring and/or fall because the brood is still small then and not much honey is present in
the colony. For simplicity, we assume that the treatment is applied three times in spring,
\[ \delta_i(t) = \begin{cases} \delta_i & \text{if } 30 \leq t < 31, 60 \leq t < 61, 90 \leq t < 91 \\ 0 & \text{otherwise} \end{cases} \]
where \( i = 1, 2, 3 \). Since there is no concerted data available for the parameters \( \delta_i \), we assume that the death rate of uninfected and infected bees (i.e., \( \delta_1 \) and \( \delta_3 \)) is small as compared to their natural death rates (given in Table 1). We assume \( \delta_1 = \delta_3 = 0.005 \). The parameters that we vary for the simulations in Figure 3.1 are \( \delta_2 \) and the brood maintenance coefficient, \( K \).

The starting point and reference point are in all cases, a stable periodic solution \( x^*(t) \) of (3.6), i.e. the model in the absence of mites and virus, according to Proposition 3.3.1. This solution is shown in Figure 3.1.a. We choose for the brood maintenance coefficient \( K \) the seasonal averages 12000, 14000, 12000, 8000 for spring, summer, fall and winter, respectively.

We first show simulations of the model without virus, i.e. with initial data \( m(0) = y(0) = 0 \), but with varroa mites present \( M(0) = 100 \) (Figure 1b). \( K \) is the same as in Figure 3.1(a). In Figure 3.1(b) the varroacide control \( \delta_2 \) is chosen strong enough (i.e. \( \delta_2 = 1.35 \), i.e \( \delta_2(t) = 1.35 \) for \( t = 30, 60, 90 \), according to Proposition 3.3.2 for the mites to be eradicated, so that the system converges to the disease and mite free periodic solution \((0, x^*, 0, 0)\). In Figure 3.1(c), the varroacide control is reduced \((\delta_2 = 1)\) such that \((0, x^*, 0, 0)\) looses its stability according to Proposition 3.3.2 and a periodic solution with bees and mites present is found. The colony strength in this case remains below \( x^* \), but the population is still strong enough to be a working colony. In Figure 3.1(d) the parameter \( \delta_2 \) is chosen to be 0.1. The colony eventually vanishes, i.e. the unconditionally stable solution \((0, 0, 0, 0)\) is attained after few years. Prior to failure, the peak colony strength in summer is already reducing from year to year.
Figure 3.1: Illustration of potential model outcomes, tracked over several years: (a) periodic solution describing a healthy honeybee colony in the absence of mites and virus with high $K$ values, (b) the same simulation scenario as in (a) but with mites present and with enough varroa treatment to fight off the mites, (c) the same simulation scenario as in (b) but with insufficient varroa treatment leading to bee-mite co-existence, (d) failure of the bee population caused by mites only (absence of ABPV) due to insufficient varroacide treatment, (e) presence of ABPV leading to the failure of the colony after more than 10 years with low $K$ values, (f) same scenario as in (e) but a rapid failure of the colony after 4 years due to milder varroa treatment application as compared to (e), (g) same scenario as in (f) but with the extent of treatment sufficient to fight off virus but not mites, (h) same simulation scenario as in (g) but with enough varroa treatment to eradicate the disease (mites as well as virus).
For Figures 3.1(e) - 3.1(h) the seasonal averages of parameter $K$ are 8000, 12000, 8000, 6000 for spring, summer, fall, and winter, respectively. We illustrate now potential model outcomes in the presence of ABPV; we choose initially $m(0) = 80$.

In a first simulation in Figure 3.1(e), the control parameter is chosen to be $\delta_2 = 0.3$. After an initial transient period of 2-3 years during which the mites establish themselves in the colony, the peak colony strength in summer is approximately the same every year; the colony seems to work properly for 6-7 years and suddenly fails. In Figure 3.1(f), the varroacide control is reduced to 0.1, which induces a faster colony failure. In Figure 3.1(g), the varroacide control is increased to a level such that ABPV is fought off but the mite population still establishes itself. The varroacide control parameter is set to be $\delta_2 = 1$ in this case. In Figure 3.1(h), finally, we choose $\delta_2 = 1.35$, strong enough to eradicate both mites and virus.

The behavior observed is sensitive with respect to parameters. For example under the parameter values for $K$ and $\alpha$ chosen in the simulations in Figures 3.1.e-h, and under conditions as in Figure 3.1.d a periodic solution with mites and bees will be found, qualitatively similar as in Figure 3.1(c) (data not shown). Under these conditions the smallest colony strength needed for the colony to survive is reduced.

In order to present a scenario of the bee-mite model where the colony collapses due to mites, as in Figure 3.1(d), we need to choose either high values of $K$ or high values of the parameter $\alpha$, to increase the number of mites to levels that can become harmful. This intricate interplay between $K$ and $\alpha$ in determining the fate of the colony has been studied in more detail previously in [36] and is not the focus of our current study.

The simulations presented here illustrate a wide range of potential solution behavior, in dependence of initial data and parameter, reaching from virus and mite free periodic solutions, over mite-bee periodic solutions, to solutions with gradual
colony failure, and solutions which over years seemingly indicate a working colony and then suddenly fail. These observations motivate a number of simulation experiments in which we investigate the relationship between parameter values and long-term colony fate.

3.4.2 Effect of initial disease infestation on the survival of the colony

In this first simulation experiment, we consider the system without varroacide treatment, i.e. $\delta_i(t) \equiv 0$ for $i = 1, 2, 3$. We will investigate the effect of the initial mite and virus infestation level, i.e. of $M_0$ and $m_0$, on the time at which the colony collapses (see Figure 3.2). A colony is assumed to collapse if $x$ becomes very small, in particular, if $x < 1$; in this case also the continuous assumption of the model is violated, i.e. the model breaks down due to small numbers. Since the trivial equilibrium has been shown to be unconditionally asymptotically stable (see Proposition 3.1), the assumption that small enough colonies imply failure seems justified.

All parameters are the same as in section 4.1 with the brood maintenance coefficient $K$ chosen to be 8000, 12000, 8000, 6000 for spring, summer, fall, and spring
respectively. We varied $M_0$ in the range of 0 to 2000 and choose $m_0 = pM_0$ where $0.1 < p < 1$. Therefore each curve is distinguished by the ratio of $M_0$ and $m_0$. It was observed that when the initial mite infestation is zero, the healthy bee population obtains a strictly positive limit cycle. As the mite infestation in the colony increases, the colony eventually dies off. The higher the mite infestation, the sooner the colony vanishes. Since the bee population is not strong enough in winter to survive in the spring, the colony collapses in winter. This pattern is observed in the natural honeybee colonies as well [41] and in Ontario in particular such wintering losses have been shown to be closely associated with varroa mites [17].

While the fate of the colony is robust, i.e. disease infestation implies eventual failure, the time to collapse depends heavily on the initial levels. This result suggests a window of opportunity for the adoption of remedial measures, e.g. by varroacide application. The stability criterion in the previous section indicated that the yearly compounded treatment efficacy is more important than the timing and local (in time) efficacy of treatment. This result together with the observation of the discrete nature of the failure event suggests that treatment strategies may be relatively robust. We investigate this possibility in more detail in the next experiment.

### 3.4.3 Comparison between a system treated with varroacide and an untreated one

In this simulation experiment, we compare a system without varroacide treatment ($\delta_i \equiv 0, \forall i$) and a system with treatment ($\delta_i \neq 0, \forall i$), all other parameters being the same in both cases and the same as in section 4.2. We will investigate whether or not the application of varroacides can protect a colony that would otherwise die off due to the virus vectored by the mites.

As a baseline for comparison, Figure 3.3(a) represents a mite infested honeybee
Figure 3.3: (a) System without varroacide treatment. (b) System with treatment. Varroacides are applied three times in spring and fall each, with an interval of one month (with $\delta_2 = 1.2$). (c) System with treatment. Varroacides are applied three times in spring and fall each, with an interval of one month (with $\delta_2 = 1.3$).
colony also infected with virus, and with no varroacide treatment. In this figure, the bee population starts increasing in spring and summer and reaches a maximum of 32,000 bees. It then starts decreasing in fall and winter to a minimum of 12,000 bees at the end of the first year. The colony appears to reach a steady maximum above 30,000 each year initially for the first three years, which indicates that it is working well. The virus is present in the colony for several years without being noticeable. After almost 4 years, the virus intensifies and has a greater effect on the bee population, reducing the number of healthy workers. The bee population decreases in spring of the fourth year but it again starts increasing in summer when the maximum birth rate increases. The maximum colony strength that years reaches about 29,000. However the virus grows rapidly, and the colony is not able survive the next winter and it vanishes.

Figure 3.3(b) and 3.3(c) represent a mite-infested colony infected with virus, where varroacide treatment is applied three times in spring and fall each, using different treatment associated death rates. In Figure 3.3(b), the death rate of mites due to varroacides ($\delta_2$) is 1.2. The bee population follows a similar pattern as in Figure 3.3(a) i.e., increases slowly in spring and reaches a maximum of 31,000 in summer. The population starts decreasing in fall and winter attaining a minimum of 14,000 bees by the end of winter season. This pattern is repeated annually. The mite population starts increasing very slowly for the first few years and then becomes established, maintaining a steady maximum and following a limit cycle (see Figure 3.4 for a magnified view of the mite population at an instance). The mite infestation level here is relatively low compared to the bee population. The virus is fought off due to the treatment but the mites are still present in the colony, albeit at relatively low levels, compared to the colony strength. In Figure 3.3(c), the death rate of mites due to varroacides ($\delta_2$) is slightly increased to 1.3. The bee population follows a similar pattern as in Figure 3.3(a) and 3.3(b). The mite population starts increasing very
Figure 3.4: Magnified version of Figure 3.3(b). Vertically downwards arrows show the times when treatment is applied and how the mite population decreases.

slowly in the first two years but the increase in population is negligible. The mite population is not able to establish itself further and dies off, indicating the effectiveness of the treatment in this case, in correspondence with the stability criterion found analytically (see Proposition 3.3).

This result suggests that a colony which would otherwise die off due to the virus, can be protected by using varroacides. Furthermore, it can be maintained as a healthy colony with zero or very low mite population levels, depending on the efficacy of the varroacides. In other words, treatment results in control of the vector and control of the viral disease.

3.4.4 Effect of varroacide treatment on the average mite population level

In this simulation experiment, we consider a system with varroacide treatment. We investigate the effect of the death rate of mites due to treatment (\(\delta_2\)), i.e. the efficacy of the varroacide compounded over one year, on the average of the total mite population over each year, see Figure 3.5. All other parameters are the same as in Section 3.4.2. The average of the mite population for each year, \(M_{av}(i)\), is calculated using
Figure 3.5: Effect of death rate of mites due to treatment (i.e., $\delta_2$) on the average mite population (scale shown on the colour bar).

the expression

$$M_{av}(i) = \frac{1}{i} \sum_{c=1}^{i} \int_{a}^{b} \frac{M(t)dt}{T}, \quad i = 1, 2, 3, ..$$

where $a = (c - 1)T$, $b = cT$ and $i$ represents the number of years and $T$ is the time period.

We vary $\delta_2$ between 0.5 and 1.5, and track the simulations over 20 years. If the annual varroacide efficacy is small, the mite population will slowly increase and a bee-mite limit cycle with a maximum of 6000 mites will be attained. As $\delta_2$ increases, the average mite population decreases over time. The mite population is not able to establish itself if the death rate is above a threshold value of approximately $\delta_2 = 1.2661$, which is the same as calculated from the analysis of the mite and virus free periodic solution.

To eradicate mites from the colony, their death rate due to varroacides must be greater than a threshold value. If the death rate due to varroacides is below the threshold value, a necessary collapse of the colony is not implied, but the mite population might become established.
3.5 Conclusions

We studied a mathematical model of infestations of honeybee colonies with varroa mites and the Acute Bee Paralysis Virus with seasonally changing coefficients. Although there is still much unknown about ABPV, the literature suggests that its virulence and transmission depend primarily on *Varroa destructor* as a mechanical vector. Therefore, a simplifying key assumption made in our model is that ABPV is transmitted by *Varroa destructor* only. Our main findings can be summarized as follows:

- In the base model without varroacide treatment, the mite and virus free solution is always unstable due to the logistic growth assumption that we made for varroa mites. If only mites are present, but no virus, then depending on parameters a periodic endemic solution can be found, where bees and mites are present, or the colony will fail. The bee population in an endemic bee-mite solution will remain below the size of the mite free solution. In the presence of the virus, for parameters in realistic ranges, the colony is likely to fail rapidly after several years of slow decline.

- In our model, the disease free equilibrium can be stabilised by the application of varroacide with sufficient intensity. This stability criterion can be given explicitly in integral form. The success of varroacide treatment depends on the cumulative efficacy over the year, rather than a specific time course. Our computer simulations suggest that varroacide treatment, at some intermediate levels, not strong enough to completely eradicate varroa mites, can keep the disease under control. In this case an endemic periodic solution can be found in which case the bee population remains slightly below the corresponding disease free solution.
• A particular difficulty in parameterizing a model like the one studied here is that normally only seasonally averaged parameter values can be obtained from available data in the literature, although it is more reasonable to assume that these parameters should vary continuously with time. We have found that different strategies to infer continuously varying parameters from seasonally averaged data lead to quantitatively different solutions, but that this has only minor impact on the qualitative longterm fate of the colony, i.e whether it survives or fails.

• Since our results suggest that annual cumulative efficacy of varroacide treatment is more important than the particular time course of treatment, continuous low dosage application of chemical or biological control agents might be possible. This suggests that it might be worthwhile to explore continuous, low maintenance, low-invasive, dispensing techniques as an alternative to current invasive treatment methods that might contribute to cross-contamination between colonies in an apiary. It might be possible, for example, that such dispensing methods use the natural air flow currents in the colony beehive that were studied and characterized in [39].

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Bibliography


[33] Moore, P.A.; Wilson, M.E.; Skinner, J.A.; Honey Bee Viruses, the Deadly Varroa Mite Associates,


Appendix

3.6 Construction of continuous parameters from seasonal averages

3.6.1 Definition based on Piecewise Cubic Hermite Interpolating Polynomials

We interpolate the average seasonal values (i.e. piecewise constant functions) to obtain continuous and periodic functions using the built-in MATLAB function PCHIP (Piecewise Cubic Hermite Interpolating Polynomial) (see [13] for details). A difficulty is to interpolate $\mu$ without having the interpolating curve becoming negative as the average value of $\mu$ in winter is zero. Therefore, the standard interpolating polynomials cannot be applied in a straightforward manner. We use PCHIP to interpolate between the seasons in two different ways to construct an interpolating function that preserves the shape of the data and monotonicity while at the same time trying to approximate the seasonal averages well. Proceeding in this manner, also the derivative of the interpolating function is continuous. Since PCHIP does
not overshoot or undershoot, it solves the purpose without having the interpolating curve becoming negative in case of the parameter $\mu$, however at the expense of not necessarily maintaining seasonal averages exactly.

Overall, three different profiles are observed in the parameters. Profile (a) is described by its highest average value is summer, lowest in winter and intermediate value in spring and fall (examples are $\mu$ and $K$). Profile (b) is described as a high average in spring and fall and lower values in summer and winter (examples are $\beta_i, i = 1, 2, 3, d_1$). Profile (c) is a high average value in spring and summer and low average in fall and winter (examples are $r$ and $d_2$). Each of these profiles is shown in Figure 3.6.

We assume that the year starts with the spring season and that each season is equal in length i.e. 91.25 days. Let us denote $s = 91.25d$. Therefore, the duration of spring is 0 to $s$, summer $s$ to $2s$, fall $2s$ to $3s$ and winter $3s$ to $4s$ days.

Method 1 for Profile (a) and (b): Reduce each season by taking off $\frac{1}{4}s$ each from the beginning and end. Consider the parameters to take average values at the reduced length of the seasons. We interpolate between the seasons (e.g. between spring and summer i.e., from $\frac{3}{4}s$ to $\frac{5}{4}s$) by using PCHIP.

Method 1 for Profile (c): Since Profile (c) is such that the average value is the same in spring and summer, Method 1 is designed in a slightly different manner. We reduce the interval each from the beginning of spring and the end of summer by $\frac{1}{4}s$. Similarly, we reduce the interval from the beginning of fall and end of winter by $\frac{1}{4}s$. We consider the parameters to take average values on the reduced intervals and we interpolate between summer and fall, and winter and spring using PCHIP.

Method 2 for Profile (a) and (b): For spring and fall, we consider the average values to be the mid point of each season instead of reducing the length of seasons
by a factor. For summer and winter, we reduce each the length of each season by taking off \( \frac{1}{4}s \) from the beginning and end of each season. Then, we use PCHIP to interpolate between all the seasons.

**Method 2 for Profile (c):** We designed this method in a way that the higher average value is considered at the mid of spring and fall, each; the lower average value is considered at the mid point of fall and winter, each. We interpolate between these mid points using PCHIP.

Seasonal average and annual average values for each of these profiles are calculated and compared against the seasonal average in Table 3.2. These methods were designed by taking into consideration that average values calculated from them should be as close as possible to the seasonal averages from literature and the interpolated functions should be almost smooth. For instance, the seasonal average for \( \mu \) by using Method 1 and Method 2 is higher than the seasonal average from the literature for all seasons except summer but the annual average using Method 1 is more closer to the annual average calculated from the literature. Therefore, Method 1 gives an annual average value more accurate as compared to Method 2 in case of Profile (a). In case of Profile (b), seasonal average of the parameter \( \beta_1 \) using Method 2 is higher than the seasonal average calculated from the literature. However the annual average using the same method is more closer to the annual average from the literature. In case of Profile (c), although the seasonal average using both methods are different (in particular Method 1 is closer to the seasonal average obtained from literature), the annual average values are the same and are close to the annual average values calculated from the literature.
Figure 3.6: Three different profiles observed in the parameters ($\mu$ and $K$ in (a), $\beta_1, \beta_2, \beta_3, d_1$ in (b), and $r$ and $d_2$ in (c)) by interpolating the piecewise constant seasonal averages using two methods.
Figure 3.7: Comparison of the bee-mite dynamics using two different methods for interpolation of the piecewise constant parameters.

Figure 3.8: Comparison of the bee-mite-virus dynamics using two different methods for interpolation of the piecewise constant parameters.
Table 3.2: Comparison between the average values of the parameters obtained from literature and their approximate forms shown in Figure 3.6

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Spring</th>
<th>Summer</th>
<th>Autumn</th>
<th>Winter</th>
<th>Annual average</th>
</tr>
</thead>
<tbody>
<tr>
<td>( \mu )</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>From [40]</td>
<td>500</td>
<td>1500</td>
<td>500</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Method 1</td>
<td>524.7214</td>
<td>1403</td>
<td>522.7622</td>
<td>55.1444</td>
</tr>
<tr>
<td></td>
<td>Method 2</td>
<td>549.6787</td>
<td>1458</td>
<td>582.8532</td>
<td>7.5580</td>
</tr>
<tr>
<td>( \beta_1 )</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>From [40]</td>
<td>0.1593</td>
<td>0.1460</td>
<td>0.1489</td>
<td>0.04226</td>
</tr>
<tr>
<td></td>
<td>Method 1</td>
<td>0.1319</td>
<td>0.1460</td>
<td>0.1332</td>
<td>0.0487</td>
</tr>
<tr>
<td></td>
<td>Method 2</td>
<td>0.1516</td>
<td>0.1474</td>
<td>0.1390</td>
<td>0.0494</td>
</tr>
<tr>
<td>( r )</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>From [29, 30]</td>
<td>0.0165</td>
<td>0.0165</td>
<td>0.0045</td>
<td>0.0045</td>
</tr>
<tr>
<td></td>
<td>Method 1</td>
<td>0.0144</td>
<td>0.0162</td>
<td>0.0063</td>
<td>0.0046</td>
</tr>
<tr>
<td></td>
<td>Method 2</td>
<td>0.0141</td>
<td>0.0142</td>
<td>0.0067</td>
<td>0.0067</td>
</tr>
</tbody>
</table>

3.6.2 Effect of different interpolated forms of parameters on the disease dynamics of the colony

Given that data are available in terms of seasonal averages, the question arises whether the model is sensitive to the particular construction of continuous coefficient functions from these discrete data. Our numerical simulations indeed show that the qualitative results are the same whether we use Method 1 or 2 for the approximation of the piecewise constant parameters, see Figures 3.7 and 3.8. However, it does affect the solutions quantitatively.

First, we considered a honeybee colony infested with mites. Co-existence of bees and mites is observed using both methods (see Figure 3.7). The quantitative difference is that in case of Method 1, the minimum of bee and mite population is higher than the case where Method 2 is used. This is explained by the observation that
for Method 2, in winter the average birth rate of bees ($\mu$) is lower and the average natural death rate of bees ($d_1$) is higher compared to the seasonal averages obtained from the literature.

Next, we consider a mite infested honeybee colony infected with virus and observed that although the colony collapses using both Method 1 and 2, the latter leads to failure of the colony one year earlier than the former, see Figure 3.8. This is explained by the observation that the minimum of the bee population is lower in case of Method 2 than in case of Method 1 and it drops below the brood maintenance coefficient $K$. This means that there are enough healthy worker bees to care for the brood present in the colony which leads to the collapse of the colony.

In another simulation experiment, we investigate how the dynamics of the bee-mite-virus system is altered by reducing the length of intervals on which average parameter value is taken in Method 1, by different proportions (i.e., $\frac{9}{20}s$ and $\frac{1}{10}s$) instead of $\frac{1}{4}s$ as we did above. It is observed that the colony collapses one year earlier if the interval for the parameters is reduced by $\frac{1}{10}s$ as compared to the case when it is reduced by $\frac{9}{20}s$, see Figure 3.9. This happens because in case of reduction by $\frac{1}{10}s$, the minimum of the bee population is lower than in case of $\frac{9}{20}s$ and after 2200 days, it falls below the brood maintenance coefficient $K$ and leads to the collapse of the colony. Although the fraction by which the interval is reduced does affect the results quantitatively but not qualitatively.

We conclude that using two different approximated forms of the parameters does not affect the qualitative results, but it can affect the results quantitatively. This suggests that data provided as the seasonal averages (i.e., piecewise constant functions) is sufficient to study the disease dynamics of the honeybee colony. For a truly
Figure 3.9: Dynamics of the bee-mite-virus system by varying the reduction of the intervals in Method 1.

quantitative predictive tool, however, better time resolved data might be required to determine the continuous model parameters with the desired accuracy
Chapter 4

The interplay between *Varroa destructor*-Acute Bee Paralysis Virus infestation and division of labour in a honeybee colony

Abstract

In this paper, we combined a mathematical model of a honeybee colony infested with *Varroa destructor* and Acute Bee Paralysis Virus with the existing bee models in which the bee population is divided into hive bees and forager bees based on tasks performed by them in the colony. The model is a system of five ordinary differential equation with dependent variables: uninfected hive bees, uninfected forager bees, infected hive bees, virus free mites and virus carrying mites. The interplay between forager loss and disease infestation has been studied. We study the stability of the disease free equilibrium of the bee-mite-virus model using the results from the analysis of the bee only model and the bee-mite model. It is observed that the disease cannot be fought off in the absence of varroacide treatment. However, the disease free equilibrium can be stable if the treatment is strong enough and also if the virus carrying mites become virus-free at a rate faster than the mite birth rate.
The critical forager mortality due to homing failure, above which the colony fails, is calculated using simulation experiments for disease-free, treated and untreated mite infested, and treated virus infested colonies. A virus infested colony without varroacide treatment fails regardless of the forager mortality rate.

**Keywords:** Honeybees, *Varroa destructor*, Acute Bee Paralysis Virus, Mathematical Model, Homing Failure

### 4.1 Introduction

A honeybee colony functions as an integrated whole performing all of the basic physiological processes that support life. Its members cannot survive on their own, yet individual honeybees are physically independent. Like other social insects, a honeybee colony shows two types of division of labour: a division of labour between queen, drones and workers for reproduction and a division of labour among workers for tasks related to colony growth and development [43]. Reproductive division of labour between queens and workers involves differences in nutrition during larval development. The only role of drones is to mate with the queen. Division of labour between worker castes is based on the age of the individuals; young adults work within the hive and perform tasks related to hive management and brood care, and older workers switch to foraging tasks [45, 46]. The size of a colony and the life span of the bees vary greatly with seasons. The queen bee starts laying eggs slowly in spring, then at an increasing increases into summer and then decreases in fall and then stops before winter.

Honeybees play an outstanding role economically and ecologically. They are responsible for a crop value of more than $2 billion each year through their pollina-
tion services in Canada [9]. One third of the human diet comes from the food crops that are pollinated by honeybees [8]. There have been dramatic losses of honeybee colonies in Canada, the USA and in Europe since 2006 [25, 40, 50]. The symptoms are different in different parts of the world and hence losses are designated by different names. The syndrome was named Colony Collapse Disorder (CCD) in the US and Wintering losses in Canada. The exact reasons for the colony losses are not clear yet; there could be single reason or a combination of several of them. Possible causes include parasites, viruses, environmental factors and management practices [5, 48]. It is suspected that a leading cause of honeybee losses is the parasitic mite *Varroa destructor* and the deadly viruses it carries [29, 47]. Any stressor that can affect the ability of the forager bees to return to the hive can lead to the colony failure [20, 39]. Failure of foragers to return to the hive could be due to a number of factors. These include precocious foraging, use of environmental pesticides, viral infections and nosema infection [1, 14, 20, 30, 37, 51]. Honey bees are regularly exposed to pesticides because they rely heavily on common blooming crops, such as oilseed rape, maize, or sunflower, that are now routinely treated against insect pests [13]. These pesticides contaminate nectar and pollen [44]. Foraging honeybees are therefore directly exposed, with possibly adverse effects on their memory, learning ability and navigational skills. Such disoriented bees fail to return to the hive which is known as homing failure. The rest of the colony is also affected as the returning foragers store or exchange contaminated material with hive individuals [12, 44]. This is our motivation to study the interplay between the individual level effect varroa-virus infestation and the colony level effects of loss of forager bees. In this section, we discuss each of these three factors i.e., varroa mite, viruses and forager loss respectively. This section will be followed by the discussion of the related mathematical models that exists in the literature.

*Varroa destructor* is an ectoparasitic mite that infests honeybee colonies. It is one
of the haplotypes of *Varroa jacobsoni*, a parasite that infests the Eastern honeybee *Apis cerana* [2]. *Varroa destructor* is the species that parasitized *Apis melifera* and spread rapidly in Western countries thereafter. The mite not only feeds on the haemolymph of individual bees but also carries and transmits deadly viruses from bee to bee. This results in a reduced life span of bees and a decrease in the survivorship. The life cycle of the varroa mite is tightly adapted to the development of honeybees. Mite reproduction takes place exclusively in the capped cells of developing bee pupae. Female mites enter the brood cell before the cell is capped, and then feeds on the developing bee and also reproduces in the capped cell. When the host bee leaves the cell, the mother mite leaves the cell with its progeny. The adult female mite becomes attached to the adult bee and feeds on it by squeezing between the overlapping segments on the ventral side of the bee’s abdomen.

Viral infections may also get transmitted to the bees when mites feed on the bees. There are more than 20 known bee viruses out of which 12 viruses are carried and transmitted by varroa mites [24, 38]. These viruses differ in pathogenesis, morphology, routes of transmission, virulence and their interaction with the host. For instance, brood infected with Acute Bee Paralysis Virus (ABPV) do not develop into adult bees and die rapidly. On the other hand, Deformed Wing Virus (DWV) also infects the brood in the hive, but they usually survive to the adult stage which has a reduced life span as compared to healthy bees [49]. In this study we focus on the Acute Bee Paralysis Virus (ABPV). It belongs to the family Dicistroviridae, which includes the Kashmir Bee Virus (KBV), Black Queen Cell Virus (BQCV) and the Israeli Acute Paralysis Virus (IAPV). ABPV is a common infective agent of honeybees that is frequently detected in apparently healthy colonies. This virus is distributed worldwide and appears to be the most common bee virus in Europe and South America [3, 4]. Bees affected by this virus are unable to fly, lose the hair from their thorax and abdomen and tremble uncontrollably. Infected pupae and adults
infected with this virus suffer rapid death. ABPV has been implicated in honeybee colony failure when transmitted by varroa mites [24]. ABPV is transmitted to the bees when mites feed on bees. A virus free phoretic mite starts carrying virus when it feeds on an infected bee. When the virus carrying mite attaches to an uninfected bee, it releases the virus into the bee’s haemolymph and the bee becomes infected [7, 32]. The level of virus infestation in a honeybee colony depends on the mite population present in the colony. Varroa mites are a mechanical vector for the transmission of ABPV, i.e., unlike other honeybee viruses such as the Deformed Wing Virus (DWV) or the Israeli Acute Paralysis Virus (IAPV), ABPV does not replicate within the mites [17, 35, 52]. Other transmission routes of ABPV have been suggested, but the literature is inconclusive and quantitative data that would allow a parameterization of a mathematical model are scarce. For example, [10] investigated the question of vertical transmission for six viruses. While they found for five of them, including DWV, that infection of the queen implied infection of her offspring, this was not found for ABPV. [11] reports of a study in which ABPV was detected in pollen but not in the bees and their glandular secretion, suggesting that the ingestion of food which contains virus might not lead to infection. Moreover, they report that in colonies without varroa mites ABPV, if it is present, is latent, whereas the presence of varroa triggers the disease, suggesting ABPV virulence is directly related to varroa infestation, cf also [17, 36, 52].

To study the interplay of varroa-ABPV infestation dynamics and forager loss due to homing failure, the forager population must be studied as a separate class of individuals. The bee population is thus divided, based on the tasks they perform, into hive bees and forager bees. Young bees nurse the brood, build the comb and perform other tasks necessary to maintain the colony and become guards or foragers when they get older are hive bees. Forager bees collect pollen and nectar for the colony. The assignment of tasks can change due to social feedback. For instance, if
there are too few foragers, young bees will start foraging at an earlier age. Similarly, if there are too few hive bees, foragers may revert to the role of hive bees. This mechanism is known as social inhibition [31]. If the social inhibition is reduced and the hive bees become foragers when they are young, this results in an overall reduction in average bee lifespan, because the foragers are at higher risk of dying [26]. Forager loss can be caused by any factor e.g. pesticides, viral infections, nosema infection etc [20, 30, 51].

There have been mathematical models developed to study the disease dynamics of a honeybee colony infested with varroa mites and viruses [15, 41, 42, 49]. There are also models which are based on division of labour that are used to study forager mortality [26, 27, 28]. A recent review of many honeybee mathematical models[5], based on a keyword search, divides the models into three categories: colony models, varroa models and foraging models. It is observed that there does not exist any mathematical model in the literature that studies the interplay of a varroa-virus infestation with division of labour [5]. In this paper, we combine the disease model in [42] with the division of labour model in [26]. The primary structure of the disease part of our model is based on [42] which in turn is based on [49] which presents a first model of the honeybee-mite-virus complex using the traditional SIR approach. The model considers two varroa transmitted bee viruses DWV and ABPV. The model quantified the critical mite population, which depends on model parameters, below which the colony survives. The total mite load in the colony is assumed to be constant but the virus carrying mite population is considered to be a dependent variable. [15] extended the model for ABPV by adding a brood maintenance term to take into account the fact that a sufficient number of healthy adult bees are required to care for the brood present in the colony. The addition of this brood maintenance term introduced a trivial equilibrium which was not present in the model of [49] because bee birth was considered to be constant. Both [49] and
[15] studied the model with constant parameters; although [15] studied the model using computer simulations to investigate the fate of the colony over multiple years assuming piecewise constant parameters. [41] extended the model in [15] by introducing a logistic growth model for the total mite population (this population was assumed to be constant in [15, 49]), with carrying capacity of the mites dependent on the total bee population. Since an explicit equation for the mite population was included, the model distinguished between natural death of bees and death due to mites. As in [15], the model in [16, 41] was studied numerically using computer simulations assuming piecewise constant parameters with discontinuous jumps between the seasons. In [42], the model was extended to study the seasonal effects on the mite and virus infested colony by considering the coefficients to be continuous functions of time. It was assumed that the coefficients are periodic in time with a period of one year, and Floquet theory was used to analyze the model. The model also included the effect of varroacide application by introducing another death term for bees and mites. The model presented in [23] followed [49] and [42] but also took into account the fact that virus transmission occurs at different biological stages of varroa mites and honeybees. It also followed [15] by including Allee effects in the honeybee population.

The division of labor aspect of our model is based on [20] which in turn is based on [26]. In [26], the authors presented the first mathematical model in which the colony population was divided based on the tasks performed. It was a two dimensional model with hive bees and forager bees as dependent variables, and is studied using phase plane analysis. The authors investigated how loss of foragers accelerates the precocious recruitment of hive bees to foragers which in turn affects the survival of the colony. The model in [20] studied the forager mortality due to exposure to pesticides as a result of which the bees fail to return to the hive. The authors incorporated the forager mortality into the model of [26] as an additional linear death term for the
forager population. They also performed field experiments to determine lower and upper bounds for forager mortality due to homing failure. A comparison between the dynamics of colonies that are exposed to the treated crops against unexposed colonies was carried out. The authors observed that the exposed colonies show a marked decline and hardly recovers afterwards. Moreover, if natural death is also considered, the colonies are not able to recover at all. In [28], the model of [26] was extended to account for a hypothetical infection that is brought into the colony by the foragers and spreads in the hive via bee-to-bee transmission. Thus model was studied in detail both analytically and numerically. The disease dynamics assumed in this paper are rather general and it is left open to what extent the results would apply to particular diseases such as ABPV and DWV, which require both a vector and a causative agent. There are other studies which are not directly relevant for our particular study but are important to study forager loss using division of labor. For instance, in [27] the model of [26] was extended by adding two new equations, one for colony food stores and one for the brood population. The authors explored the interactions between food availability and forager mortality on colony fate. In other work, a generic disease model similar to [28] was studied in [6]. This model explicitly accounts for food storage as in [27] and assumes that birth rate is limited by both the the worker population and food availability. The resulting system of five ODEs is studied numerically through a sensitivity analysis, including an investigation of Wintering effects, by adjusting the growth rate, forager recruitment rate and food production rate. As in [28], [6] assumes direct transmission between bees, without a vector.

In this paper, we present a mathematical model for the dynamics of a honeybee colony affected by varroa mites, ABPV, and division of labor between hive and forager bees. The model is a combination of existing models that independently describe the varroa-ABPV [42] and division of labor [26] systems, with a provision
for increased forager bee mortality due to homing failure [20]; the combined system consists of five non-linear ODEs. Using a combination of stability analysis and numerical simulations, we investigate (i) stability of equilibria in an autonomous presentation of the model, and (ii) the effect of forager mortality parameters on the strength and survival of the colony under various varroacide treatment conditions in a non-autonomous (full) presentation of the model.

4.2 Mathematical model

4.2.1 Model assumptions

Our model follows the assumptions given below.

1. Following [26], the healthy bee population is divided into hive bees and foragers. The base model is combined with the model in [42] to incorporate the effect of mites and virus. The resulting model is formulated in terms of the dependent variables (i) uninfected hive bees (ii) uninfected forager bees (iii) infected hive bees (iv) virus carrying mites and (v) virus free mites.

2. Unlike [41] and [42], where the mite population is categorized into virus carrying mites and the total mite population, the mite population is categorized into virus carrying mites and virus free mites. This allows us to study the virus free mites as a separate class of individuals. We also assume that the maximum birth rate for virus-free and virus carrying mites is the same.

3. Since a minimum number of healthy worker bees are required to take care of the brood, bee birth is dependent on the number of worker bees which we assume to be the sum of the hive bees and foragers based on [26]. Following [15], we formulate this assumption in the form of a Sigmoidal Hill function,
which introduces an Allee effect.

4. Following [6, 15, 26, 28, 41, 42, 49], we assume that the queen bee is not affected by the disease. This implies that the egg laying rate of the queen is independent of the mites and virus.

5. We assume that the only route of virus transmission is horizontal transmission vectored by varroa mites. In accordance with [17, 35, 52] the mites are assumed to be a mechanical vector only. In particular, no virus replication takes place within the mites.

6. In accordance with [33, 36], we assume that the pupae affected with ABPV die quickly before developing into adult bees and so all newly born bees are uninfected. To incorporate this assumption, we follow [49] and include a term that represents the decrease in bee birth rate due to virus carrying mites.

7. Following [42], we account for varroacide treatment by introducing additional sink terms for the mites and bees depending on varroacide treatment. However, we assume that the varroacide has a stronger effect on the mites than the bees.

8. We assume that hive bees, forager bees, and infected bees die due to both natural cause and due to mites feeding on them and/or infecting them with virus. As in [41, 42], the death term is divided into two components one that depends on mites and one that does not. Since the mite population was considered to be a constant in [15, 49], the death due to mites was not needed to be incorporated in the model. In case of foragers, along with the natural death rate and death rate due to mites, there is another linear death term that represents the loss of foragers due to homing failure. We further assume that the death rate of infected hive bees is higher than the death rates of uninfected
hive bees.

9. Following [26, 27], we assume that in the absence of foragers, the hive bees are recruited as foragers at a maximum rate. As the number of foragers increases, the rate of recruitment of hive bees to foraging decreases following social inhibition. We formulate this process of social inhibition as a Holling type II functional response.

10. The mite population is dependent on the availability of brood in the hive. This leads to the fact that the increase in the mite population is limited by the colony strength which is a measure of brood size, as in [41, 42]. We use a logistic model to describe the growth of the mite population.

11. The dynamics of disease transmission for ABPV is described as originally worked out in [49] and later used in [15, 41, 42].

12. We assume that there is no flow of mites into and out of the colony via foragers. The only process through which mites leave the colony through the varroacide treatment.
4.2.2 Model Equations

Our model is obtained by combining the models in [26, 42]. It reads as

\[
\frac{dx_h}{dt} = \mu g(x_h + x_f)h(m) - \beta_1 m \frac{x_h}{x_h + y + x_f} - (d_1 + \delta_1) x_h - \gamma_1 (m + n) x_h - x_h R(x_h, x_f)
\]  
(4.1)

\[
\frac{dx_f}{dt} = x_h R(x_h, x_f) - \beta_2 m \frac{x_f}{x_h + y + x_f} - (p + d_2 + \delta_2) x_f - \gamma_2 (m + n) x_f
\]  
(4.2)

\[
\frac{dy}{dt} = \beta_3 m \frac{x_h + x_f}{x_h + y + x_f} - (d_3 + \delta_3) y - \gamma_3 (m + n) y
\]  
(4.3)

\[
\frac{dm}{dt} = r_m \left(1 - \frac{m + n}{\alpha(x_h + y + x_f)}\right) + \beta_4 n \frac{y}{x_h + y + x_f} - \delta_4 m
\]  
(4.4)

\[
\frac{dn}{dt} = r_n \left(1 - \frac{m + n}{\alpha(x_h + y + x_f)}\right) - \beta_5 n \frac{y}{x_h + y + x_f} + \beta_5 m \frac{x_h + x_f}{x_h + y + x_f} - \delta_5 n
\]  
(4.5)

where

\(x_h\): number of uninfected hive bees

\(x_f\): number of uninfected forager bees

\(y\): number of infected hive bees

\(m\): virus carrying mites

\(n\): virus free mites

The parameters are assumed to be non-negative and periodic functions of time with period \(T\); in practice \(T = 1\) year.
The parameter $\mu$ in (4.1) is the maximum birth rate, specified as the number of worker bees (i.e., hive bees) born per day.

The function $g(x_h + x_f)$ expresses that a sufficiently large number of healthy worker bees (i.e., hive bees as well as foragers) is required to care for the brood. We think of $g(x_h + x_f)$ as a switch function. If $x_h + x_f$ falls below a critical value, which may seasonally depend on time, essential work in the maintenance of the brood cannot be carried out anymore and no new bees are born. If $x_h + x_f$ is above this value, the birth of bees is not hampered. Thus $g(0, \cdot) = 0$, $\frac{dg(0)}{dx_h} \geq 0$, $\frac{dg(0)}{dx_f} \geq 0$, $\lim_{x_h + x_f \to \infty} g(x_h + x_f) = 1$. A convenient formulation of such switch like behavior is given by the sigmoidal Hill function

$$g(x_h + x_f) = \frac{(x_h + x_f)^i}{K^i + (x_h + x_f)^i}, \quad (4.6)$$

where the parameter $K$ is the size of the bee colony at which the birth rate is half of maximum possible rate and the integer exponent $i > 1$. If $K = 0$ is chosen, then the bee birth term of the original model of [49] is recovered. Then the brood is always reared at maximum capacity, independent of the actual bee population size, because $g(x_h + x_f) \equiv 1$.

The function $h(m)$ in (4.1) indicates that the birth rate is affected by the presence of virus-carrying mites in the hive. This modulation of the birth rate is particularly important for viruses like ABPV that kill infected pupae before they develop into adult bees. The function $h(m)$ is assumed to decrease as $m$ increases, $h(0) = 1$, $\frac{dh}{dm}(m) < 0$ and $\lim_{m \to \infty} h(m) = 0$; [49] suggests that this is an exponential function $h(m) \approx e^{-mk}$, where $k$ is non-negative. We will use this expression in computer simulations.

The parameter $\beta_4$ in (4.4) is the rate at which mites that do not carry the virus acquire it. The rate at which infected mites lose their virus to an uninfected host is
The rate at which uninfected hive bees become infected is $\beta_1$, in bees per virus carrying mite and time. The rate at which uninfected forager bees become infected is $\beta_2$, in bees per virus carrying mite and time. We assumed that the rate at which hive bees get infected (i.e. $\beta_1$) is the same as the rate at which foragers get infected (i.e. $\beta_2$). With this assumption, the first term in ?? becomes the rate at which total bees get infected (i.e., $\beta_3$ from [42]).

Finally, $d_1$, $d_2$ and $d_3$ are the death rates for uninfected hive bees, uninfected foragers, and infected hive bees. We can assume that infected bees live shorter lives than healthy bees, thus $d_3 > d_1$ and $d_3 > d_2$. The parameter $d_2$ is assumed to be [0.04762, 0.025, 0.005376, 0.025] for spring, summer, fall and winter respectively. These values are calculated using the average life span of bee (from [49]) and the age at which hive bees are recruited as foragers (i.e., using parameter $\sigma_1$ from [26]).

The seasonal averages of the parameters $\beta_i (i = 1, 2, 3, 4, 5)$, $d_1$, $d_2$, $d_3$, $\mu$, $k$, $\alpha$, $r$, $K$, $\sigma_1$, $\sigma_2$ and $\gamma_i (i = 1, 2, 3)$ are given in Table 4.1.

By $r$ we denote the maximum mite birth rate. The carrying capacity for the mites changes with the host population size, $x_h + y + x_f$, and is characterized by the parameter $\alpha$ which indicates the average number of mites that can be sustained per bee.

The parameter $p$ in equation (4.2) represents the rate at which foragers are lost i.e., forager mortality due to homing failure.

Mites contribute to an increased mortality of bees. This factor is considered in (4.1), (4.2) and (4.3) by including death terms that depend on the total mite population ($m + n$); the parameters $\gamma_{1,2,3}$ are the rates at which mites kill bees. We assume that the mites kill the sick bees more quickly. Thus, $\gamma_3 > \gamma_1$ and $\gamma_3 > \gamma_2$. 

115
Table 4.1: Seasonal averages of some of the model parameters, derived from the data in [26, 33, 34, 41, 49].

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Spring</th>
<th>Summer</th>
<th>Autumn</th>
<th>Winter</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\beta_1 = \beta_2 = \beta_3$</td>
<td>0.1984</td>
<td>0.1460</td>
<td>0.1900</td>
<td>0.03384</td>
<td>Assumed</td>
</tr>
<tr>
<td>$\beta_4$</td>
<td>0.1593</td>
<td>0.1460</td>
<td>0.1489</td>
<td>0.04226</td>
<td>[49]</td>
</tr>
<tr>
<td>$\beta_5$</td>
<td>0.04959</td>
<td>0.03721</td>
<td>0.04750</td>
<td>0.008460</td>
<td>[49]</td>
</tr>
<tr>
<td>$d_1$</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>Assumed</td>
</tr>
<tr>
<td>$d_3$</td>
<td>0.2</td>
<td>0.2</td>
<td>0.2</td>
<td>0.005300</td>
<td>[49]</td>
</tr>
<tr>
<td>$\mu$</td>
<td>500</td>
<td>1500</td>
<td>500</td>
<td>0</td>
<td>[49]</td>
</tr>
<tr>
<td>$k$</td>
<td>0.000075</td>
<td>0.00003125</td>
<td>0.000075</td>
<td>N/A</td>
<td>[49]</td>
</tr>
<tr>
<td>$r$</td>
<td>0.0165</td>
<td>0.0165</td>
<td>0.0045</td>
<td>0.0045</td>
<td>[33, 34]</td>
</tr>
<tr>
<td>$\alpha$</td>
<td>0.4784</td>
<td>0.5</td>
<td>0.5</td>
<td>0.4784</td>
<td>[41]</td>
</tr>
<tr>
<td>$\gamma_1$</td>
<td>$10^{-7}$</td>
<td>$10^{-7}$</td>
<td>$10^{-7}$</td>
<td>$10^{-7}$</td>
<td>[41]</td>
</tr>
<tr>
<td>($= \gamma_2 = \gamma_3$)</td>
<td>$10^{-7}$</td>
<td>$10^{-7}$</td>
<td>$10^{-7}$</td>
<td>$10^{-7}$</td>
<td></td>
</tr>
<tr>
<td>$K$</td>
<td>8000</td>
<td>12000</td>
<td>8000</td>
<td>6000</td>
<td>[41]</td>
</tr>
<tr>
<td>$\sigma_2$</td>
<td>0.75</td>
<td>0.75</td>
<td>0.75</td>
<td>0.75</td>
<td>[26]</td>
</tr>
</tbody>
</table>
As in [26], the term $R(x_h, x_f)$ in equation (4.1) represents the effect of social inhibition on the recruitment rate and is equal to $\sigma_1 - \sigma_2 \left( \frac{x_f}{x_h + x_f} \right)$ where $\sigma_1$ is the maximum rate at which hive bees are recruited as foragers when there are no foragers present in the colony. The second term $\sigma_2 \left( \frac{x_f}{x_h + x_f} \right)$ represents social inhibition that is, the process whereby a surplus of foragers causes the foragers to revert to being hive bees. We assume that social inhibition is directly proportional to the forager population present in the colony.

Remark 7. Our model is a general framework which encapsulates the features of existing models in the literature [26, 28, 41] under particular assumptions. For instance, the model in [26] can be obtained if we study a honey bee colony with neither parasites nor viruses (i.e., $y = m = n = 0$), eclosion rate of bees is modelled by Holling type II term (i.e., $i = 1$) and the hive bees and forager bees do not die from natural death ($d_1 = d_2 = 0$).

In [28], a hypothetical infection is considered which is transmitted from bee to bee via direct contact with each other while communicating about feeding site locations. It is assumed that there is no vector involved in the disease transmission i.e., $m = n = 0$. It is also assumed that the eclosion rate of bees depends only on the hive bees and not on the total bee population i.e., $g(x_h + x_f) = g(x_h)$. It is also assumed that hive bees do not die of natural death i.e. $d_1 = 0$; they are only recruited as foragers. The assumption regarding the brood maintenance term in [26] still holds in [28].

The model in [41] can be obtained from our model by simply assuming that the total population is not divided into categories based on the division of tasks i.e. if $x_h + x_f = x$. 

117
4.3 Model with constant parameters

We first study the model with constant coefficients as in [15, 41, 49]. This will help in determining critical parameter values of the model. In order to prepare for the analysis of the complete five dimensional model (4.17)-(4.21), we start our investigation by studying smaller, more easily accessible sub-models. We begin by discussing the model for a healthy bee colony without mites and virus. In a second preliminary step we will introduce mites into the system but not the virus. The complete model will be studied with the help of the results of these simpler special cases.

4.3.1 The two dimensional disease-free bee model

In the absence of mites and viruses, the model becomes

\[ \dot{x}_h = \mu g(x_h + x_f) - d_1 x_h - x_h \left( \sigma_1 - \sigma_2 \frac{x_f}{x_h + x_f} \right) \] (4.7)

\[ \dot{x}_f = x_h \left( \sigma_1 - \sigma_2 \frac{x_f}{x_h + x_f} \right) - (p + d_2)x_f \] (4.8)

where \( g(x_h + x_f) = \frac{(x_h + x_f)^i}{K^i + (x_h + x_f)^i} \).

We assume that the parameters are positive and \( i > 1 \). The differential equations (4.7)-(4.8) with (4.6) has either one steady state i.e \( A(0, 0) \) or three steady states \( A(0, 0), B(x_{h_1}^*, F x_{h_1}^*) \) and \( C(x_{h_2}^*, F x_{h_2}^*) \) where \( x_{h_2}^* > x_{h_1}^* \) and

\[ F = \frac{1}{2} \left( \frac{\sigma_1 - \sigma_2 - p - d_2}{p + d_2} \right) + \sqrt{\left( \frac{\sigma_1 - \sigma_2 - p - d_2}{p + d_2} \right)^2 + \frac{4\sigma_1}{p + d_2}}. \] (4.9)

For \( i \geq 2 \), Descarte’s rule of signs gives the number of positive steady states.

For \( i = 2 \), we can explicitly calculate the expressions for \( x_{h_1,2}^* \).
\[ x_{h_{1,2}}^* = \frac{1}{2} \left[ \frac{\mu}{d_1 + \sigma_1 - \frac{\sigma_2 F}{1+F}} \pm \sqrt{\left( \frac{\mu}{d_1 + \sigma_1 - \frac{\sigma_2 F}{1+F}} \right)^2 - 4 \left( \frac{K}{1+F} \right)^2} \right]. \] (4.10)

Therefore, the two real positive \( x_{h_1}^* \) and \( x_{h_2}^* \) exist if

\[
\frac{\mu}{d_1 + \sigma_1 - \frac{\sigma_2 F}{1+F}} > \frac{2K}{1+F}.
\] (4.11)

The trivial equilibrium \( A(0, 0) \) of the model is asymptotically stable. This is proved using differential inequalities. For this, we note that for \( x_h \geq 0 \) and \( x_f \geq 0 \),

\[
\dot{x}_h + \dot{x}_f = \mu g(x_h + x_f) - d_1 x_h - (p + d_2) x_f \\
\leq \mu g(x_h + x_f) - \delta(x_h + x_f) \quad \text{where} \quad \delta = \min \{d_1, d_2 + p\} \\
=: G(x_f + x_f)
\]

Let \( x \) be the solution of \( \dot{x} = G(x) \). Then for small enough \( x \) we have \( G(x) < 0 \), i.e. \( x(t) \to 0 \). By the comparison theorem, we have \( x(t) \geq x_h + x_f \), i.e., \( x_h + x_f \to 0 \).

This means that in order to establish itself as a properly working healthy colony, a sufficiently large healthy adult bee population is required to take care of the brood. If the number of bees in the colony falls below this critical value, the colony will die off.

To study the stability of the non trivial equilibria \( B(x_{h_1}^*, Fx_{h_1}^*) \) and \( C(x_{h_2}^*, Fx_{h_2}^*) \), we look at the Jacobian matrix \( J(x_{h_1}^*, Fx_{h_1}^*) \) of the system (4.7)-(4.8),

\[
J(x_{h_1}^*, Fx_{h_1}^*) = \begin{bmatrix}
\mu \frac{\partial g}{\partial x_h} - d_1 - \sigma_1 + \frac{\sigma_2 F^2}{(1+F)^2} & \mu \frac{\partial g}{\partial x_f} + \frac{\sigma_2}{(1+F)^2} \\
\sigma_1 - \frac{\sigma_2 F^2}{(1+F)^2} & -\frac{\sigma_2}{(1+F)^2} - (p + d_2)
\end{bmatrix}
\] (4.12)
where

$$\frac{\partial g}{\partial x_h^*} = \frac{\partial g}{\partial x_f^*} = \frac{iK^i x_h^{i-1}(1 + F)^{i-1}}{(K^i + x_h^i(1 + F)^i)^2}$$

(4.13)

Since \(\sigma_1, \sigma_2, F, p, d_2\) are positive, we have \(J_{12} > 0\) and \(J_{22} < 0\). However, the sign of the \(J_{11}\) and \(J_{21}\) cannot be easily determined due to algebraic complexity. Thus we explore the stability of the equilibria numerically using a trace-determinant diagram. We plot the steady state solutions for parameters \(p, \sigma_1\) and \(\sigma_2\) on the trace-determinant plane (see Figure 4.1). We choose to vary the parameters \(p, \sigma_1\) and \(\sigma_2\) (from 0 to 2) to observe the effect of forager mortality and recruitment rate on the stability of the steady state solutions. We use the parameters corresponding to the summer season from Table 1, however, the results are qualitatively the same for spring and fall.

We observe that the steady states \(A\) and \(C\) are stable sinks because the solution lie in the first quadrant and below the solid black curve representing \(\Delta = (\text{trace})^2/4\). Since the solution corresponding to the steady state \(B\) stays in the negative half plane, the steady state \(B\) is an unstable saddle. Moreover, it is observed that as the parameters \(p\) and \(\sigma_2\) decreases to zero, and the parameter \(\sigma_1\) increases from 0 to 2, the steady state solution approaches the bifurcation point which lies on the x-axis.

**Remark 8.** Unlike [26], it is not possible to carry out a complete analysis of the two dimensional model due to the algebraic complexity of Holling type III growth function. The use of the Holling type III function introduces an Allee effect. Thus, the trivial equilibrium is found to be asymptotically stable while it is unstable in [26]. Moreover, the authors in [26] calculated a critical value for forager loss (due to natural death and homing failure) below which the hive bees and forager bees coexist and above which the colony fails. Again, due to the algebraic complexity, which arises from the Holling type III formulation for the bee eclosion term in our model, it is not possible to calculate the exact critical value of forager mortality. In
Figure 4.1: Trace-determinant plot of the Jacobian (4.12) for steady states $A(0,0)$, $B(x^*_{h1},Fx^*_{h1})$ and $C(x^*_{h2},Fx^*_{h2})$ of the two dimensional disease free model. Red, blue and cyan curves are obtained by varying the parameters $p$, $\sigma_1$ and $\sigma_2$ respectively over the range from 0 to 2. The solid black curve represents $\Delta = \tau^2/4$. Summer parameters from Table 4.1 are used for this Figure.

[26], the authors observed one stable non-trivial co-existence equilibrium whereas in our model we observe two non trivial co-existence equilibria one of which is stable and the other unstable.

### 4.3.2 The three dimensional bee-mite model

We investigate now how the stability of the equilibria $A$, $B$ and $C$ changes when virus free mites infest the colony. To this end we study the bee-mite subsystem of (4.17)-(4.21),

\[
\begin{align*}
\dot{x}_h &= \mu g(x_h + x_f) - (d_1 + \delta_1)x_h - \gamma_1 n x_h - x_h \left( \sigma_1 - \sigma_2 \frac{x_f}{x_h + x_f} \right) \\
\dot{x}_f &= x_h \left( \sigma_1 - \sigma_2 \frac{x_f}{x_h + x_f} \right) - (p + d_2 + \delta_2)x_f - \gamma_2 n x_f \\
\dot{n} &= r n \left( 1 - \frac{n}{\alpha(x_h + x_f)} \right) - \delta_5 n
\end{align*}
\]

The differential equations (4.14)-(4.16) with (4.6) has either one trivial steady state
(0, 0, 0) or six steady states \((0, 0, 0), (x_{h_1}^*, Fx_{h_1}^*, 0), (x_{h_2}^*, Fx_{h_2}^*, 0), (x_{h_3}^*, Fx_{h_3}^*, n_3^*), (x_{h_4}^*, Fx_{h_4}^*, n_4^*)\) and \((x_{h_5}^*, Fx_{h_5}^*, n_5^*)\) if \(F_1 > 0\) and \(r - \delta_5 > 0\).

For \(i > 2\), Descarte’s rule of signs gives the number of non-negative steady states.

Here, \(n_j^* = \frac{\alpha(r - \delta_5)F_1(1+x_j^*)}{r}\) where \(j = 3, 4, 5;\)

\(F\) is given by (4.9) and \(F_1\) is given by

\[
F_1 = \frac{r(\sigma_2 - \sigma_1 + p + d_2 + \delta_2) + 2\gamma_2\alpha(r - \delta_5)}{2(r\sigma_1 - \gamma_2\alpha(r - \delta_5))} \\
\pm \frac{\sqrt{(r(\sigma_2 - \sigma_1 + p + d_2 + \delta_2) + 2\gamma_2\alpha(r - \delta_5))^2 - 4(r\sigma_1 - \gamma_2\alpha(r - \delta_5))(r(p + d_2 + \delta_2) + \gamma_2\alpha(r - \delta_5))}}{2(r\sigma_1 - \gamma_2\alpha(r - \delta_5))}
\]

Also, \((x_{h_1}^*, Fx_{h_1}^*)\) and \((x_{h_2}^*, Fx_{h_2}^*)\) are the steady states of the bee-only model (4.7)-(4.8).

For \(i = 2\), we can explicitly calculate the expression for \(x_{h_1, 2}\) which is the same as (4.10) and the condition for the existence of the real and positive roots is (4.11).

The trivial equilibrium \((0, 0, 0)\) of the model (4.14)-(4.16) is asymptotically stable which can be proved using differential inequalities. For this proof, we use an argument similar to the one used in the case of the two dimensional model. From (4.14)-(4.15), it follows that for \(x_h + x_f = x\) and for all \(0 < x < \bar{x},\)

\[
\dot{x}_h + \dot{x}_f = \mu g(x_h + x_f) - (d_1 + \delta_1)x_h - (p + d_2 + \delta_2)x_f - (\gamma_1x_h + \gamma_2x_f)n \\
\leq \mu g(x_h + x_f) - \delta(x_h + x_f) < 0 \quad \text{where} \quad \delta = \min\{d, d_2\}, \quad d = d_1 + \delta_1
\]

Moreover, for all \(n > \hat{n},\)

\[
\hat{n} = r\alpha \left(1 - \frac{n}{\alpha(x_h + x_f)}\right) - \delta_5 n < 0
\]
where $\tilde{n} \geq \alpha(x_h + x_f)$. For small enough $\tilde{x}$ and $n > \tilde{n}$, the set

$$Z_{(\tilde{x}, \tilde{n})} = \{ x, n : 0 < x < \tilde{x}, n > \tilde{n}, n > 0 \}$$

is positively invariant with inward pointing flux. So every solution starting from a point in the set $Z_{(\tilde{x}, \tilde{n})}$ enters a positively invariant set.

This means that to establish itself as a properly working colony, a sufficiently large number of healthy worker (hive and forager) bees is required to maintain the hive.

The stability of the mite-free equilibria $B(x^*_h, Fx^*_h, 0)$ and $C(x^*_h, Fx^*_h, 0)$ can be studied by using the Jacobian matrix $J(x^*_h, Fx^*_h, 0)$ with (4.13), which is

$$J(x^*_h, Fx^*_h, 0) = \begin{bmatrix}
\mu \frac{\partial g}{\partial x_h} - d_1 - \delta_1 - \sigma_1 + \frac{\sigma_2 F^2}{(1+F)^2} & \mu \frac{\partial g}{\partial x_f} + \frac{\sigma_2}{(1+F)^2} & -\gamma_1 x^*_h \\
\sigma_1 - \frac{\sigma_2 F^2}{(1+F)^2} & -\frac{\sigma_2}{(1+F)^2} - (p + d_2 + \delta_2) & -\gamma_2 Fx^*_h \\
0 & 0 & r - \delta_5
\end{bmatrix}$$

One eigenvalue of the Jacobian matrix is given by:

$$\lambda_1 = r - \delta_5$$

The remaining two eigenvalues are the eigenvalues of the Jacobian matrix (4.12).

If $\lambda_1 < 0$, then the stability of the mite-free equilibria is the same the stability of the non-trivial equilibria of the two dimensional model, the maximum birth rate of mites is less than their death rate due to varroacide treatment. This means that if the varroacide treatment is strong enough, the mite infestation can be fought off. It is also observed that in the absence of varroacide treatment, it is not possible to fight off the mites.

On the other hand, if the mite-free equilibrium is unstable then it is not clear whether the system converges to the trivial equilibrium or an endemic equilibrium. We will
use numerical simulations to investigate this behaviour. It is important to note that these results are in agreement with the results corresponding to the stability of the mite free equilibrium in [42].

### 4.3.3 The complete bee-mite-virus model

We investigate now whether or not a stable, mite infested honeybee colony can fight off the virus. To this end we consider the complete five-dimensional model (4.17)-(4.21)

\[
\begin{align*}
\frac{dx_h}{dt} &= \mu g(x_h + x_f)h(m) - \beta_1 m \frac{x_h}{x_h + y + x_f} - (d_1 + \delta_1)x_h \\
&\quad - \gamma_1(m + n)x_h - x_h \left( \sigma_1 - \sigma_2 \frac{x_f}{x_h + x_f} \right) \quad (4.17) \\
\frac{dx_f}{dt} &= x_h \left( \sigma_1 - \sigma_2 \frac{x_f}{x_h + x_f} \right) - \beta_2 m \frac{x_f}{x_h + y + x_f} \\
&\quad - (p + d_2 + \delta_2)x_f - \gamma_2(m + n)x_f \quad (4.18) \\
\frac{dy}{dt} &= \beta_3 m \frac{x_h + x_f}{x_h + y + x_f} - (d_3 + \delta_3)y - \gamma_3(m + n)y \quad (4.19) \\
\frac{dm}{dt} &= rm \left( 1 - \frac{m}{\alpha(x_h + y + x_f)} \right) + \beta_4 n \frac{y}{x_h + y + x_f} \\
&\quad - \beta_5 m \frac{x_h + x_f}{x_h + y + x_f} - \delta_4 m \quad (4.20) \\
\frac{dn}{dt} &= \frac{rn}{\alpha(x_h + y + x_f)} - \beta_4 n \frac{y}{x_h + y + x_f} \\
&\quad + \beta_5 m \frac{x_h + x_f}{x_h + y + x_f} - \delta_5 n \quad (4.21)
\end{align*}
\]

The local stability of the disease free equilibria can be studied by linearization, using the Jacobian matrix \( J(x_h^*, Fx_h^*, 0, 0, 0) \) with (4.13), which is given by
\[
J(x^*_h, Fx^*_h, 0, 0, 0) = 
\begin{bmatrix}
\mu \frac{\partial g}{\partial x} - d_1 - \delta_1 - \sigma_1 + \frac{\sigma_2 F^2}{(1+F)^2} & \mu \frac{\partial g}{\partial x} + \frac{\sigma_2}{(1+F)^2} & 0 & \mu g(x^*_h + x^*_f)h'(0) - \beta_1 \frac{1}{1+F} - \gamma_1 x_h - \gamma_1 x_h \\
\sigma_1 - \frac{\sigma_2 F^2}{(1+F)^2} & -\frac{\sigma_2 F^2}{(1+F)^2} - (p + d_2 + \delta_2) & 0 & -\beta_2 \frac{F}{1+F} - \gamma_2 F x_h & -\gamma_2 F x_h \\
0 & 0 & -d_3 - \delta_3 & \beta_3 & 0 \\
0 & 0 & 0 & r - \beta_5 - \delta_4 & 0 \\
0 & 0 & 0 & \beta_5 & r - \delta_5 \\
\end{bmatrix}
\]
Three eigenvalues are given by

\[ \lambda_1 = -d_3 - \delta_3, \quad \lambda_2 = r - \beta_5 - \delta_4, \quad \lambda_3 = r - \delta_5. \]

The remaining two eigenvalues are the eigenvalues of the Jacobian matrix (4.12) for the two dimensional model.

The eigenvalue \( \lambda_1 \) is always negative. The eigenvalues \( \lambda_2 \) and \( \lambda_3 \) will be negative if the maximum birth rate of mites is less than the varroacide death rate of virus carrying mites and the rate at which the virus carrying mites lose their virus. This means that the disease can be fought off if the varroacide treatment is strong enough to eradicate the virus free mites; also if the virus carrying mites lose their virus faster than the rate at which they are born. The disease free equilibrium is always unstable in the absence of varroacide treatment. In [42], there is no condition on the transmission rate of virus because the population is divided into virus carrying mites and total number of mites that infest the colony. In the absence of treatment, the stability conditions for our model are in agreement with [42].

### 4.3.4 Numerical simulations of the model with constant parameters

We now perform two computer simulation experiments on the model with constant coefficients. In the first experiment, we observe the effect of different forager mortality rates on the dynamics of the colony that is infested with mites and virus. In the second experiment, we compare the dynamics of a disease free colony with the dynamics of a mite-virus infested colony when both are exposed to crops treated with
pesticides \( (p > 0) \). We simulate the loss of foragers due to exposure to the crops treated with pesticides; forager mortality rate is a measure of the level to which bees are exposed to the crops treated with pesticides. Following [20], we study the first 3 months of a beekeeping season (i.e., the spring season) encompassing the blooming period of crops such as oilseed rape, maize etc, that are treated with pesticides and visited by bees. We assume that the bees are exposed to the treated crops for 30 days (i.e., \( t = 5 \) to \( t = 35 \)) in the beginning of spring. The exposure period is delineated by the shaded region in Figures 4.2 and 4.3. The parameters \( \mu, \beta_1, \ldots, 5, d_1, \ldots, 3, k, r, \sigma_1, \sigma_2, \alpha \) and \( \gamma_1, \ldots, 3 \) for the spring season are taken from Table 4.1.

**Effect of exposure to treated crops on a colony that has fought off the virus:**

We begin the simulation experiment with the bee-mite steady state solution where virus is present initially but fought off. We investigate whether the population grows back to the steady state population level after being exposed to a treated crop (see Figure 4.2). We consider a base case when the colony is not exposed to the treated crops which means that the forager mortality due to homing failure is 0 \( (p = 0) \). In the absence of exposure the total bee population is constant at 20300. For a low rate of forager mortality due to homing failure \( (i.e., p = 0.1) \), the colony population decreases from 20300 to 11400 during the exposure period. After the exposure period ends, the population starts increasing and recovers to the same level from where it started before exposure. However, it takes about a year for the solution to revert to the pre-exposure equilibrium, which is much longer than the season for which the parameters hold. For a higher rate of forager mortality due to homing failure, \( i.e., p = 0.7 \), the population before the exposure period starts is 20330 and it decreases quickly to 1118 bees by the end of the exposure period. The population rapidly goes to zero after the exposure ends.
Figure 4.2: Comparison of the dynamics of a mite-virus infested honeybee population between simulated colonies with no homing failure (i.e., \( p = 0 \)), a low rate of homing failure (i.e., \( p = 0.1 \)) and a high rate of homing failure (i.e., \( p = 0.7 \)). Shaded areas delineate the time period of increased homing failure (i.e., when the colonies are exposed to a treated crop). These results are obtained with parameters fixed at the spring values.

Comparison of the effect of the increased forager loss between a disease free and a mite-virus infested colony:

In this simulation experiment, we compare the effect of exposure to treated crops on the dynamics of a disease free colony with a mite-virus infested colony (Figure 4.3). It is observed that the disease infested colony follows the same trajectory as the disease free colony but the latter curve lies below the former. The reason that the solutions lie so close to each other is that Figure 4.3 captures only the first season of the first year. To observe the effect of disease on the dynamics of the colony with increased homing failure, we need to study the case of seasonally varying parameters case instead of focusing on one season.

4.4 Model with seasonally varying parameters

4.4.1 Bee-mite model with periodic coefficients
Figure 4.3: Comparison of the dynamics of honeybee population between an exposed colony that is disease free and an exposed colony ($p = 0.1$) that is infested with mites and virus. **Note that** the curve for the disease-infested case lies below the curve for the disease free case but it is difficult to distinguish them as they are very close to each other.

A stability analysis of the disease free equilibrium of the full bee-mite-virus model cannot be easily carried out due to the algebraic complexity of the model equations. Numerical simulations however suggest the existence of periodic solutions to (4.17)-(4.21). Since a formal proof of the existence of periodic solutions seems out of reach at this point, we conjecture the existence of periodic solutions, as observed in simulations. We study the stability of the mite-free equilibrium of the bee-mite model using Floquet theory.

**Proposition 4.4.1.** Suppose $(x^*_h(t), x^*_f(t))$ is a periodic positive solution of (4.7)-(4.8). Then $(x^*_h, x^*_f, 0)$ is a periodic solution of (4.14)-(4.16). It is is stable if the periodic solution $(x^*_h, h^*_f)$ of (4.7)-(4.8) is stable and if $\int_0^T (r - \delta_5)dt \leq 0$.

**Proof.** That a positive periodic solution of (4.7)-(4.8) defines a disease free solution of (4.14)-(4.16) is immediate from the model equations. In order to analyse its stability, we use linearization and Floquet theory. We linearize the system about the periodic solution $(x^*_h, x^*_f, 0)$, i.e., we investigate the longterm behaviour of the perturbation $u := x_h - x^*_h, v := x_f - x^*_f, w := n - 0$. 

129
The Jacobian of the system is obtained as

\[
J(x^*_h, Fx^*_h, 0) = \begin{bmatrix}
\mu \frac{\partial g}{\partial x} - d_1 - \delta_1 - \sigma_1 + \frac{\sigma_2 F^2}{(1+F)^2} & \mu \frac{\partial g}{\partial x_f} + \frac{\sigma_2}{(1+F)^2} & -\gamma_1 x^*_h \\
\sigma_1 - \frac{\sigma_2 F^2}{(1+F)^2} & -\frac{\sigma_2}{(1+F)^2} - (p + d_2 + \delta_2) & -\gamma_2 F x^*_h \\
0 & 0 & r - \delta_5
\end{bmatrix}
\]

Thus, the linearized system about \((x^*_h, x^*_f, 0)\) is

\[
\begin{bmatrix}
\dot{u} \\
\dot{v} \\
\dot{w}
\end{bmatrix} = \begin{bmatrix}
\mu \frac{\partial g}{\partial x} - d_1 - \delta_1 - \sigma_1 + \frac{\sigma_2 F^2}{(1+F)^2} & \mu \frac{\partial g}{\partial x_f} + \frac{\sigma_2}{(1+F)^2} & -\gamma_1 x^*_h \\
\sigma_1 - \frac{\sigma_2 F^2}{(1+F)^2} & -\frac{\sigma_2}{(1+F)^2} - (p + d_2 + \delta_2) & -\gamma_2 F x^*_h \\
0 & 0 & r - \delta_5
\end{bmatrix}
\begin{bmatrix}
u \\
v \\
w
\end{bmatrix}.
\]

Let \((u_1(t), v_1(t), w_1(t)), (u_2(t), v_2(t), w_2(t))\) and \((u_3(t), v_3(t), w_3(t))\) be linearly independent solutions of the linearized system with corresponding linearly independent set of initial conditions

\[
\begin{align*}
u_1(0) &= 1, & u_2(0) &= 0, & u_3(0) &= 0, \\
v_1(0) &= 0, & u_2(0) &= 1, & v_3(0) &= 0, \\
w_1(0) &= 0, & w_2(0) &= 0, & w_3(0) &= 1.
\end{align*}
\]

The fundamental matrix \(A(t)\) of the linearized system over the interval \(0 \leq t \leq T\), where \(T\) is the period, is obtained as

\[
A(t) = \begin{bmatrix}
u_1(t) & u_2(t) & u_3(t) \\
v_1(t) & v_2(t) & v_3(t) \\
w_1(t) & w_2(t) & w_3(t)
\end{bmatrix}
\]

where

\[
130
\]
\[
\begin{align*}
\mathbf{u}_1(t) &= e^{\int_{\delta_5}^{t} \mu g(x_h^*) - d_1 - \sigma_1 + \frac{\sigma_2}{(1+F)^2} d\rho} \left[ \int_0^t e^{-\int_0^\rho \mu g(x_h^*) - d_1 - \sigma_1 + \frac{\sigma_2}{(1+F)^2} d\tau} \left( \mu g(x_f^*) + \frac{\sigma_2}{(1+F)^2} \right) v_1(\rho) d\rho + 1 \right] \\
\mathbf{u}_2(t) &= e^{\int_{\delta_5}^{t} \mu g(x_h^*) - d_1 - \sigma_1 + \frac{\sigma_2}{(1+F)^2} d\rho} \left[ \int_0^t e^{-\int_0^\rho \mu g(x_h^*) - d_1 - \sigma_1 + \frac{\sigma_2}{(1+F)^2} d\tau} \left( \mu g(x_f^*) + \frac{\sigma_2}{(1+F)^2} \right) v_2(\rho) d\rho \right] \\
\mathbf{u}_3(t) &= e^{\int_{\delta_5}^{t} \mu g(x_h^*) - d_1 - \sigma_1 + \frac{\sigma_2}{(1+F)^2} d\rho} \left[ \int_0^t e^{-\int_0^\rho \mu g(x_h^*) - d_1 - \sigma_1 + \frac{\sigma_2}{(1+F)^2} d\tau} \left( \mu g(x_f^*) + \frac{\sigma_2}{(1+F)^2} \right) v_3(\rho) d\rho \right] \\
\mathbf{v}_1(t) &= e^{-\int_{\delta_5}^{t} \frac{\sigma_2}{(1+F)^2} + p + d_2 + \delta_2 d\rho} \left[ \int_0^t e^{\int_0^\rho \frac{\sigma_2}{(1+F)^2} + p + d_2 + \delta_2 d\tau} \left( \sigma_1 - \frac{\sigma_2 F^2}{(1+F)^2} \right) u_1(\rho) d\rho \right] \\
\mathbf{v}_2(t) &= e^{-\int_{\delta_5}^{t} \frac{\sigma_2}{(1+F)^2} + p + d_2 + \delta_2 d\rho} \left[ \int_0^t e^{\int_0^\rho \frac{\sigma_2}{(1+F)^2} + p + d_2 + \delta_2 d\tau} \left( \sigma_1 - \frac{\sigma_2 F^2}{(1+F)^2} \right) u_2(\rho) d\rho + 1 \right] \\
\mathbf{v}_3(t) &= e^{-\int_{\delta_5}^{t} \frac{\sigma_2}{(1+F)^2} + p + d_2 + \delta_2 d\rho} \left[ \int_0^t e^{\int_0^\rho \frac{\sigma_2}{(1+F)^2} + p + d_2 + \delta_2 d\tau} \left( \sigma_1 - \frac{\sigma_2 F^2}{(1+F)^2} \right) u_3(\rho) d\rho \right] \\
\mathbf{w}_1(t) &= 0 \\
\mathbf{w}_2(t) &= 0 \\
\mathbf{w}_3(t) &= \int_{\delta_5}^{t} (r - \delta_5) d\rho
\end{align*}
\]
The transition matrix at $t = T$ is

$$C = A(T) = \begin{bmatrix}
u_1(T) & u_2(T) & u_3(T) \\
v_1(T) & v_2(T) & v_3(T) \\
0 & 0 & e^{\int_0^T (r-\delta_5)dt}
\end{bmatrix}.$$  

One eigenvalue of the matrix is

$$\lambda_1 = e^{\int_0^T (r-\delta_5)dt}.$$  

The remaining two eigenvalues are the same as the eigenvalues of the Jacobian matrix of the bee-only model. Therefore the stability of $(x_h^*, x_f^*)$ carries over to the bee-mite model if $\int_0^T (r-\delta_5)dt \leq 0$. \hfill \Box

This result indicates that the mite infestation in a colony can be fought off if (i) the cumulative death rate of mites due to treatment is greater than or equal to their birth rate, and (ii) the periodic solution of the bee-only model is stable. The mite-free equilibrium is always unstable in the absence of varroacide treatment, when $\delta_5 = 0$. That is, a mite invasion cannot be fought off by the bees alone as a consequence of the logistic growth assumption for mites. This generalizes the findings in [41] for the autonomous models presented there. If $(x_h^*, x_f^*, 0)$ is unstable, it is not clear whether the system will converge to the trivial state or whether, for example, an endemic periodic solution will be obtained in which the bee colony persists in the presence of mites. The simulations in [16, 41, 42] suggest the possibility of such an endemic periodic bee-mite solution for certain parameters. While in principle Floquet theory could be used to derive a stability condition for such a periodic solution, algebraic complexity prevented this. Instead, we study the system behavior through numerical simulations.
4.4.2 Numerical results

We perform simulation experiments to investigate how an increased loss of foragers due to homing failure affects the average total bee population in the hive. Following [20], we assume that the bees are exposed to treated crops in the environment for 30 days (i.e., $t = 5$ to $t = 35$) at the beginning of spring every year. The average bee population presented in Figure 4.4a is the average of the total bee population (hive bees and foragers) calculated over the last year of the simulation experiment. We vary the parameter $p$ from 0 to 1.5 and track the simulations for 20 years. As in [41, 42], we assume the parameters to be seasonally constant. The parameter values for $\beta_1, \ldots, 5, d_1, 3, \mu, \sigma_1, \gamma_1, \ldots, 3, r$ and $k$ are those listed in the Table 4.1. The parameter values for $d_2$ and $\sigma_1$ are assumed to be $[0.087318 \ 0.154 \ 0.087354 \ 0.020405]$ and $[0.14175 \ 0.25 \ 0.14175 \ 0.033125]$ for spring, summer, fall and winter respectively [26, 49].

We observe that in the case of a disease free colony (Figure 4.4a), as $p$ increases from 0 to a critical value of 1.02, the average population decreases from 40,000 to 35,000 bees. The decrease in average population is fast for small values of $p$ and then slows down as $p$ increases. After $p$ reaches the critical value ($p = 1.02$) the average bee population suddenly drops to zero and stays there for all higher values of $p$. When mites infest the colony and there is no varroacide treatment applied, the average bee population follows the same pattern as in case of the disease free colony but the population level is lower as compared to the disease free case. The average bee population starts from 35,200 and decreases to 31,820 as the parameter $p$ increases from 0 to 0.86. The population drops to 0 when the critical value $p = 0.86$ is reached. This critical $p$ value is lower than the critical value in the disease free case. This difference means that a lower forager mortality due to homing failure will result in collapse of a colony infested with mites.
We next investigate how the varroacide treatment affects the dynamics of the mites and virus infested colony. For this purpose, we follow the same treatment strategy as we did in [42]. We assume that the treatment is applied three times in the spring, 

\[
\delta_i(t) = \begin{cases} 
\delta_i, & \text{if } 30 \leq t < 31, 60 \leq t < 61, 90 \leq t < 91 \\
0, & \text{otherwise,}
\end{cases}
\]

where \( i = 1, \ldots, 5 \). Since there is no concerted data available for the parameters \( \delta_i \), we assume that the death rate of uninfected and infected bees due to treatment (i.e., \( \delta_1, \delta_2 \) and \( \delta_3 \)) is small as compared to their natural death rates (given in Table 4.1). Thus, we assume \( \delta_1 = \delta_2 = \delta_3 = 0.005 \). For the mite infested case in Figure 4.4a, the varroacide control \( \delta_5 \) is chosen strong enough (\( \delta_5 = 0.5 \) i.e., \( \delta_5(t) = 0.5 \) for \( t = 30, 60, 90 \)) for the mites to be eradicated. Since there is no virus present in this case, the parameter \( \delta_4 \) is assumed to be 0. For the virus infested case in Figure 4.4a, we choose the varroacide control for virus free and virus carrying mites strong enough (\( \delta_4 = \delta_5 = 0.5 \) i.e., \( \delta_4(t) = \delta_5(t) = 0.5 \) for \( t = 30, 60, 90 \)) for the virus to be fought off so that colony survives.

When the colony infested with mites is treated with varroacides, the average population is maintained at a higher level as compared to the case without treatment. Also, it is important to note that the critical value of the parameter \( p \) is higher (i.e., \( p = 0.9 \)) than in the case when no varroacide treatment is applied. This means that a mite infested colony can support a higher forager mortality and maintain itself at a higher population level if a sufficient varroacide treatment is applied. When the colony is infested with mites and virus and a strong enough varroacide treatment is applied, the average bee population follows the same pattern and maintains exactly the same population level as in the case of a virus-free colony treated against mites. As an example, we present the temporal dynamics of the honeybee colony infested with mites and virus when the virus is fought off due to the application of varroacide treatment. We choose two values of the parameter \( p \), one below the
critical value \((p = 0.89)\) and one above the critical value \((p = 0.9)\). For \(p = 0.89\), the colony shows an oscillatory bee-mite pattern and survives as a properly working colony (Figure 4.4b). When \(p = 0.9\) (Figure 4.4c), the colony dies off immediately after it is exposed to the treated crops (i.e. during the first spring season). When the colony is infested with mites and virus and no varroacide treatment is applied, the colony usually dies off in the first season.

4.5 Summary and Conclusion

- Our model is a general framework that combines the existing bee-mite-virus models without division of labour and the models based on the division of labour but do not include disease infestation. In particular, our model allows us to study the interplay between increased forager loss and infestation of the colony with varroa mites and the Acute Bee Paralysis Virus. The combined model allows us to investigate scenarios where a disease leads to increased forager loss/mortality, or where external causes of forager loss/mortality (e.g. exposure to environmental pesticides) affect a disease infested honeybee colony. The models in [26, 28, 42] are special cases of our model under certain parameter conditions. For instance, our model can be reduced to the model in [26] if we assume that there is no disease present in the colony. Our model can be reduced to the model in [28] if we assume that there is no vector involved in the transmission of disease in the colony. The model in [42] can be obtained if we do not divide the bee population into hive bees and forager bees.

- Our simulations suggest that a disease free colony dies off if a threshold value of forager mortality due to homing failure is reached. The threshold value is lower in the case of a mite infestation that is not treated with varroacides.
Figure 4.4: (a) Comparison of average total bee population between a disease free colony, a colony infested with mites, a colony infested with mites but treated with varroacides and a colony infested with mites and virus but treated with varroacides by varying the forager mortality due to homing failure i.e., $p$ from 0 to 1.5. The average total bee population is calculated at the final time (i.e., after $t = 20$ years). **Note that** the curve for the mite-infested but treated and the mite-virus infested but treated case overlap with each other. (b) Temporal dynamics of a colony infested with mites and virus where the virus is fought off due to the varroacide treatment when the forager mortality rate $p$ is 0.89. (c) Temporal dynamics of a colony infested with mites and virus where the virus is fought off due to the varroacide treatment and the forager mortality rate $p$ is 0.9.
In the presence of varroacide treatment, a mite infested colony can tolerate a higher forager mortality due to homing failure and maintain itself at a higher population level as compared to the case without varroacide treatment.

- In our model, the analysis suggests that the absence of varroacide treatment, the mite and virus free solution is always unstable; this result is in agreement with the results from [42]. This result means that the solution might converge to the trivial equilibrium or the endemic equilibrium, a possibility that is not known from the local analysis. Simulation experiments suggest that in a colony that is infested with only mites (no virus), the system converges to the endemic equilibrium if the forager mortality is below the critical value, and it converges to the trivial equilibrium if the forager mortality is above the critical value. The bee population level throughout the year is lower as compared to the bee population in the mite-free case. Simulation experiments also suggest that in the case of a colony infested with both mites and virus with no varroacide treatment applied, the colony is not able to fight off the virus and dies off. This result is in agreement with [42], and indicates that in the absence of varroacides, the additional feature added to the model (i.e., division of labor) does not affect the stability of the disease free equilibria.

- A disease free colony may survive as a properly working healthy colony for particular parameter values. Key parameters are forager mortality due to homing failure, recruitment rate of hive bees to foragers and social inhibition level. This result is in agreement with [26] in which a critical value of forager loss is calculated above which the colony fails, but below which the colony continues to function. It is not possible to calculate a criterion in our model because of the algebraic complexity involved.

- In order to understand the role of forager mortality due to homing failure in
a colony which is infested with disease, it is important to study the seasonal variations in colony dynamics. Seasonality is important because the dynamics of the disease infested colony may seem to be the same as the disease free colony in the first few years and then significantly different afterwards.

- Based on our model and its assumptions, our analysis suggests that the mite free equilibria can be stable if a sufficiently strong varroacide treatment is applied. This condition also appears in [42]. In order to fight off the virus, in addition to the application of a strong enough varroacide treatment, it is necessary that the virus carrying mites lose their virus at a rate which is higher than their maximum birth rate. This result is also observed in the simulation experiments.

**Bibliography**


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Chapter 5

A discrete-continuous modeling framework to study the role of swarming in a honeybee colony infested with Varroa destructor and Acute Bee Paralysis Virus

Abstract

In this paper, we present a general discrete-continuous modeling framework to study the effect of swarming on the dynamics of a honeybee colony infested with varroa mite and Acute Bee Paralysis Virus. Two scenarios are studied under which swarming takes place i.e., swarming due to congestion and swarming at fixed time intervals. For this purpose, we use an existing mathematical model in the literature. The dependent variables in the model are uninfected bees, infected bees, virus carrying mites and total mites that infest the colony. The model is studied in variable coefficients, in particular, step functions with each season as a constant in time. It
is observed that the percentage of healthy bees leaving with the swarm has a great impact on the strength and survival of the parent colony. A colony, that otherwise dies off due to virus, survives as a properly working colony if the percentage of the mites leaving the parent colony is above a critical value.

5.1 Introduction

A honeybee colony consists of a single reproductive queen, 20,000-60,000 adult workers, 10,000-30,000 individuals at brood stage (eggs, larvae and pupae), and several hundred drones. A large population of workers is needed to carry out the tasks of the bee colony, including cleaning, brood rearing, guarding the hive etc. In order to maintain a high reproduction level in the colony, the bees start preparing for swarming. Swarming is the natural method of reproduction of honeybee colonies. In the process of swarming, the original single colony reproduces to two or more colonies. During this event, almost 50 – 70% of the worker bees leave the parent colony with the queen (old mated queen in case of the first swarm) to a new site [3, 14]. The colony starts preparing for the swarm one month before the swarm is issued. Swarming normally takes place in mid-spring [14]. The timing of swarming varies with seasons and location of the hives. Since swarming affects pollination and honey production, it has an impact on agriculture and economy as well. The main symptom of swarming is the preparation of brood cups and queen rearing. The causes of swarming could be (i) large colony size, (ii) high proportion of young worker bees, (iii) reduced queen pheromone due to congestion, and (iv) abundance of pollen and nectar leading to congestion. There is a common cause behind all the symptoms i.e congestion in the colony.

When a swarm issues, the parasites present in the parent colony are divided among
the parent colony and the new colony formed after swarming [3]. This may reduce the disease infestation in the parent colony. We investigate the effect of swarming on the colony infested with a parasite *Varroa destructor* and Acute Bee Paralysis Virus. *Varroa destructor* is an ectoparasitic mite that not only feeds on the bees but also carries and transmits fatal viruses in the colony. The mite feeds on bees’ haemolymph by piercing their inter-segmental membrane and transmits the virus while feeding on them. When a virus carrying mite feeds on an infected bee, it releases the virus into the bee’s haemolymph. Thus, the uninfected bee becomes infected and mite becomes virus free. When a virus free mite feeds on an infected bee, it begins to carry virus. There are 20 bee viruses known so far, out of which atleast 14 viruses are reported to be associated with mites [8, 10]. These viruses have different routes of transmission and different levels of virulence. One of the most common virus is the Acute Bee Paralysis Virus. It has also been implicated in the colony losses [4, 8, 15]. The bees infected by this virus are unable to fly, loose their body hair and tremble uncontrollably. Unlike the Deformed Wing Virus, where brood infested with the virus develop into an adult sick bee, the brood infected with ABPV does not survive to the adult stage and dies immediately.

There have been several SIR-type mathematical models developed for honeybee-varroa mite-virus systems [2, 11, 12, 13]. There have also been models on some aspects of swarming such as the use of bee dance, design of nest selection and decision-making processes [1, 6, 9]. However, none of these models studied the combined effect of swarming and the varroa-virus infestation in a honeybee colony. In this paper, we provide a general framework of difference-differential equations to incorporate the process of swarming taking place as discrete events. We also use numerical simulations to study (i) swarming due to congestion (ii) swarming after a fixed time interval mimicking the natural death cycle of a queen bee. We vary the proportion of healthy bees leaving the parent colony and observe its effect.
on the dynamics of the colony. We numerically calculate a critical value of mites (leaving the parent colony) below which the parent colony dies off and above which it survives.

5.2 Model Equations

The underlying model of honeybee-varroa-ABPV disease dynamics [11] is:

\[
\frac{dm}{dt} = \beta_1 (M - m) \frac{y}{x + y} - \beta_2 m \frac{x}{x + y}, \quad (5.1)
\]
\[
\frac{dx}{dt} = \mu g(x) h(m) - \beta_3 m \frac{x}{x + y} - d_1 x - \gamma_1 M x, \quad (5.2)
\]
\[
\frac{dy}{dt} = \beta_3 m \frac{x}{x + y} - d_2 y - \gamma_2 M y, \quad (5.3)
\]
\[
\frac{dM}{dt} = r M \left(1 - \frac{M}{\alpha(x + y)}\right). \quad (5.4)
\]

The parameters are assumed to be non-negative. Because the size of the bee colony and the life span of bees vary drastically with the seasons, the parameters are assumed to be seasonally varying. In particular, we assume the parameters to be periodic functions of time with a period \(T\); in practice \(T = 1\) year.

The parameter \(\mu\) in (5.2) is the maximum birth rate, specified as the number of worker bees emerging as adults per day.

The function \(g(x)\) expresses that a sufficiently large number of healthy worker bees is required to care for the brood. We think of \(g(x)\) as a switch function. If \(x\) falls below a critical value, which may seasonally depend on time, essential work in the maintenance of the brood cannot be carried out anymore and no new bees are born. If \(x\) is above this value, the birth of bees is not hampered. Thus \(g(0, \cdot) = 0, \quad \frac{dg(0)}{dx} \geq 0, \lim_{x \to \infty} g(x) = 1\). A convenient formulation of such switch like behavior
is given by the Sigmoidal Hill function

\[ g(x) = \frac{x^n}{K^n + x^n} \]  \hspace{1cm} (5.5)

where the parameter \( K \) is the size of the bee colony at which the birth rate is half of the maximum possible rate and the integer exponent \( n > 1 \). If \( K = 0 \) is chosen, then the bee birth terms of the original model in [13] is recovered. Then the brood is always reared at maximum capacity, independent of the actual bee population size, because \( g(x) \equiv 1 \).

The function \( h(m) \) in (5.2) indicates that the birth rate is affected by the presence of mites that carry the virus. This is in particular important for viruses like ABPV that kill infected pupae before they develop into bees. The function \( h(m) \) is assumed to decrease as \( m \) increases, \( h(0) = 1, \frac{dh}{dm}(m) < 0 \) and \( \lim_{m \to \infty} h(m) = 0; \) [13] suggests that this is an exponential function \( h(m) \approx e^{-mk} \), where \( k \) is non-negative. We will use this expression in the computer simulations later on.

The parameter \( \beta_1 \) in (5.1) is the rate at which mites that do not carry the virus acquire it. The rate at which infected mites lose their virus to an uninfected host is \( \beta_2 \). The rate at which uninfected bees become infected is \( \beta_3 \), in bees per virus carrying mite and time.

Finally, \( d_1 \) and \( d_2 \) are the death rates for uninfected and infected honeybees. We can assume that infected bees live shorter than healthy bees, thus \( d_2 > d_1 \).

Equation (5.4) is a logistic growth model for varroa mites. By \( r \) we denote the maximum mite birth rate. The carrying capacity for the mites changes with the host population site, \( x + y \), and is characterized by the parameter \( \alpha \) which indicates how many mites can be sustained per bee on average. The parameters \( \gamma_{1,2} \) in the equations (5.2) and (5.3) represent the mortality rates of bees due to mites feeding on them.
Table 5.1: Seasonal averages of model parameters, derived from the data presented in the literature[5, 6, 11, 13]. The parameters included here are kept constant for all simulations; the values of the parameters that are varied are given in the text.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Spring</th>
<th>Summer</th>
<th>Autumn</th>
<th>Winter</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\beta_1$</td>
<td>0.1593</td>
<td>0.1460</td>
<td>0.1489</td>
<td>0.04226</td>
<td>[13]</td>
</tr>
<tr>
<td>$\beta_2$</td>
<td>0.04959</td>
<td>0.03721</td>
<td>0.04750</td>
<td>0.008460</td>
<td>[13]</td>
</tr>
<tr>
<td>$\beta_3$</td>
<td>0.1984</td>
<td>0.1460</td>
<td>0.1900</td>
<td>0.03384</td>
<td>[13]</td>
</tr>
<tr>
<td>$d_1$</td>
<td>0.02272</td>
<td>0.04</td>
<td>0.02272</td>
<td>0.005263</td>
<td>[13]</td>
</tr>
<tr>
<td>$d_2$</td>
<td>0.2</td>
<td>0.2</td>
<td>0.2</td>
<td>0.005300</td>
<td>[13]</td>
</tr>
<tr>
<td>$\mu$</td>
<td>500</td>
<td>1500</td>
<td>500</td>
<td>0</td>
<td>[13]</td>
</tr>
<tr>
<td>$k$</td>
<td>0.000075</td>
<td>0.00003125</td>
<td>0.000075</td>
<td>N/A</td>
<td>[13]</td>
</tr>
<tr>
<td>$K$</td>
<td>8000</td>
<td>12000</td>
<td>8000</td>
<td>6000</td>
<td>[11]</td>
</tr>
<tr>
<td>$r$</td>
<td>0.0165</td>
<td>0.0165</td>
<td>0.0045</td>
<td>0.0045</td>
<td>[5, 6]</td>
</tr>
<tr>
<td>$\gamma_1 = \gamma_2$</td>
<td>$10^{-7}$</td>
<td>$10^{-7}$</td>
<td>$10^{-7}$</td>
<td>$10^{-7}$</td>
<td>[11]</td>
</tr>
</tbody>
</table>
5.3 Mathematical Formulation of Discrete Interventions

We formulate the process of swarming as discrete interventions in a continuous system, thus creating a hybrid system. The discrete interventions \((t_i's)\) may depend on the time or the state variables. For instance, if we assume that swarming takes place after fixed time intervals i.e., mimicking the natural life cycle of a queen bee, the time at which discrete interventions takes place will be given \emph{a priori}. On the other hand, if we assume that swarming takes place due to overcrowding in the hive, the occurrence of discrete interventions will be state dependent.

The mathematical formulation in terms of hybrid dynamical systems is written

\[
\dot{z}(t) = f(t, z(t)), \quad t \in (t_i, t_{i+1}), \quad z(t_0) = z_0, \quad z(t_i) = X_i, \quad (5.6)
\]

\[
X_{i+1} = F(z_{i+1}), \quad \text{where} \quad z_{i+1} = \lim_{t \rightarrow t_{i+1}} z(t). \quad (5.7)
\]

Here \(t_i\) are the discrete times at which events take place and \(t_0 < \ldots < t_i < t_{i+1}\).

Also, \(z \in \mathbb{R}^4, f \in C^1[\mathbb{R} \times \mathbb{R}^4, \mathbb{R}^4], t \in \mathbb{R}^+, i \in \mathbb{N}, X \in \mathbb{R}^4, D \in \mathbb{R}^{4 \times 4}\).

In the case of swarming, we assume that \(F(X) = DX\).
Also, \( z = (m, x, y, M)^T \), \( f \) is the RHS of (5.1)-(5.4), and, \( X \) and \( D \) are given by

\[
X = \begin{bmatrix} m \\ x \\ y \\ M \end{bmatrix}, \quad D = \begin{bmatrix} a & 0 & 0 \\ 0 & b & 0 \\ 0 & 0 & 1 \\ 0 & 0 & a \end{bmatrix}.
\]

We assume that the infected bees do not leave the parent colony. We also assume that the percentage of total mites and virus carrying mites leaving the parent colony is the same. Thus, two new parameters \( a \) and \( b \) are introduced. The parameter \( a \) is the percentage of mites staying in the parent colony and the parameter \( b \) is the percentage of uninfected bees staying in the parent colony after the swarm leaves.

### 5.4 Computer Simulations

In the simulation experiments, we study the process of swarming taking place due to overcrowding in the hive and due to events like queen failure. We investigate how these two causes of swarming affect the strength and survival of the parent colony infested with mites and virus. In the case where swarming takes place due to overcrowding in the hive, discrete interventions take place when

\[
x(t) = cx^* \quad \text{where} \quad 0 < c \leq 1.
\]

(5.8)

The quantity \( x^* \) is calculated numerically by running the disease free model (without swarming) until the steady state is reached and then taking the maximum of the steady state solution over a two year period. For the simulation experiments, we fix \( c = 0.95 \). In the case where swarming takes place due to queen failure, the time at which discrete interventions \( (t_i's) \) take place are fixed \( a \text{ priori} \) as \( t_i = t_0 + i(\Delta t) \).
where $\Delta t = 2T$, $T = 365$ days and $i = 1, 2, \ldots$. We assume that $t_0 = 45$ i.e., swarming takes place in mid May [14].

The seasonal averages of the parameters $\beta_i(i = 1, \ldots, 3), r, d_1, d_2, k, K$ and $\mu$ are given in Table 5.1. Two sets of seasonal averages of the parameter $\alpha$, $[0.4784, 0.5, 0.5, 0.4784]$ and $[0.1 0.1 0.1 0.1]$, for spring, summer, fall and winter respectively, are used depending upon the cause of swarming under study (see [11] for the choice of these values). Lacking more detailed information about parameters, we use these values to construct piecewise constant time varying parameter functions, assuming four equally long seasons of 91.25 days[11]. In order to better present the simulation experiments better, we introduce two new variables $a_1 = 1 - a$ and $b_1 = 1 - b$. Here, $a_1$ is the proportion of mites leaving the parent colony and $b_1$ is the proportion of uninfected bees leaving the parent colony during swarming.

**Illustrative Simulation:**

The purpose of this simulation is to (i) show a typical simulation of the temporal dynamics of a honeybee colony infested with mites and virus (ii) compare the system with and without the process of swarming. In Figure 5.1a, we consider a honeybee-mite-virus system with no swarming taking place. We assume the lower value of the parameter $\alpha$ i.e., $[0.1 0.1 0.1 0.1]$ for spring, summer, fall and winter respectively, so that the colony fights off the virus but not the mites [11]. The uninfected bee population increases from 13350 in the beginning of spring and reaches its maximum of 31195 in the summer, decreases in the fall and reaches its minimum of 13350 in the winter. This pattern repeats annually. After an initial transient period of 2 years, the mites establish themselves in the colony and follow the same pattern as the bee population. In Figure 5.1b, we consider a honeybee colony infested with mites and virus where swarming takes place due to overcrowding i.e.,
swarming takes place if the bee population exceeds a certain threshold value \( x^* \) (see Equation 5.8). For this experiment, we assume that \( a_1 = 0.65 \) and \( b_1 = 0.5 \) which means 50% of the uninfected bees and 65% of the mites leave the parent colony during swarming. In Figure 5.1b, we assume the higher value of the parameter \( \alpha \) i.e., \([0.5 0.4784 0.4784 0.5]\) . We choose the parameters, \( a_1, b_1 \) and \( \alpha \), to present a reference case. The bee population follows the same pattern as in Figure 5.1a in the first year. In the second year, the population increases in the spring and summer and then swarming takes place when the bee population reaches the threshold value \( x^* \) which in this case is 31342. The population drops down from 29670 to 15207 bees during swarming and then increases to 23780 due to the model dynamics. The population starts decreasing again in the fall and winter and reaches its minimum of 13180. This pattern repeats itself annually. After a transient period of 1 year, the mite population also follows the same oscillatory behavior as the bee population.

**Simulation Experiment I:**

In this simulation experiment, we consider the case where swarming takes place due
to overcrowding. As in the simulation experiment I, we assume that swarming takes place if the bee population exceeds a certain threshold value, \( x^* \). We use the value of the parameter \( \alpha \) to be \([0.5 \ 0.4784 \ 0.4784 \ 0.5]\) for the spring, summer, fall and winter respectively. In Figure 5.2a, we compare a disease free colony, mite infested colony in which only 5% of the mites leave the parent colony \( (a_1 = 0.05) \), and, a mite infested colony in which 70% of the mites leave the parent colony \( (a_1 = 0.7) \).

We vary the percentage of healthy bees leaving the parent colony over \( 50 \% - 100\% \) which covers the range \((50 - 70\%)\) given in the literature \([3, 14]\) i.e., we vary \( b_1 \) from 0.5 to 1. In the case of the disease-free colony, the average population starts from 19000 and decreases gradually as the parameter \( b_1 \) increases. The average population suddenly drops down when \( b_1 = 0.87 \). In the case of the mite-infested colony with \( a_1 = 0.05 \), the average bee population starts at a lower level (i.e., at 18000) than in the disease-free case and decreases to 11000 bees as \( b_1 \) increases followed by a sudden drop to 0 when \( b_1 = 0.87 \). When \( a_1 = 0.7 \), the average bee population starts at 18500 which is in between the initial average population in the disease-free case and the case when \( a_1 = 0.05 \). The critical value for the percentage of bees leaving the parent colony is the same in all three cases. Figure 5.2b and Figure 5.2c show the effect of the percentage of uninfected bees leaving the parent colony \( (b_1) \) on the dynamics of the colony; we fix the parameter \( a_1 = 0.65 \). In Figure 5.2b, the colony fights of the virus and survives as a properly working colony when \( b_1 = 0.5 \). In Figure 5.2c, the colony dies off after 7000 days when \( b_1 = 0.6 \).

Figure 5.2d and Figure 5.2e show how the colony, that otherwise dies off due to virus, survives as a properly working colony if the percentage of mites leaving the parent colony is above a threshold value; we fix the parameter \( b_1 = 0.5 \). In Figure 5.2d, the colony dies off due to virus after 6600 days when \( a_1 = 0.64 \). Figure 5.2e shows that when \( a_1 = 0.65 \), the colony fights off the virus and works as a properly working colony.
Simulation Experiment II:

In this simulation experiment, we assume that swarming occurs at fixed time intervals of two years mimicking the natural death cycle of the queen bee. We assume that the swarm leaves the colony every two years in the mid of May [14]. We use the value of the parameter $\alpha$ to be $[0.1 \ 0.1 \ 0.1 \ 0.1]$ for the spring, summer, fall and winter respectively. In Figure 5.3a, we compare a disease free colony, mite infested colony with $a_1 = 0.05$ and, a mite infested colony with $a_1 = 0.7$. We investigate the effect of the percentage of bees leaving with the swarm ($b_1$) on the average population of the parent colony. The parameter $b_1$ is varied from 0.5 to 1. In case of the disease free colony, the average bee population starts from 21000 and remains constant when the parameter $b_1$ is varied from 50-76% and suddenly drops down to 0 when $b_1$ reaches 0.77. In case of the mite infested colony with $a_1 = 0.05$, the average bee population starts below the disease free population and remains constant until the parameter $b_1$ reaches 0.75 when it suddenly drops down to 0. In case of the mite infested colony where $a_1 = 0.7$, the average bee population starts at the same level as in case of $a_1 = 0.05$ and remains constant until $a_1$ reaches 0.76 and then it suddenly drops down to 0. It is interesting to note that the threshold value of the parameter $b_1$ is the maximum in case of the disease free colony which is followed by the mite infested case with $a_1 = 0.7$ which in turn is followed by the mite infested case with $a_1 = 0.05$.

Figure 5.3b and Figure 5.3c show the effect of the percentage of the uninfected bees leaving the parent colony ($b_1$) on the survival of the colony. The parameter $a_1$ is fixed to be 0.7. In Figure 5.3b, the colony fights off the virus and survives as a properly working colony when $b_1 = 0.76$. In Figure 5.3c, the colony dies off after 1000 days when $b_1 = 0.77$. Figure 5.3d and Figure 5.3e show how the
Figure 5.2: When swarming takes place due to overcrowding: (a) Effect of the percentage of the healthy bees leaving the parent colony on the average healthy bee population of the (i) disease free colony, (ii) mite infested colony with $a_1 = 0.05$, and (iii) mite infested colony with $a_1 = 0.7$. (b) The colony fights off the virus when $b_1 = 0.5$ and $a_1 = 0.65$. (c) The colony dies off after 7000 days when $b_1 = 0.6$ and $a_1 = 0.65$. (d) The colony dies off after 6600 days when $a_1 = 0.64$ and $b_1 = 0.5$. (e) The colony fights off the virus when $a_1 = 0.65$ and $b_1 = 0.5$. 

157
colony, that otherwise dies off due to virus, survives as a properly working colony if the parameter $a_1$ is above a threshold value. The parameter $b_1$ is fixed to be 0.5. In Figure 5.3d, the colony dies off due to virus after 6000 days when $a_1 = 0.91$. Figure 5.3e shows that when $a_1 = 0.92$, the colony fights off the virus and survives as a properly working colony.

5.5 Conclusion

- A general framework is provided to incorporate the discrete interventions into the model using a discrete-continuous model. This framework is applied to the process of swarming which involves two types of discrete interventions: (i) due to queen failure and, (ii) due to congestion.

- In case of a disease free colony and a mite-infested colony, a critical value of the percentage of bees leaving the colony plays an important role. The colony survives only if the percentage of bees leaving with the swarm is below this critical value.

- In our model, the percentage of virus carrying mites and virus free mites leaving the colony during swarming has a huge impact on the survival of the parent colony. In particular, a colony, that otherwise dies off due to virus, can survive if the percentage of mites leaving the parent colony is above a critical value.

- The critical value of the percentage of bees leaving the colony is lower in case of swarming due to congestion as compared to the case where swarming takes place after fixed intervals. This difference could be due to the fact that swarming due to congestion takes place every year, however, swarming after fixed intervals is basically every two years. The parent colony is able
Figure 5.3: When swarming takes place every two years: (a) Effect of the percentage of the healthy bees leaving the parent colony on the average healthy bee population of the colony that is (i) disease free, (ii) mite infested with $a_1 = 0.05$, and (iii) mite infested with $a_1 = 0.7$ (b) The colony fights off the virus when $b_1 = 0.76$ and $a_1 = 0.7$ (c) The colony dies off after 1000 days when $b_1 = 0.77$ and $a_1 = 0.7$ (d) The colony dies off after 6000 days when $a_1 = 0.91$ and $b_1 = 0.5$ (e) The colony fights off the virus when $a_1 = 0.92$ and $b_1 = 0.5$. 
to tolerate greater loss of bees because it gets longer time to establish itself before the next swarming event takes place.

Bibliography


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Chapter 6

Conclusion and Future Work

6.1 Research Findings

The objective of the thesis was to gain a good qualitative insight into the complex interaction between the honeybees and their diseases viz. varroa mites and viruses. The main findings of this thesis are as follows:

- The SIR modeling framework for infectious diseases can be adapted to describe mite vectored honeybee viruses and their effect on host colonies. It is important here to account for the seasonal variations in honeybee an mite biology, i.e. to consider non-autonomous models, to obtain a qualitative prediction of long-term effects. While we have carried out our work for the Acute Bee Paralysis Virus, in principle these modelling techniques should be applicable to other honeybee viruses as well.

- Floquet Theory is the usual technique to study such models with seasonal fluctuations that are represented by time-periodic parameters. In the case of honeybee-varroa-ABPV models this is possible only for some simple diseases free cases. Algebraic complexity prevents in particular a rigorous analytical treatment of the ecologically important scenario where varroa mites (not car-
rying viruses) establish themselves in a honeybee colony without bringing them to collapse. Therefore, numerical simulation is an important tool in the investigation of such systems. This requires the availability estimates for the model parameters.

- It is possible to combine traditional SIR-like models for honeybee diseases with a recently proposed model of honeybee colonies, in which a distinction between hive and forager worker bees is made. This becomes important, for example, to investigate scenarios where a disease leads to increased forager loss/mortality, or where external causes of forager loss/mortality (e.g. exposure to environmental pesticides) affect a diseases infested honeybee colony. Our results suggest that a disease infested colony which otherwise survives in the absence of forager loss, dies off if the forager mortality is taken into account. Also, a disease infested colony can tolerate a lower forager mortality and dies off faster as compared to a disease free colony.

- Our model simulations suggest that in particular the transition from Winter to Spring is critical for the survival of honeybee colonies. Since no new bees are born during Winter, this means by extension that the colony strength at the end of fall determines the fate of the colony. Our model implies that a mite and ABPV infested colony can sometimes work for several years properly but then fail suddenly. During this initial transient time the colony strength decreases slightly this effect is not strong enough to be clearly noticeable and the level of virus infestation builds up which leads eventually to a breakdown of the colony. These observation seem in line with field observations and correspond to reports that varroa-ABPV infestations often manifest themselves in the form of Wintering Losses, e.g. as has been reported in Canada and Germany.
• Varroa mites are a mechanical vector for ABPV. A varroacide treatment, at some intermediate levels, even if it is not strong enough to completely eradicate the parasite, can keep the viral disease under control. Our model suggests that for the parameter ranges tested without such parasite control a mite and ABPV infested colony will eventually fail.

• We have also proposed a hybrid discrete-continuous modeling framework to describe discrete interventions and instantaneous occurring events in honeybee colonies. The underlying idea is to couple a discrete time scale with the continuous time-scale. Discrete events can occur at a priori determined time instances or the time of the event can be state dependent. We have illustrated this concept in an application to swarming, due to congestion or queen replacement, and its interplay with mite and ABPV infestation of the mother colony.

6.2 Future Work

Although our study yields a good qualitative insight into the progression of the bee diseases, one has to realize that there might be certain relevant effects that are yet to be taken into consideration. The various lines of research arising from this work, which should be pursued, are as follows:

• For the bee and the mite biology, the data is available only as seasonal averages. Moreover, the available data is just a default parameter set with inherent uncertainties due to geographical and ecological variations. To overcome these shortcomings and to study the model quantitatively, a thorough data set would be helpful.
• The complexity of the models allowed us to study mainly the stability of the disease free steady state of the systems. Whether the introduction of disease leads to extinction or endemic steady state is not known yet. The next step would be to perform a complete stability analysis of the models which is expected to be algebraically more involved.

• Throughout the thesis, it is assumed that the queen bee is always unaffected by mites and virus. One can think of incorporating the crucial event of queen failure into the model in terms of sudden discrete interventions and investigates how that changes the dynamics of the colony.

• In this thesis, it is assumed that each season is of equal length and each year is identical to the next i.e., the parameters are periodic without accounting for weather changes and for systematic changes of the environment (e.g. due to human development activities). It would be interesting to investigate the more realistic scenarios (e.g. longer Winter seasons) and study how bees survive and emerge the next Spring.

• We implemented the logistic growth model for the mite population because the mite population is limited by the brood population. However the logistic model also implicitly introduces the inability of the bees to fight off the mite population. It is suggested that a more detailed growth model which captures the essential features of mite population and its dependence on the host population, should be opted.

• This thesis focusses on a particular bee virus, Acute Bee Paralysis Virus (ABPV); an obvious extension will be to apply this framework to other bee viruses like the Deformed Wing Virus, the Israel Acute Paralysis Virus, the Kashmir Bee Virus etc. Since different viruses have different biological characteristics (routes of transmission, virulence etc.), the extended models will
have their own challenges involved. For instance, unlike the ABPV, the brood infected with the DWV survives to the adult stage. To account for the brood population, another dependent variable would have to be introduced. Also, the varroa mite does not act as a mechanical vector for some other viruses i.e., it does not merely carry the virus, the virus may also replicate within the mite’s body. These added characteristics are expected to make the models algebraically and numerically more challenging but worthwhile exploring.

- Our results from Chapter 3 suggest that annual cumulative efficacy of varroacide treatment is more important than the particular time course of treatment, continuous low dosage application of chemical or biological control agents might be possible. This suggests that it might be worthwhile to explore continuous, low maintenance, less invasive, dispensing techniques as an alternative to current invasive treatment methods that might contribute to cross-contamination between colonies in an apiary.

- One of the routes of viral infection to enter the hive is via food brought by the forager bees. Since we have developed a model to account for the foragers, it will be easier incorporate the food contamination into the model. There are existing models on the division of labor and the availability of food in the hive. There are also models that study division of labor and a hypothetical bee infection brought into the hive by foragers. None of the models study division of labor and availability of food and take into account specific diseases simultaneously. The interplay of all these factors would be very interesting to explore.

- We studied the combined effect of forager loss and the mite-ABPV infestation where forager loss could occur due to any reason. Another important extension will be to study the interplay of forager loss specifically due to
neonicotinoid exposure and disease. The disease can be *Nosema spp.* or the viral diseases (e.g., Deformed Wing Virus, Israel Acute Paralysis Virus). The model will be cast in the framework of Ordinary Differential Equations and studied with a blend of analytical and computational techniques.

- In Chapter 5, a general formulation of the discrete-continuous model is presented. It is suggested to perform the complete mathematical analysis of the hybrid model and to implement and study the model numerically as well. Moreover, an additional equation for the brood population should be added to the model for the better understanding of the process of swarming particularly if we consider congestion or lack of ventilation to be the cause of swarming.

- This thesis studies the dynamics within an isolated hive without any interference from other hives e.g., the migration of bee and mites from one hive to the other. It will be interesting to study the interaction between various colonies in an apiary. In order to capture the spacial effects i.e., exchange of bees and mites between hives, one can formulate the model using meta-population models.