A SIMULATION MODEL FOR THE SPREAD OF SWINE FLU PANDEMIC

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INTRODUCTION

This is a collaborative interdisciplinary study performed by students from the Biological Sciences Department and the Mathematics Department at City Tech.

The world has seen a couple of pandemics over the last 10 years and chances are that we may have to face even more pandemics in the near future. Realistic Mathematical models, simulating the spread of contagion can be used to great benefit by state and federal government agencies as well as health organizations around the world to better prepare and quickly contain the spread of pandemics. A novel Influenza A H1N1 virus outbreak emerged in April 2009 and by December 2009, spread across the world. This marked the beginning of the first influenza pandemic of the 21st century. Our study describes the etiology, transmission, symptoms, treatment and prevention of swine flu. We focused on the epidemiology of the disease in the US and worldwide.

On the mathematical side, the main goal of this project was to design and implement in MATLAB a stochastic model (i.e. a mathematical model with random variables) that simulates the spread of swine flu on a square grid of susceptible individuals, using realistic dynamics. The model depends on a small number of parameters, mostly various probabilities that define the different interactions in the model. Some key probabilities for which we would need realistic numerical values based on historical data collected from the swine flu pandemic in 2009, are the following: the probability that an infected individual will spread the disease to an immediate neighbor on the grid and the probability that an infected individual may recover from the disease and become immune or die. One of the main questions we want to answer using simulations is how sensitive the size of a pandemic is to the epidemiological parameters of the model.

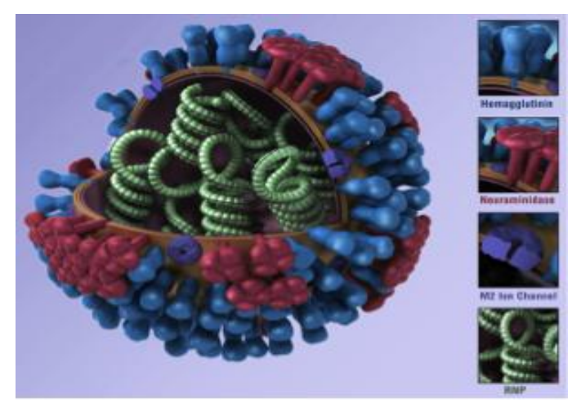
SWINE FLU

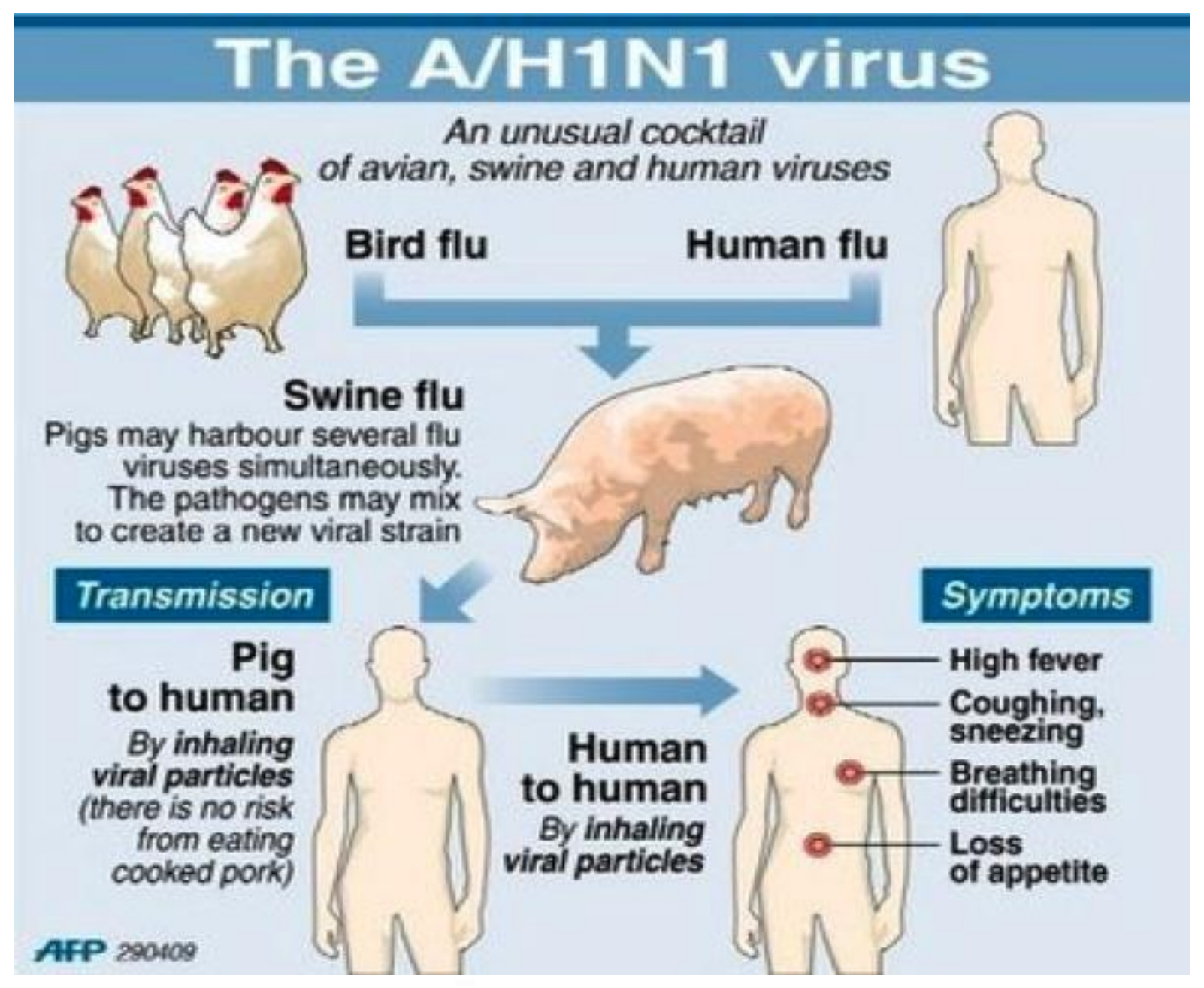
- Infection that initially affected only pigs;
- The Human Swine Flu, caused by H1N1 influenza, is a respiratory contagious disease;
- In mid-April, 2009 the H1N1 "Swine Flu" was recognized as the first pandemic influenza of the 21st century ;
- CDC's Influenza Division laboratories in Atlanta were the first in the world to identify the new 2009 H1N1 virus strain.

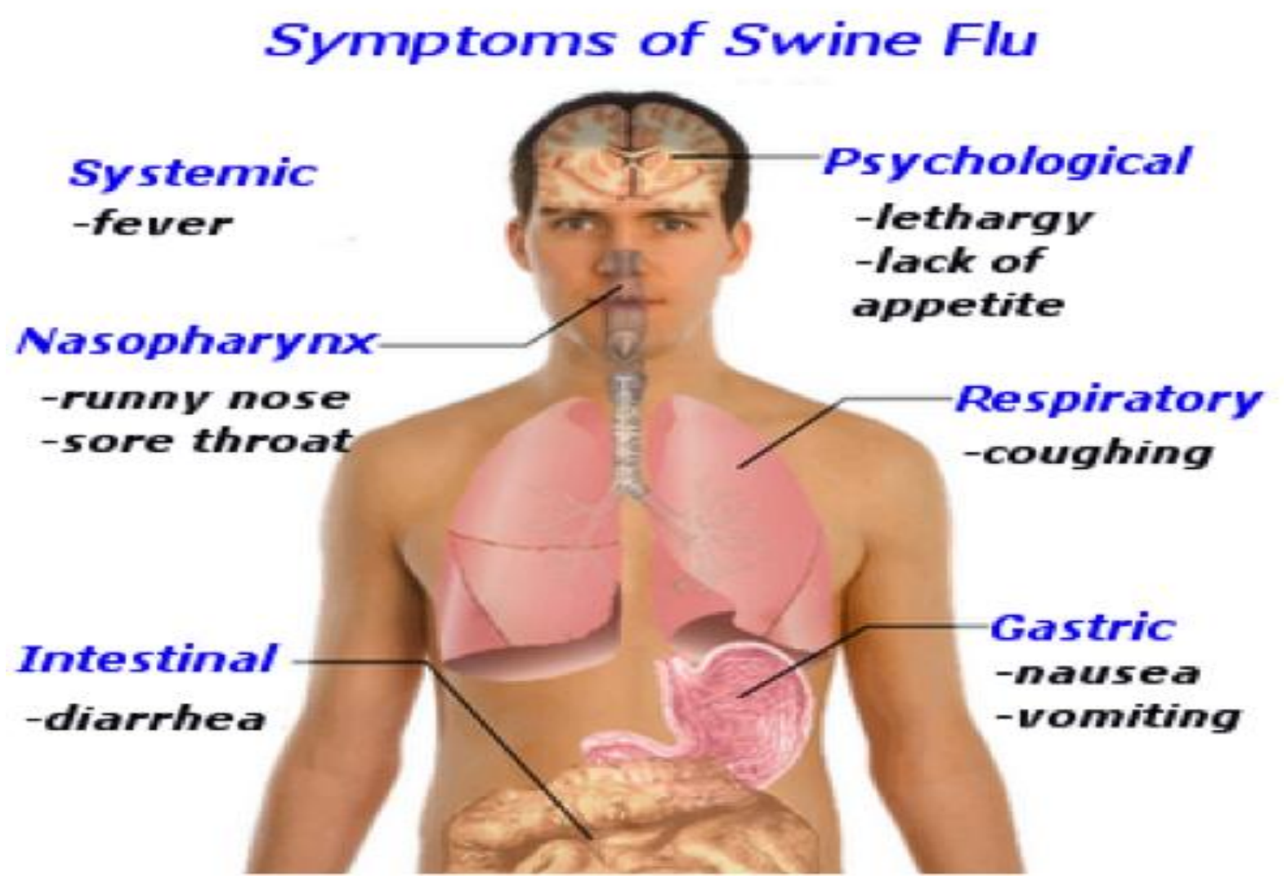
KEY INFLUENZA VIRAL FEATURES

Surface Proteins

A. Hemagglutinin (HA)
B. Neuraminadase (NA)
C. M2 Ion Channel
D. Ribonucleoprotein (RNP)







INFLUENZA INCUBATION PERIOD

- 1- 7 days (typically 2-3 days);
- Viral shedding can begin 1 day before illness onset;
- People can be contagious to others from the day before illness;
- Most people will shed virus and possibly able to spread flu to others for 5-7 days after illness onset;
- Children, severely ill persons, and those with weakened immune systems may shed virus for longer than 7 days.

DETECTION OF 2009 H1N1 VIRUS

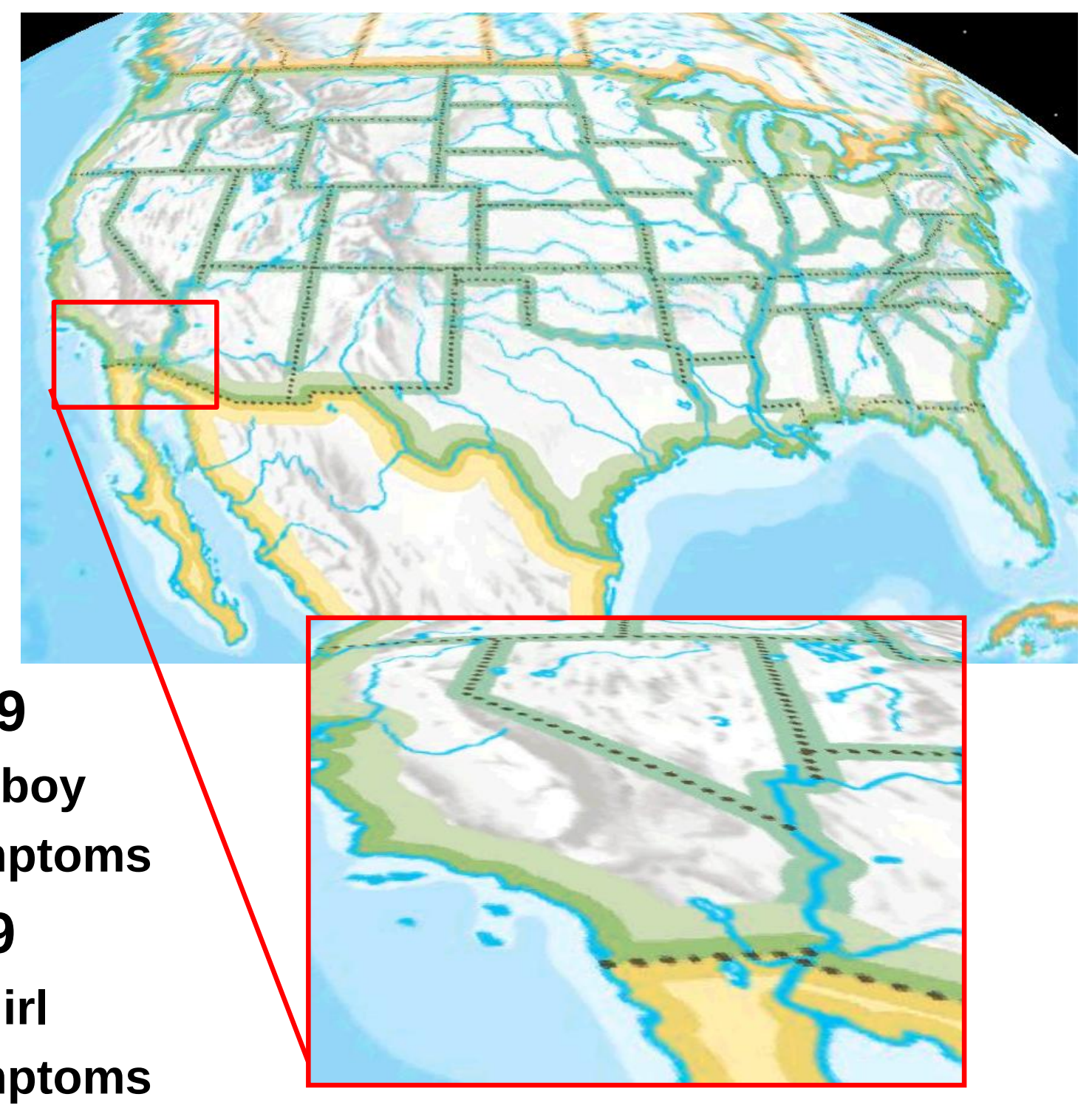
- 2009 pandemic influenza A (H1N1) virus testing began at CDC on April 15th;
- June 11, 2009 WHO declared Global pandemic of novel influenza A (H1N1) virus.

MMWR April 24, 2009

Swine Influenza A (H1N1) Infection in Two Children — Southern California, March–April 2009

On April 21, this report was posted as an MMWR Early Release on the MMWR website (http://www.cdc.gov/mmwr).

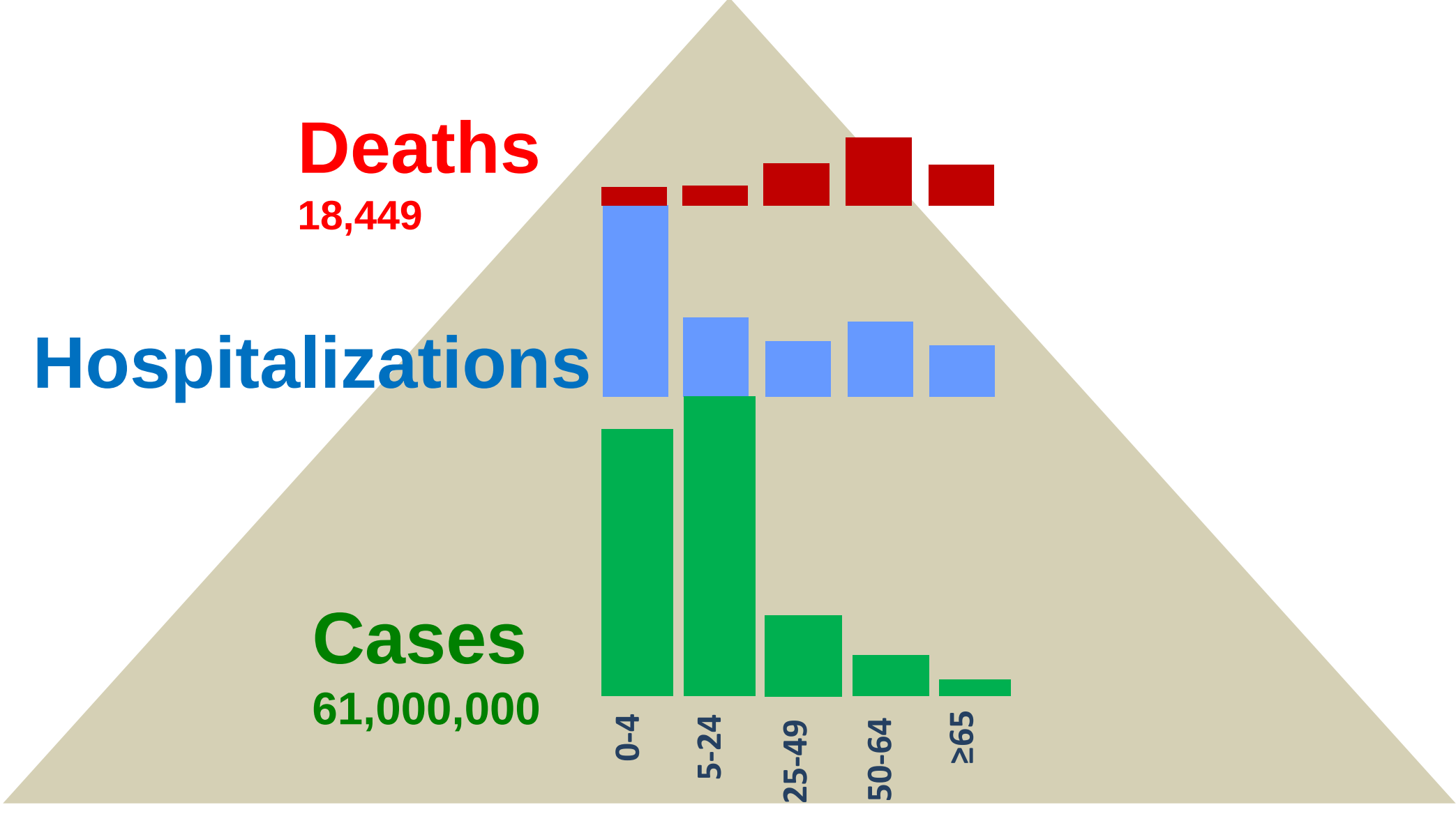
NOVEL SWINE INFLUENZA DETECTED



- April 15, 2009
  - 10-year-old boy
  - Mild flu symptoms
- April 17, 2009
  - 8-year-old girl
  - Mild flu symptoms

Southern California, US

More than 214 countries and overseas territories had reported laboratory confirmed cases of pandemic influenza H1N1 2009, including at least 18,449 deaths (WHO August 6, 2010)



Approximate Rate per 100,000 population

2009 H1N1 ACCOMPLISHMENTS

- One of the most important laboratory activities performed at CDC was the selection and development of a candidate vaccine virus for use in the 2009 H1N1 vaccine;
- CDC's laboratories took the first step of picking a candidate vaccine virus, which involves choosing a 2009 H1N1 virus that can be grown in mass quantities in chicken eggs;
- Once the virus is grown in mass quantities, the parts of the virus that are important for forming an immune response to the vaccine (the virus antigens), are purified to make the vaccine;
- Clinical trials of the vaccine conducted by the National Institutes of Health (NIH) found that one dose of 2009 H1N1 vaccine was enough to provide an effective immune response in people 10 years of age and older, and no significant vaccine-related health concerns from the vaccine were reported.

GROUPS AT INCREASED RISK OF SEVERE INFLUENZA INFECTION (2009 H1N1)

Most impacted populations

- Children, young adults
- Persons with underlying chronic medical conditions (e.g. chronic lung disease, heart disease, immunosuppression, neurological and neurodevelopment diseases)
- Pregnant women
- Indigenous populations

Possible risk groups

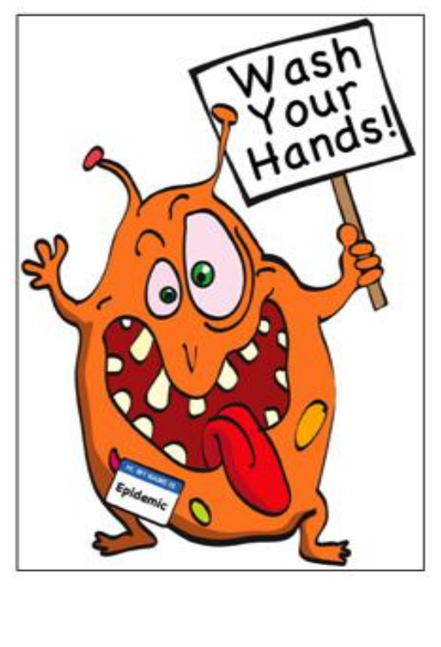
- Obesity (Body Mass Index ≥35)
- Extreme/Morbid obesity (Body Mass Index ≥40)

HOW TO PROTECT YOURSELF

✓Take time to get a flu vaccine - the single best way to protect against influenza illness;

✓Take everyday preventive actions to stop the spread of germs;

✓Take flu antiviral drugs such as ZANAMIVIR(Relenza) and TAMIFLU or others that your doctor prescribes.



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THE SIR SIMULATION MODEL

SIR stands for Susceptible, Infected, and Removed. In this model we suppose that individuals can be one of three types: susceptible if they have not yet caught the disease, infected if they currently have the disease, and removed if they have had the disease and have since recovered (and are now immune) or died, or if the individual was missing from the cell in the grid before the pandemic begins, reflected in the simulations by an initial random distribution of susceptibles and empty cells. In our computer simulations, we use 0,1,2 to represent removed, susceptible and infected, and we assign yellow, green and red colors to these cells, respectively. We measure time in discrete steps. At each time step, each infected can infect susceptibles or can recover/die, at which point the infected is removed.

Let S(t), I(t) and R(t) be the number of susceptible, infected and removed individuals at time t. At each time step each infected has probability α of infecting each susceptible. This assumes that each infected has equal contact with all susceptibles. This is called a mixing assumption. At the end of each time step, after having had a chance to infect people, each infected has probability β of being removed. Initial conditions: S(0) = N-1, I(0) = 1, R(0) = 0.
The total population is N and this remains fixed. That is: S(t) + I(t) + R(t) = N for all t.

SIR MODEL DYNAMICS

$$S(t+1) \sim Binom(S(t),(1-\alpha)^{I(t)})$$
$$R(t+1) \sim R(t) + Binom(I(t),\beta)$$
$$I(t+1) = N - R(t+1) - S(t+1)$$

MATLAB CODE FOR THE SIR MODEL COMPUTER SIMULATION

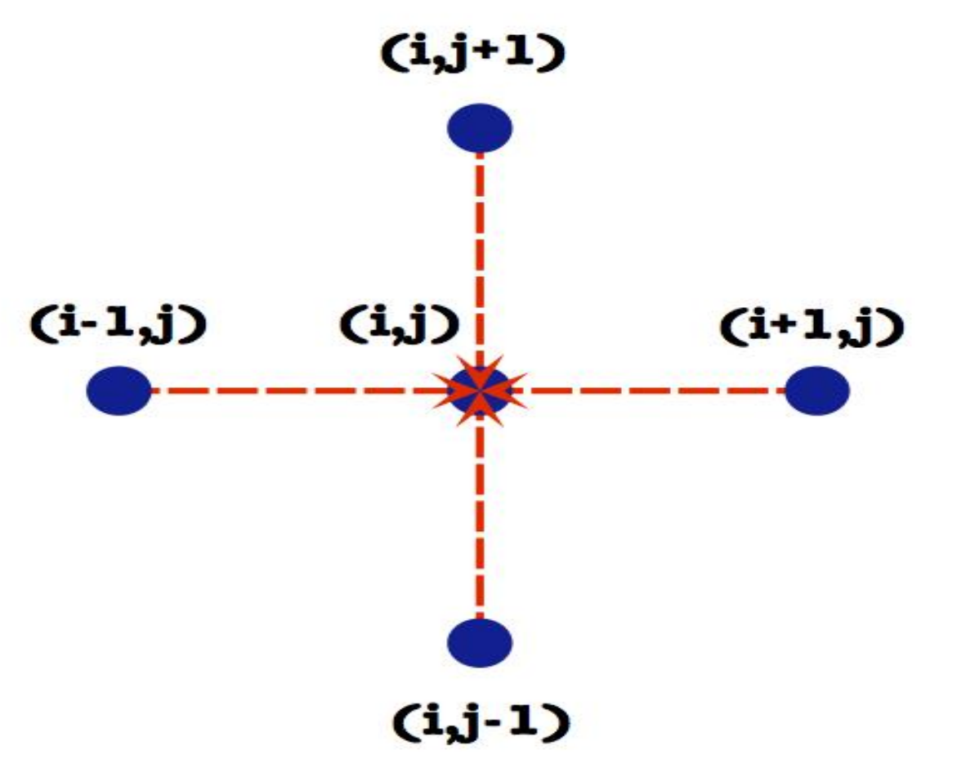
```
%% Main Simulation of Discrete SIR Epidemic Model
% Output:
% A matrix whose 3 columns are particular realizations
% of the number of susceptile (S), infected (I) and
% removed (R) individuals, over T time steps.
% Input:
% a = 0.0005; % the infection rate
% b = 0.10;   % the removal rate
% N = 1e3;    % initial number of susceptible people
% T = 1e2;    % time steps = simulation length

function SIRpaths=sir(a,b,N,T)
S = zeros(T+1,1);
I = zeros(T+1,1);
R = zeros(T+1,1);
I(1) = 1; % a single initial infected case
S(1) = N - I(1);
for t = 1:T
    % the evolution of SIR paths over time
    % sample from the Binomial distribution
    S(t+1) = binornd(S(t),(1-a)^I(t));
    R(t+1) = R(t) + binornd(I(t),b);
    I(t+1) = N - S(t) - R(t);
end
SIRpaths=[S I R];
```

THE SIR SIMULATION MODEL WITH SPATIAL INTERACTIONS ON A GRID

This model incorporates spatial interactions. Like the SIR model we suppose that we have a population made up of susceptible, infected, and removed individuals. The difference is that the individuals are placed on a grid and an infected individual can only infect a susceptible individual if they are neighbors. We define the neighbors of a point (x,y) to be the four points (x−1,y), (x,y−1), (x,y+1), (x+1,y)(smaller or larger neighborhoods can also be considered). We take time in discrete steps. At each step an infected individual has a probability α of infecting each of its susceptible neighbors. Thus for a susceptible individual, the probability of remaining uninfected is $(1 - \alpha)^x$ where x is the number of infected neighbors. After having had a chance to infect its neighbors, an individual is removed with probability β. We restrict our simulation to a grid of size N x N. Let X_t be our grid, that is a matrix of size N × N representing the population at time t:

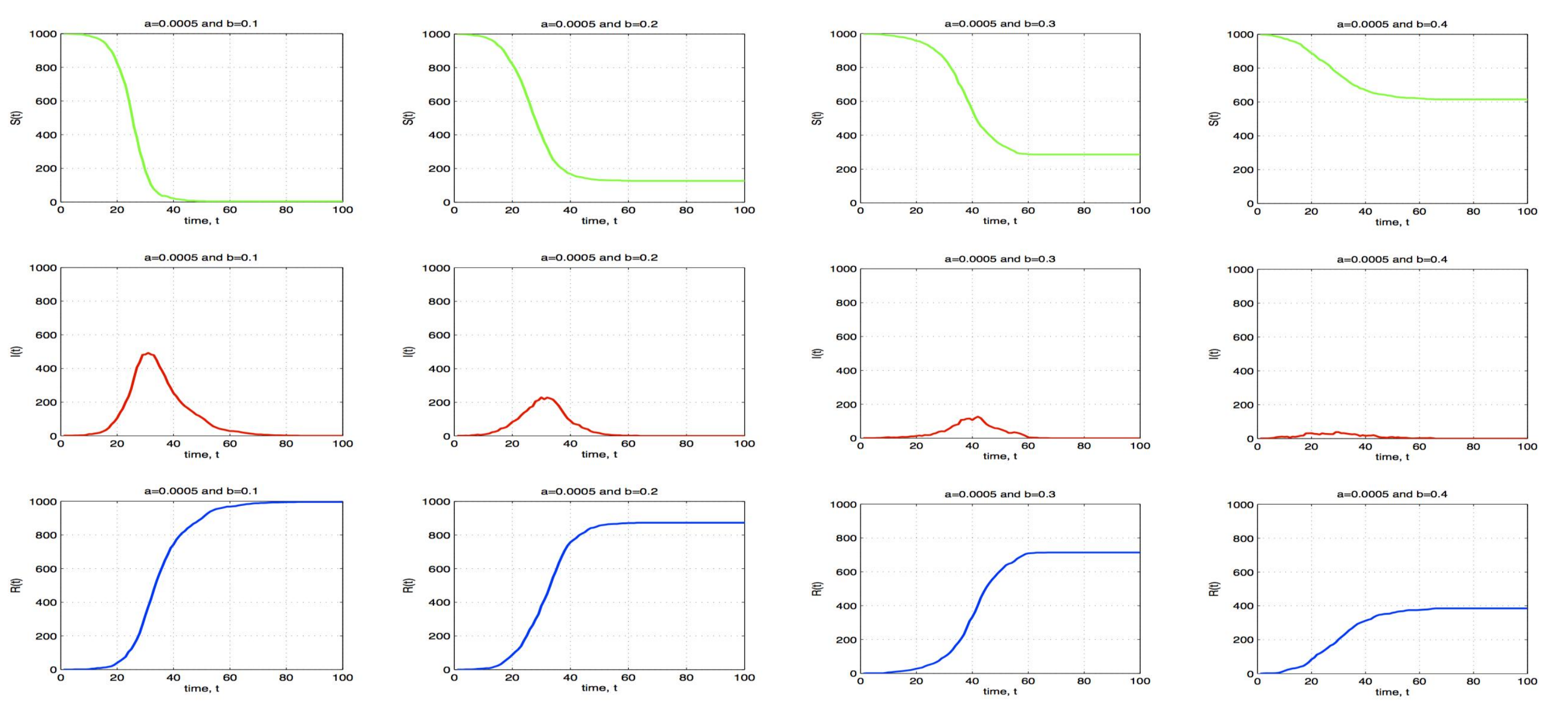
$$X_t(i,j) = \begin{cases} 2 & \text{if } (i,j) \text{ is infected;} \\ 1 & \text{if } (i,j) \text{ is susceptible;} \\ 0 & \text{if } (i,j) \text{ is removed.} \end{cases}$$

Spatial Interactions in the Grid

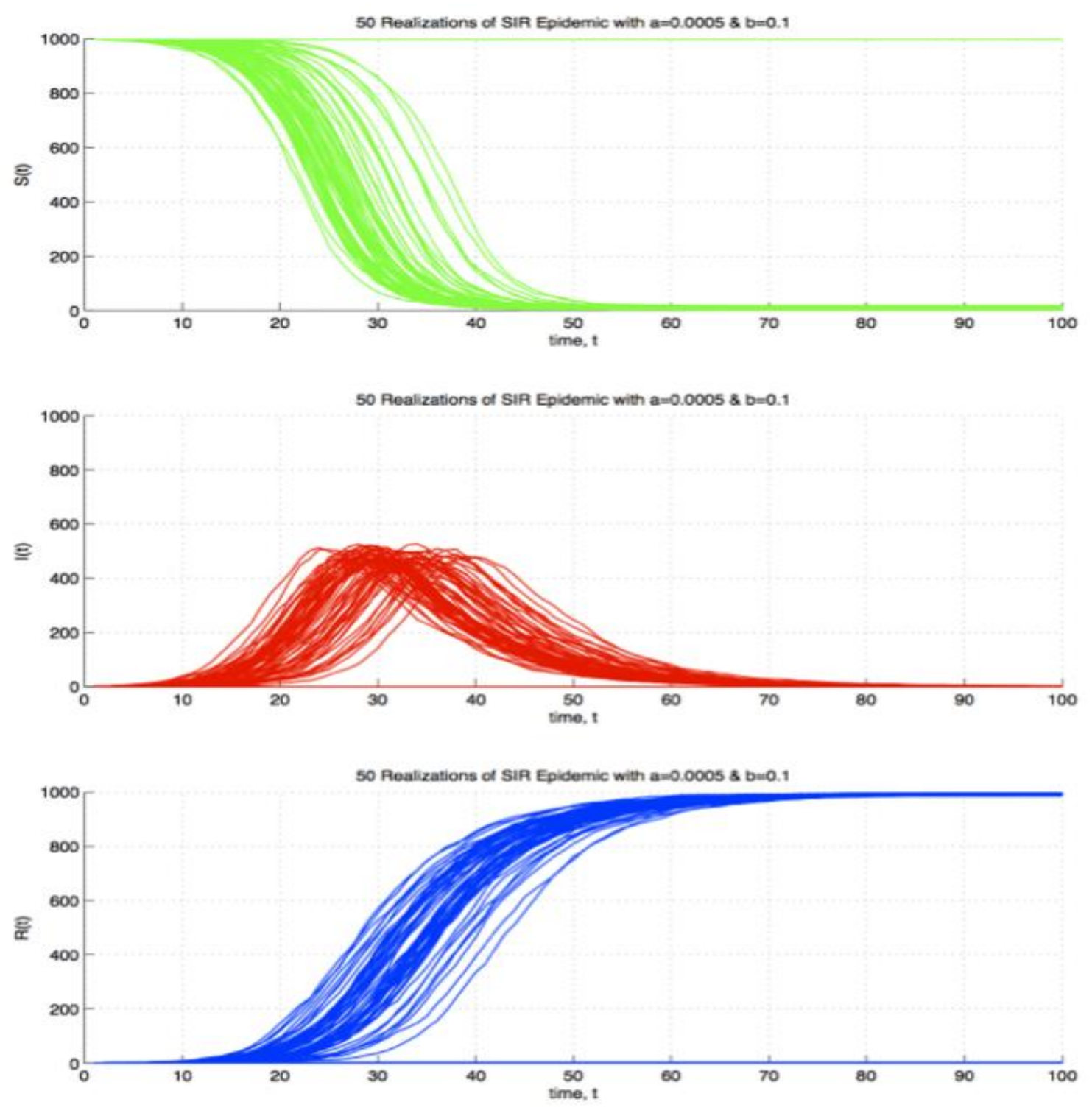


The four immediate neighbors of (i,j).

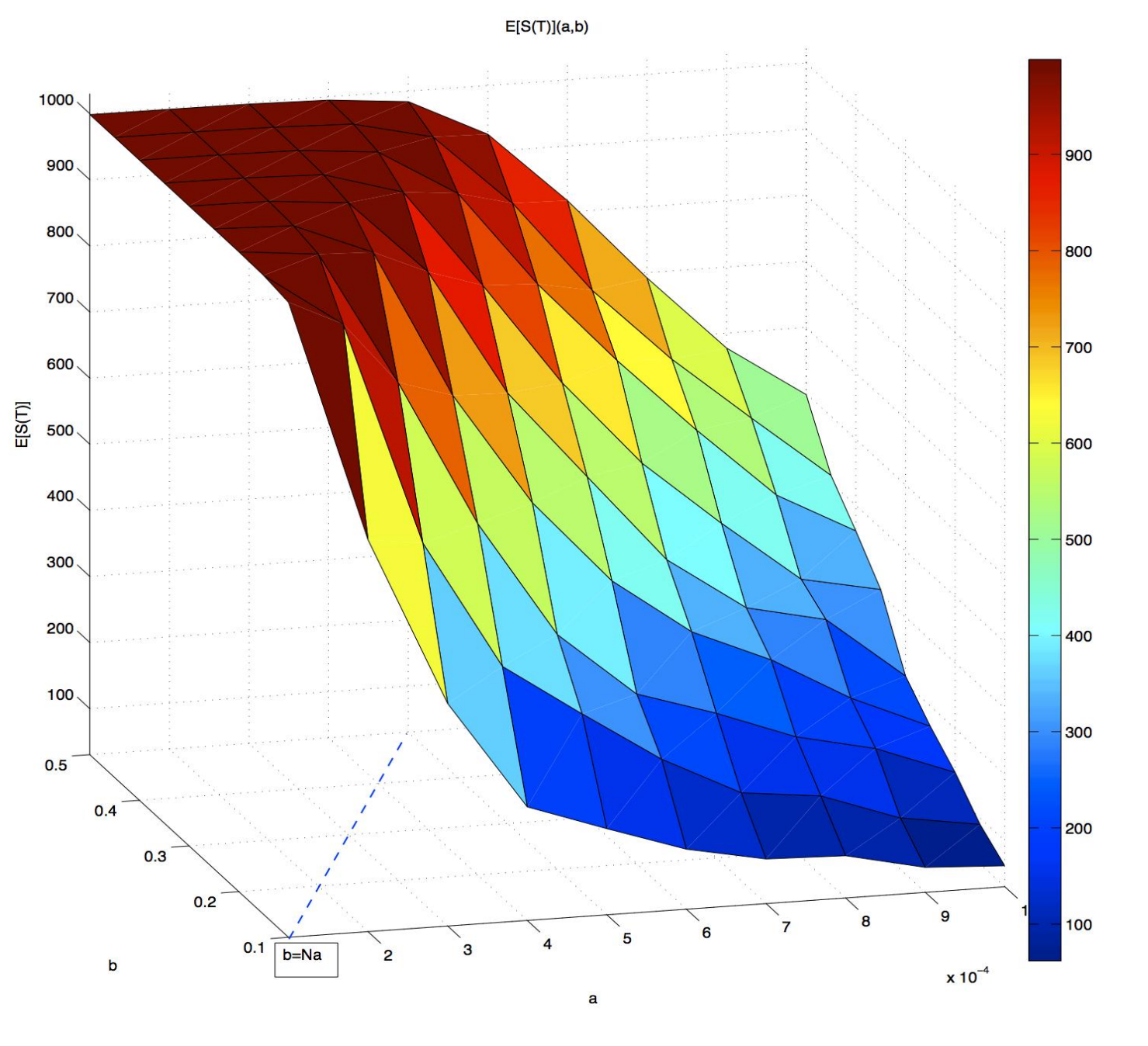
RESULTS OF THE SIMULATION FOR THE SIR MODEL



In the figures above we plot S(t), I(t), and R(t) for four separate simulations, with α = 0.0005 and β = 0.1, 0.2, 0.3, and 0.4.
The conclusion is that as β increases, the size of the epidemic decreases, in terms of I(T), the number of infections (in red).



To see the range of possible behavior for a single choice of α and β, we plot 50 realizations of the SIR simulation on the same graph.



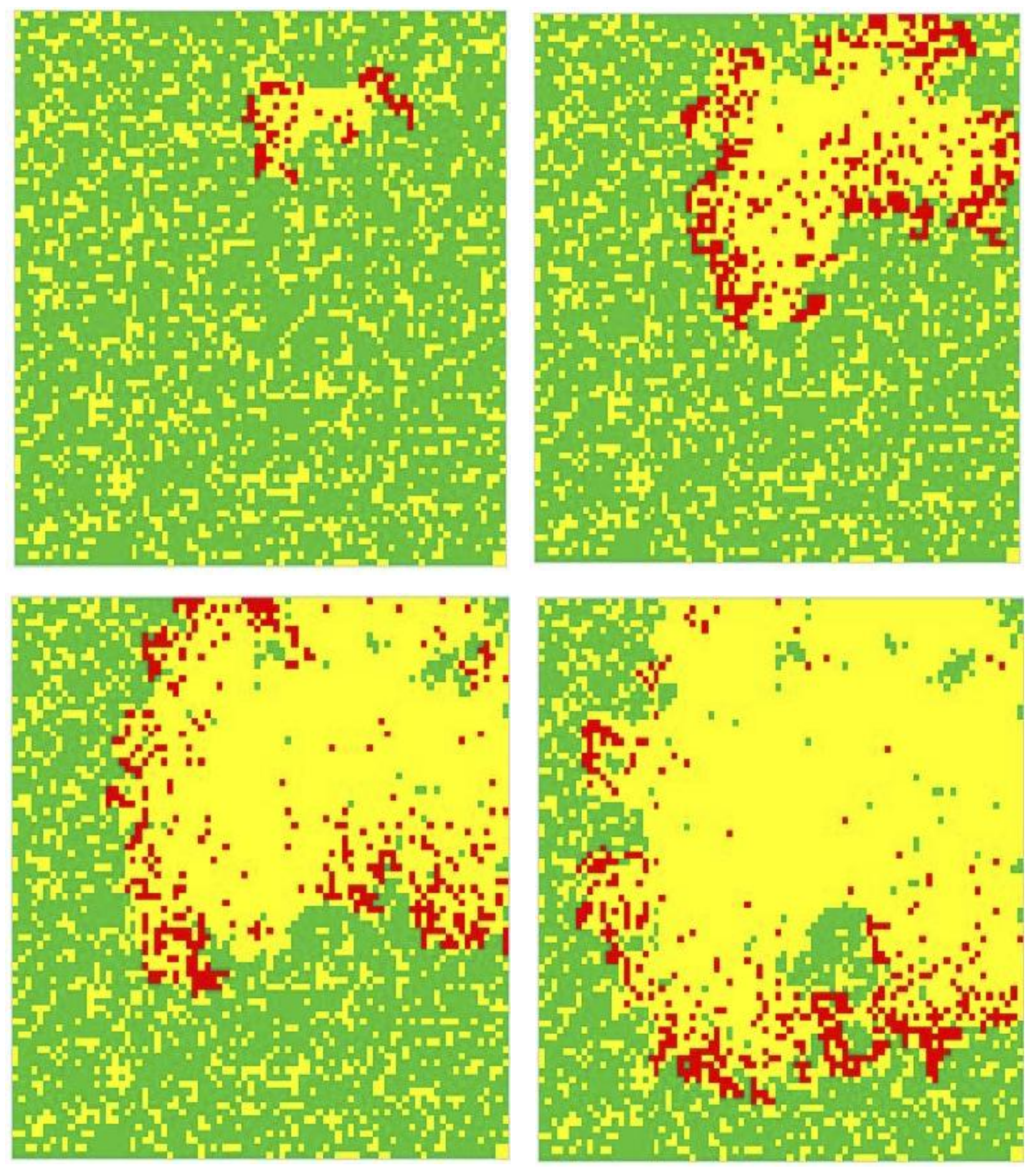
Using simulation we estimate E[S(T)] for different values of α and β and plot the surface E[S(T)](α,β). We do this for α ∈ [0.0001, 0.001] and β ∈ [0.1, 0.5] and plot the results on the 3D-graph below.

RESULTS OF THE MATLAB SIMULATION FOR THE SIR MODEL WITH SPATIAL INTERACTIONS ON A GRID

```
%% Main Simulation for the Spread of Pandemic

iDist=0.75; % probability of having a susceptible individual in a cell
ncol=80; % grid dimensions
nrow=80;
time=100; % time steps
a=0.35; % probability of infection, see function Spread()
b=0.1; % probability of removal, see function Spread()

% initial distribution of susceptible individuals
M=1*(rand(nrow,ncol)<iDist);
% the pandemic begins at some random cell in the grid
M(randi(nrow,1),randi(ncol,1)) = 2;
map=[1 1 0;0.1 0.75 0.2;1 0 0]; % yellow, forest green and red
%map=[1 1 1;0 1 0;1 0 0]; % white, green and red colors
colormap(map); % creates a color map to visualize the grid
%pcolor(M); % an alternative way to visualize the grid
image(M+1)
axis off
axis square
F(1)=getframe; % record the first frame into a movie
% iterate the pandemic simulation over time
for k=2:time
        M=Spread(M,a,b,@infNbs); % pass infNbs as a function handle
        %subplot(3,3,k)
        if any(any(M==2))
            map=[1 1 0;0.1 0.75 0.2;1 0 0];
            %map=[1 1 1;0 1 0;1 0 0];
        else
            % if no infection left in the grid, remove the color red
            map=[1 1 0;0.1 0.75 0.2];
            %map=[1 1 1;0 1 0];
        end
        colormap(map);
        %pcolor(M);
        image(M+1)
        axis off
        axis square
        F(k)=getframe; % records the current frame into a movie
end
movie2avi(F, 'pandemic', 'compression', 'None','fps',4,'quality',100);
```

```
%% Main Simulation Function for the Spread of Pandemic
% Output:
% The function Spread returns a matrix, representing the state
% of infection in the grid of individuals, after one time step.
% Input:
% M is the matrix of initial distribution of susceptible individuals
% in the grid with a single infected individual in a random cell.
% a is the probability an infected individual will infect a neighbor.
% b is the probability an infected individual will be removed,
% that is, die or recover and become immune to the disease.
% infNbs(M,i,j) is a custom function, which counts the number of
% infected neighbors around the cell (i,j), given a grid M.
% The simulation has 3 states: 0,1,2; 0=Removed, 1=Susceptible, 2=Infected

function state = Spread(M,a,b,infNbs)

[nrow ncol] = size(M);
bM = zeros(nrow+2,ncol+2); % insulating boundary (with 0's around the grid)
bM(2:nrow+1,2:ncol+1) = M;

for i=2:nrow+1
    for j=2:ncol+1
        % if the cell is 0 don't do anything
        if bM(i,j)==1 % if susceptible then ...
            ninfNbs = infNbs(bM,i,j); %count the number of infected neighbors
            bM(i,j) = 1+(rand > (1-a)^ninfNbs);%simulate the new state:1 or 2
        elseif bM(i,j)==2 % if infected then ...
            bM(i,j) = 2*(rand > b); % simulate the new state: 0 or 2
        end
    end
end

state = bM(2:nrow+1,2:ncol+1);
```

```
%% Count the number of infected neighbors
% Output:
% The function infNbs returns the number
% of infected neighbors, given a matrix
% M, and a cell (i,j) in M.
% Input:
% M is a matrix with a boundary condition,
% representing the grid of individuals and
% (i,j) is the cell position in the matrix,
% around which we count the infected cells.
% a state of 2 represents an infected cell.

function ninfNbs = infNbs(M,i,j)

ninfNbs=0; % initialize the counter

% count infected neighbors
if M(i-1,j) == 2
    ninfNbs=ninfNbs+1;
end
if M(i+1,j) == 2
    ninfNbs=ninfNbs+1;
end
if M(i,j-1) == 2
    ninfNbs=ninfNbs+1;
end
if M(i,j+1) == 2
    ninfNbs=ninfNbs+1;
end
```



Simulation of a pandemic at 25, 50, 75, and 100 time steps. Here α = 0.35 and β = 0.10. We started with a single infected individual placed at random in the grid.

CONCLUSIONS

In the SIR model, we see that epidemics either die out quickly or grow to be quite large. We observe a change in behavior about the line Nα = β. When Nα > β then we almost always get a big epidemic, but when Nα ≤ β the size of the epidemic decreases sharply.

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