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Chronic Wasting Disease:
The Effects of Environmental Prion Density and Interactions Between Populations on Disease Dynamics

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Abstract

Chronic wasting disease (CWD) is a degenerative and fatal prion disease affecting cervid (deer and elk) populations in North America. While the disease exists in captive herds throughout the western United States and southern Canada, the only free-ranging populations afflicted are in northern Colorado, southeastern Wyoming, and the western panhandle of Nebraska. CWD, similar to other prion diseases such as scrapie in sheep, bovine spongiform encephalopathy in cattle, and Creutzfeldt-Jacob disease in humans, attacks the central nervous system via an accumulation of abnormal prion proteins.

For this investigation, we use both analytical and computational approaches to model the dynamics of the disease in mule deer populations. We focus on modifying the structure of an existing model by integrating sources of infection previously excluded. We proceed to model the effects of two interacting populations and the subsequent impact on disease dynamics. We hope that our analysis and simulations will help in the development of spatial models to be used in CWD management, a central goal of wildlife management agencies.

1 Introduction

1.1 Disease Background

Chronic wasting disease (CWD) belongs to a class of diseases known as transmissible spongiform encephalopathies (TSEs). More specifically, CWD is a degenerative and fatal prion disease afflicting cervid (deer and elk) populations in North America. CWD is similar to other prion diseases, such as scrapie in sheep and goats, bovine spongiform encephalopathy in cattle, and kuru and Creutzfeldt-Jacob disease in humans, as it affects the central nervous system via an accumulation of abnormal prion proteins. These abnormal prions are resistant to degradation by proteases, the enzymes responsible for catalyzing protein breakdown. The accumulation of prions results in reduced neurological function that leads to a lack of coordination, weakness, fatigue, excessive salivation, emaciation, and invariably death.[1]

While the disease exists in captive herds throughout the western United States and southern Canada, the only free-ranging populations afflicted are in northern Colorado, southeastern Wyoming, and the western panhandle of Nebraska. CWD was first recognized in free-ranging cervids in 1981, but the origin of the causative agent is unknown [7]. Thus far, the disease has been observed in mule deer, white-tailed deer, and elk. There is uniform transmission of the disease within a species irrespective of age and sex, although CWD is more prevalent in deer species than in elk. In epidemic areas, prevalence among the two deer species is as high as 11% versus 1% for elk.[5]

1.2 Epidemiology of CWD in Mule Deer

Chronic wasting disease is a progressive disease that advances as the prion proteins accumulate in the nervous system. Individuals typically have the infection for 18-36 months, during which there is an initial period that is asymptomatic and likely not infectious. As the disease progresses and prions accumulate, individuals likely become increasingly infectious as more prions are shed from the lymph system via mucous membranes. The time from onset of symptoms to death ranges from 2 weeks to 8 months.[7, 10]

Many aspects of the epidemiology of this disease are poorly understood. It is unclear as to whether or not the current population is at equilibrium or whether the population is experiencing an epidemic, although the latter seems more probable. While relatively little is known about the way in which the disease is spread among individuals, the agent is very likely transferred through exposure to the saliva, urine, feces, and/or carcasses of infected individuals via the alimentary canal. It has been estimated that less than 3.4% of cases result from maternal transmission, therefore it is assumed that the impact of vertical transmission on disease dynamics is negligible. Some sources suggest that infectious material is able to persist in the environment for significant periods of time, which would certainly complicate disease management

in wild populations. [7, 5, 6]

1.3 Existing Chronic Wasting Disease Models

Researchers and wildlife management agencies have employed mathematical models and computational techniques to learn more about the dynamics of chronic wasting disease in cervid populations. Two of these models come from Gross and Miller and from Miller et al (2000), and each will be introduced here briefly to provide familiarity with the models that have been constructed thus far.

Gross and Miller developed an individual-based model that tracked the sex, age, and death of each individual. The stages of infection were also tracked for individuals. The model included annual recruitment, aging, natural death, population monitoring and harvesting. Density-dependent changes in the rates of recruitment or survival were not incorporated into the model, instead harvesting was used to regulate the population. Since it is unclear whether or not excreta and carcasses of infected individuals transmit the disease, these effects were not incorporated into the model. In this case, the model was able to simulate the currently observed conditions within the mule deer populations that have been studied in the Colorado-Wyoming study area. The model predicted that CWD prevalence would continue to increase in infected areas, with the spread of the disease only stopping once the deer populations were extinct. Indeed, no realistic parameter values were found that supported an endemic existence of the disease in the deer population.[3]

Miller et al constructed a discrete deterministic model for CWD, taking into consideration sex and age classes. Fixed survival rates were used and recruitment was not compensatory. The disease classes were divided into susceptible, infected-but-not-infectious, and infectious classes. For this model, their primary focus was to explore some basic assumptions about CWD and to estimate ranges of the different parameter values that resulted in plausible disease dynamics.[7]

In the above models, field data were available and used to estimate parameter values. Therefore, much of the work here employs parameter value ranges and dynamic results from these two earlier models. Hopefully we can show that a simpler disease model with similar parameter values can be used to generate disease dynamics similar to those generated by more complex models.

1.4 Research Goals & Objectives

The goals of our research are two-fold. The first goal is the establishment of a simple yet realistic disease model for CWD that incorporates the effects of infectious materials in the environment. The second goal is to study the effects of population

interactions on the disease dynamics within mule deer using a two-patch model.

The remainder of this paper consists of four sections. The second section in the paper introduces our first model where we explore the dynamics of the model and identify parameter values that result in realistic behavior of the system. The next section introduces the refined model and simulations to illustrate that it describes the desired behavior. The following section introduces the two-patch model and presents the results of the two-patch system and its dynamics. Lastly, our results are summarized in section 5.

2 Preliminary Model

2.1 Assumptions

While many of the epidemiological details of this disease have yet to be revealed, there is sufficient evidence for making simplifying assumptions that can be incorporated into a model of the disease [3, 6]. First, we assume that the progression of the disease can be considered in terms of susceptible, exposed, and infectious classes. In addition, all individuals are born into the susceptible class; and birth, death, and harvest rates are proportional to population size. Transmission is assumed to be strictly horizontal, from infectious individuals and/or infectious materials to susceptible individuals, with random-mixing within the population. We assume that infectious individuals produce infectious materials and carcasses that accumulate in the environment and lead to infection of susceptible individuals. Additionally, we assume that prion build up hastens the rate of movement of individuals from the exposed class to the infectious class. It is also assumed that there is homogeneity among ages and sexes within the population with respect to disease prevalence. Finally, there is no recovery from the disease once an individual is infected.

2.2 Model

From the sketch of the model (Figure 3), the system can be represented by the following set of ordinary differential equations (shown below). For details of the parameters, see Table 2.5

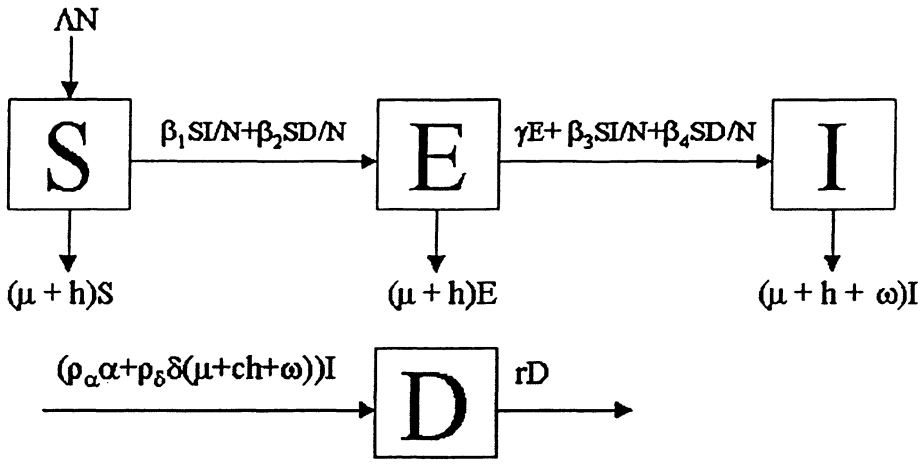

Figure 1: Diagram of the preliminary CWD model.

$$\begin{aligned}
\dot{S} &= \Lambda N - (\mu + h)\ S - \beta_1 \frac{S}{N} I - \beta_2 \frac{S}{N} D \\
\dot{E} &= \beta_1 \frac{S}{N} I + \beta_2 \frac{S}{N} D - (\mu + h + \gamma)\, E - \beta_3 \frac{E}{N} I - \beta_4 \frac{E}{N} D \\
\dot{I} &= \gamma E + \beta_3 \frac{E}{N} I + \beta_4 \frac{E}{N} D - (\mu + h + \omega)\, I \\
\dot{D} &= \rho_\alpha \alpha I + \rho_\delta \delta\, (\mu + ch + \omega)\, I - rD \\
\dot{N} &= \Lambda N - (\mu + h)\, N - \omega I
\end{aligned} \tag{1}$$

Due to the difficulties in obtaining useful analytical results for this model, we can assume constant population for certain analytical purposes, such as calculating R_0. The system can then be reduced to the following equations, where $s = \frac{S}{N}$, $i = \frac{I}{N}$, $e = \frac{E}{N}$, and $d = \frac{D}{N}$ with $s + e + i = 1$.

$$\begin{aligned}
\dot{s} &= \mu + h + \omega i - (\mu + h)\, s - \beta_1 si - \beta_2 sd \\
\dot{e} &= \beta_1 si + \beta_2 sd - (\mu + h + \gamma)\, e - \beta_3 ei - \beta_4 ed \\
\dot{i} &= \beta_3 ei + \beta_4 ed - (\mu + h + \omega)\, i + \gamma e \\
\dot{d} &= \rho_\alpha \alpha i + \rho_\delta \delta\, (\mu + ch + \omega)\, i - rd
\end{aligned}$$

2.3 R_0 Calculation From The Disease-Free Equilibrium

R_0 was calculated using the next generation operator approach for the constant-population model at the disease-free equilibrium (1,0,0,0) [2]. Thus, our model is put

in the form:

$$\vec{X} = [s],\ \vec{Y} = [e],\ \vec{Z} = [i, d]$$

where $m_{ij} \geq 0$ and $d_{ii} \geq 0$ and D is a diagonal matrix given by

$$M = \begin{bmatrix} \frac{\gamma\beta_1}{\mu+h+\gamma} & \frac{\beta_2\gamma}{\mu+h+\gamma} \\ \rho_\alpha\alpha + \rho_\delta\delta(\mu + ch + \omega) & 0 \end{bmatrix}$$

$$D = \begin{bmatrix} \mu + h + \omega & 0 \\ 0 & r \end{bmatrix}$$

It then follows that R_0 is given as the dominant eigenvalue of the matrix MD^{-1}, thus

$$R_0 \equiv \frac{1}{2}\left(\beta_1\frac{\gamma}{\mu+h+\gamma}\frac{1}{\mu+h+\omega} + \sqrt{\left(\beta_1\frac{\gamma}{\mu+h+\gamma}\frac{1}{\mu+h+\omega}\right)^2 + 4\beta_2\frac{\rho_\alpha\alpha+\rho_\delta\delta(\mu+ch+\omega)}{r}\frac{\gamma}{\mu+h+\gamma}\frac{1}{\mu+h+\omega}}\right)$$

While the next generation operator method does give the proper boundary condition for the stability of the disease-free equilibrium, the form of this threshold may not be in the form of R_0. However, this form of the threshold does make biological sense as R_0. In Table 2.3, the terms in the above representation of R_0 are interpreted.

Term	*Interpretation*
$\frac{\gamma}{\mu+h+\gamma}$	Proportion of infected individuals who become infectious
$\frac{1}{\mu+h+\omega}$	Average time spent in infective state
β_1	Rate of infections per infected individual
β_2	Rate of infections per unit of infectious material
$\frac{\rho_\alpha\alpha+\rho_\delta\delta(\mu+ch+\omega)}{r}$	Amount per area of infectious material produced per infectious individual

Table 1. Interpretation of terms in R_0 expression.

It should be mentioned again that this definition for R_0 comes from the analysis of the disease-free equilibrium where constant population is assumed. Given that the population is currently increasing in the low-density areas where the disease is present [4], this basic reproductive number should only be considered as a close approximation.

2.4 Endemic Equilibrium

$$\begin{aligned} i_\infty &= \frac{B \pm \sqrt{B^2 + 4AC}}{2A} \\ s_\infty &= \frac{\mu + h + \omega i_\infty}{\mu + h + (\beta_1 + \beta_2\frac{\alpha+\delta(\mu+ch+\omega)}{r})i_\infty} i_\infty \\ e_\infty &= \frac{\mu + h + \omega}{\gamma + (\beta_3 + \beta_4\frac{\alpha+\delta(\mu+ch+\omega)}{r})i_\infty} i_\infty \\ d_\infty &= \frac{\alpha + \delta(\mu + ch + \omega)}{r} i_\infty \end{aligned}$$

where,

$$
\begin{aligned}
A &= (\mu+h)\left(\beta_1+\beta_2\frac{\rho_\alpha\alpha+\rho_\delta\delta(\mu+ch+\omega)}{r}\right)\left(\beta_3+\beta_4\frac{\rho_\alpha\alpha+\rho_\delta\delta(\mu+ch+\omega)}{r}\right)\\
B &= \left(\beta_1+\beta_2\frac{\rho_\alpha\alpha+\rho_\delta\delta(\mu+ch+\omega)}{r}-\mu-h\right)\left(\beta_3+\beta_4\frac{\rho_\alpha\alpha+\rho_\delta\delta(\mu+ch+\omega)}{r}\right)(\mu+h)\\
&\quad+(\omega\gamma-(\mu+h+\omega)(\mu+h+\gamma))\left(\beta_1+\beta_2\frac{\rho_\alpha\alpha+\rho_\delta\delta(\mu+ch+\omega)}{r}\right)\\
C &= \left(\left(\beta_1+\beta_2\frac{\rho_\alpha\alpha+\rho_\delta\delta(\mu+ch+\omega)}{r}\right)\gamma-(\mu+h+\omega)(\mu+h+\gamma)\right)(\mu+h)
\end{aligned}
\tag{2}
$$

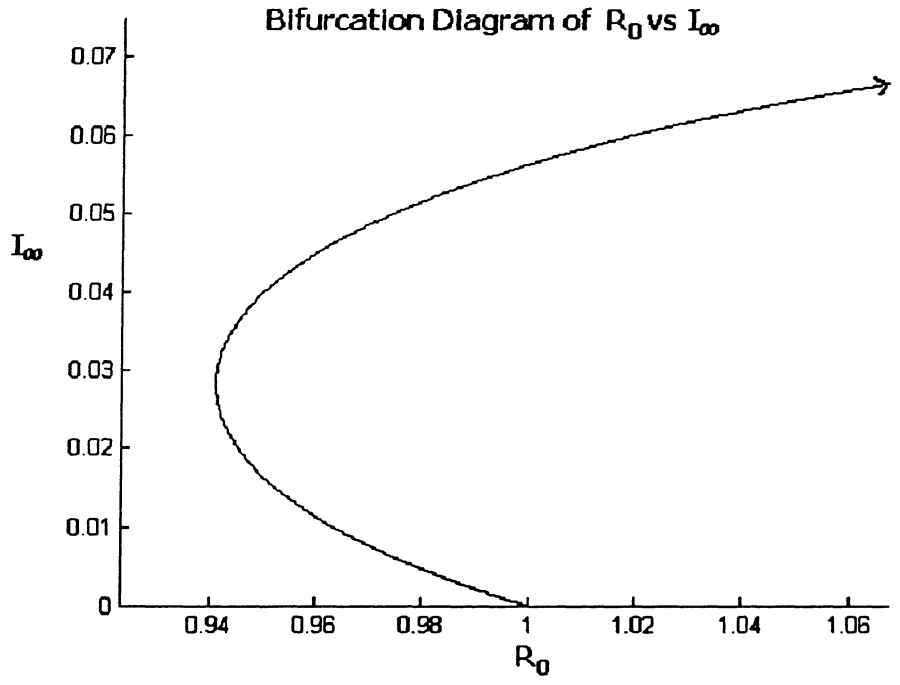

Figure 2: Bifurcation graph illustrating the backwards bifurcation.

There are two endemic equilibria in our model. There is a backward bifurcation for certain parameter values (Figure); however, these parameter values are not biologically significant, some being two orders of magnitude greater than biologically reasonable estimates. For biologically significant parameter values we have a single positive endemic equilibrium (Figure). We did not perform further analysis of this bifurcation.

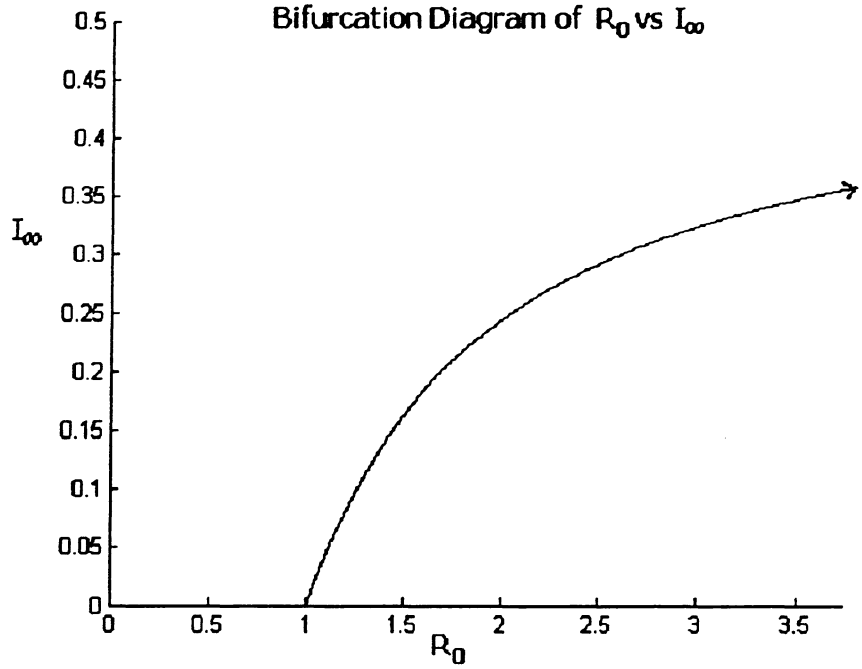

Figure 3: Bifurcation graph using realistic parameter values.

2.5 Parameter Estimation

To investigate the plausible range of parameter values for this model, literature values were used, when available. For parameter values that could not be estimated in this manner, reasonable estimates were made that fit the observed behavior of this disease and agreed with the results of the earlier CWD models.

Parameter	*Value*	*Description*	*Units*
Λ	0.57	Recruitment rate[3, 7]	$year^{-1}$
β_1	$1.8 - 2.2$	Annual infectious contacts per infectious individual	$year^{-1}$
β_2	$1 \cdot 10^{-2}$	Annual infectious contacts per infectious individual	$year^{-1}$
β_3	≤ 1	Annual infectious contacts per infectious individual	$year^{-1}$
β_4	$\leq 1 \cdot 10^{-2}$	Annual infectious contacts per infectious individual	$year^{-1}$
μ	0.2	Rate of death due to natural causes	$year^{-1}$
h	0.3687	Rate of death due to hunting	$year^{-1}$
ω	$.6 - 1.2$	Death rate due to disease[7]	$year^{-1}$
γ	$.7 - 1.3$	Rate of leaving the latent class and becoming infectious[3, 7]	$year^{-1}$
c	0.3	Proportion of hunted carcass left in the wild	-
r	0.4	Rate of infectious material removal from the environment	$year^{-1}$
α	3.79	Density of waste produced annually per individual[8, 9]	$g \cdot km^{-2} \cdot year^{-1}$
δ	0.47	Density of biomass per carcass[8, 9]	$g \cdot km^{-2}$
ρ_α	0.001	Amount of infectious material in waste	g^{-1}
ρ_δ	0.001	Amount of infectious material in carcasses	g^{-1}

Table 2. Parameters

Reported literature values for β were in the range (1, 1.5)[3]. For β_1, however, this range proved to be somewhat small. Changing $\beta_1$to a range of (1.5, 2) gave us more realistic disease dynamics. This discrepancy between infection rates is very likely the result of having such different models, with our model certainly being less complex.

Experimenting with different parameter values for ρ_α, ρ_δ, r, and β_2 yielded varied insights. While different densities of infectious material in the environment resulted in the expected changes in the disease dynamics, the system was most sensitive to the chosen value of β_2. Indeed, this would be an expected result in light of the notion that it is individual interactions that drive the disease, which might lead one to believe that $\beta_1 \gg \beta_2$. Therefore, a value roughly two orders of magnitude less than β_1 was chosen for β_2.

The constants α and δ are defined as the rates of production of excreta and carcass biomass per area per individual, respectively. These values were calculated from approximate values of food intake, body mass, and estimated home range size for mule deer.[8, 9] Given that deer have variable home-range sizes, the larger of the areas was used because the deer populations in the Colorado-Wyoming study area exist at relatively low densities. [4, 9]

Individual interactions are likely the primary force driving the spread of this disease throughout cervid populations [6]. Based on this assumption, computer simulations were done where values of ρ_α and ρ_δ were varied while fixing other parameter values.

Indeed, values that were used in our simulations vary from the literature values in some cases, however this is reasonable given the differences between our model and previous models.

2.6 Computer Simulations

Computer simulations using MatLab were used to further explore certain components of the preliminary model, the main objectives being to approximate parameter values, determine the importance of the $\beta_3 \frac{E}{N} I + \beta_4 ED$ terms, and to determine whether or not proportional growth and death was a satisfactory approximation for this model.

Figures 2, 3, and 4 show that overall population dynamics are not influenced significantly by the term $\beta_3 \frac{E}{N} I + \beta_4 \frac{E}{N} D$, which increases the rate of exposed individuals becoming infectious as they come into contact with more sources of infection. As the figures demonstrate, even a substantial change in β_3 and β_4 have little influence on the population dynamics. In addition, and perhaps more importantly, neither term appears in R_0. Given their relative unimportance to the disease dynamics, these

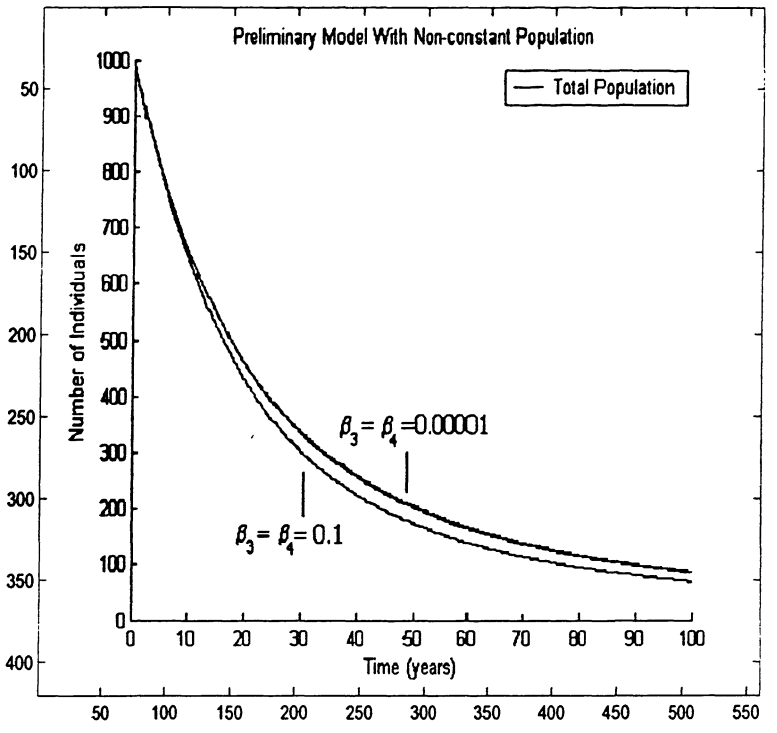

Figure 4: The effects of varying values of β_3 and β_4. Population size only.

terms may be omitted from the model without any significant effect, and are therefore dropped in our revised model. This of course makes sense, given that relatively large doses of prions would be needed to increase the present levels within an individual to any significant degree.

Figure 5 shows population growth or decline is very sensitive to birth and death rates in the population. A proportional recruitment rate is most reasonable given the reproductive capabilities of cervids, and therefore anything more than a proportional recruitment function seems unreasonable. Indeed, when a slightly more compensatory model is used the dynamics for the system become much more inclined to stabilize about some endemic equilibrium values which does not agree with current research. Therefore, in this case, proportional recruitment appears to be a better model for this process.

In practice, populations are regulated in part by variable harvesting in the form of hunting. For the model developed here, this process was not taken into account, but instead an average rate of h was used. While the resulting system dynamics were still within the realm of those observed in deer populations, a variable hunting rate as a function of prior population size may help to further improve the model.

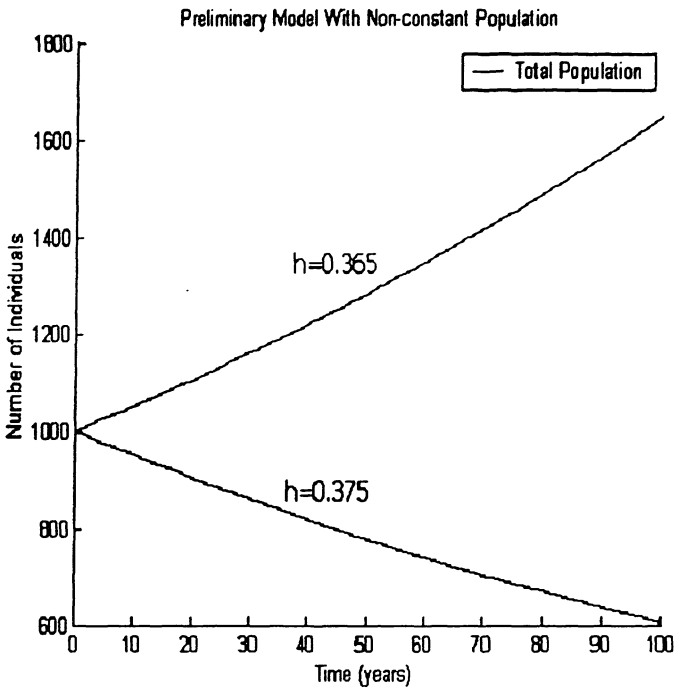

Figure 5: Population explosion for $h = 0.375$.

2.7 Preliminary Findings

The original model did not fulfill our expectations and was unable to correctly model the dynamics of the disease. It did let us find parameter values (listed in Table 2). The most important estimation that was achieved was the two-orders of magnitude difference between β_1(dee r-to-deer transmission) and β_2 (environment-to-deer transmission). The β_3 and β_4 terms were also found to not contribute to the dynamics of the disease and, therefore, can be dropped in future models.

The original model used the term D/N (density of prions in the environment per individual). This was an assumption to allow us to study a constant population model, and while it could be justified biologically it compromised the accuracy of the model. In light of the removal of the constant population model, this assumption is no longer needed and will be removed in further models.

The numerical analysis of the model (constant and non-constant population) showed that the constant-population assumption does not allow us to study the dynamics of the disease which result in extinction of the population.

3 The Revised Model

As a result of the computational analysis we removed the β_3 and β_4 terms as explained in 2.8. We also replaced the standard incidence terms for the interaction between susceptibles and infectious material with mass-action terms. Therefore, we have the following model.

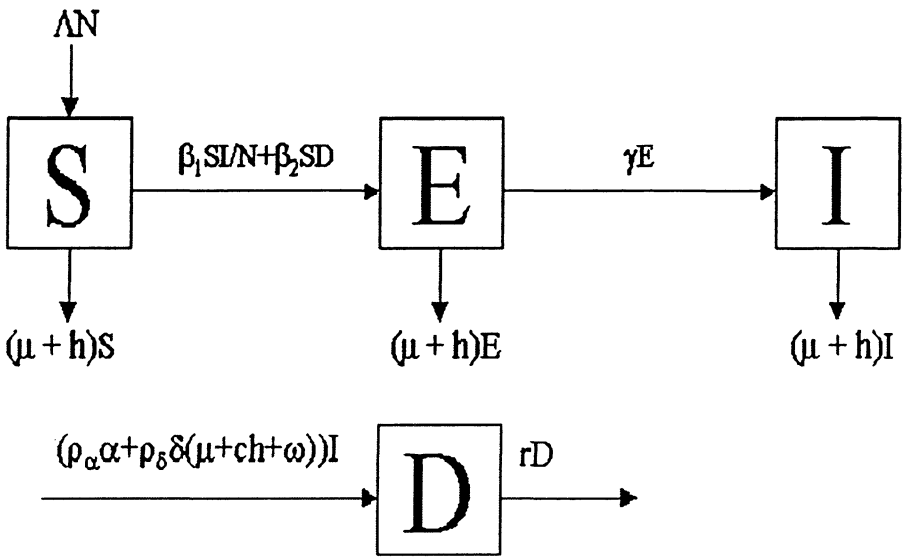

Figure 6: A diagram of the revised model.

$$
\begin{aligned}
\dot{S} &= \Lambda N - (\mu + h)\ S - \beta_1 \frac{S}{N} I - \beta_2 SD \\
\dot{E} &= \beta_1 \frac{S}{N} I + \beta_2 SD - (\mu + h + \gamma)\, E \\
\dot{I} &= \gamma E - (\mu + h + \omega)\, I \\
\dot{D} &= \rho_\alpha \alpha I + \rho_\delta \delta\, (\mu + ch + \omega)\, I - rD
\end{aligned}
$$

It should be noted here that for this model, the same parameter values were used (see Table 2).

3.1 R_0 Calculation From the Disease-Free Equilibrium

The revised model does not have a disease free-equilibrium for a non-constant population. Indeed, at (E,I,D)=(0,0,0) we find that

$$S(t) = e^{\Lambda - \mu - h}$$

This shows that the population will either grow exponentially or die out without the disease. As a result the model does not have a R_0 in the usual meaning of the term. However, under the assumption of a constant population we were able to obtain an R_0 using the next generation operator approach[2]. From this method, we find that R_0 is identical to the basic reproductive number in the first model.

$$R_0 \equiv \frac{\gamma\beta_1}{(\mu+h+\gamma)(\mu+h+\omega)} + \sqrt{\left(\frac{\gamma\beta_1}{(\mu+h+\gamma)(\mu+h+\omega)}\right)^2 - 4\frac{\gamma\beta_2(\rho_\alpha\alpha+\rho_\delta\delta(\mu+ch+\omega))}{r(\mu+h+\gamma)(\mu+h+\omega)}}$$

3.2 Endemic Equilibrium

Additionally, we were able to calculate the endemic equilibrium for a variable population:

$$\begin{aligned}
S_\infty &= \frac{\beta_1(\mu+h+\gamma)(\mu\omega(h+\mu+\omega)+\beta_1(\lambda-\mu-h-\omega))+\beta_1\lambda\omega}{\gamma\omega\beta_2\frac{\rho_\alpha\alpha+\rho_\delta\delta(\mu+ch+\omega)}{r}} \\
I_\infty &= \frac{(\lambda-\mu-h)(\omega\lambda\beta_1\gamma-(\mu+h+\gamma)(\mu+h+\omega)((\mu+h)\omega+\beta_1(\lambda-\mu-h)))}{((\lambda-\mu-h)(\mu+h+\omega)(\mu+h+\gamma)-\gamma\lambda\omega)\beta_2\omega\frac{\rho_\alpha\alpha+\rho_\delta\delta(\mu+ch+\omega)}{r}} \\
E_\infty &= \frac{(\mu+h+\omega)(\lambda-\mu-h)(\omega\lambda\beta_1\gamma-(\mu+h+\gamma)(\mu+h+\omega)((\mu+h)\omega+\beta_1(\lambda-\mu-h)))}{((\lambda-\mu-h)(\mu+h+\omega)(\mu+h+\gamma)-\gamma\lambda\omega)\beta_2\omega\gamma\frac{\rho_\alpha\alpha+\rho_\delta\delta(\mu+ch+\omega)}{r}} \\
D_\infty &= \frac{(\lambda-\mu-h)(\omega\lambda\beta_1\gamma-(\mu+h+\gamma)(\mu+h+\omega)((\mu+h)\omega+\beta_1(\lambda-\mu-h)))}{((\lambda-\mu-h)(\mu+h+\omega)(\mu+h+\gamma)-\gamma\lambda\omega)\beta_2\omega} \\
N_\infty &= \frac{(\omega\lambda\beta_1\gamma-(\mu+h+\gamma)(\mu+h+\omega)((\mu+h)\omega+\beta_1(\lambda-\mu-h)))}{((\lambda-\mu-h)(\mu+h+\omega)(\mu+h+\gamma)-\gamma\lambda\omega)\beta_2\frac{\rho_\alpha\alpha+\rho_\delta\delta(\mu+ch+\omega)}{r}}
\end{aligned} \tag{3}$$

Consider the case where $\Lambda < \mu + h$. Observe that $N_\infty = I_\infty\frac{\omega}{\Lambda-\mu-h}$. Therefore, in this case I_∞ and N_∞ would have opposite signs. Biologically, it does not make sense to have negative population values, thus they will not be considered.
Now, let us consider the case where $\Lambda > \mu + h$. Then,

$$I_\infty,\ E_\infty,\ D_\infty,\ N_\infty > 0$$

which implies that

$$\frac{(\omega\lambda\beta_1\gamma-(\mu+h+\gamma)(\mu+h+\omega)((\mu+h)\omega+\beta_1(\lambda-\mu-h)))}{((\lambda-\mu-h)(\mu+h+\omega)(\mu+h+\gamma)-\gamma\lambda\omega)} > 0 \tag{4}$$

In order for this fraction to be greater than 0, it follows that both the numerator and denominator must have the same sign. For the case where both are positive, we have

$$(\omega\lambda\beta_1\gamma-(\mu+h+\gamma)(\mu+h+\omega)((\mu+h)\omega+\beta_1(\lambda-\mu-h))) > 0 \tag{5}$$
$$((\lambda-\mu-h)(\mu+h+\omega)(\mu+h+\gamma)-\gamma\lambda\omega) > 0 \tag{6}$$

We see that equation 5 implies that

$$(\mu+h+\gamma)(\mu+h+\omega)(\mu+h)\omega+\beta_1(\mu+h+\gamma)(\mu+h+\omega)(\lambda-\mu-h))<\omega\lambda\beta_1\gamma \quad (7)$$

From equation 6 we see that multiplying through by β_1 yields the inequality

$$\beta_1(\lambda-\mu-h)(\mu+h+\omega)(\mu+h+\gamma)>\beta_1\gamma\lambda\omega \quad (8)$$

Thus, from 7 and 8 it follows that

$$(\mu+h+\gamma)(\mu+h+\omega)(\mu+h)\omega+\beta_1(\mu+h+\gamma)(\mu+h+\omega)(\lambda-\mu-h))< \beta_1(\lambda-\mu-h)(\mu+h+\omega)(\mu+h+\gamma)$$

This implies that $(\mu+h+\gamma)(\mu+h+\omega)(\mu+h)\omega<0$ which is a contradiction. Thus, it follows that 5 and 6 must be negative. Therefore, we reach the following conditions for the endemic equilibrium:

$$\begin{aligned}&(\omega\lambda\beta_1\gamma-(\mu+h+\gamma)(\mu+h+\omega)((\mu+h)\omega+\beta_1(\lambda-\mu-h)))<0\\&((\lambda-\mu-h)(\mu+h+\omega)(\mu+h+\gamma)-\gamma\lambda\omega)<0\\&\Lambda>\mu+h\end{aligned}$$

These conditions are independant of each other, so none of them can be disregarded. Numerical analysis has shown that the equilibrium is locally stable and it is positive only if these conditions are met. (No further stability analysis was conducted at this time).

3.3 Computer Simulations

The main purpose of running simulations was to show that the model still behaves in accordance with the observed disease dynamics, given biologically-reasonable parameter values.

The growth rate of mule deer has been predicted at 6 % over 50 years without CWD. Figure 6 shows that this is indeed true for our parameter values. The behaviors of the disease after a 50-100 year period are not important since by then there would be changes in the deer population and/or their environment:

The influence of the environment on the disease is important when the disease is beginning in a population, however it is the deer-to-deer infections that drive the model. A lack of this would slow down the spread of the disease, but would not stop it, given realistic parameter values.

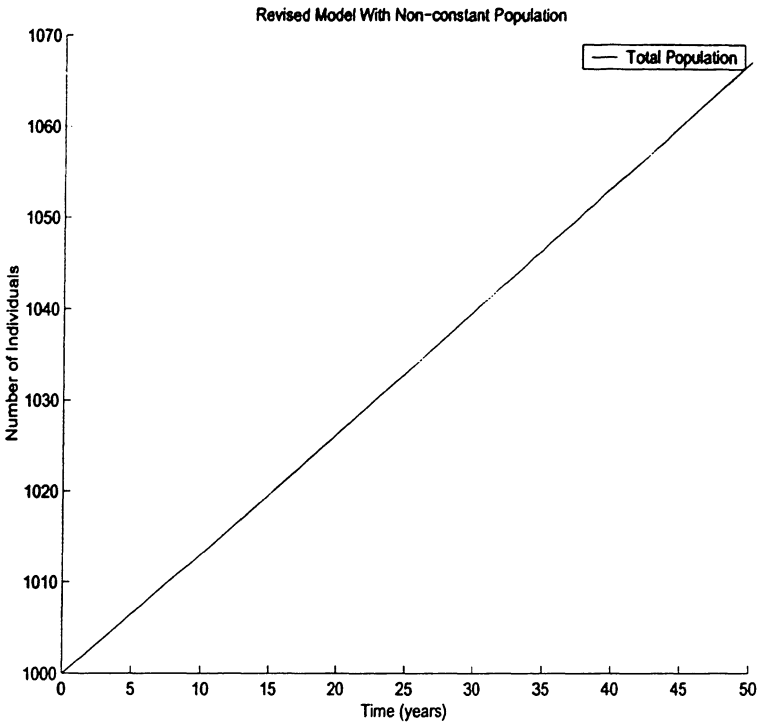

Figure 7: 6% population growth for $h = 0.3687$, $\mu = 0.2$, $\Lambda = 0.57$.

Figure 7 shows the population dying out within 50 years, which agrees with current, more complex models. The value of β has to be larger than current estimates to achieve this behavior, which may be due to the differences between this model and other models. In addition, other parameters may have been underestimated.

3.4 Preliminary Findings

The revised model was altered to further simplify the first model and more accurately model the chronic wasting disease. The β_3 and β_4 terms were discarded from the revised model and the standard incidence terms for interactions between individuals and the density of infectious material in the environment were replaced with mass-action terms. The population dies out in 25 to 40 years based on realistic parameter values, which agrees with other research. Having constructed a model that approximates the disease dynamics within a single given deer population reasonably well, the first aim of this investigation has been achieved.

4 The Two-Patch Model

We look at a two-patch model to simiulate two interacting deer populations. In this model, individual deer populations interact by two means. The first is from interactions between deer at the borders of the two populations. The second is through

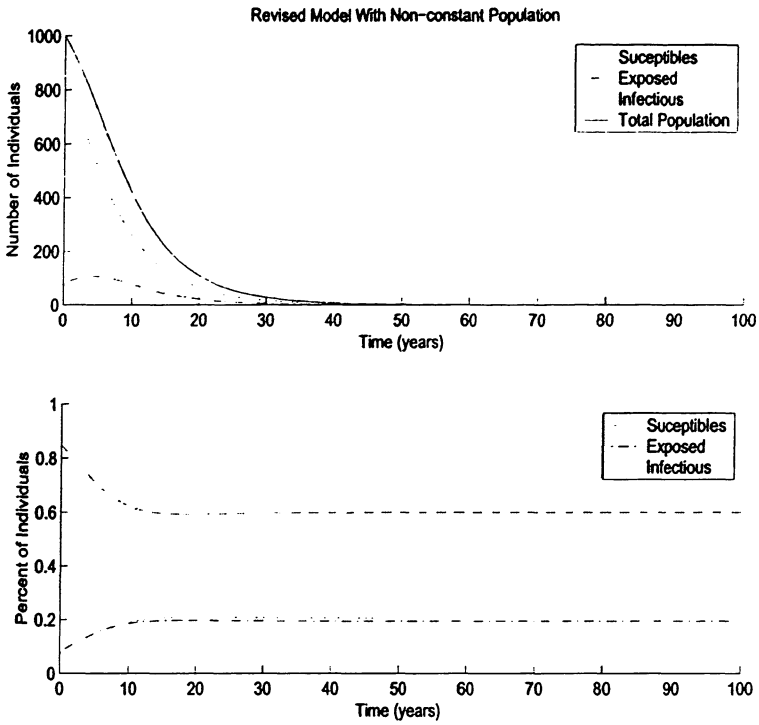

Figure 8: The population dies out within 25 to 40 years

the migration of deer between the two populations. We assume that the two populations have separate S, E, I, and D classes and that individuals from each of the three population classes migrate at the same rate (τ_1 and τ_2, respectively) regardless of their disease-state. We further assume that border interactions are dependent on the percentage of the adjacent population that is infected (I_2/N_2), the size of the susceptible population (S_1, and a force of infection for border interactions (β_3 and β_6). We also assume that both $\beta_3$and $\beta_6$are small given the relatively lower number of interactions between individuals in two different populations.

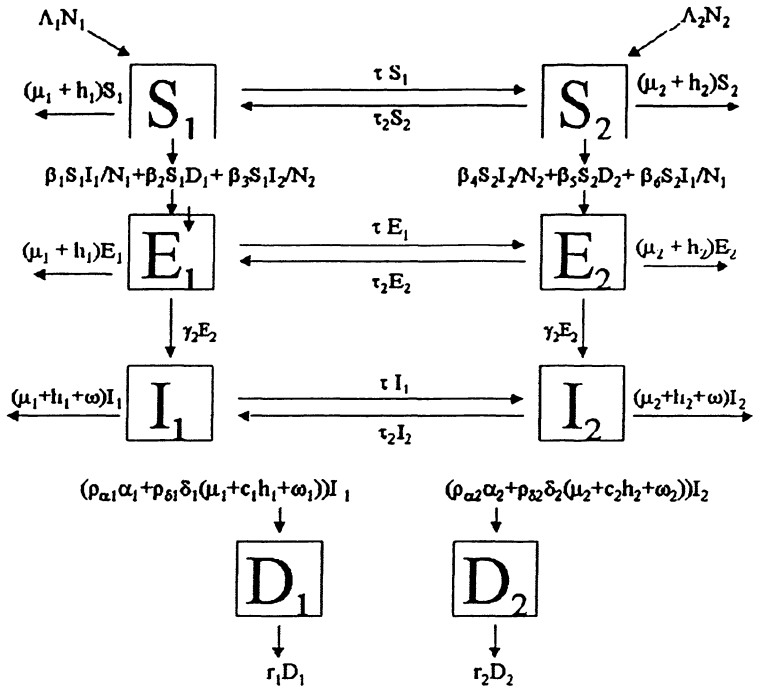

Figure 9: Diagram of the two-patch model.

$$
\begin{aligned}
\frac{dS_1}{dt} &= \Lambda_1 N_1 + \tau_2 S_2 - \left(\beta_1 \frac{I_1}{N_1} + \beta_2 D_1 + \mu_1 + h_1 + \tau_1 + \beta_3 \frac{I_2}{N_2}\right) S_1 \\
\frac{dE_1}{dt} &= \left(\beta_1 \frac{I_1}{N_1} + \beta_2 D_1 + \beta_3 \frac{I_2}{N_2}\right) S_1 + \tau_2 E_2 - (\mu_1 + h_1 + \gamma_1 + \tau_1) E_1 \\
\frac{dI_1}{dt} &= \gamma E_1 + \tau_2 I_2 - (\mu_1 + h_1 + \omega_1 + \tau_1) I_1 \\
\frac{dD_1}{dt} &= (\rho_{\alpha 1}\alpha_1 + \rho_{\delta 1}\delta_1(\mu_1 + c_1 h_1 + \omega_1)) I_1 - r_1 D_1 \\
\frac{dS_2}{dt} &= \Lambda_2 N_2 + \tau_1 S_1 - \left(\beta_4 \frac{I_2}{N_2} + \beta_5 D_1 + \beta_6 \frac{I_1}{N_1} + \mu_2 + h_2 + \tau_2\right) S_2 \\
\frac{dE_2}{dt} &= \left(\beta_4 \frac{I_2}{N_2} + \beta_5 D_1 + \beta_6 \frac{I_1}{N_1}\right) S_2 + \tau_1 E_1 - (\mu_2 + h_2 + \gamma_2 + \tau_2) E_2 \\
\frac{dI_2}{dt} &= \gamma_2 E_2 + \tau_1 I_1 - (\mu_2 + h_2 + \omega_2 + \tau_2) I_2 \\
\frac{dD_2}{dt} &= (\rho_{\alpha 2}\alpha_2 + \rho_{\delta 2}\delta_2(\mu_2 + c_2 h_2 + \omega_2)) I_2 - r_2 D_2
\end{aligned}
$$

The model does not have a disease-free equilibrium for a non-constant population and, as such, it does not have an R_0. In this case, no approximation was made to calculate R_0 for this model at the disease-free equilibrium.

The model appears to have a number of equilibria, however no further analytical search for equilibria was conducted at this time.

4.1 Parameters

As in the previous models, the same parameter values were used with the addition of the rates of migration (τ_i) and the infectious force between the two populations (β_3 and β_6).

Parm.	*Value*	*Description*	*Units*
Λ_i	0.57	Recruitment rate for patch i[3, 7]	$year^{-1}$
β_1	$1.8 - 2.2$	Annual infectious contacts per infectious individual in a population	$year^{-1}$
β_2	$1 \cdot 10^{-2}$	Annual infectious contacts per infectious material	$year^{-1}$
β_3	$1 \cdot 10^{-2}$	Annual infectious contacts per infectious individual between populations	$year^{-1}$
μ_i	0.2	Rate of death due to natural causes in patch i	$year^{-1}$
h_i	0.3687	Rate of death due to hunting in patch i	$year^{-1}$
ω_i	$.6 - 1.2$	Death rate due to disease in patch i[7]	$year^{-1}$
γ_i	$.7 - 1.3$	Rate of leaving the latent class and becoming infectious in patch i[3, 7]	$years^{-1}$
c_i	0.3	Proportion of hunted carcass left in the wild in patch i	——
r_i	0.4	Rate of infectious material removal from the environment in patch i	$year^{-1}$
α_i	3.79	Density of waste produced annually per individual in patch i[8, 9]	$g \cdot km^{-2} \cdot year^{-1}$
δ_i	0.47	Density of biomass per carcass in patch i[8, 9]	$g \cdot km^{-2}$
$\rho_{\alpha i}$	0.001	Amount of infectious material in waste in patch i	g^{-1}
$\rho_{\delta i}$	0.001	Amount of infectious material in carcasses in patch i	g^{-1}
τ_i	$0 - 0.2$	Annual rate of migration out of patch i	$year^{-1}$

Table 3. Parameters for two-patch model.

4.2 Computer Simulations

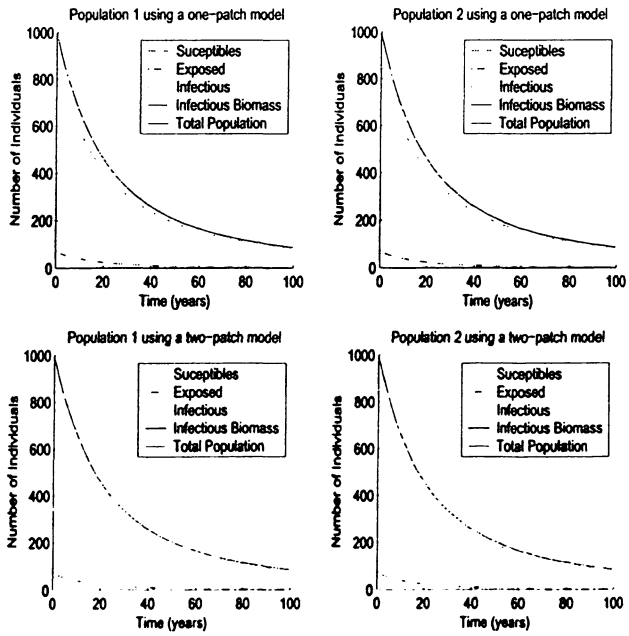

Figure 10: The two-patch model with each population having identical parameters yields no change in the disease progression.

Computer simulations using MatLab were run to further explore certain components of the model. The objectives were primarily to investigate the disease dynamics within a population with and without the interactions. The results are given for each population with both a one- and two-patch model. As can be seen in Figure 8, the top two graphs represent two separate individual populations, while the bottom two graphs are those same two populations after they are coupled via the two-patch model presented above.

Figure 10 illustrates the case where two populations exist in proximity to one another and one of the populations has the disease. In the disease-free population we see that interaction with the second population causes infection, resulting in the population quickly acquiring the disease. As a result, one could conjecture that the deer populations would die out around the same time in the adjacent area, even if the disease began later in some areas (the disease in the second area started causing population death 10 years later than the first one, however the population died out around the same time).

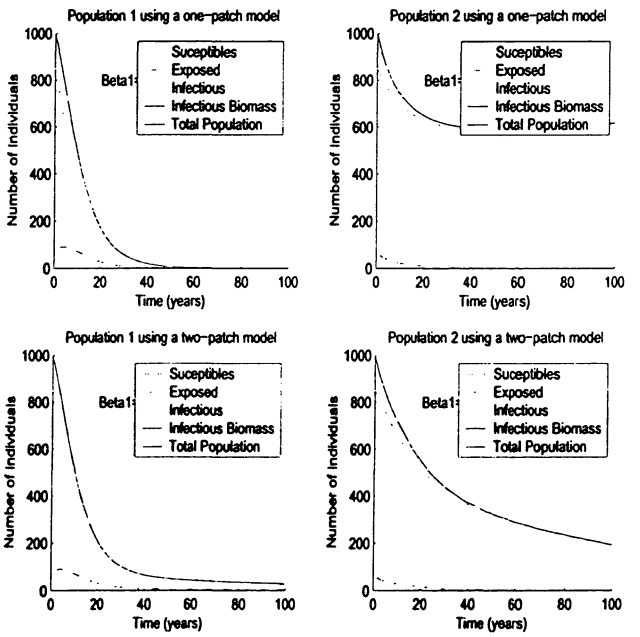

Figure 11: In a one-patch model the second population would survive, however due to the adjacent population with a higher infective force, both populations die out.

4.3 Preliminary Findings

The two-patch model adds a number of interesting dynamics to the population. Some of these dynamics show that the deer population may survive using a two-patch model

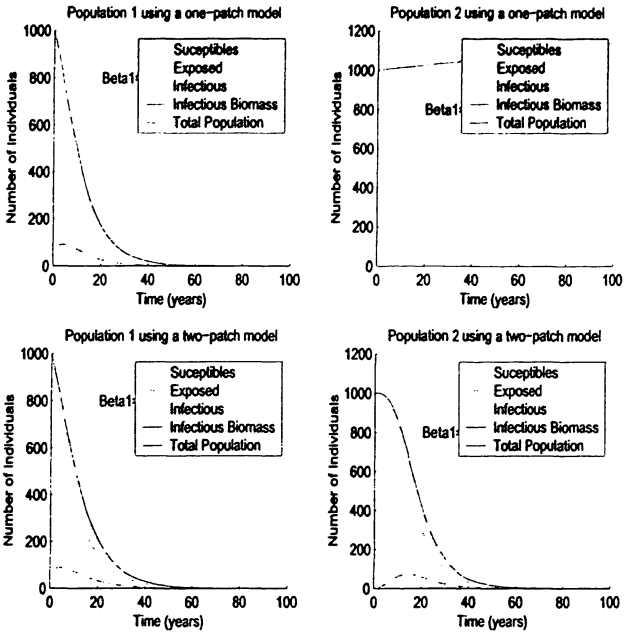

Figure 12: The infection of one population leads to a rapid infection of an adjacent population.

while not surviving as long with a one-patch model due to migration. Further computational analysis shows that endemic equilibria likely occur with a very low disease rate in some cases. Indeed, we see that in the case of two populations interacting, a patch which would survive alone may die off due to a adjacent patch which has the disease.

5 Summary

From this investigation, we were able to meet our two main goals. The first was to construct a reasonable yet simple model of chronic wasting disease in deer populations and to incorporate the effects of diseased material in the environment. The second was to investigate how two interacting populations of deer would effect the dynamics of the disease in each population.

In constructing a mathematical model of CWD the deer population was thought of as being divided into susceptible (S), exposed but not infectious (E), and infectious classes (I). In addition, the density of infectious material in the environment (D) produced by infectious individuals was also taken into account and incorporated into the model. This model was then studied and refined to yield our final disease model.

Following the construction of the disease model, two of these single-patch models were

coupled together via migration between populations and interaction at the border between populations. This two-patch model was then investigated using computational methods to gain some insight into the impact of population interactions on the dynamics of the disease in each population. It was observed that population interactions do little to increase the health of a population with the disease (i.e., decreasing the severity of the epidemic) for reasonable parameter values, but instead serve primarily to spread the disease from the population with the higher prevelance to the healthier population. While these results are preliminary and more analysis of this disease model should be done, this study serves to illustrate that a simple disease model of CWD can be used to obtain useful results.

6 Future Work

We are planning to look at the two-patch model more in-depth, including analytical analysis of the endemic equilibrium and stability analysis. In addition, numerical analysis should be performed on three- and four-patch models to see if there are any changes in the dynamics. For the one-patch model, analytical analysis and endemic quilibrium stability analysis require completion.
There are many aspects of the dynamics of chronic wasting disease that merit further attention. For example, multi-patch and spatial models, as well discrete or stochastic models could be studied. Additionally, interactions between different cervid species or models involving captive populations may be insightful. It may also be beneficial to include aspects such as seasonal birth and hunting, as well as age and gender structures. Hopefully, further research employing mathematical models will be utilized for investigating those measures proposed for controlling the spread of chronic wasting disease.

7 Acknowledgements

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A Appendix: MatLab Code

A.1 CallModel1.m

```
function CallModel1();
%This calls the CWD model with constant population and four betas using the
%parameters defined below

x0=[950 25 25 .1];      % Initial values of [S E I D]
tspan=100;              % Time Period to look at (time units are years)

% Parameter Values:
lambda=.57;              % Proportional birth rate
h=0.39;                 % Hunting death rate
r=.6;                    % rate of decay of infectious material
rhoa=.001;               % Density of infectious material in waste per gram per area
rhod=.001;               % Density of infectious material in carcass
beta1=0;                 % Infection rate of susceptible-environmen t interaction
beta2=.0;               % Infection rate of susceptible-infective interaction < 1.45
c=.1;                    % proportion of carcass left in field from hunt
gamma=1.15;              % 1/time spent in exposed class
omega=.65;               % Disease death rate (infecteds only)
mu=0.2;                  % Natural death rate
alpha=3.79;              % Infectious material made per I individual per year
delta=.47;               % Infectious material made per avg I death per year
beta3=.0;               % Rate at which increased contact with infectious individuals
                %speeds up travel into infectious class
beta4=.0;               % Rate at which increased contact with infectious material
                %speeds up travel into infectious class

[t,x]=ode45('Model1',ts pan,x0,[],lambda,beta1,beta2,beta3,beta4,mu, h,omega,gamma,
c,r,delta,alpha,rhoa,rh od);

%Population totals
hold on
plot(t,x(:,1),'--g');                    %Susceptible population
plot(t,x(:,2),'-.b');                    %Exposed population
plot(t,x(:,3),':r');                     %Infectious population
plot(t,x(:,1)+x(:,2)+x( :,3),'k');       %Total population

xlabel('Time (years)');
ylabel('Number of Individuals');
legend('Susceptible','E xposed','Infectious','Total  Population');
title(['Beta1 =',num2str(beta1),',Beta2 =',num2str(beta2),',Beta3  =',num2str(beta3),',Beta4
=',num2str(beta4),',lam bda-mu-h (effective reproduction number)=',n um2str(lambda-mu-h),'']);
hold off

%Population percentages
figure(2)
hold on
plot(t,x(:,1)./(x(:,1)+ x(:,2)+x(:,3)),'--g');      %Susceptible population percentage
plot(t,x(:,2)./(x(:,1)+ x(:,2)+x(:,3)),'-.');       %Exposed population percentage
plot(t,x(:,3)./(x(:,1)+ x(:,2)+x(:,3)),':r');       %Infectious population percentage
```

```
xlabel('Time (years)');
ylabel('Percent of Individuals');
legend('Susceptible','E xposed','Infectious');
title(['Beta1 =',num2str(beta1),',Beta2 =',num2str(beta2),',Beta3 =',num2str(beta3),',Beta4
=',num2str(beta4),',lam bda-mu-h (effective reproduction number)=',n um2str(lambda-mu-h),'']);
%title(['Lambda =',num2str(lambda),',Beta1 =',num2str(beta1),',Beta 2 =',num2str(beta2),',
Beta3 =',num2str(beta3) ,',Beta4=',num2str(beta4),',mu =',num2str(mu ),',h =',num2str(h),',
gamma =',num2str(gamma) ,',omega =',num2str(omega),',c=',num2str(c), ',r =',num2str(r),',alpha
=',num2str(alpha),',del ta =',num2str(delta),',rhoa =',num2str(rhoa) ,',rhod =',num2str(rhod),
'']);
hold off
```

A.2 CallModel2.m

```
function CallModel2();
%ecstasyode solves 'connecto' function (ODE system) and plots it...
%
%  Some param values...
%    cwdode(x0,tf,tspan ,v1,v2,v3,beta1,beta2,beta3,beta4,mu,h,omega ,gamma,c,r,delta,alpha,
lambda)
%    cwdode([400,0,1,0] ,50,100,1,2,3,1.1,.04,.3,.01,.1,.05,.69,1,.5 ,.1,.04,.05,.16)
% v1,v2,v3-if true (1) then Rc,q,Ro will be put in the title respectively.

x0=[850 75 75 .1];      % Initial values of [S E I D]
tspan=100;              % Time Period to look at (time units are years)

% Parameter Values:
lambda=.57;              % Proportional birth rate
h=0.3687;                % Hunting death rate
r=.4;                    % rate of decay of infectious material
rhoa=.001;               % Density of infectious material in waste per gram per area
rhod=.001;               % Density of infectious material in carcass
beta1=1.85;                 % Infection rate of susceptible-environ ment interaction
beta2=.01;               % Infection rate of susceptible-infective interaction < 1.45
c=.3;                    % proportion of carcass left in field from hunt
gamma=1.15;              % 1/time spent in exposed class
omega=.65;               % Disease death rate (infecteds only)
mu=0.2;                  % Natural death rate
alpha=3.79;              % Infectious material made per I individual per year
delta=.47;               % Infectious material made per avg I death per year

% Computationally solves system of differential equations
% with the above parameter values and initial conditions.
[t,x]=ode45('Model2',ts pan,x0,[],lambda,beta1,beta2,mu,h,omega,gamm a,c,r,delta,alpha,
rhoa,rhod);


%Population totals
subplot(211), hold on
plot(t,x(:,1),'--g');                  %Susceptible population
plot(t,x(:,2),'-.b');                  %Exposed population
plot(t,x(:,3),':r');                   %Infectious population
plot(t,x(:,.4),'.k');                   %Infectious population
plot(t,x(:,1)+x(:,2)+x( :,3),'k');      %Total population
```

```
xlabel(['Time (years) -','- Beta1 =',num2str(beta1)]);
ylabel('Number of Individuals');
legend('Susceptible','E xposed','Infectious','Total  Population');
title('Preliminary Model With Non-constant Population');
hold off

%Population percentages
subplot(212), hold on
plot(t,x(:,1)./(x(:,1)+ x(:,2)+x(:,3)),'--g');       %Susceptible population percentage
plot(t,x(:,2)./(x(:,1)+ x(:,2)+x(:,3)),'-.b');        %Exposed population percentage
plot(t,x(:,3)./(x(:,1)+ x(:,2)+x(:,3)),':r');        %Infectious population percentage

xlabel(['Time (years)']);
ylabel('Percent of Individuals');
legend('Susceptible','E xposed','Infectious');
%title(['Lambda =',num2str(lambda),',Beta1 =',num2str(beta1),',Beta 2 =',num2str(beta2),
',mu =',num2str(mu),',h =',num2str(h),',gamma =',num2str(gamma),',o mega =',num2str(omega)
,',c =',num2str(c),',r =',num2str(r),',alpha =',num2str(alpha),',de lta =',num2str(delta)
,',rhoa =',num2str(rhoa),',rhod =',num2str(rhod),'']);
hold off
```

A.3 CallModel3.m

```
function CallModel3();
%Calls the two patch CWD model and evaluates it for the parameters given below:

x0=[850 75 75 .1 850 75 75 .1];     % Initial values of [S E I D]
tspan=1000;                 % Time Period to look at.

% Parameter values for patch 1 deer:  (time units are years)
lambda=.57                  % Proportional birth rate
h=0.3687                    % Hunting death rate
r=.6                        % rate of decay of infectious material
rhod=.001                   % Density of infectious material in waste per gram per area
rhoa=.001                   % Density of infectious material in a carcass per area
beta1=1.85                     % Infection rate of susceptible-infectiv e interaction
betab1=.01                  % Infection rate of susceptible-infecti ous material interaction
betac1=.001                 % Infection rate of interactions with other patch
c=.1                        % proportion of carcass left in field from hunt
gamma=1.15                  % Rate of progression from exposed to infectious
omega=.65                   % Disease death rate (infecteds only)
mu=0.2                      % Natural death rate
tau=.01                    % Migration rate
alpha=2.53                  % Infectious material made per I individual per year
delta=.315                  % Infectious material made per avg I death per year

% Parameter values for patch 2 Deer:
lambda2=.57                 % Proportional birth rate
h2=0.3687                   % Hunting death rate
r2=1                       % rate of decay of infectious material
rhod2=.0001                  % Density of infectious material in waste per gram per area
rhoa2=.0001                  % Density of infectious material in a carcass per area
```

```
beta2=.5                    % Infection rate of susceptible-infective interaction
betab2=.01                  % Infection rate of susceptible-infecti ous material interaction
betac2=.001                 % Infection rate of interactions with other patch
c2=.1                       % proportion of carcass left in field from hunt
gamma2=1                  % Rate of progression from exposed to infectious
omega2=.5                   % Disease death rate (infecteds only)
mu2=0.2                     % Natural death rate
tau2=.01                    % Migration rate
alpha2=2.53                 % Infectious waste made per I individual per year
delta2=.315                 % Infectious material made per avg I death per year


[t,x]=ode45('Model3',ts pan,x0,[],beta1,betab1,betac1,mu,h,tau,omega ,gamma,c,r,delta,alpha,
lambda,rhoa,rhod,beta2, betab2,betac2,mu2,h2,tau2,omega2,gamma2,c2,r 2,delta2,alpha2,lambda2,
rhoa2,rhod2);

[tt,xx]=ode45('Model2', tspan,x0(1:4),[],lambda,beta1,betab1,mu,h,om ega,gamma,c,r,delta,alpha,
rhoa,rhod);
% Plot of patch one:

subplot (221);
hold on
plot(tt,xx(:,1),'--g');
plot(tt,xx(:,2),'-.b');
plot(tt,xx(:,3),':r');
plot(tt,xx(:,4),'k');
plot(tt,xx(:,1)+xx(:,2) +xx(:,3),'k');
hold off

xlabel('Time (years)');
ylabel('Number of Individuals');
legend('Susceptible','E xposed','Infectious','Infectious  Biomass','Total Population');
title('Population 1 using a one-patch model')%['Beta1 = ',num2str(b eta1),', Beta2 = ',
num2str(beta2),''']);

hold off
subplot (223);
hold on
plot(t,x(:,1),'--g');
plot(t,x(:,2),'-.b');
plot(t,x(:,3),':r');
plot(t,x(:,4),'k');
plot(t,x(:,1)+x(:,2)+x( :,3),'k');
hold off

% Title, legend and axis labels:
xlabel('Time (years)');
ylabel('Number of Individuals');
legend('Susceptible','E xposed','Infectious','Infectious  Biomass','Total Population');
title('Population 1 using a two-patch model')%['Beta1 = ',num2str(b eta1),', Beta2 = ',
num2str(beta2),''']);
hold off

[ttt,xxx]=ode45('Model2 ',tspan,x0(5:8),[],lambda2,beta2,betab2,mu2, h2,omega2,gamma2,c2,
```

```
r2,delta2,alpha2,rhoa2, rhod2);
% Plot of patch two:
subplot (222);
hold on
plot(ttt,xxx(:,1),'--g' );
plot(ttt,xxx(:,2),'-.b' );
plot(ttt,xxx(:,3),':r') ;
plot(ttt,xxx(:,4),'k');
plot(ttt,xxx(:,1)+xxx(: ,2)+xxx(:,3),'k');
hold off

xlabel('Time (years)');
ylabel('Number of Individuals');
legend('Susceptible','E xposed','Infectious','Infectious  Biomass','Total Population');
title('Population 2 using a one-patch model')
num2str(beta2),'']);
hold off

subplot (224);
hold on
plot(t,x(:,5),'--g');
plot(t,x(:,6),'-.b');
plot(t,x(:,7),':r');
plot(t,x(:,4),'k');
plot(t,x(:,5)+x(:,6)+x( :,7),'k');
hold off

% Title, legend and axis labels:
xlabel('Time (years)');
ylabel('Number of Individuals');
legend('Susceptible','E xposed','Infectious','Infectious  Biomass','Total Population');
title('Population 2 using a two-patch model')
num2str(beta2),'']);
hold off
```