An Epidemiological Approach to the Dynamics of Chytridiomycosis on a Harlequin Frog Population

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Abstract

Amphibious species around the world are experiencing catastrophic decline and extinction. Chytridiomycosis, a newly recognized emerging infectious disease, is now thought to be a major contributor to observed rapid decline. Chytridiomycosis is a skin disease caused by the Chytrid fungus, a water-borne pathogen prevalent in Neotropical habitats. The Harlequin Frog, *Atelopus Varius*, native to the montane regions of Costa Rica, is one of the hundreds of species threatened by this epidemic disease. We study the dynamics (primarily through numerics) of this host-pathogen system in a spatial-explicit setting. In order to gain qualitative understanding on the nature of this system, we conduct a mean field approximation, pair approximation, and computer simulation.

1 Introduction

Amphibian is a classification of organisms that includes four-legged vertebrates and all tetrapods. Amphibians generally spend part of their life span on land; although, some have entirely adapted to terrestrial or aqueous habitat. Amphibians are not amniotic, usually undergoing a metamorphosis from waterborne tadpoles to four legged, air breathing adults. There are four main groups of amphibians: the salamanders, caecilians, frogs and toads [9].

There is an increasing concern for amphibious populations around the world. More than one third (1,187) of all amphibious species are facing the threat of extinction [12].

The number of threatened amphibious species exceeds that of both mammal and bird species. There are also 500 species classified as critically endangered i.e. on the brink of extinction [12]. Numerous studies suggest this population decline is not localized to a specific area but is widespread. The majority of threatened amphibious species are primarily concentrated in areas of Mexico, Panama, Guatemala, the Andes of Colombia and Ecuador, Costa Rica and Brazil [9].

Since the early 1980s scientists and conservationists have concluded that amphibious declines are the result of natural fluctuations intrinsic to their ecology. Although amphibious species are known to exhibit oscillation in population size overtime, they cannot explain the observed widespread and rapid decline of the amphibious species in the 1990's [8]. The magnitude of the documented fluctuations have stirred debate on the possible factors leading to this decline. An enigmatic agent responsible for the sudden catastrophic declines has been identified [1], but the belief that a single factor maybe driving the amphibian population to extinction is not universal. Some studies subscribe to the view that several causative agents are responsible for the alarming levels of precipitous amphibious population decline. Habitat destruction and recently discovered epidemiological factors are two of the leading suspects [16, 17]. Other factors include environmental pollutants, new predators, and international trading [8, 9].

The Harlequin Frog (Atelopus Varius) is a Neotropical montane, stream-breeding species native to Monteverde, Costa Rica and western Panama [9]. It can be found in the Cordilleras de Tilaran on both the Atlantic and Pacific slopes. It inhabits Tropical lowland and lower montane regions. These environmental landscapes include both wet and dry areas interspersed with stream routes. Its Neotropical habitat has a wet season (May-November) and dry season [12]. Although the Harlequin frog is a stream-breeding amphibian, it is mainly terrestrial, rarely entering water, and spending most of its time near wetlands.

There has been controversial debate over the causative factor for the sudden decline of the species population in relatively undisturbed habitat. Recent studies have observed mysterious decline to regions of high elevation in the tropics [1, 17] . A newly discovered infectious disease (Chytridiomycosis) has been sited in several amphibious species and is considered a major contributor to catastrophic decline [5]. The virulence of the fungal disease is increased among species inhabiting streams of high elevation. Atelopus Varius is one of hundreds of amphibious species threatened to extinction due to disease.

The pattern of the Harlequin Frog's mortality and population decline is attributed to the pathogenic Chytrid fungus (*Batrachochytium dendrobatidis*), the causative agent of Chytridiomycosis. The appearance of the Chytrid fungus was synchronous with the initial decline of the frog population [5, 15]. The fungus is known to be endemic to several countries including Costa Rica, but may have recently become more virulent or the frog population may have increased its susceptibility to such infections. Reduced frog resistance to infection may be due to environmental or climate changes that have facilitated increased fungal outbreaks population becoming less resistant thus more susceptible or with the increased fungal outbreak and persistence in the environment. These factors of increased

pathogenicity are ascribed to the climatic fluctuation [6].

Global climate change seems to be the leading culprit associated with the changes in the dynamics of this infectious disease [2, 5, 10, 6]. Part of the rational is based on the facts that rising temperatures create a distinct effect specific to a geographical locale. The local region of the frog responds to the climate change with increased cloud cover and humidity. This effectively creates the necessary conditions for optimal growth of the Chytrid fungus. Of the nearly 500 amphibious species currently listed as critically endangered, nearly 50 percent of the declining population trends have been directly attributed to the skin disease Chytridiomycosis [12].

Chytridiomycosis was first discovered and diagnosed in dead amphibians in 1998. Tissue samples of epidermal skin collected from these mass deaths contained developing sporangia of the Chytrid fungus [4]. The fungus penetrates the surface or epidermal layer of skin, which causes damage to the keratin layer. It is not known exactly how the fungus kills the frog. Upon invasion of the skin, it may release toxins and disrupt the respiratory track. Clinical signs of infection include lethargy, hemorrhaging of the skin, muscle and eye [4].

There is a high mortality rate for the victims of the disease which is causing devastating population declines and even extinction [14, 15]. While such levels of mortality may normally create a disease free state this is not the case since the tadpoles act as a reservoir population creating a situation where the disease may persist. According to a recent study, there will be hundreds of amphibious species becoming extinct over the next few decades [8]. The consistency in outbreaks and persistence of the disease has been a cause for alarm for the countries of the affected regions. Several studies by J. Alan Pounds, et. al. have linked the fungi population increase to global climate change [6]. With increased reproductive rates of the fungus, pathogen transmissibility becomes more prevalent. With biological diversity at stake, it is vital that research is continued to discover a way to control this disease [6, 7, 18].

The ecology of the Harlequin Frog and Chytrid fungal biology has to be considered in determining the impact of Chytrid fungus on the population. The Chytrid fungus has two main stages of development. It is first a waterborne mobile zoospore that becomes a stationary thallus for asexual reproduction [3]. Driven by the flagellum, the saprobe or saprophyte can easily spread and readily persist in a host population that resides in water. The fungus aptly takes advantage of the stream-breeding nature of the Harlequin frog, using the abundant tadpoles for increased propagation. Since the fungus only infects the keratinized areas, the tadpole death associated with fungal infection is often rare given the lack of keratin on the tadpoles. The fungus may reproduce and survive as a saprophytic organism (spore), thriving on keratin from the carcass of other dead frogs and from shedding [3]. The ability of the organism to survive outside the host accelerates the declination of the frog population. The fungi usually reside in water or in moist soil. The frogs are believed to contract the disease with contact of the fungal spores in the water or from contact with infected frogs [3]. There is still more research needed to fully understand the spread of the fungi and its ability to cause mortality among amphibians.

2 Research Goals and Objectives

The first goal of our project is to understand and review the current research of amphibious population extinction resulting from an emerging infectious disease. The second goal is to establish two models that incorporate the interaction between the disease causing Chytrid fungus and the Harlequin frog population. We want to study and analyze the effects of an infectious disease on the Harlequin frog, while concurrently exploring prevention measures. Further objectives include comparative analysis of two models in approximating the computer simulation of the Harlequin frog population and disease dynamics.

3 Model

We employ a stochastic spatial-temporal model to simulate the interaction between the Harlequin frog and the Chytrid fungus. It is important to address the spatial arrangement of the frog and fungi in order to capture the spreading dynamics of the disease. The infection dynamics between frog and fungus take place primarily in wet areas, specifically near waterfalls or streams. The model used is a continuous-time lattice-based epidemiological model where each site on the lattice contains a numeric value representing one of six states (see Table 1). The model uses eight events, defining the focus of the simulated interaction between the two organisms.

#	State	Description
0	empty	wetland with no fungus or frog
1	fungus	wetland occupied by a fungus
2	frog	wetland occupied by a single healthy frog
3	infected frog	wetland occupied by one infected frog, fungi has been lodged in the epidermal layer of the skin
4	fungus & frog	wetland occupied by one healthy frog and fungi, more specifically it reflects a healthy frog occupying the same space as a patch of fungi
5	fungus & infected frog	wetland occupied by one infected frog and fungi

Table 1: State variables representing the sites of the lattice.

These state variables will be dispersed onto a lattice, thereby creating a potential environment representing the distribution of the frogs, infected frogs, and fungi.

To describe an event, we have defined eight parameters as follows:

Parameters of System Dynamics

Symbol	Description	Estimated Biological Values	Ranges
ϕ_f	fungus successful birth rate	$\frac{1}{3}$	[0,10]
μ_f	fungus death rate	$\frac{1}{49}$	[0,1]
ϕ_h	frog successful birth rate	1	[0,1]
μ_i	infected frog death rate	$\frac{1}{3}$	fixed
m_i	infected frog movement rate	12	[0,24]
m_h	healthy frog movement rate	24	[12,48]
σ_f	rate of successful fungus to frog infection	$\frac{1}{4}$	$[0,\frac{1}{3}]$
σ_i	rate of successful infected frog to frog infection	$\frac{1}{8}$	$[0,\frac{1}{3}]$

Table 2: This table shows the eight parameters used in our system of equations and the values and ranges of values estimated for those parameters. All parameters are expressed as rates (per day).

- ϕ_f is defined as the successful birth rate of a fungus. We make a reasonable assumption that there is local dispersion of the zoospores and they only choose one of their four orthogonal neighbors to whom they spread. The life cycle of the fungus from its first production of zoospores to the point it is infectious is roughly estimated to take three days. We have considered a range of values from no birth to ten births in a day.
- μ_f is defined as the fungus death rate. The average life span of the fungus is 7 weeks, so $\mu_f = \frac{1}{49}$. This estimation can be found from a study published by the Center for Disease Control & Prevention [13].
- ϕ_h is defined as the successful birth rate of a healthy frog. Realistically there should be a time delay on the healthy frog successful birth rate, but for the sake of simplification we have not included this delay, thus ϕ_h is the per capita birthrate.
- μ_i is defined as the death rate of the infected frog. This parameter will be fixed throughout the analysis. The estimated time until death whence a frog is infected is three days, so $\mu_i = \frac{1}{3}$.
- m_i is defined as the infected frog movement rate. This parameter value will always remain lower compared to the movement rate of a healthy frog. This assumption is made from the knowledge that an infected frog is lethargic [4].
- m_h is defined as the per healthy frog movement rate.
- σ_f is defined as the rate of successful fungus to frog infection rate.
- σ_i is defined as the rate of successful infected frog to frog infection rate.

The legal transitions of single sites according to our biological assumptions are described in the chart below.

Transitions of States

[0]	⇒	[1], [2], [3]
[1]	⇒	[0], [4], [5]
[2]	⇒	[0], [3], [4]
[3]	⇒	[0], [1], [5]
[4]	⇒	[1], [2], [5]
[5]	⇒	[1], [3]

Table 3: This table shows the possible transitions from one state to another state. For example, [0] can become [1], [2], or [3].

- State [0]: State [1] can become [0] if the fungus dies, State [2] can become [0] if a healthy frog moves from the current site to an empty site, or State [3] can become [0] if an infected frog moves from the current site to an empty site. State [0] can turn into [1] if a fungus is born from one of its neighbors, [2] if a healthy frog is born onto the site or if a healthy frog moves there, or [3] if an infected frog moves to that site.

- State [1]: State [0] can become [1] if a fungus is born from one of its neighbors and State [3] can become [1] if an infected frog dies or State [5] may become [1] due to infected frog death or movement. We have thus assumed that the event of the death of an infected frog will leave that site occupied by fungus. State [1] can turn into [0] if a fungus dies, [4] if a healthy frog is born or moves to that site, or [5] if an infected frog moves to that site.

- State [2]: State [0] can become [2] if a healthy frog is born or if a healthy frog moves to that site and State [4] can become [2] if the fungus dies. State [2] can turn into [0] if a healthy frog moves away from the site, can turn into [3] if a healthy frog becomes infected, or can turn into [4] if a fungus is born on that site.

- State [3]: State [0] can become [3] if an infected frog moves to that site, State [2] can become [3] if the healthy frog is infected by an infected frog from one of the neighboring sites, and State [5] can become [3] if the fungus dies. State [3] can turn into [0] if the infected frog moves to an empty site, [1] if the infected frog dies, or [5] if a fungus is born from a fungus in one of the neighboring sites.

- State [4]: State [1] can become [4] if a healthy frog is born or a healthy frog moves to that site from one of the neighboring sites and State [2] can become [4] if a fungus

is born. State [4] can turn into [1] if the healthy frog moves to an empty site, [2] if the fungus dies, [5] if the healthy frog becomes infected.

- State [5]: State [1] can become [5] if infected frog moves to the site, State [3] can become [5] if a fungus is born, and State [4] can become [5] if the healthy frog becomes infected. State [5] can turn into [1] if the infected frog dies or if the infected frog moves from the current site to an empty site or can turn into [3] if the frog dies.

In our model we do not include the per-capita natural death of healthy frogs because the model reflects only the dynamics of single outbreaks, that is, it does not adequately capture the dynamics over a long period of time (lack of adaptive parameters). We also assume that a healthy frog that is occupying the same spot as fungus can be infected by the fungus at a rate of σ_f. This is the only way that a frog can become infected by a fungus. There is also infection from an infected frog onto a random adjacent healthy frog at rate σ_i. If there is movement of an infected frog, we conjecture that the infected frog will not leave behind any fungi, but its death will leave behind fungus on that patch.

4 Pair Approximation

Our approach in analyzing the dynamics of the spreading of an epidemic disease is through the incorporation of spatial-temporal dimensions with local neighborhood interactions. The pair-approximation is an applicable method employed as an analytical tool providing behavioral dynamics of the host population and the infectious disease.

Pair Approximation utilizes a system of ordinary differential equations to describe the probability of pairs of adjacent sites being in particular combinations of states. It can be used to model both deterministic and stochastic processes of spatial dispersal, interaction, disturbance, etc. This method is useful in models where the spatial arrangement between states needs to be considered. Refer to Table 4 for all possible combinations of pairs of neighboring sites. Specifically for our model a pair of sites can only be transformed into certain pairs of sites as defined within the realm of biological significance. The lattice of cells will represent a certain configuration of states, and while the proportion of a given pair of states will change over time, it is assumed to be only dependent on its immediate neighbors. A particular site will have a probability of being updated to another state, which may be conditioned on the state of its four orthogonal neighbors. The pair approximation method will be used as a continuous time Poisson process; only a single event can happen per time-step.

Since our system has six state variables, there will be a total of thirty-six equations when we consider each possible pair of state variables. We have listed below in Table 4 all possible combinations of the state variables.

Assuming rotational symmetry, $P[jk] = P[kj] = P\begin{bmatrix} j \\ k \end{bmatrix} = P\begin{bmatrix} k \\ j \end{bmatrix}$ as described in Hiebeler 2004 [11]; therefore, the probabilities are equal and we only need to consider one.

[00]	~~[10]~~	~~[20]~~	~~[30]~~	~~[40]~~	~~[50]~~
[01]	[11]	~~[21]~~	~~[31]~~	~~[41]~~	~~[51]~~
[02]	[12]	[22]	~~[32]~~	~~[42]~~	~~[52]~~
[03]	[13]	[23]	[33]	~~[43]~~	~~[53]~~
[04]	[14]	[24]	[34]	[44]	~~[54]~~
[05]	[15]	[25]	[35]	[45]	~~[55]~~

Table 4: All possible pairs of combinations of the state variables. Fifteen pairs have been eliminated due to symmetry. That last pair [55] has been eliminated since the sum of the probabilities of all the pairs is equal to one.

As shown in Table 3, we have eliminated fifteen pairs due to the property of symmetry. Further note the sum of all of the probabilities is equal to one. This will eliminate one more equation. We have chosen to eliminate the pair [55]; thus $P[55]$=1-$\sum_{j,k} P[jk]$ where $j = k$ and $k \neq 5$.

4.1 Equations

Our first equation is the rate of change of the probability of [00].

The notation y, f, h, and i is used for simplicity. The notation y is used for an empty space not occupied by a frog. An empty site consists of the state variables [0] and [1]. If a fungus is occupying a site, we use the notation f to describe the state. These conditions describe the states [1], [4] and [5]. The notation h is used to describe a site that is occupied by a healthy frog, representing the state variables [2] and [4]. Finally, we use i to represent a site occupied by an infected frog: [3] and [5].

To find $\frac{dP[00]}{dt}$, we find the possible outflow of [00] and subtract that from the possible inflow. For example, [01], [10], [02], [20], [03], and [30] may become [00] in a single event. If an empty site is paired with a fungus in either orientation, and that fungus dies, we will be left with two empty sites. Should an empty site be paired with a site containing only a frog, infected or healthy, then movement of this frog may result in the pair becoming [00]. We assume the movement of an infected frog does not leave fungus on the site. The inflow terms are the following:

$$P[01]\mu_f + P[10]\mu_f + P[02]\frac{3}{4}m_h Q_{y|2}$$
$$+P[20]\frac{3}{4}m_h Q_{y|2} + P[03]\frac{3}{4}m_i Q_{y|3} + P[30]\frac{3}{4}m_i Q_{y|3}$$

The term $Q_{j|k}$ is the conditional probability that a randomly chosen neighbor of a site in state k is in state j. More succinctly:

$$Q_{j|k} = \frac{P[jk]}{P[k]}$$

We can simplify since we know that $P[jk]$=$P[kj]$; therefore, the inflow terms are simplified:

$$2P[01]\mu_f + 2P[02]\frac{3}{4}m_h Q_{y|2} + 2P[03]\frac{3}{4}m_i Q_{y|3}$$

When we consider the outputs, we must also consider symmetry. In a single event, the pair [00] can become [01], [02], or [03] if there is a successful birth of a fungus, a successful birth of a frog, or a healthy or infected frog moves onto the pair. Thus, the equation of the total rate change of the probability of [00] is

$$\begin{aligned}\frac{dP[00]}{dt} &= 2P[01]\mu_f + 2P[02]\frac{3}{4}m_h Q_{y|2} + 2P[03]\frac{3}{4}m_i Q_{y|3} \\ &\quad -2P[00]\left(\frac{3}{4}\phi_f Q_{f|0} + P[h]\phi_h + \frac{3}{4}m_h Q_{h|0} + \frac{3}{4}m_i Q_{i|0}\right). \qquad (1)\end{aligned}$$

When we find the total rate of change over time of a pair of sites that is symmetric, we will always get equal terms in pairs of two, as was such in the first equation. However, this will not be true when our pair of sites is asymmetric.

Let us consider $\frac{dP[01]}{dt}$.

The inflow will be [00], [03], [04], [05], [21], [11], and [31]. Note that we have reduced our thirty-six equations to twenty equations, so we are only using twenty pairs. The probabilities of [21] and [31] will appear as $P[12]$ and $P[13]$ in our equation since these are included in the twenty pairs that we initially decided would be solved.

The outflow will consist of the single events when the fungus dies [00], a healthy frog moves onto the one site [04], a successful birth of a frog occurs on a zero site [21], a successful birth of a frog occurs on a one site [04], an infected frog moves onto a zero site [31], an infected frog moves onto a one site [05], and the event that a successful birth of a fungus occurs on a zero site [11].

The final equations is

$$\begin{aligned}\frac{dP[01]}{dt} &= P[00]\frac{3}{4}\phi_f Q_{f|0} + P[03]\mu_i + P[04]\frac{3}{4}m_h Q_{y|4} + P[05]\left(\frac{3}{4}m_i Q_{y|5} + \mu_i\right) \\ &\quad + P[12]\frac{3}{4}m_h Q_{y|2} + P[11]\mu_f + P[13]\frac{3}{4}m_i Q_{y|3} - P[01]\left(\mu_f + \frac{3}{4}m_h Q_{h|0}\right. \\ &\quad \left. + \frac{3}{4}m_h Q_{h|1} + 2P[h]\phi_h + \frac{3}{4}m_i Q_{i|0} + \frac{3}{4}m_i Q_{i|1} + \frac{3}{4}\phi_f Q_{f|0} + \frac{\phi_f}{4}\right). \qquad (2)\end{aligned}$$

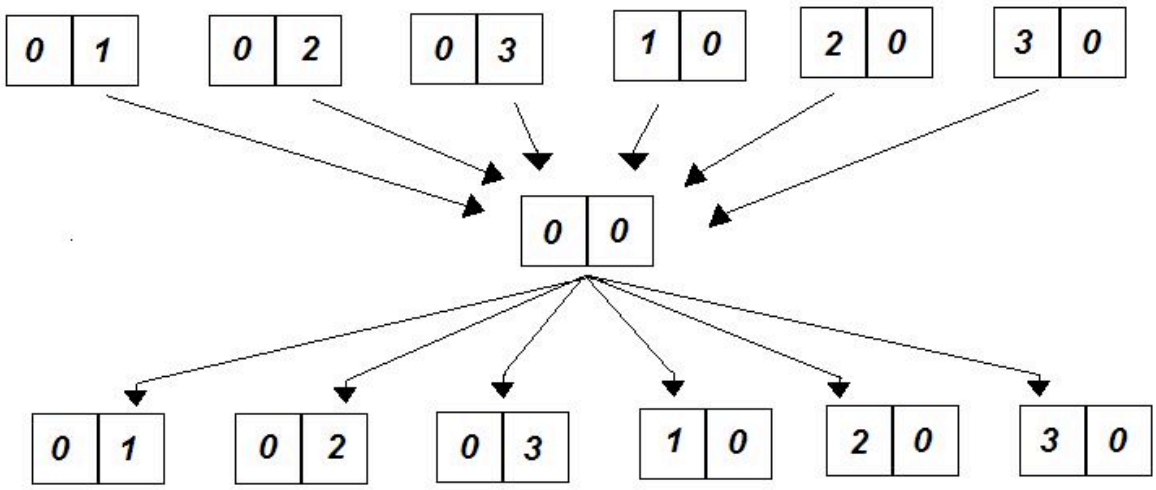

Figure 1: This figure shows the possible pairs of states that can become [00] and the outflow of pairs that [00] can turn into, given a single event.

Below we show the next eighteen equations.

$$\begin{aligned}
\frac{dP[02]}{dt} &= P[00]\left(P[h]\phi_h + \frac{3}{4}m_h Q_{h|0}\right) + P[02]\frac{m_h}{4} + P[04]\mu_f \\
&+P[12]\mu_f + P[22]\frac{3}{4}m_h Q_{y|2} + P[23]\frac{3}{4}m_i Q_{y|3} \\
&-P[02]\left(\frac{3}{4}m_h Q_{y|2} + \frac{m_h}{4} + \frac{3}{4}\sigma_i Q_{i|2} + \frac{3}{4}\phi_f Q_{f|2}\right. \\
&\left.+\frac{3}{4}\phi_f Q_{f|0} + P[h]\phi_h + \frac{3}{4}m_h Q_{h|0} + \frac{3}{4}m_i Q_{i|0}\right) \qquad (3) \\
\frac{dP[03]}{dt} &= P[00]\frac{3}{4}m_i Q_{i|0} + P[02]\frac{3}{4}\sigma_i Q_{i|2} + P[05]\mu_f + P[03]\frac{m_i}{4} \\
&+P[13]\mu_f + P[23]\frac{3}{4}m_h Q_{y|2} + P[33]\frac{3}{4}m_i Q_{y|3} \\
&-P[03]\left(\frac{3}{4}m_i Q_{y|3} + \mu_i + \frac{3}{4}\phi_f Q_{f|3} + \frac{3}{4}\phi_f Q_{f|0} + P[h]\phi_h\right. \\
&\left.+\frac{3}{4}m_h Q_{h|0} + \frac{3}{4}m_i Q_{i|0} + \frac{m_i}{4}\right) \qquad (4)
\end{aligned}$$

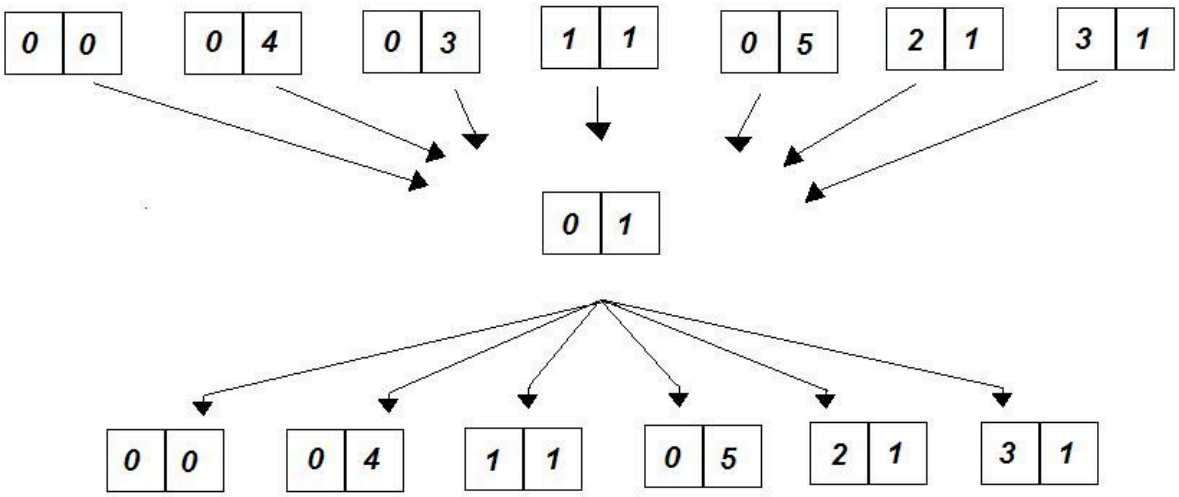

Figure 2: This figure shows the possible pairs of states that can become [01] and the outflow of pairs that [01] can turn into, given a single event.

$$
\begin{aligned}
\frac{dP[04]}{dt} &= P[01]\left(\frac{3}{4}m_h Q_{h|1} + P[h]\phi_h\right) + P[02]\frac{3}{4}\phi_f Q_{f|2} + P[12]\frac{m_h}{4} \\
&\quad + P[14]\mu_f + P[24]\frac{3}{4}m_h Q_{y|2} + P[34]\frac{3}{4}m_i Q_{y|3} \\
&\quad - P[04]\left(\frac{3}{4}m_h Q_{y|4} + \mu_f + \sigma_f + \frac{3}{4}\sigma_i Q_{i|4} + \frac{m_h}{4}\right. \\
&\quad \left. + \frac{3}{4}\phi_f Q_{f|0} + \frac{\phi_f}{4} + \frac{3}{4}m_h Q_{h|0} + P[h]\phi_h + \frac{3}{4}m_i Q_{i|0}\right) \qquad (5) \\
\frac{dP[05]}{dt} &= P[01]\frac{3}{4}m_i Q_{i|1} + P[03]\frac{3}{4}\phi_f Q_{f|3} + P[04]\left(\sigma_f + \frac{3}{4}\sigma_i Q_{i|4}\right) \\
&\quad + P[13]\frac{m_i}{4} + P[15]\mu_f + P[25]\frac{3}{4}m_h Q_{y|2} + P[35]\frac{3}{4}m_i Q_{y|3} \\
&\quad - P[05]\left(\mu_i + \frac{3}{4}m_i Q_{y|5} + \mu_f + \frac{3}{4}\phi_f Q_{f|0} + \frac{\phi_f}{4}\right. \\
&\quad \left. + P[h]\phi_h + \frac{3}{4}m_h Q_{h|0} + \frac{3}{4}m_i Q_{i|0} + \frac{m_i}{4}\right) \qquad (6)
\end{aligned}
$$

$$\begin{aligned}
\frac{dP[11]}{dt} &= 2P[01]\left(\frac{3}{4}\phi_f Q_{f|0}+\frac{\phi_f}{4}\right)+2P[14]\frac{3}{4}m_h Q_{y|4} \\
&\quad +2P[15]\left(\frac{3}{4}m_i Q_{y|5}+\mu_i\right)+2P[13]\mu_i-2P[11]\left(\mu_f+\phi_f\right. \\
&\quad \left.+\frac{3}{4}m_h Q_{h|1}+\frac{3}{4}m_i Q_{i|1}\right) \qquad (7) \\
\frac{dP[12]}{dt} &= P[01]\left(P[h]\phi_h+\frac{3}{4}m_h Q_{h|0}\right)+P[04]\frac{m_h}{4}+P[02]\frac{3}{4}\phi_f Q_{f|0} \\
&\quad +P[23]\mu_i+P[14]\mu_f+P[24]\frac{3}{4}m_h Q_{y|4}+P[25]\left(\mu_i+\frac{3}{4}m_i Q_{y|5}\right) \\
&\quad -P[12]\left(\frac{3}{4}m_h Q_{y|2}+\frac{3}{4}\sigma_i Q_{i|2}+\frac{3}{4}\phi_f Q_{f|2}+\frac{\phi_f}{4}\right. \\
&\quad \left.+\mu_f+P[h]\phi_h+\frac{3}{4}m_h Q_{h|1}+\frac{3}{4}m_i Q_{i|1}+\frac{m_h}{4}\right) \qquad (8) \\
\frac{dP[13]}{dt} &= P[01]\frac{3}{4}m_i Q_{i|0}+P[12]\frac{3}{4}\sigma_i Q_{i|2}+P[15]\mu_f \\
&\quad +P[03]\frac{3}{4}\phi_f Q_{f|0}+P[05]\frac{m_i}{4}+P[33]\mu_i+P[34]\frac{3}{4}m_h Q_{y|4} \\
&\quad +P[35]\left(\mu_i+\frac{3}{4}m_i Q_{y|5}\right)-P[13]\left(\frac{3}{4}m_i Q_{y|3}+\mu_i+\frac{3}{4}\phi_f Q_{f|3}\right. \\
&\quad \left.+\frac{\phi_f}{4}+\mu_f+P[h]\phi_h+\frac{3}{4}m_h Q_{h|1}+\frac{3}{4}m_i Q_{i|1}+\frac{m_i}{4}\right) \qquad (9) \\
\frac{dP[14]}{dt} &= P[11]\left(P[h]\phi_h+\frac{3}{4}m_h Q_{h|1}\right)+P[12]\left(\frac{3}{4}\phi_f Q_{f|2}+\frac{\phi_f}{4}\right) \\
&\quad +P[04]\left(\frac{3}{4}\phi_f Q_{f|0}+\frac{\phi_f}{4}\right)+P[34]\mu_i+P[14]\frac{m_h}{4} \\
&\quad +P[44]\frac{3}{4}m_h Q_{y|4}+P[45]\left(\mu_i+\frac{3}{4}m_i Q_{y|5}\right) \\
&\quad -P[14]\left(\frac{3}{4}m_h Q_{y|4}+\frac{3}{4}\sigma_i Q_{i|4}+\sigma_f+\mu_f\right. \\
&\quad \left.+P[h]\phi_h+\frac{3}{4}m_h Q_{h|1}+\frac{3}{4}m_i Q_{i|1}+\frac{m_h}{4}+\mu_f\right) \qquad (10) \\
\frac{dp[15]}{dt} &= P[11]\frac{3}{4}m_i Q_{i|1}+P[13]\left(\frac{3}{4}\phi_f Q_{f|3}+\frac{\phi_f}{4}\right) \\
&\quad +P[14]\left(\sigma_f+\frac{3}{4}\sigma_i Q_{i|4}\right)+P[15]\frac{m_i}{4}+P[05]\left(\frac{3}{4}\phi_f Q_{f|0}+\frac{\phi_f}{4}\right) \\
&\quad +P[35]\mu_i+P[45]\frac{3}{4}m_h Q_{y|4}+P[55]\left(\mu_i+\frac{3}{4}m_i Q_{y|5}\right)-P[15]\left(\mu_i\right. \\
&\quad \left.+\frac{3}{4}m_i Q_{y|5}+2\mu_f+P[h]\phi_h+\frac{3}{4}m_h Q_{h|1}+\frac{3}{4}m_i Q_{i|1}+\frac{m_i}{4}\right) \qquad (11)
\end{aligned}$$

$$
\begin{aligned}
\frac{dP[22]}{dt} &= 2P[02]\left(P[h]\phi_h + \frac{3}{4}m_h Q_{h|0}\right) + 2P[24]\mu_f \\
&\quad -2P[22]\left(\frac{3}{4}m_h Q_{y|2} + \frac{3}{4}\sigma_i Q_{i|2} + \frac{3}{4}\phi_f Q_{f|2}\right) \qquad (12)\\
\frac{dP[23]}{dt} &= P[02]\frac{3}{4}m_i Q_{i|0} + P[22]\frac{3}{4}\sigma_i Q_{i|2} + P[25]\mu_f + P[34]\mu_f \\
&\quad +P[03]\left(P[h]\phi_h + \frac{3}{4}m_h Q_{h|0}\right) - P[23]\left(\frac{3}{4}m_i Q_{y|3} + \mu_i\right. \\
&\quad \left.+\frac{3}{4}\phi_f Q_{f|3} + \frac{3}{4}m_h Q_{y|2} + \frac{3}{4}\sigma_i Q_{i|2} + \frac{\sigma_i}{4} + \frac{3}{4}\phi_f Q_{f|2}\right) \qquad (13)\\
\frac{dP[24]}{dt} &= P[12]\left(P[h]\phi_h + \frac{3}{4}m_h Q_{h|1}\right) + P[22]\frac{3}{4}\phi_f Q_{f|2} + P[04]\left(P[h]\phi_h + \frac{3}{4}m_h Q_{h|0}\right) \\
&\quad +P[44]\mu_f - P[24]\left(\frac{3}{4}m_h Q_{y|4} + \sigma_f + \frac{3}{4}\sigma_i Q_{i|4}\right. \\
&\quad \left.+\frac{3}{4}m_h Q_{y|2} + \frac{3}{4}\sigma_i Q_{i|2} + \frac{3}{4}\phi_f Q_{f|2} + \frac{\phi_f}{4} + \mu_f\right) \qquad (14)\\
\frac{dP[25]}{dt} &= P[12]\frac{3}{4}m_i Q_{i|1} + P[23]\frac{3}{4}\phi_f Q_{f|3} + P[24]\left(\sigma_f + \frac{3}{4}\sigma_i Q_{i|4}\right) \\
&\quad +P[05]\left(P[h]\phi_h + \frac{3}{4}m_h Q_{h|0}\right) + P[45]\mu_f - P[25]\left(\mu_i + \frac{3}{4}m_i Q_{y|5}\right. \\
&\quad \left.+\mu_f + \frac{3}{4}m_h Q_{y|2} + \frac{3}{4}\sigma_i Q_{i|2} + \frac{\sigma_i}{4} + \frac{3}{4}\phi_f Q_{f|2} + \frac{\phi_f}{4}\right) \qquad (15)\\
\frac{dP[33]}{dt} &= 2P[03]\frac{3}{4}m_i Q_{i|0} + 2P[23]\left(\frac{3}{4}\sigma_i Q_{i|2} + \frac{\sigma_i}{4}\right) + 2P[35]\mu_f \\
&\quad -2P[33]\left(\frac{3}{4}m_i Q_{y|3} + \mu_i + \frac{3}{4}\phi_f Q_{f|3}\right) \qquad (16)\\
\frac{dP[34]}{dt} &= P[13]\left(P[h]\phi_h + \frac{3}{4}m_h Q_{h|1}\right) + P[23]\frac{3}{4}\phi_f Q_{f|2} + P[04]\frac{3}{4}m_i Q_{i|0} \\
&\quad +P[24]\frac{3}{4}\sigma_i Q_{i|2} + P[45]\mu_f - P[34]\left(\frac{3}{4}m_h Q_{y|4} + \frac{3}{4}m_i Q_{y|3} + \mu_i\right. \\
&\quad \left.+\sigma_f + \frac{3}{4}\sigma_i Q_{i|4} + \frac{\phi_f}{4} + \frac{3}{4}\phi_f Q_{f|3} + \mu_f\right) \qquad (17)\\
\frac{dP[35]}{dt} &= P[13]\frac{3}{4}m_i Q_{i|1} + P[33]\frac{3}{4}\phi_f Q_{f|3} + P[34]\left(\sigma_f + \frac{3}{4}\sigma_i Q_{i|4}\right) \\
&\quad +P[05]\frac{3}{4}m_i Q_{i|0} + P[25]\left(\frac{3}{4}\sigma_i Q_{i|2} + \frac{\sigma_i}{4}\right) + P[55]\mu_f - P[35]\left(2\mu_i\right. \\
&\quad \left.+\frac{3}{4}m_i Q_{y|5} + \mu_f + \frac{3}{4}m_i Q_{y|3} + \frac{3}{4}\phi_f Q_{f|3} + \frac{\phi_f}{4}\right) \qquad (18)
\end{aligned}
$$

$$\frac{dP[44]}{dt} = 2P[14]\left(P[h]\phi_h + \frac{3}{4}m_hQ_{h|1}\right) + 2P[24]\left(\frac{3}{4}\phi_fQ_{f|2} + \frac{\phi_f}{4}\right)$$
$$-2P[44]\left(\mu_f + \frac{3}{4}m_hQ_{y|4} + \sigma_f + \frac{3}{4}\sigma_iQ_{i|4}\right) \quad (19)$$

$$\frac{dP[45]}{dt} = P[14]\frac{3}{4}m_iQ_{i|1} + P[34]\left(\frac{3}{4}\phi_fQ_{f|3} + \frac{\phi_f}{4}\right) + P[44]\left(\sigma_f + \frac{3}{4}\sigma_iQ_{i|4}\right)$$
$$+P[15]\left(P[h]\phi_h + \frac{3}{4}m_hQ_{h|1}\right) + P[25]\left(\frac{3}{4}\phi_fQ_{f|2} + \frac{\phi_f}{4}\right) - P[45]\left(\mu_i\right.$$
$$\left.+\frac{3}{4}m_iQ_{y|5} + 2\mu_f + \frac{3}{4}m_hQ_{y|4} + \sigma_f + \frac{3}{4}\sigma_iQ_{i|4} + \frac{\sigma_i}{4}\right) \quad (20)$$

These equations will be analyzed numerically to obtain quantitative behavior (for a limited range of parameters) and then be compared with mean field approximation to approximate the computer simulation (full model).

5 Computer Simulations

We simulate a spatial Poisson process in continuous time, and as such the time between two events is exponentially distributed. First we construct a 100×100 lattice using toroidal (wrap-around) boundary conditions i.e. exiting the lattice from the left means entering the lattice from the right. Next we decide on the dispersal of the initial amount of fungi, healthy frogs, and infected frogs. The placement of the initial amounts is assumed to be uniformly distributed on the lattice.

The process is modeled by randomly choosing one of the eight events. Depending on the chosen event, a position or cell of the appropriate type is selected at random. For example, upon the selection of a successful healthy frog birth event, the simulation will choose a random cell not occupied by a frog. In this specific example, the birth event will be wasted if all sites are occupied by a frog, healthy or infected. The lattice may be produced visually as a grid with each cell set to a specific state designating each of the 6 states. Upon execution of the simulation, we track the lattice coordinates of all 6 states (refer to Table 1 for list and descriptions). The importance of bookkeeping all 10,000 cells in our lattice becomes evident as only certain states may transform into selected others. After every event we save the data, updating the matrix containing the current value or proportion of each state on our lattice. This data is effectively tracking the population of the fungus, infected frog, and healthy frog after each event. We use this data for comparative numerical analysis.

In our program we code rules for each simulation event as follows:

- Movement of the healthy frog is local, meaning that every frog can move to one of its four cardinal neighbors. After selection of the movement of the healthy frog event,

the program will randomly select a neighbor and check to see if the healthy frog is allowed to move into the site. The healthy frog may move into a site not occupied by another frog. The movement of a healthy frog event will be a wasted event if the site is not empty.

- Movement of an infected frog is also local. The infected frog does not leave fungus behind when it leaves the cell.
- Death of an infected frog leaves fungus in its place.
- Birth of a healthy frog may take place on any cell that is not occupied by a frog. Under these conditions a healthy frog may be born to a site occupied by a fungus or empty site.
- Fungus is also a locally dispersing vector spreading to a randomly chosen cardinal neighbor. A fungus birth event is wasted if the chosen neighbor already has fungus.
- Infected frog to frog transmission requires an infected frog adjacent to a healthy frog.
- Fungus to frog transmission requires a healthy frog and fungus to occupy the same cell.

6 Mean Field Model

The mean field approximation models a way of using a system of differential equations that describes the rate of change of the probabilities of states under simplified conditions. This method neglects any spatial arrangement and assumes a well mixing, effectively an infinite neighborhood where "space does not matter". Such approximation is carried out by assuming independence between all states, that is, the local structure is neglected. In short the mean field approximation assumes that $P[ij] = P[i]P[j]$.

6.1 Equations

We consider the state variables alone rather than as a pair of sites since there is independence between all states. Note that the notation y, f, h, and i is again used to describe the states empty, fungus, healthy frog, and infected frog. The differential equations are formed by subtracting the outflow from the inflow, describing the total rate of change.

$$\begin{aligned} \frac{dP[0]}{dt} &= P[1]\mu_f + P[2]m_h P[y] + P[3]m_i P[y] \\ &\quad -P[0]\left(\phi_f P[f] + \phi_h P[h] + m_h P[h] + m_i P[i]\right) \end{aligned} \tag{21}$$

$$\begin{aligned}\frac{dP[1]}{dt} &= P[0]\phi_f P[f] + P[3]\mu_i + P[4]m_h P[y] \\ &\quad + P[5]\mu_i + P[5]m_i P[y] - P[1]\left(\mu_f\right. \\ &\quad \left. + \phi_h P[h] + m_h P[h] + m_i P[i]\right) \end{aligned} \tag{22}$$

$$\begin{aligned}\frac{dP[2]}{dt} &= P[0]\phi_h P[h] + P[0]m_h P[h] + P[4]\mu_f \\ &\quad - P[2]\left(m_h P[y] + \sigma_i P[i] + \phi_f P[f]\right) \end{aligned} \tag{23}$$

$$\begin{aligned}\frac{dP[3]}{dt} &= P[0]m_i P[i] + P[2]\sigma_i P[i] + P[5]\mu_f \\ &\quad - P[3]\left(m_i P[y] + \mu_i + \phi_f P[f]\right) \end{aligned} \tag{24}$$

$$\begin{aligned}\frac{dP[4]}{dt} &= P[1]\phi_h P[h] + P[1]m_h P[h] + P[2]\phi_f P[f] \\ &\quad - P[4]\left(m_h P[y] + \mu_f + \sigma_i P[i] + \sigma_f\right) \end{aligned} \tag{25}$$

$$\begin{aligned}\frac{dP[5]}{dt} &= P[1]m_i P[i] + P[3]\phi_f P[f] + P[4]\sigma_i P[i] \\ &\quad + P[4]\sigma_f - P[5]\left(m_i P[y] + \mu_i + \mu_f\right) \end{aligned} \tag{26}$$

By solving for the Jacobian, we analyze three trivial equilibriums: frog-free, fungus-free, and disease-free. These equilibriums are unstable and only occur if the entire lattice consists of empty sites or the entire lattice consists of healthy frogs.

7 Results

We have numerically integrated the systems of equations for the pair approximation model and the mean field model to obtain solutions using a fourth-order Runge-Kutta technique. Preliminary numerical solutions using varied initial values and fixed parameter values indicate the healthy frog population, infected frog population and the fungus population reach their respective equilibrium values regardless of the initial values. As we range our parameters, the proportion of sites used to plot against parameters are equilibrium values. The estimated biological parameters from Table 2 are used to plot the graphs.

	M.F.	P.A.	F.S.
Fungus	95.4	95.4	94.1
Infected Frog	33.6	33.7	32.8
Healthy Frog	38.5	38.5	40.0
Empty	27.9	27.8	27.2

Table 5: This table displays the equilibrium percentages of the healthy frog, infected frog, and fungus population evaluated numerically with mean field, pair approximation, and full model (computer simulation). We used the fixed parameter values defined in Figure 2.

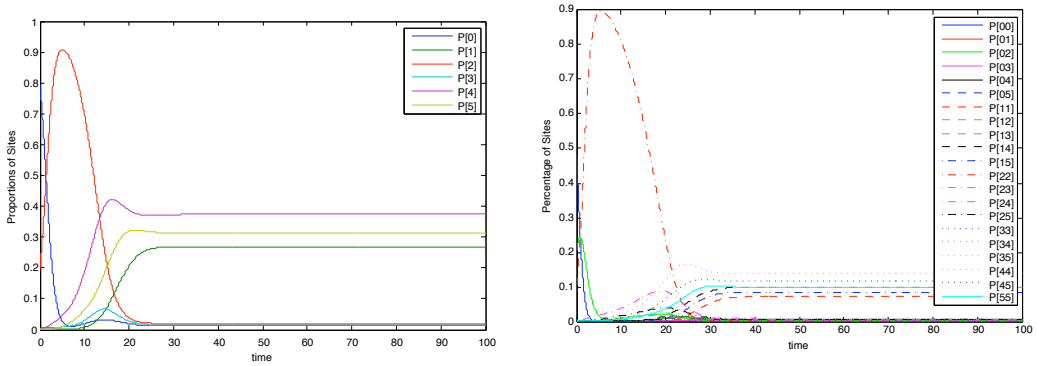

Figure 3: These figures show all state variables plotted against time using of the mean field approximation using the estimated biological parameters from Table 2 showing the change of percentage of sites of all state variables over time.

In Figure 4 plot the state variables versus time. We also plot empty, fungus, healthy frog, and infected frog proportions versus time to allow for comparison between the simulations, mean field approximation and pair approximation.

The mean field model assumes well-mixing among all sites. This allows for more contacts, which drives the behavior of the equilibria. Comparing the outcomes of a well-mixing model of the frogs and fungi to the outcomes of a spatially explicit model, do not show strong differences over time, in fact, both models behave quite similarly. Equilibria appear to be nearly the same. In the pair approximation model the solution takes slightly longer to reach equilibrium than the mean field model. This is due to the combination of spatial dynamics and movement considered in the pair approximation model.

Since the parameters can not be determined with certainty due to the unavailability of data, we isolate one parameter and vary it within an acceptable range and observe the response of the system. Refer to Table 2 to see the range of values tested. First we vary

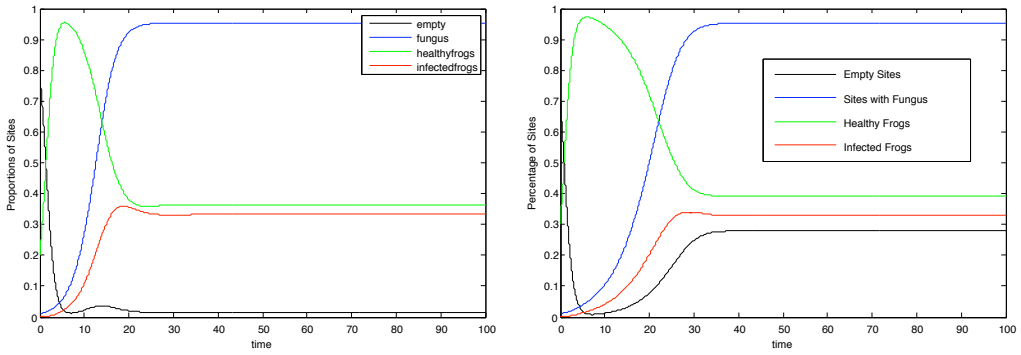

Figure 4: These figures show the six equations of the mean field approximation and the 21 equations of the pair approximation as separated in the categories empty, fungus, healthy frog, and infected frog plotted against time.

our parameters in the mean field model.

The population of fungus, healthy frog, and infected frog at equilibrium are not affected by the values of the movement rate of infected frogs or the movement rate of healthy frogs if these movement rates are not zero. Refer to Figure 8. We find that the fungus occupies 95.4% of the lattice, healthy frog occupies 38.5%, infected frog occupies 33.6%, and empty sites occupy 27.9%, respectively, at equilibrium. We conclude that movement is negligible to the equilibrium values in the mean field model.

We vary the successful birth rate of healthy frogs on the interval [0,1] (Refer to Figure 5). The proportion of fungi experiences little change as ϕ_h increases while the proportions of empty sites, infected frog sites, and healthy frog sites have drastic changes. As expected, the proportion of empty sites decreases as the proportion of healthy frogs and infected frogs increases. According to pair approximation, with ϕ_h initially small, on the order of less than 1 birth of frog every 5 days, the healthy frog population will not persist. Same can be said for the infected frog population given the healthy frogs are driven to zero. Increasing the birth rate greater than 1 birth of a frog every 5 days will allow for persistence of both the healthy frog population and infected frog population. The proportion of the healthy frogs and infected frogs will increase for higher values of ϕ_h. The rate at which the population changes, for higher values of ϕ_h, decreases and levels off. The fungus population with a fixed birth and death rate will approach a near saturation of the lattice. We conclude that the density of the fungi in the lattice is not affected by the number of frogs born. Furthermore, the mean field model and the pair approximation model support the conclusion that increasing the birth rate of this species will not suffice in allowing for the persistence of the healthy frog at higher population levels..

In Figure 6 we show the variation in the parameter ϕ_f in the interval [0,1]. We have found on this interval rather than observing the interval [0,10] since the most interesting

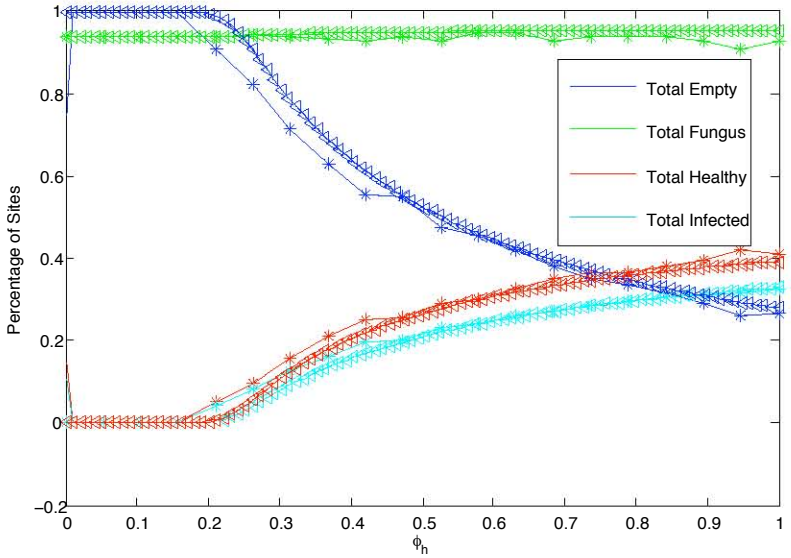

Figure 5: This Figure displays the healthy frog, infected frog, and fungus populations plotted against the successful healthy frog birth rate (units of healthy frog births per day). The solid line represents the graph of the pair approximation, the starred line represents the simulation, and the line with triangles represents the mean field model.

dynamics occur near zero. According to the mean field model, we find a threshold value at approximately 0.2 where the proportions display sharp increases or decreases. Unfortunately for the Harlequin frog population, this figure shows that the successful birth rate of the fungi must be significantly decreased in order for healthy frogs to persist in high proportions. The birth rate of the fungus is relatively insensitive. The fungus will eventually saturate the entire lattice, thus increasing ϕ_f will not affect or influence any change in the frog or infected frog population. Similarly with the pair approximation the birth rate of the fungus is relatively insensitive. The fungus will eventually saturate the entire lattice, thus increasing ϕ_f will not affect or influence any change in the frog or infected frog equilibrium population. Both the mean field and pair approximation model suggest that reducing the successful fungus birth rate is not the most efficient plan of action.

According to the mean field model, the variation of the infected frog to frog infection rate σ_i in the interval $[0,\frac{1}{3}]$ gave us a constant equilibrium for the proportion of fungus sites at 95.3% of the lattice (Refer to Figure 9). As σ_i increases, we notice how the healthy frog equilibrium decreases linearly while the infected frog equilibrium and empty equilibrium increase linearly. Similarly, in the pair approximation model, the healthy frog population declines in a linear fashion with increasing transmission rate. The infected frog population

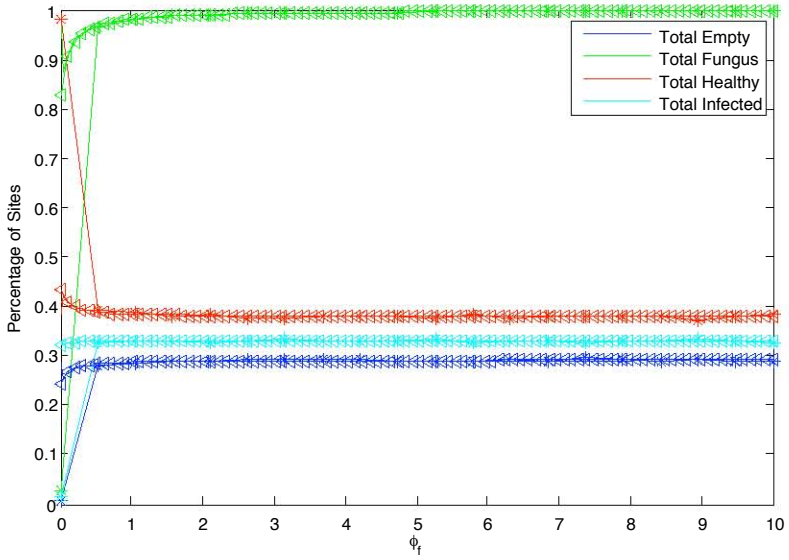

Figure 6: This Figure displays the healthy frog, infected frog, and fungus populations plotted against the birth rate of the fungus (units of fungus births per day). The solid line represents the graph of the pair approximation, the starred line represents the simulation, and the line with triangles represents the mean field model.

slowly increases with increasing values of σ_i, eventually exceeding the population level of healthy frogs. Biologically this implies that decreasing the fungus to frog infection rate is a more effective solution than decreasing the infected frog to frog infection rate.

With the pair approximation model increasing the rate of transmission will steadily decrease the size of the healthy frog population. From our observations if we increased the transmission rate beyond 1 transmission per three days, the healthy frog population could be driven to extinction (Refer to Figure 9). The population of the infected frog increases with increasing transmission rate. The rate of increase of the infected frog population decreases with increasing transmission rates. Increasing (σ_f) beyond our interval will allow the population of infected frog to persist at a higher level as compared to the population level of healthy frogs. According to the mean field model, increasing σ_f we see a decrease in healthy frogs as empty sites and infected frogs increase; however, these changes appear to be exponential. Again, fungus stays relatively constant, varying only by a slight increase.

In the pair approximation model and mean field model, increasing the death rate of the fungus to about .3 gradually lowers the equilibrium population of fungus and empty sites (Refer to Figure 10). The equilibrium population of infected frogs declines linearly. This observed behavior changes as the death rate approaches .4 . The equilibrium population of the infected frog, empty sites, and fungus experience a sharp decline. They eventually

are driven to zero once μ_f approaches and exceeds .5 .

Comparing the mean field to pair approximation reveal that the population of healthy frogs, infected frogs, and fungi are not sensitive to the variation of movement rates of both the healthy frog and infected frog. Variation of the fungus death rate and fungus to frog infection rate show the most deviation between the pair approximation and mean field approximation. Both methods approximate the computer simulation very closely (Refer to table [comparison table]); the two methods accurately capture the qualitative behavior of the computer simulation.

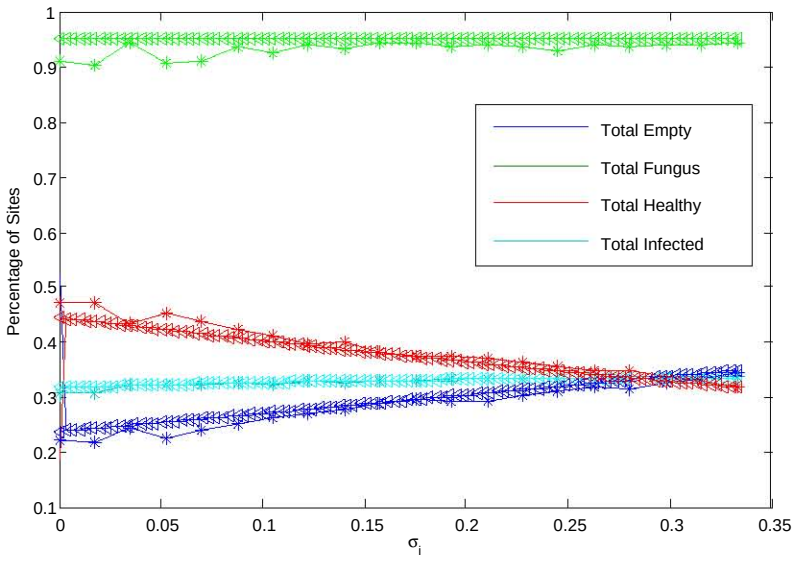

Figure 7: This Figure displays the healthy frog, infected frog, and fungus populations plotted against the rate of infected frog to frog transmission rate (units of infected frog

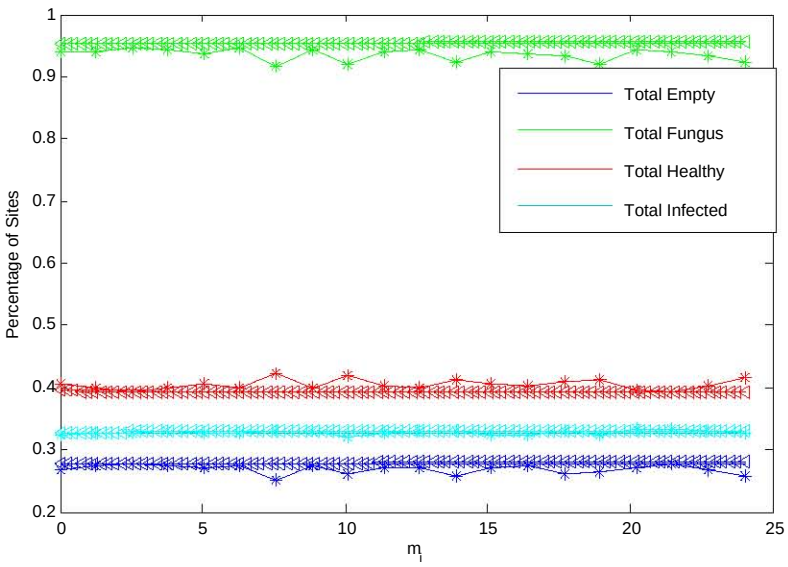

Figure 8: This Figure displays the healthy frog, infected frog, and fungus populations plotted against the movement of an infected frog (units of movements per day). The

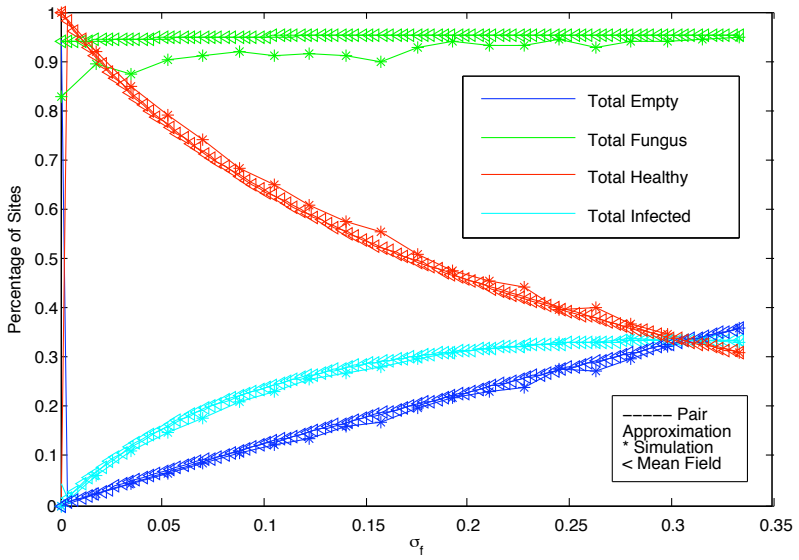

Figure 9: This Figure displays the healthy frog, infected frog and fungus populations plotted against the fungus to frog transmission rate (units of fungus to frog infections per day). The solid line represents the graph of the pair approximation, the starred line represents the simulation, and the line with triangles represents the mean field model.

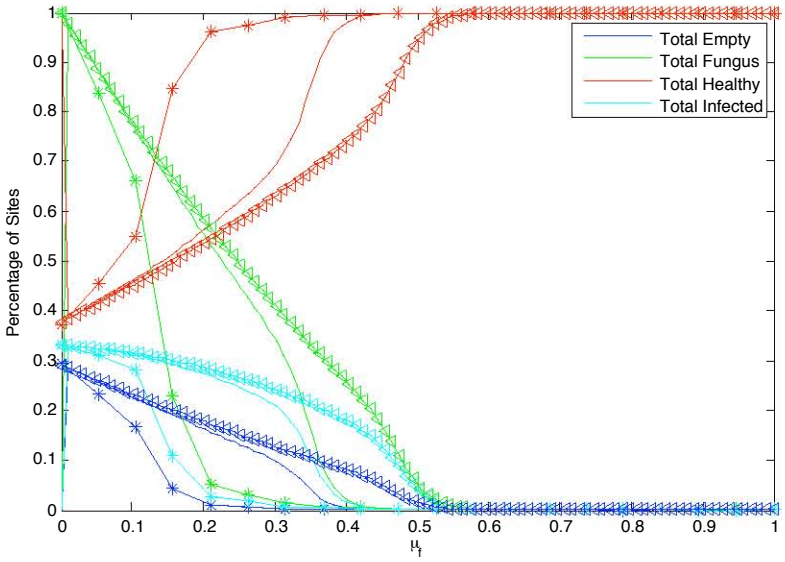

Figure 10: This Figure displays the healthy frog, infected frog and fungus populations plotted against the fungus death rate. The solid line represents the graph of the pair approximation, the starred line represents the simulation, and the line with triangles represents the mean field model.

8 Conclusions

From our research we have met our goals and objectives. The first goal was to develop an understanding of the current amphibious population declination crisis. The second goal was to construct two models that capture the interaction of an infectious disease and the Harlequin frog population. Finally, we compared our two models with the computer simulation.

The reasons behind the documented declining population of the Harlequin frog species and Chytridiomycosis are widely debated. The complexity of interaction between the Chytrid fungus and the frog population while unclear represent an important factor whose impact must be considered. Although there exists circumstantial evidence for increased fungus virulence with climate fluctuations, the evidence is not conclusive. Further research needs to be explored to better understand the Chytrid fungal interaction with the changing climate.

We explored the interaction between the Chytrid fungus and the Harlequin frog by varying parameter values to better understand the qualitative effects of each parameter on the healthy frog population, infected frog population and the fungus population. Our simulations and sensitivity analysis show that the populations are more sensitive to the fungus to frog infection rate and death rate of the fungus, meaning slight changes to these rates have more influence on the healthy frog, infected frog, and fungus populations. When considering prevention measures to reduce the level at which the infected frog population persists and increase the level at which healthy frogs persists, we need to focus our attention to the rate of fungus to frog infection and the death rate of the fungus. To reduce the rate of infection, we need to remove the opportunity for the fungus to make contact with the frog. This could be achieved by relocating the extant frog population to a wildlife preserve. Another approach would be increasing the death rate of the fungus. A chemical could be developed to treat the frog population and reduce the level of the fungus.

The fungus population saturates the entire lattice for all parameter sweeps except for the fungus death rate. As long as the death rate remains low and the birth rate is above zero, the fungus will eventually spread over the entire lattice. A fungus can only give birth to one of its four neighbors. Eventually a fungus will become surrounded by fungus, resulting in wasted birth events. For this reason increasing the birth rate beyond a certain value does not change the population of the fungus because the lattice is fully occupied by fungus.

9 Discussion & Future Work

Within the mean field approximation we assume that space does not matter and well mixing of all sites. This essentially, in the differential equation, gives every site an infinite neighborhood for dispersal, movement, and interaction. Spatial structure is entirely neglected and we are only concerned with the actual state within a given site. Within this

framework we have that a site containing a frog is dependant upon the state of the fungus in that site (hence the need for $P[2]$ and $P[4]$).

In the pair approximation, we assume that the dynamics are driven by the interaction of a site with its adjacent neighbors. While we ignore correlations forming over a distance greater than two sites, it captures to a certain extent, how the spread and movement of the respective species influence steady state outcomes for the system. There is a particular fashion of coupling betwixt the two species. We have maintained the mean field single site dependency of state but have extended the dependency to involve adjacent neighbors. This is reflected in the fact that we maintain the difference between a [2] and a [4] but now also extending the dependency to involve differences between [02], [12], ... , [34], [54].

The question becomes: What is the interdependency between the frogs and the fungus? If we were to assume no dependency of the state of a frog within a site given the fungus content of that site, we could formulate a new system of ODE's. This would include state variables $P[yy], P[yh], P[yi], P[hh], P[ii], P[nn] and P[ff]$, where y is a site without a frog, h is a site with a healthy frog, i is a site with an infected frog, n is a site with no fungus, and f is a site with fungus. This assumption is put more succinctly as $P(frog\ here \mid fungus\ here) = P(frog\ here) = P(frog\ here \mid no\ fungus\ here)$. This system has loosened the assumptions on how the frog and fungus interact but the reader who is paying attention will still notice that the $P(fungus\ here) \neq P(fungus\ here \mid Infected\ Frog\ was\ here)$; thus, we still have two coupled systems.

The previous system still maintained the local structure of the frogs, presumably due to the biology of their movement. Considering the difference in magnitude between the movement rates and the rest of the parameters a different assumption may be legitimate. Recall that there is already some sort of mean field behavior within the frog population due to tadpoles (i.e. birth may target any non-occupied site). What is holding us back from rescaling the movement rates while adjusting the movement to al so be mean field? Not much. We are able to strip away the pair structure of the frogs and reach a system with even fewer state variables $P[h], P[i], P[nn], P[ff]$. The only change in this hybrid method from the last is the introduction of well mixing amongst the frog population. This seems to be justified by previous models (mean field and pair approximation) due to the near complete insensitivity to the value of m_h and m_i thus making it possible to let the movement rates approach infinity.

Now consider a fungus that doesn't die or spread but can infect frogs. With our mean field approximation, moving frogs may come in contact with the stationary fungus which infects the frog. The frog wanders off to a randomly chosen site and dies, thus spreading the fungus in a mean field fashion. Now pulling back a little closer the models we had before with normal fungus behavior the fungus is a local disperser. With the mean field frog movement we have, as the toy example above pointed out, these potentials to do essentially long distance dispersal, thus we can make another assumption that the fungus behaves in a mean field manner. This assumption transforms the system into three state variables $P[h], P[i]$, and $P[f]$. Through a particular series of decoupling, we have reduced a twenty dimensional pair approximation system to a three dimensional mean field system.

There are several questions raised throughout this formulation, including biological validity. Perhaps the time scales of the ecology for a particular pair species is such that it naturally lends itself to this reduction. What are the major differences in the dynamics between these systems? Perhaps the smallest system is just as rich in qualitative behavior as the most complicated or maybe the quantitative measures are way off. Or maybe end states are preserved throughout the reduction process but the intermediate dynamics differs dramatically. A very involved study could be conducted in order to properly formulate each of these unfolding layers. This could uncover different paths of reduction, where the steps are made clear and the information lost along the way made apparent.

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Appendix

```
%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%
%%%%                                                                      %%%%
%%%%MTBI 2006                                                             %%%%
%%%%Revised on:    July 18, 2006                                          %%%%
%%%%Created by:    Cassie Pawling                                         %%%%
%%%%               Mario Ayala                                            %%%%
%%%%               Adrian Smith                                           %%%%
%%%%               Ben Morin
%%%%
%%%%Function:  Will simulate our harlequin frog project                   %%%%
%%%%           at MTBI in 2006.  Simulates pair approximation             %%%%
%%%%           model where chytrid fungus can infect and kill             %%%%
%%%%           the frog population.  We will change our                   %%%%
%%%%           parameters to show the difference between the              %%%%
%%%%           wet season and the dry season.                             %%%%
%%%%                                                                      %%%%
%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%

function  frogs(fp,hp,ip,phif,phih,muf,mui,movei,moveh,sigmai,sigmaf, placement, dry)
%multstep(.2, .1, .1, .15, 1, 1/49, 1/3, 12, 24, 1/3, 1/4, [1, 1, 1], 1),
%fungus prevails
%multstep(.2, .1, .1, .4, 1, 1/49, 1/3, 12, 24, 1/3, 1/4, [1, 1, 1], 1)
%%%%%%%%%%%%%%%%%%%%%%%%%%%%INPUTS%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%
% fp          initial proportion of fungus
% hp          intial prortion of healthy frogs
% ip          initial proportion of infected frogs
% phih        successful birth rate of healthy frogs
% phif        successful birth rate of fungus
% muf         fungus death rate
% mui         infected frog death rate
% movei       infected frog movement rate
% moveh       healthy frog movement rate
% sigmaf      rate of successful fungus to frog infection
% sigmai      rate of successful infected frog to frog infection
% placement   A vector with three values to determine the distributions of
%             fungus, frogs, and infected frogs in initial placement
%dry          The effective percentage of certian parameters during the dry
%             season
%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%
% State variables
```

```
% state 0 : empty water/wetland
% state 1:  fungus
% state 2;  healthy frog
% state 3:  infected frog
% state 4:  heaalthy frog with fungus
% state 5:  infected frog with fungus
%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%


n=100; % lattice dimension
lattice=zeros(n,n); %creates a lattice of zero with dimension n by n
M=n^2; %total number of sites
Fungus_Coordinates=zeros(M,2); % tracking addresses of the sites occupied
% by a fungus(sites of state 1, 4, 5)
H_Frogs_Coordinates=zeros(M,2);% tracking addresses of the sites occupied
% by a healthy frog (h_frog)(sites of state 2, 4)
I_Frogs_Coordinates=zeros(M,2);% tracking addresses of the sites occupied
% by a infected frog (i_frog)(sites of state 3, 5)

cf=0; % cf is the number of sites on lattice with fungus at the moment.
fpop=floor(fp*M); % initial fungus population is equal to percentage of
% fungus times M, floor is used in case it is a decimal

ch=0; % ch is the number of sites on lattice with h_frog at the moment.
hpop=floor(M*hp); % initialization of healthy frog population size

ci=0; % ci is the number of sites on lattice with i_frog at the moment.
ipop=floor(M*ip); % initialization of infected frog population size

% handling potential initialization abnomalities.
if ((hp+ip)>1)
disp('the initial proportion of frogs has to be less than one')
return
end

if (fp>1)
    disp('Reducing Fungus proportion to one')
    fp=1;
end

if (fp<0||hp<0||ip<0)
    disp('How dare you put a negative!')
```

```
    return
end

switch placement(1)
% Placement is one of inputs, this calls the first value of the vector,
% with specifies the distribution of fungus.
    case 1 %uniform distribution
        disp('Fungus_uniform')
        while (cf<fpop) % place fungus on the lattice
            row=unidrnd(n); % row is a random number between 1 and n.
            col=unidrnd(n);
             if (~lattice(row,col))
                lattice(row,col)=1;
                cf=cf+1; % Current fungus site count is increased by 1
                Fungus_Coordinates(cf,1)=row;
                Fungus_Coordinates(cf,2)=col;
                % store the address of fungus sites in 'Fungus address
                % book'
            end
        end
    case 2 %distributed in center
        disp('Fungus_normal')
        var=ceil(sqrt(fpop)/6); %The most appropriate value for variance
        while (cf<fpop)
            row=mod(ceil(n/2+normrnd(0,var))-1+n,n)+1; %Ask Ben
            col=mod(ceil(n/2+normrnd(0,var))-1+n,n)+1; %Ask Ben
           if (~lattice(row,col))
                lattice(row,col)=1;
                cf=cf+1;
                Fungus_Coordinates(cf,1)=row;
                Fungus_Coordinates(cf,2)=col;
            end
        end
end

switch placement(2) % Calls the second value of the placement vector
    case 1 % H_frog is uniform distribuited
        disp('Uniform-Healthy Frog')
        while (ch<hpop)
            row=unidrnd(n);
            col=unidrnd(n);
            if (lattice(row,col)==0)
```

```
                % The site is empty, put a frog there, it turns to 2.
                lattice (row,col)=2;
                ch=ch+1;
                H_Frogs_Coordinates(ch,1)=row;
                H_Frogs_Coordinates(ch,2)=col;
            elseif (lattice(row,col)==1)
                % The site has fungus, put a frog there, it turns to 4.
                lattice (row,col)=4;
                ch=ch+1;
                H_Frogs_Coordinates(ch,1)=row;
                H_Frogs_Coordinates(ch,2)=col;
            end
        end
end

switch placement(3)
    case 1 %uniform distribuited
        disp('Uniform-Infected Frog')
        while (ci<ipop)
            row=unidrnd(n);
            col=unidrnd(n);
            if (lattice(row,col)==0)
                %If the site is empty, put an i_frog, it turns to 3
                lattice (row,col)=3;
                ci=ci+1;
                I_Frogs_Coordinates(ci,1)=row;
                I_Frogs_Coordinates(ci,2)=col;
            elseif (lattice(row,col)==1)
                % The site has a fungus, put an i_frog there, it turns to 5
                lattice (row,col)=5;
                ci=ci+1;
                I_Frogs_Coordinates(ci,1)=row;
                I_Frogs_Coordinates(ci,2)=col;
            end

        end
end

colormap([0,0,0;0,0,1;0,1,0;1,0,0;0,1,1;1,0,1;]);
image(lattice + 1);
```

```
max=n^2; % Number of events

A=zeros(max,1);  % A(i) is the time elapsed till the event i-1
B=A;             % save in this matrix the frog population in every step
C=A;             % save the fungus population size

A(1)=0;                 % start at the time 0
B(1)=floor(M*(hp+ip));  % the intial frogs population size
C(1)=floor(M*fp);       % the initial fungus population size

%Here we are going to find the coordinates of the empty sites ( with no
%frogs) and then store them in the matrix Empty_Coordinates.

Empty_Coordinates=zeros(M,2); % define the address book of empty sites
cE=0; % cE is the number of empty sites.
for i=1:n
    for j=1:n
        if(lattice(i,j)==0 || lattice(i,j)==1)
            cE=cE+1;
            Empty_Coordinates(cE,1:2)=[i,j];
        end
    end
end

Tr= ch*(phih + moveh)+ci*(movei+sigmai+mui)+cf*(phif+sigmaf+muf);
% Tr here is the initial value of total rates of all events.

% The major loop starts here
%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%
k=1000;   % number of steps in the process
H_frogs=zeros(k,1);
I_frogs=zeros(k,1);
Fungus=zeros(k,1);
H_frogs(1)=floor(M*hp);
I_frogs(1)=floor(M*ip);
Fungus(1)=floor(M*fp);

step=1;
slope = 1;
%for step=1:k
while ((slope > 0.1) & (step <=k))
for count=1:max  % NOW LET US START WITH THE SIMULATION
```

```
if(Tr==0)
disp('Tr=0')
pause
end

Tr= ch*(phih + moveh)+ci*(movei+sigmai+mui)+cf*(phif+sigmaf+muf);
Pphih=(phih*ch)/Tr;
Pmoveh=(moveh*ch)/Tr;
Pmovei=(movei*ci)/Tr;
Psigmai=(sigmai*ci)/Tr;
Pmui=(mui*ci)/Tr;
Pphif=(phif*cf)/Tr;
Pmuf=(muf*cf)/Tr;
Psigmaf=(sigmaf*cf)/Tr;
P1=[Pphih, Pmoveh, Pmovei, Psigmai, Pmui, Pphif, Pmuf, Psigmaf];
P=cumsum(P1);
A(count+1)=A(count)+ exprnd(1/Tr);

r=rand(1);  % Choose an event out of 8 possible events

w=unidrnd(4);  % Choose a nearest-neighbor for event
if (w==1)
 a=1;
 c=0;
elseif(w==2)
 a=0;
 c=1;
elseif(w==3)
 a=-1;
 c=0;

elseif(w==4)
 a=0;
 c=-1;
end

if (r<P(1))     % birth of a frog
%    disp('p(1): birth of a frog')
    if (cE==0)
        continue;
    end
```

```
    b=unidrnd(cE);  % choose an empty site randomly
    if (lattice(Empty_Coordinates(b,1),Empty_Coordinates(b,2))==1)
        lattice(Empty_Coordinates(b,1),Empty_Coordinates(b,2))=4;
    elseif (lattice(Empty_Coordinates(b,1),Empty_Coordinates(b,2))==0)
            lattice(Empty_Coordinates(b,1),Empty_Coordinates(b,2))=2;
    else
        disp('error-birth of a frog')
        break
    end
    ch=ch+1;
    H_Frogs_Coordinates(ch,:)=Empty_Coordinates(b,:);
    Empty_Coordinates(b,:)=Empty_Coordinates(cE,:);
    cE=cE-1;

elseif (r<P(2))   % movement of a healthy frog

     if (cE==0 || ch==0) % if no empty sites or healthy frogs, abort the operation.
        continue
     end
     d=unidrnd(ch);  % pick a health frog
     old_address_x =H_Frogs_Coordinates(d,1);
     old_address_y =H_Frogs_Coordinates(d,2);
     % Now find the address of the nearest_neighbor the healtht frog
     % will move into, provided it is empty. Boundaries
     % are wrapped around (torus lattice)
     destination_x =mod(old_address_x+a-1+n,n)+1;
     destination_y =mod(old_address_y+c-1+n,n)+1;

     if (lattice (destination_x,destination_y)==0)
        lattice(destination_x,destination_y)=2;
     elseif (lattice (destination_x,destination_y)==1)
        lattice(destination_x,destination_y)=4;
     else
         continue  % if the destination already has a frog, skip the rest.
     end
     H_Frogs_Coordinates(d,1)=destination_x;
     % the frog moved, change address
     H_Frogs_Coordinates(d,2)=destination_y;
     % the new address was empty, find it's id in the Empty A_book.
     findrow=find(Empty_Coordinates(:,1)==destination_x & Empty_Coordinates(:,2)==destinatio
     % The destionation in the Empty A_book is replaced by old_location of the frog.
```

```
      Empty_Coordinates(findrow(1),1)=old_address_x;
      Empty_Coordinates(findrow(1),2)=old_address_y;

      % Now change state in the old address, for frog has left.
      if(lattice(old_address_x,old_address_y)==2)
        lattice(old_address_x,old_address_y)=0;
      elseif(lattice(old_address_x,old_address_y)==4)
        lattice(old_address_x,old_address_y)=1;
      end

elseif (r<P(3))    %movement of an infected frog
      if (cE==0 || ci==0)     % if no empty sites or infected frogs, abort the operation.
         continue
      end
      d=unidrnd(ci);  % pick an infected frog

      old_address_x =I_Frogs_Coordinates(d,1);
      old_address_y =I_Frogs_Coordinates(d,2);
      % Now find the address of the nearest_neighbor the infected frog
      % will move into, provided it is empty. Boundaries
      % are wrapped around (torus lattice)
      destination_x =mod(old_address_x+a-1+n,n)+1;
      destination_y =mod(old_address_y+c-1+n,n)+1;

      if (lattice (destination_x,destination_y)==0)
         lattice(destination_x,destination_y)=3;
      elseif (lattice (destination_x,destination_y)==1)
         lattice(destination_x,destination_y)=5;
      else
          continue  % if the destination already has a frog, skip the rest.
      end
      I_Frogs_Coordinates(d,1)=destination_x;
      % the frog moved, change address
      I_Frogs_Coordinates(d,2)=destination_y;
      % the new address was orginally empty, find it's id in the Empty A_book.
      findrow=find(Empty_Coordinates(:,1)==destination_x & Empty_Coordinates(:,2)==destinatio
      % The destionation in the Empty A_book is replaced by old_location of the frog.

      Empty_Coordinates(findrow(1),1)=old_address_x;
      Empty_Coordinates(findrow(1),2)=old_address_y;

      % Now change state in the old address, for frog has left.
```

```
     if(lattice(old_address_x,old_address_y)==3)
       lattice(old_address_x,old_address_y)=0;
     elseif(lattice(old_address_x,old_address_y)==5)
       lattice(old_address_x,old_address_y)=1;
     end

elseif (r<P(4))  %an infected frog infects a neighbor frog
     if ci==0
         continue
     end
     d=unidrnd(ci);  % Choose an infected frog
     % Now find the address of the nearest_neighbor this infected frog
     % will infect, provided it has a healthy frog. Boundaries
     % are wrapped around (torus lattice)
     target_x =mod(I_Frogs_Coordinates(d,1)+a-1+n,n)+1;
     target_y =mod(I_Frogs_Coordinates(d,2)+c-1+n,n)+1;

     if (lattice (target_x,target_y)==2)
        lattice(target_x,target_y)=3; ci=ci+1;
     elseif(lattice (target_x,target_y)==4)
        lattice(target_x,target_y)=5; ci=ci+1;
     else
       continue% if the destination doesn't have a healthy frog, skip rest.
     end

     I_Frogs_Coordinates(ci,1)=target_x;
     I_Frogs_Coordinates(ci,2)=target_y;

     findrow=find(H_Frogs_Coordinates(:,1)==target_x & H_Frogs_Coordinates(:,2)==target_y);

     H_Frogs_Coordinates(findrow(1),:)=H_Frogs_Coordinates(ch,:);
     ch=ch-1;

elseif (r<P(5))   % death of an infected frog
    if ci==0
        continue
    end
    d=unidrnd(ci);

    if (lattice(I_Frogs_Coordinates(d,1),I_Frogs_Coordinates(d,2))==3)
        lattice(I_Frogs_Coordinates(d,1),I_Frogs_Coordinates(d,2))=1;
        cf=cf+1; %update fungus count
```

```
        Fungus_Coordinates(cf,:)=I_Frogs_Coordinates(d,:);
    elseif (lattice(I_Frogs_Coordinates(d,1),I_Frogs_Coordinates(d,2))==5)
        lattice(I_Frogs_Coordinates(d,1),I_Frogs_Coordinates(d,2))=1;
    else
        disp('error-death of frog')
        pause
    end
    % update empty (frog-free) count.
    cE=cE+1;
    Empty_Coordinates(cE,:)=I_Frogs_Coordinates(d,:);

    I_Frogs_Coordinates(d,:)=I_Frogs_Coordinates(ci,:);
    % update infected frog count.
    ci=ci-1;

elseif (r<P(6))    %birth of fungus
      b=unidrnd(cf);
      target_x = mod(Fungus_Coordinates(b,1)+a-1+n,n)+1;
      target_y = mod(Fungus_Coordinates(b,2)+c-1+n,n)+1;

      if (lattice(target_x,target_y)==0)
          lattice(target_x,target_y)=1;
      elseif (lattice(target_x,target_y)==2)
          lattice(target_x,target_y)=4;
      elseif (lattice(target_x,target_y)==3)
          lattice(target_x,target_y)=5;
      else
        continue
      end
      cf=cf+1;
      Fungus_Coordinates(cf,1)=target_x;
      Fungus_Coordinates(cf,2)=target_y;

elseif(r<P(7))    %death of fungus
    if (cf==0)
        continue
    end
    b=unidrnd(cf);
    if (lattice(Fungus_Coordinates(b,1),Fungus_Coordinates(b,2))==1)
        lattice(Fungus_Coordinates(b,1),Fungus_Coordinates(b,2))=0;
    elseif (lattice(Fungus_Coordinates(b,1),Fungus_Coordinates(b,2))==4)
        lattice(Fungus_Coordinates(b,1),Fungus_Coordinates(b,2))=2;
```

```
    elseif (lattice(Fungus_Coordinates(b,1),Fungus_Coordinates(b,2))==5)
        lattice(Fungus_Coordinates(b,1),Fungus_Coordinates(b,2))=3;
    end
   Fungus_Coordinates(b,:)=Fungus_Coordinates(cf,:);
   cf=cf-1;

elseif(r<P(8))  %the fungus infects one frog
    if (ch==0 || cf==0)
        continue
    end
    b=unidrnd(cf);
    if (lattice(Fungus_Coordinates(b,1),Fungus_Coordinates(b,2))==4)
       lattice(Fungus_Coordinates(b,1),Fungus_Coordinates(b,2))=5;
       ci=ci+1;
       I_Frogs_Coordinates(ci,:)=Fungus_Coordinates(b,:);
       findrow=find(H_Frogs_Coordinates(:,1)==Fungus_Coordinates(b,1) & H_Frogs_Coordinates(

       H_Frogs_Coordinates(findrow(1),:)=H_Frogs_Coordinates(ch,:);
       ch=ch-1;
    else
        continue;
    end
end % of an event (started at "if r<P(1)")
% display the lattice in motion every 100 events.
if(mod(count,10^3)==0)
    subplot(211),
    H=image(lattice+1);drawnow;pause(.001);
    hold on;
end

end % of the count_loop, one step
% store size of H_frogs, I_frogs and fungus in a vector, later in data
% file after each step.

H_frogs(step)=ch/M;
I_frogs(step)=ci/M;
Fungus(step)=cf/M;

% regresson as stopping criteria
if (step>399 & mod(step,100)==0)
    x=step-99:step;
    y=Fungus(step-99:step);
```

```
    numerator=100*sum(x.*y)-sum(x)*sum(y);
    denominator=100*sum(x.^2)-(sum(x))^2;
    slope=abs(numerator/denominator)
end

end % of while

t=1:k;
subplot(212),
plot(t,H_frogs,'-g',t,I_frogs,'*r',t,Fungus,'+b')
hold on

save -ascii Parameter1H H_frogs;
save -ascii Parameter1I I_frogs;
save -ascii Parameter1F Fungus;
```