Simulating Vaccination Control and Herd Immunity Threshold in EcoDemics

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Abstract: Modeling infectious diseases and exploring immunization interventions has been a major concern for the last century. Deadly pandemics transmitted from animals to humans such as SARS, rabies, H1N1 and the lack of extensive parameters in most of the epidemic simulations, imposes a great importance on simulating realistic ecosystems to study different aspects of epidemics and mitigation strategies. To this end, EcoDemics was built upon EcoSim to model epidemics in an evolutionary ecosystem simulation. Due to the high mitigation capacity and significance of the immunization intervention, we explore vaccination techniques with various time delays and population proportions. Based on the herd immunity theory, the whole population can be protected against a contagious disease by vaccination of a fraction of individuals. We investigate this principle in EcoDemics and compare our results with real epidemics data.

1 INTRODUCTION

Infectious pandemic diseases transmitted from animals to humans (zoonotic infections) such as SARS, rabies, and H1N1 have had a deadly effect throughout the world. Although the final number of infections, illnesses, and deaths could vary tremendously depending on the pandemic and other multiple factors, it is certain that without adequate planning and preparations, a pandemic in the 21st century has the potential to cause enough illnesses to overwhelm public health system at all levels.

During the last few decades, several models have been developed to explore mitigation strategies in the disease models. Tsunoda, et al. simulated the spread of influenza for exploring the most efficient mass vaccination strategies to prevent an epidemic (Tsunoda et al., 2011). In another study, the role of travel restrictions in delaying and ending the H1N1 pandemic has been explored (Bajardi et al., 2011). A large-scale epidemic simulation was used in (Ferguson et al., 2006) to examine intervention options in an influenza outbreak. Keeling, et al. modeled vaccination strategies against foot-and-mouth disease (Keeling et al., 2003). The roles of individual imitation behavior and population structure in vaccination were explored in (Fu et al., 2010) to control infectious diseases. In these models, however, many details of the progression of infection and individual behaviors are neglected. Additionally, either unrealistic mixed-populations have been assumed or the number of different subpopulation types is small.

On the hand, network analysis has been used as an explanatory tool to describe the evolution and spread of epidemics (Eubank et al., 2004), (Keeling and Eames, 2005), and (Meyers et al., 2005). Pourbohloul, et al. used contact network epidemiology to predict several control policies for a mildly contagious disease (Pourbohloul et al., 2005). However, all network-based simulations are limited by the fact that there is no simple way to ascertain the sensitivity of the epidemiological results to the details of the network structure. Other challenges also concern data collection, modeling dynamics in network connections and dealing with complexity of the models. A recent example of this problem exists in the spatial network model presented in (Kim et al., 2011) which focuses on the disease spread from the central point of a static vertices graph and fails to model the dynamics of the network structure.

This imposes a great importance on simulating realistic ecosystems to study the spread of diseases and control strategies. There are a number of evolutionary artificial life ecosystems, the most notable ones are Tierra (Ray, 1991), Avida (Adami, 1998), Echo (Harber, 1995), PolyWorld (Yaeger, 1993), Framsticks (FRAMSTICKS), and EcoSim (Gras et al., 2009). Among them, to our knowledge,

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the only one that integrated some notions of diseases diffusion is EcoSim. EcoDemics (Majdabadi Farahani et al., submitted) is built upon EcoSim to allow the study of the spread of an epidemic associated with mitigation strategies. EcoSim was first introduced and developed by Gras, et al. This powerful complex ecosystem simulation tries to gain knowledge about natural ecosystems by simulating intelligent adaptive agents interacting and evolving in a large and dynamic environment. The novelty of modeling disease in EcoDemics comes from the fact that each agent has a behavioral model which evolves during the simulation. Unlike classic disease models which assume a well-mixed static population or a uniform population with random movements, EcoDemics is based on a dynamic population with respect to both the number of births and deaths, as well as the migration of the individuals. These dynamic properties that affect the disease spread and mitigation strategy are emergent from the behavioral model of the agents.

The previously built framework gave us a rich ground, with more depth and details to study different epidemic outbreaks along with different strategies that control the spread. Due to the high mitigation capacity and significance of the immunization intervention in the literature of epidemiology, we explore vaccination technique with various scenarios in this paper. The rest of the paper is organized as follows. The next section is dedicated to a brief description of the EcoSim. We next present the disease model used in EcoDemics, followed by the vaccination and herd immunity explanation. The experiments and results will be discussed afterwards. We then conclude our work and discuss our future plans in the conclusion section.

2 AGENTS, BEHAVIOUR, AND ENVIRONMENT IN ECOSIM

The individuals (or agents) of this simulation are prey or predators acting in a simulated environment. Individuals act in a dynamic environment composed of 1000×1000 cells. Each cell may contain several individuals and some amount of food. Each individual possesses several physical characteristics such as: age, minimum age for breeding, speed, vision distance, possibility of disease, immunity, levels of energy, and amount of energy transmitted to the offspring. Energy is provided to individuals by the resources (food) they find in their environment. Prey consume grass, which is dynamic in quantity and location, whereas predators hunt prey individuals. An individual consumes some energy each time it performs an action. Each individual performs one unique action during a time step, based on its perception of the environment. Each agent possesses a Fuzzy Cognitive Map (FCM) to compute the next action (Kosko, 1986). In each FCM, three kinds of concepts are defined: sensitive (such as distance to foe or food, amount of energy, etc.), internal (fear, hunger, curiosity, satisfaction, etc.), and motor (evasion, socialization, exploration, breeding, etc.). The FCM of an individual, which also represents its genome, is transmitted to its offspring after being combined with the mate's genome and after the possible addition of some mutations. The behavior model of each individual is therefore unique.

For the study of disease we focus on patterns of epidemic outbreaks in prey as they have higher populations. The possible actions for prey are:

1. Evasion, which is in the opposite direction of the barycenter of the five closest predators within the prey's range of vision. The new position of the prey is computed using the speed of the prey.
2. Search for food, which is toward the closest food (grass) within the prey's range of vision.
3. Socialization, which is the direction toward the closest possible mate within the prey's range of vision.
4. Exploration, in which the individual moves at its speed in a random direction.
5. Resting, in which nothing happens.
6. Eating, which includes a change in the cell grass amount and also in the individual's energy and hunger levels.
7. Breeding: If the energy levels of two individuals in a same cell are more than a certain threshold, their two genomes are similar, and their both choices of action are breeding, then mating will occur.

The detailed explanations regarding individuals FCM and associated concepts along with the values for the initial parameters and actions can be found in (Gras et al., 2009).

Our simulation iterates through a loop such that every execution of the loop represents a single time step in which every individual makes a decision and performs an action. The parameters of the environment are updated at the end of each time step.

3 DISEASE MODEL AND VACCINATION IN ECODEMICS

EcoDemics (Farahani et al., submitted) applies a modified Susceptible-Infected-Removed (SIR) model of transmission disease. The EcoDemics strength is based on modeling a natural ecosystem with a predator-prey interaction. Individual based modeling, genome representation, and modeling birth, death, and evolution are all points making our system unique and more realistic. In this section we review briefly the disease model used in EcoDemics.

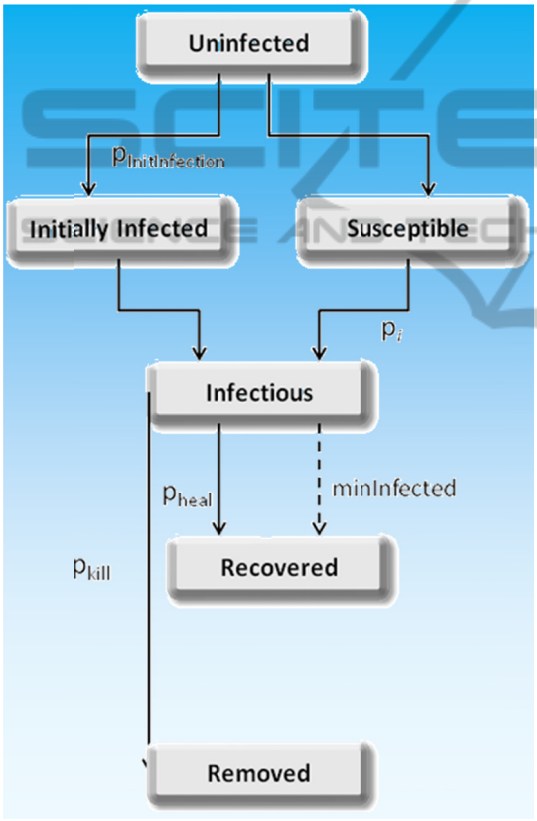

Figure 1: The disease model representing different states within host disease progression.

The disease starts in a user specified time step and not from the beginning of the simulation. This provides the system with a chance to stabilize and for species to group together, as at initialization the individuals are mostly uniformly distributed in the world. The initial location of the infection is set in a small window having 1/256 of the size of the world and prey are infected according to the probability $p_{InitInfection}$. Individuals subjected to the disease become infected based on a probability function presented later in equation (1). The infected individuals then enter different SIR disease stages; infected and then recovered based on the probabilities presented in Table 1. In addition, we set a minimum time (minInfected) for the individual to carry the disease before it is able to heal. Also, certain individuals are given immunity to disease according to the parameter p_{immune}.

Table 1: Probabilities of the disease model along with their description.

Name	Description
$p_{InitInfection}$	Probability of initially infecting an individual with the disease, which happens once in the simulation.
p_{immune}	Probability of the individual being immune to the disease.
p_{heal}	Probability of recovering from infection.
p_{kill}	Probability that describes an optional step that would kill the infected individual.

Infected individuals can spread the disease to other individuals in the same cell and the 8 closest adjacent cells. The interaction between individuals comes from the fact that individuals belonging to the same species tend to group together: individuals from the same prey species are not randomly distributed in the world but are spatially close to each other (Aspinal, and Gras, 2010). At each time step, the uninfected individuals have the possibility to be infected based on a probability function p_i introduced in (1):

$$p_i = \begin{cases} 0, & \sum s + \sum r = 0 \\ 1/\left(1 + \beta \exp\left(\alpha\left(2\sum s + \sum r - 1\right)\right)\right), & \sum s + \sum r \neq 0 \end{cases} \quad (1)$$

Where p_i is the probability of individual i being infected with the disease, s is the number of infected individuals in the same cell as i, and r represents the number of infected individuals in the adjacent cells.

The values of α and β are the parameters of the infection. We define two different values for α and β according to the age group of the individual. Middle-aged individuals are at low risk, while young and old-aged individuals are at greater risk of being infected.

At each time step some individuals recover based on the parameter p_{heal}, given that they have passed the minimum time to carry the disease (minInfected). This model is based on the SIR-type epidemic, which is characterized by the fact that recovered individuals will become immune. In addition, individuals would be subjected to death as a result of the disease based on p_{kill}. Figure 1

represents different states of disease progression.

The role of the predator-prey interaction and the significance of the behavioral model of each individual in forming the population, as well as its consequence on spreading the infection, have been highlighted in EcoDemics (Majdabadi Farahani, et al., submitted). Including a behavioural model to the population and the spatial distribution of the individuals in the environment, have led to a novel disease model that has shown reasonable concordance with real wildlife epidemics. Since the ultimate goal in any epidemiological modeling is to study possible control strategies that help mitigate the spread of diseases, three different control techniques have been implemented in the EcoDemics: vaccination, pharmaceutical interventions, and quarantine. The fact that vaccination control strategy has shown the highest mitigation rate among the three tested, has motivated us to further explore immunization control and verify the existence of the herd immunity threshold. We would like to see if the implementations regarding vaccination strategies lead to results conform to the ones observed in wildlife epidemics to confirm the interest of our approach for more in deep epidemiological studies.

3.1 Vaccination and Herd Immunity Threshold

We assume no initial immunity to the infection for individuals in the general disease model and full immunity for those susceptible individuals being vaccinated.

3.1.1 Variation in Time Delay

As intervention timing has had a great interest in many disease mitigation studies including mathematical (Garner et al., 2011), (Kelso et al., 2009) and real-data epidemic simulations (Ferguson et al., 2006), we explore the effect of immunization delay in the first experiment. We apply the vaccination with various time delays from the initiation of the infection and observe the difference in the magnitude of infection.

3.1.2 Variation in Proportion of Population

In another experiment we study the effect of vaccinating various population percentages. In this case, vaccination starts immediately after the initiation of the disease and is performed in 3 different phases. Each phase consists of 3 steps in which the number of vaccinated individuals are the same. In the first phase, the number of vaccinated individuals in each step is high to accelerate the mitigation process. We call this number Vaccination Capacity (VC). In the second and third phase, the number of vaccinated individuals in each step decreased to 2/3 and 1/3 of VC, respectively. Therefore, to ascertain the immunization of the chosen total percentage, VP, of the population during the whole 3 phases of vaccination, maximum vaccination capacity is defined as follows:

$VC = VP * S/6$

Where VC is maximum vaccination capacity in a step, VP is total vaccination percentage of the population and S is the number of susceptible agents. This process guaranties that the total number of individuals vaccinated during the 9 steps that cover the 3 phases is equal to VP * S.

3.1.3 Herd Immunity

There is an important theory in epidemiology known as *herd immunity* which proposes that, all the individuals can be protected against a contagious disease by vaccination of a fraction of a population (John and Samuel, 2000). The proportion of vaccinated individuals in a population above which a contagious disease eradicates is the *herd immunity threshold*. This value depends on the type of the infection and population parameters, such as individual interactions and spatial distribution (Fine, 1993). We are interested to investigate this principle in EcoDemics. This will be explored by varying the VP value and observe the epidemic trend over time in the next section.

4 RESULTS

The simulation is implemented in C++ and all experiments are performed on Sharcnet (SHARCNET) using the Linux XC cluster. At the beginning stage of the simulation, the prey and predator populations are set to 12000 and 500 respectively. The life span of an individual is from 1 to maxAge, where maxAge is computed randomly for each individual to be centred around 46. Initiation of the infection occurs after the stabilization stage that is, after 750 time steps of the simulation. At this stage of the simulation run, the prey and predator populations grow to 178340 and 29656 respectively. Due to the large number of parameters in our EcoDemics, numerous scenarios can be defined and experimented on. Different range of values for the disease parameters along with their

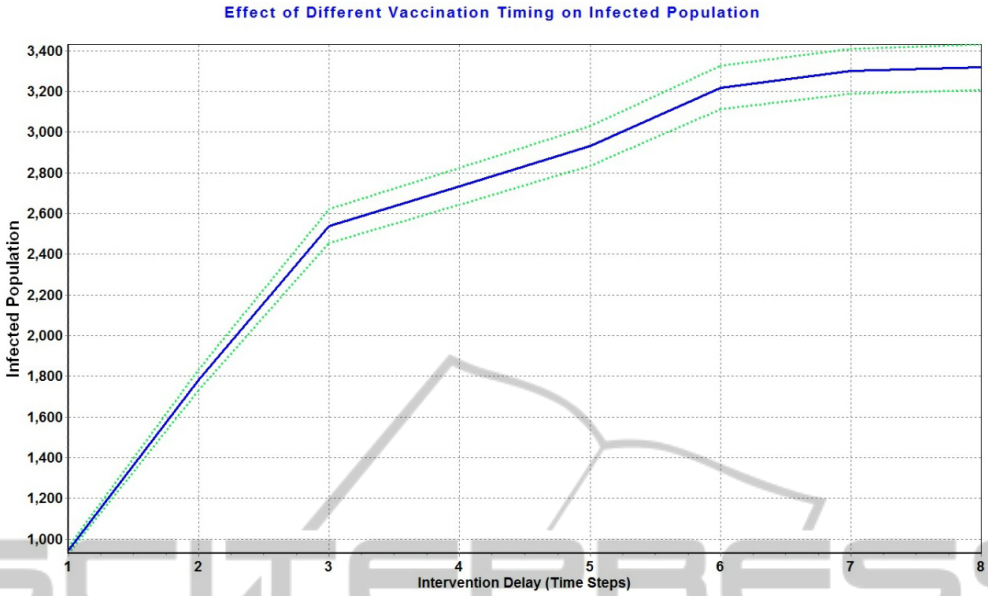

Figure 2: Effect of varying the vaccination delay on the number of infections. Dotted lines represent one standard deviation.

principal effect on the epidemic have been studied in EcoDemics (Farahani et al., submitted). For this experiment we chose one set of parameters but many such sets have been tested and led to the same results.Using probability of $p_{InitInfection}$ = 0.05, only 5% of the susceptible prey in the initial window are set to be infected during the initial infection stage. The infected individual goes through different states based on the parameters and probabilities of the disease model. We define the general infection model with the following specifications: susceptible individuals become infected with the disease based on the probability function (1) with α = -0.2 and β = 2 for high risk individuals, and α = -0.15 and β = 4 for low risk individuals, infected individuals may recover from the disease after a minimum of 10 time steps (minInfected) and with the probability (p_{heal}) of 60% and the recovered individual is naturally immune. The killing rate of 1% is also assigned to this infection model according to p_{kill}.

4.1 Variation in Time Delay

In order to study the effect of timing in vaccination, we applied various time delays to the vaccination from the initiation of the infection, and then observe the corresponding values of the total number of infections. We vaccinated 90% of the population in delays ranging from 1 to 8 time steps after the initiation of the infection. We computed the average of 10 different independent runs of the simulation. Our results show that with the early initiation of the vaccination, which correspond to an intervention delay of 1, the number of infections would be around 900, 5% of the population; however, having an intervention delay of 3, would increase the number of infections to 2500, 14% of the population. In other words, a delay of only 2 time steps in the application of the vaccination increases the magnitude of infection in the population by a factor of 2.7 (Figure 2). This result follows the process of the studies presented in (Kelso, et al. 2009), in which final attack rates in a worst case epidemic increased by a factor of 3.2 between the intervention delays of 1 and 3 time steps.

4.2 Variation in Percentage of Population Vaccinated

To study the importance of the quantity of the vaccination, different proportions of the population are vaccinated. For this purpose, the value of VP is varied from 10% to 90% of the population. The average numbers of infected individuals and epidemic duration for 10 runs using the same VC value are computed. Figure 3 shows the effect of different vaccination rates on the total infected population.

Similarly, Figure 4 shows the effect of different vaccination rates on the total duration of the infection. These results are similar to other vaccination models such as (Keeling et al., 2003), which used the 2001 real cattle epidemic as a template (see the appendix). As shown in the Figure 3, the infection has a maximum value of almost

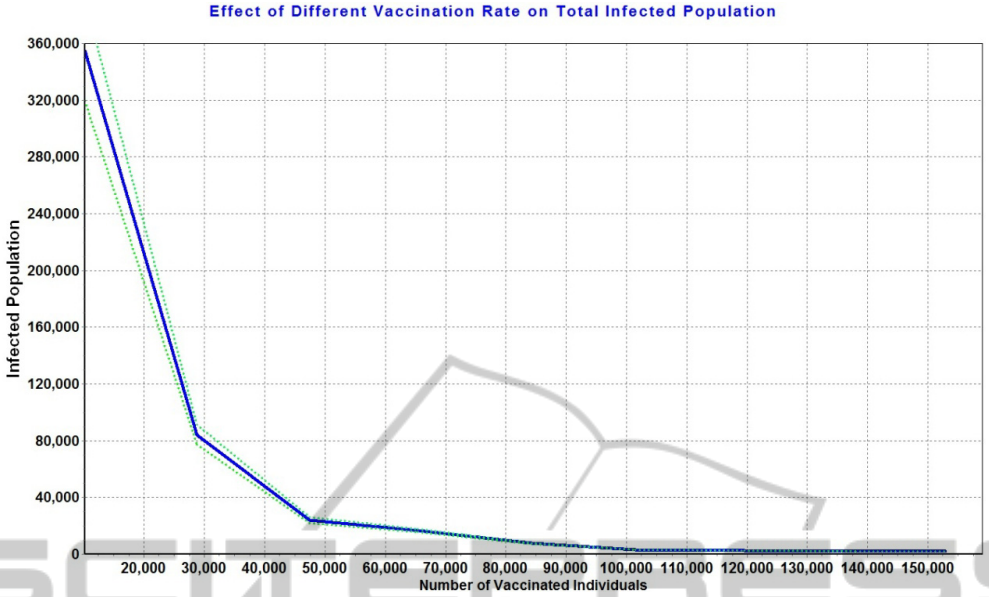

Figure 3: Effect of varying the number of vaccinated individuals on total infected population. The total number of vaccinated individuals is in abscissa and the cumulative total number of infected individual during the whole epidemic duration is in ordinate. Highest and lowest values in infected population correspond to the lowest (10%) and highest (90%) VP values respectively. Dotted lines represent one standard deviation.

355,000 individuals, which is a cumulative value over more than 100 time steps, while the number of vaccinated individuals is around 10,000, which represents approximately 10% of the population. However, the number of infections decreases drastically to less than 10,000 agents when the number of vaccinated individuals is more than 60% of the population and even decreases to 2000 infections when 90% of the population is vaccinated. The comparison of actual infections with the study that used a real cattle epidemic (Keeling et al., 2003) is not applicable, as it considered the number of infected farms instead of the infected population; however, the obtained curves have exactly the same trend: the average size of epidemic declines rapidly with the vaccination rate at each time step, reaching a lower plateau that corresponds to a disease eradication threshold (Keeling et al., 2003).

In Figure 4, it can be seen that the epidemic lasts for a period of 466 time steps with 10% vaccination; however, the duration is substantially reduced to less than 22 time steps while the vaccination percentage is more than 70% of the population. Similarly, this trend matches the reactive vaccination for cattle (Keeling et al., 2003) which started with 400 days for the lowest vaccination rate, versus 466 time steps in our study, and achieved the herd immunity threshold in around 25 days, versus 22 time steps in our study.

Figure 5 depicts epidemic curves for different VP values. The curves with the highest and lowest peak represent the VP values of 10% and 90% respectively, and each curve is the average for 10 independent runs. Only the first 50 time steps of the infection are depicted, as they are the most characteristic part of the epidemic patterns. For the VP of 60%, 70%, 80% and 90%, which are the four lowest curves, the epidemic was significantly mitigated and finally eradicated. For the lower VP values, although the trend of the epidemic over the first 15 time steps is similar to the 4 aforementioned curves, the vaccination strategy was unable to fully suppress the infection at the desired time and we observed jumps of infection after the global decline. This phenomenon suggests an immunity threshold to ensure the eradication of the epidemic over an acceptable duration. For this study the vaccination percentage of the total population needs to be equal or above a threshold of 60% to stop the disease diffusion. In qualitative context, this result is validated by the study about the herd immunity: high levels of herd immunity in cattle can prevent the long tail of the epidemic and is necessary to inhibit stochastic jumps of infection for a given special transmission kernel (Keeling et al., 2003). This correspondence only applies to the threshold for eradication of infection by vaccination: lower levels of vaccination can generate complex, nonlinear, spatio-temporal disease dynamics (Keeling et al., 2003). As mentioned earlier, we observed this

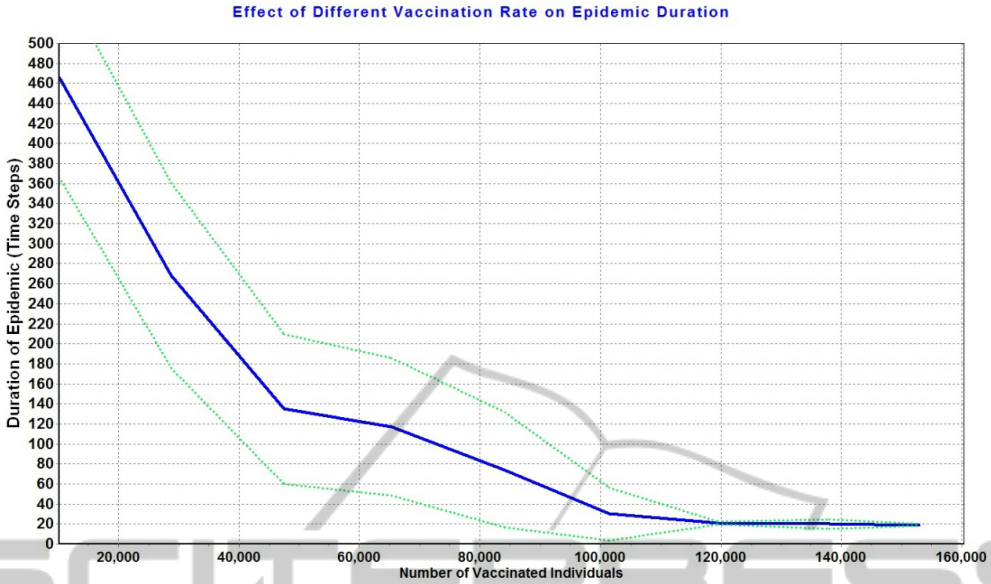

Figure 4: Effect of varying the number of vaccinated individuals on the infection duration. The total number of vaccinated individuals is in abscissa and the duration of the epidemic is in ordinate. Highest and lowest values in epidemic duration correspond to the lowest (10%) and highest (90%) VP values respectively. Dotted lines represent one standard deviation.

nonlinear complex behaviour in lower VP values that are unable to eradicate the disease.

The above results show that our system, which includes much more complex mechanisms than the others, like the ability to model concepts such as complex individual behaviours, multi-level food chains, reproduction, evolution or speciation, produces results similar to the ones observed in systems dedicated to epidemic modeling. This is a significant result for the evaluation of EcoDemics' potential as a platform for studying open complex problems in epidemiology that are unable to be tackled in simpler simulations.

5 CONCLUSIONS

We simulated vaccination strategies in EcoDemics to model the mitigation of epidemics. We explored the effect of this technique with various timing and population percentage parameters. Our experiments revealed that there is a threshold value for the parameter setting the percentage of the population that is vaccinated. This is the same result observed in the herd immunity study: lower levels of vaccination can generate complex, nonlinear, spatio-temporal disease dynamics (Keeling et al., 2003). We observed that with a value greater than 60%, the pattern of the disease spread changes abruptly. However, these measures may not be appropriate to apply directly as quantitative values, as extensive disease specific parameters need to be adjusted depending on the different situations (Harvey et al., 2007); (Keeling et al., 2003); (Holland, 1995). Nevertheless, this study highlighted the importance of effective vaccination policies in mitigating the infection and confirms the fundamental role of increasing individual's immunity over a relatively wide area to inhibit stochastic jumps of infection (Keeling et al., 2003).

We have shown that the results obtained with our simulation are in reasonable concordance with the ones already obtained with other studies. The interest of our approach is that we do not design a system dedicated to disease spread modeling.

Our system is based on a large scale evolving ecosystem simulation which has already proved its interest for the study of complex ecological problems such as community composition (Devaurs and Gras, 2010) or speciation mechanisms (Aspinal and Gras, 2010).

The proof that our system can easily integrate disease models and generate realistic data of disease spread for various mitigation strategies is essential to give us the opportunity to study other situations that cannot be described with a simpler system. Indeed, EcoDemics can easily be extended to tackle numerous difficult open problems.

We are currently studying the precise effect of predators in prey infections, with the assumption that infected preys are more vulnerable to predation. This help us to analyze different scenarios in an

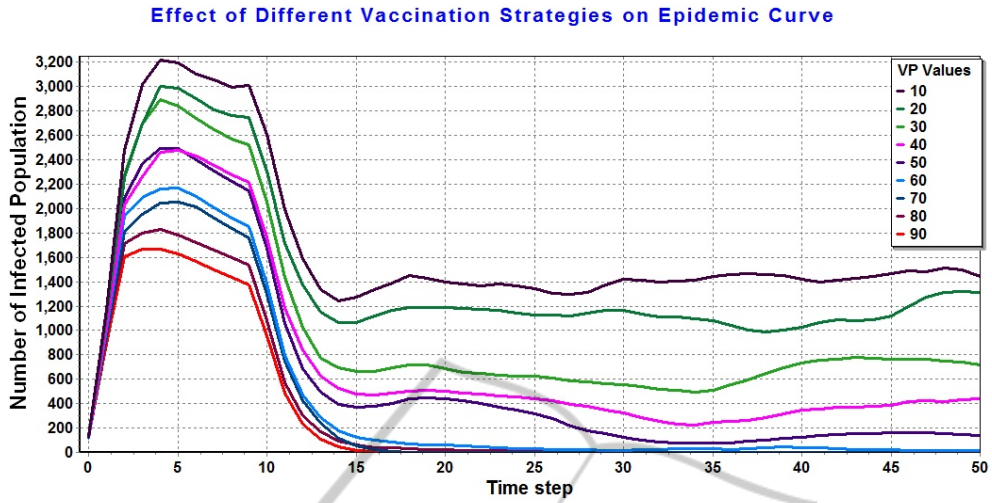

Figure 5: Effect of varying the number of vaccinated population on epidemic curve. Each curve is the average of 10 independent runs for the corresponding VP value.

ecosystem; for instance if the infection can be eradicated by the predators, or if predator removal can increase the incidence of parasitic infection.

As the individuals in our system search for mates and breed, sexually transmitted diseases can easily be integrated. This will allow for studying the specific properties of sexually transmitted disease in large multi-species populations.

The way a disease impacts the genome through the course of evolution is also an interesting question to investigate. Several biological and ecological studies have tried to argue these types of impacts in the evolution of individuals and the necessity of their recognition and interpretation for both public health (Gluckman and Hanson, 2005) and the population of the ecosystem (Bar-David, 2006). As our system integrates the notions of genome, transmission of genome and evolution, we will have the ability to analyze how individuals try to adapt and overcome a disease spread through evolution. Co-evolution of diseases and hosts could also be represented. We will be able to track and analyze the way that one affects the other and influences its evolution over long time periods.

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APPENDIX

Figure 6 shows how an epidemic can be controlled by the rapid vaccination of cattle during the early stages, using the 2001 epidemic of Great Britain as a template. Throughout, vaccination is of cattle only and assumed to be at 90% efficacy. Expected number of farms reporting infection against the number of cattle vaccinated per day (bottom axis) or the corresponding time to achieve the disease eradication threshold of around 5.5 million cattle (top axis). Solid and dashed lines show the result when different culling is performed. Solid lines depict the average size of the simulated epidemic, which declines rapidly with daily vaccination rate, reaching a lower plateau at a rate of around 300,000 cattle per day. This rate corresponds to achieving the deterministic vaccination threshold in around 25 days. Similarly, Figure 7 represents the expected duration of the epidemic by varying the number of vaccinated cattle (Keeling et al., 2003).

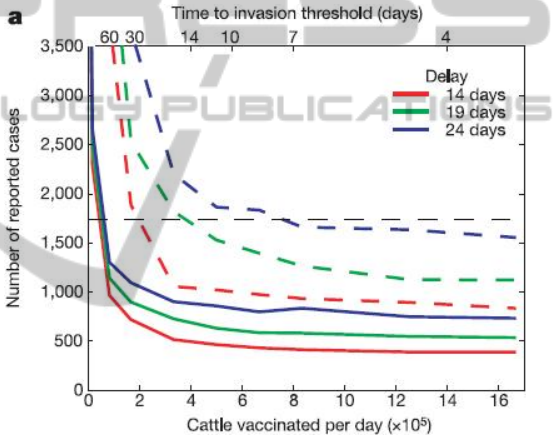

Figure 6: Effect of varying the number of vaccinated cattle on total infected population using the 2001epidemic of Great Britain as a template (Keeling et al., 2003).

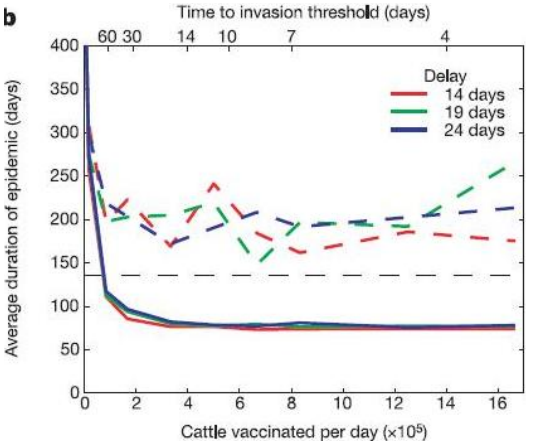

Figure 7: Effect of varying the number of vaccinated cattle on the epidemic duration using the 2001epidemic of Great Britain as a template (Keeling et al., 2003).