Epidemiology and Chaos

Jonathan Wills
Math 053: Chaos!
Prof. Alex Barnett
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Abstract:

Mathematical epidemiological models for the spread of disease through a population are used to predict the prevalence of a disease or to study the impacts of treatment or prevention measures. Initial conditions for these models are measured from statistical data collected from a population – since these initial conditions can never be exact, the presence of chaos in mathematical models has serious implications for the accuracy of the models as well as how epidemiologists interpret their findings. This paper confirms the chaotic behavior of a model for dengue fever by investigating sensitive dependence, chaotic attractors, and Lyapunov exponents under a variety of initial conditions.

Mathematical Epidemiological Models:

Mathematical models for the spread of disease through a population have a variety of uses. A good mathematical model can be used to predict the prevalence of a disease within a population. Different parameters in the model reflect the average lifespan of a population, the survival rate for a disease, the infectiousness of a disease, the rate of loss of immunity over time, the rate of recovery from the disease, or a number of other factors that vary by disease. Varying these constants allows epidemiologists to approximate the effects of prevention measures such as vaccinations or treatment measures. Models also allow epidemiologists to predict whether a disease or virus will die out over time under certain conditions. From the models, mathematicians can calculate reproduction numbers and other measures of how much the disease will spread at a given time, or threshold values necessary for certain conditions such as eradication to be achieved (Hethcote). Finding which conditions will achieve eradication lets epidemiologists know where it will be most effective to concentrate their efforts. More advance models differentiate between age groups or seasonal variations in disease prevalence caused by climate changes or school terms.

The standard epidemiological model for disease prevalence is the MSEIR model, a set of differential equations that categorizes percentages of the population, as shown in the figure below (Hethcote). The M portion of the population represents those infants who have temporary maternal passive immunity from the disease. Over time, those in M will move in to the S group, those susceptible to the disease. If a susceptible individual has contact with an infectious individual and the contact is sufficient to contract the disease, then the susceptible one will move into E, the exposed group. Those in E will spend a certain amount of time specific to the disease before the start to show symptoms and become infectious, at which point they will move into the I group. If they survive the disease, they recover and move into the R group, and will remain immune to the disease for an amount of time specific to each disease.

In the MSEIR model, it is assumed for the sake of mathematical simplicity that the birth rate is the same as the death rate; the total population stays constant and there is

constant input into the M and S categories. More complicated mathematical models include populations that vary over time.

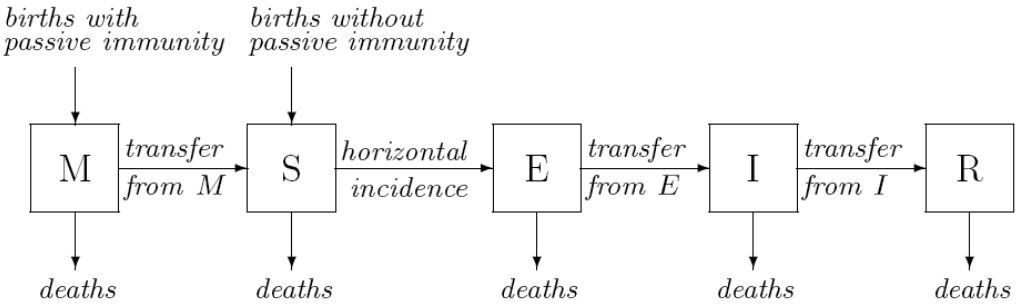


Fig. 1. The general transfer diagram for the MSEIR model with the passively-immune class M, the susceptible class S, the exposed class E, the infective class I, and the recovered class R.

MSEIR represents a general case that can be adapted to better reflect many specific diseases. For some cases, the time between exposure and display of symptoms or the ability of mothers to transfer antibodies to their fetuses may be negligible, in which case the E or M group would be omitted from the model. Different parameters in each model will further reflect the specific properties of a single disease.

Limitations:

While these models are powerful tools for predicting the behavior of diseases within a population, it is important to remember that they are drastic simplifications of reality. Disease dynamics in real life are not deterministic – human behavior can affect outcomes for any set of initial conditions. These models are merely approximations of what should happen for sufficiently large populations. They assume constant total population (although they account for births and deaths at an equal rate) and they assume that the population will mix homogeneously (that each individual will come into contact with the same constant number of other individuals).

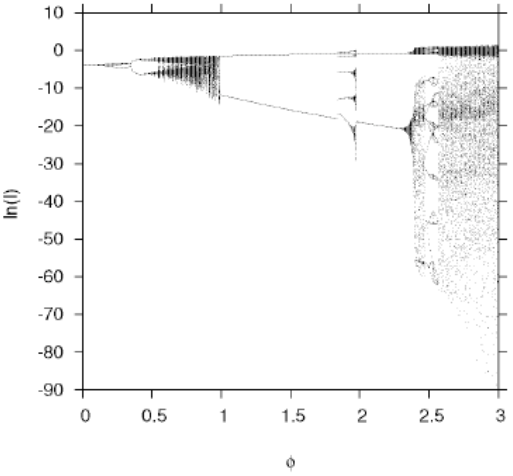
It is also impossible to obtain perfect information about the constants that fit into the model to characterize the disease. Statistical information about real diseases is gathered, but one must always account for unreported cases of the disease or instances of the disease that have been affected by other variables. More complicated models require more and more parameters to fully model the spread of a disease; when choosing how to study a disease, a mathematician or epidemiologist must balance the accuracy of the mathematical model against the feasibility of obtaining all the necessary parameters to fully characterize the a disease.

Chaos and sensitive dependence further complicate this dynamic. Epidemiologists can only approximate initial conditions, and the possibility that two very similar sets of initial conditions could have results that diverge at an exponential rate has serious ramifications for the accuracy of their models. The production of vaccines takes a significant amount of time, and which diseases or strains of a virus the mathematical models predict will be most prevalent in the future and will be most affected by mass vaccinations govern their production.

Chaos in Dengue Fever:

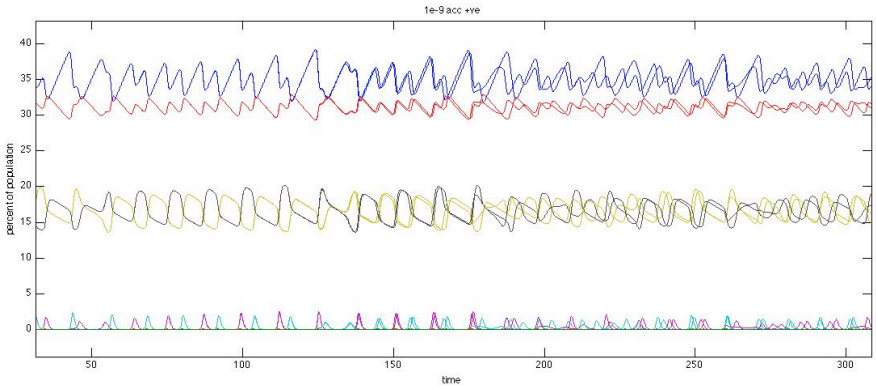
$$
\begin{aligned}
\frac{d}{dt}S &= -\frac{\beta}{N}S(I_1+\phi I_{21}) - \frac{\beta}{N}S(I_2+\phi I_{12}) + \mu(N-S)\\
\frac{d}{dt}I_1 &= \frac{\beta}{N}S(I_1+\phi I_{21}) - (\gamma+\mu)I_1\\
\frac{d}{dt}I_2 &= \frac{\beta}{N}S(I_2+\phi I_{12}) - (\gamma+\mu)I_2\\
\frac{d}{dt}R_1 &= \gamma I_1 - (\alpha+\mu)R_1\\
\frac{d}{dt}R_2 &= \gamma I_2 - (\alpha+\mu)R_2\\
\frac{d}{dt}S_1 &= -\frac{\beta}{N}S_1(I_2+\phi I_{12}) + \alpha R_1 - \mu S_1\\
\frac{d}{dt}S_2 &= -\frac{\beta}{N}S_2(I_1+\phi I_{21}) + \alpha R_2 - \mu S_2\\
\frac{d}{dt}I_{12} &= \frac{\beta}{N}S_1(I_2+\phi I_{12}) - (\gamma+\mu)I_{12}\\
\frac{d}{dt}I_{21} &= \frac{\beta}{N}S_2(I_1+\phi I_{21}) - (\gamma+\mu)I_{21}\\
\frac{d}{dt}R &= \gamma(I_{12}+I_{21}) - \mu R \quad .
\end{aligned}
$$

I investigated chaos in an adaptation of the SIRS model (shown to the right, and taken from a study by Aguiar, Kooi, and Stollenwerk) for two coexisting strains of dengue fever. Dengue is essentially a human disease, but is passed through a population by transfer of blood, most often by mosquitoes. In many epidemiological models for dengue fever, it is assumed that mosquitoes are mixing homogeneously with the human population (Derouich et al). Note also that in this case, the creators of the model deemed the time and number of infants with maternal passive immunity and the length of time between exposure and display of symptoms to be negligible; hence the M and E groups have been omitted. In this model, those infected with one strain or another of dengue will temporarily have cross immunity to the other strain. Those with the first strain cannot get the second until a certain period of time after recovering from the first, and vice versa. Chaos has been found in this model, as seen in some regions of the bifurcation diagram to the right, obtained by varying the parameter φ (Aguiar).

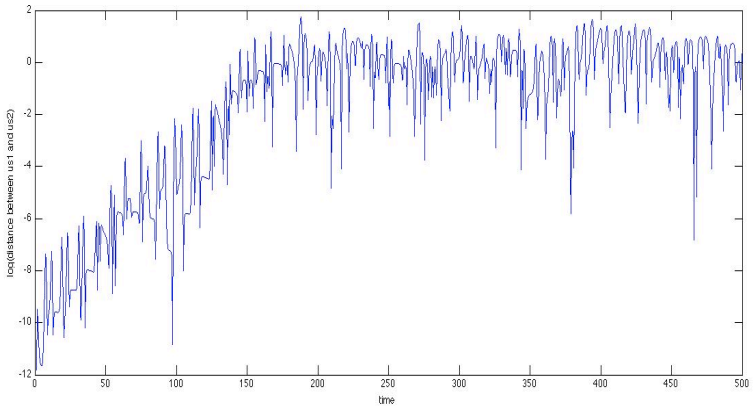


Mathematical analysis was done using Matlab. Total population was set at 100 so that results would reflect percentages of the population rather than absolute numbers. The other parameters that approximate those for dengue fever are as follows: μ = 1/65, $\gamma = 52$, $\beta = 2\gamma$, $\alpha = 2$, and the parameter φ , a measure of infectiousness that can reflect what proportion of the population is vaccinated, will be varied.

I first kept φ constant at 0.9 to search for sensitive dependence. After finding an orbit that appeared to be chaotic, I mapped two trajectories with very similar initial conditions (uo = [35.8207; 0.0001; 0.0074; 0.0196; 0.0768; 19.0634; 14.3108; 0.0040; 0.0000; 30.6972] and uo2 = uo + 1e-4 * [1; zeros(8,1); -1]). The initial distance between the two sets of starting values was 1.4142e-04. These trajectories diverged at an exponential rate, as is apparent in the figure below.

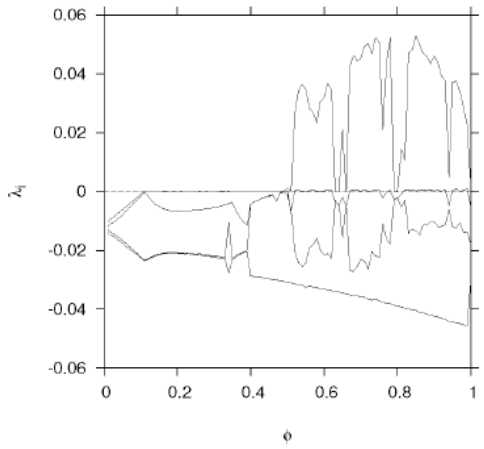


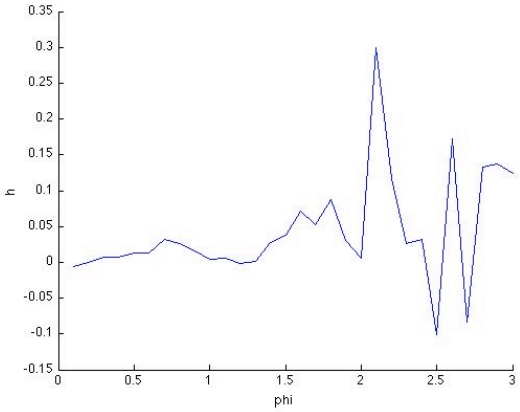
To calculate the rate of divergence, I mapped time against the log of the distance between the two trajectories (results below). There is a clear upward slope followed by a plateau at which the trajectories cannot diverge any more. I measured the slope of the region before the plateau from time 10 until the first time that the distance between the two trajectories was greater than 1. This slope gave me an approximation for the leading Lyapunov exponent.



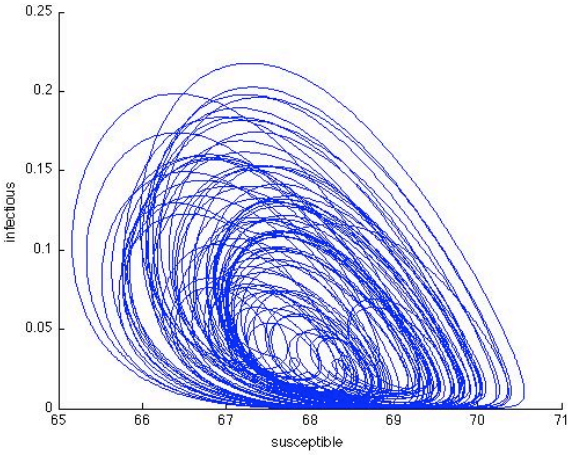
To make my approximation more accurate, I repeated the calculations for 15 different sets of initial values and averaged the results. This yielded a weakly positive average leading Lyapunov exponent of $h = 0.0247$ when $\varphi = 0.9$.

To further investigate the effects of the φ parameter, I repeated this estimate of the leading Lyapunov exponent for values of φ between 0 and 3. Each reported leading Lyapunov exponent is the average of the calculated Lyapunov exponent for 15 different initial conditions. My results are shown below on the right. On the left for comparison are four Lyapunov exponents for the same model in the smaller range $0 < \varphi < 1$, calculated by Aguiar, Kooi, and Stollenwerk with very different methods. My calculations seem to confirm the small peak of $0.4 < h < 0.6$ for φ close to 0.8, but does not capture the sharp drop-off of h as φ decreases below 0.5 or the downward spikes in the $0.5 < \varphi < 1$ range, most likely because I only calculated h in 0.1 intervals of φ. My calculations also seem to confirm the chaos found by Aguiar et al. in the range $2 < \varphi < 3$, but my model also finds some chaos in the $1.5 < \varphi < 2$ range, which may be erroneous.





My results, shown to the right above, give an approximation for the Lyapunov exponent for a given φ, but suffer from some limitations. First, I was only able to average 15 different initial conditions for each φ, and I calculated the Lyapunov exponent only for φ values that are multiples of 0.1; thus, the model has limited predictive capability for intermediate values of φ between those calculated. Furthermore, there is no guarantee that the chosen orbits will remain chaotic when φ is changed. The Lyapunov exponents remain weakly positive for the majority of φ values, but the calculated Lyapunov exponent could be influenced positively or negatively by my methods for calculations of slope. It should be used only to draw general conclusions about the positive Lyapunov exponents of the model.



Having identified chaos in the model, I wanted to characterize it further. Below is the chaotic attractor for the first initial conditions used in the calculations for Lyapunov exponent. It is shown on a graph of total percent of susceptible individuals in the population versus total percentage of infectious individuals in the population. Percent recovered in the population is omitted because it can be determined by subtracting infectious and susceptible populations from the total population. Graphed in three dimensions, the strange attractor lies on a plane for which the total population adds up to 100%; therefore, graphing the chaotic attractor in two dimensions still retains all information.

Conclusions:

My findings confirmed and expanded upon the results found by other researchers of this model with other methods. My findings cannot conclusively confirm chaos in the dynamics of actual dengue fever, ruled by a system involving complex and changing interactions and behaviors that are not necessarily determined by initial conditions.

Rather it confirms the presence of chaos for many values of φ in this particular model for the disease, calling into question the predictive capabilities of the model and raising the possibility of sensitive dependence in the actual disease dynamics to the extent that the disease reflects the model. A better understanding of the chaos in this and other models for epidemics can allow epidemiologists to calculate threshold values for asymptotic stability to approach eradication of a disease, and to better understand the limitations the models have and the effects their treatment programs might have.

Sources:

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Appendix: Matlab Code

First code is for plotting divergent trajectories, plotting chaotic attractor in 3d and 2d, and plotting graph for calculations of Lyapunov exponents:

```
%Searching for Chaos in the MSEIR model for infectious diseases
%Jonathan Wills, Fall 2009

%Dengue fever is a multi-strain system that can be modeled by a
permutation
%of the SIR model: here are the differential eqns.

%Constants:
N = 100;          %puts values in percentages of total population
M = (1/65);       %years^(-1)    %average life span/death rate
Y = 52;           %years^(-1)     rate of recovery from infection, In-
>Rn, where n=1 or n=2
B = 2*Y;                          %infection rate from either of groups
I1 or I2
A = 2;            %years^(-1)    %rate of loss of cross immunity from
R1->S1

%the constant Q will be varied.
            %the rate of infection of S1 by I12 is Q*B

if 0
%Differential Equations:
S = @(t) -B/N*S*(I1+Q*I21)-B/N*S*(I2+Q*I12)+M*(N-S);  %susceptible
I1 = @(t) B/N*S*(I1+Q*I21)-(Y+M)*I1;        %infected with strain 1 but
not strain 2
I2 = @(t) B/N*S*(I2+Q*I12)-(Y+M)*I2;
R1 = @(t) Y*I1-(A+M)*R1;                    %recovered from strain 1,
temporarily cross immune
R2 = @(t) Y*I2-(A+M)*R2;
S1 = @(t) -B/N*S1*(I2+Q*I12)+A*R1-M*S1;     %immune to strain 1 but
susceptible to strain 2
S2 = @(t) -B/N*S2*(I1+Q*I21)+A*R2-M*S2;     %and vice versa
I12 = @(t) B/N*S1*(I2+Q*I12)-(Y+M)*I12;     %rezinfected from S1 with
strain 2
I21 = @(t) B/N*S2*(I1+Q*I21)-(Y+M)*I21;
R = @(t) Y*(I12+I21)-M*R;                   %recovered from both
strains

%now comes the differential equations part
%eps = 0.1;
%F = @(t,u) [S; I1; I2; R1; R2; S1; S2; I12; I21; R];
end
%commented out the above functions because it was simpler to write them
all
%out as one function F below.



Q = 0.9;  %varied parameter

eps = 0.1;
F = @(t,u) [-B/N*u(1)*(u(2)+Q*u(9))-B/N*u(1)*(u(3)+Q*u(8))+M*(N-u(1));
```

```
B/N*u(1)*(u(2)+Q*u(9))-(Y+M)*u(2); B/N*u(1)*(u(3)+Q*u(8))-(Y+M)*u(3);
Y*u(2)-(A+M)*u(4); Y*u(3)-(A+M)*u(5); -B/N*u(6)*(u(3)+Q*u(8))+A*u(4)-
M*u(6); -B/N*u(7)*(u(2)+Q*u(9))+A*u(5)-M*u(7); B/N*u(6)*(u(3)+Q*u(8))-
(Y+M)*u(8); B/N*u(7)*(u(2)+Q*u(9))-(Y+M)*u(9); Y*(u(8)+u(9))-M*u(10)];
uo = [35.6932; 0.0005; 0.0068; 0.0622; 0.0731; 19.0647; 14.3795;
0.0036; 0.0002; 30.7162];
%uo = [27;16;14;12;10;8;6;4;2;1];
%uo = [27;16;14;22;0;12;6;0;2;1];
%uo = [18.3878;0;0.0119;0.0048;0.0538;13.5421;9.0077;0.0088;0;58.9831];
%uo = [97;1;1;0;0;0;0;0;0;1];
s1 = ode45(F,[0 500],uo,odeset('abstol',1e-9,'nonnegative',1:10));
ts1 = 1:0.01:500;
us1 = deval(s1,ts1)';


eps = 0.1;
F = @(t,u) [-B/N*u(1)*(u(2)+Q*u(9))-B/N*u(1)*(u(3)+Q*u(8))+M*(N-u(1));
B/N*u(1)*(u(2)+Q*u(9))-(Y+M)*u(2); B/N*u(1)*(u(3)+Q*u(8))-(Y+M)*u(3);
Y*u(2)-(A+M)*u(4); Y*u(3)-(A+M)*u(5); -B/N*u(6)*(u(3)+Q*u(8))+A*u(4)-
M*u(6); -B/N*u(7)*(u(2)+Q*u(9))+A*u(5)-M*u(7); B/N*u(6)*(u(3)+Q*u(8))-
(Y+M)*u(8); B/N*u(7)*(u(2)+Q*u(9))-(Y+M)*u(9); Y*(u(8)+u(9))-M*u(10)];
uo2 = uo + 1e-4 * [1; zeros(8,1); -1];
%uo2 =
[18.3877;0;0.0119;0.0048;0.0538;13.5421;9.0077;0.0088;0;58.9834];
s2 = ode45(F,[0 500],uo2,odeset('abstol',1e-9,'nonnegative',1:10));
ts2 = 1:0.01:500;
us2 = deval(s2,ts2)';


a=1:numel(ts1);
b=1:numel(ts2);
figure;
plot3 (us1(a,1)+us1(a,6)+us1(a,7), us1(a,2)+us1(a,3)+us1(a,8)+us1(a,9),
us1(a,4)+us1(a,5)+us1(a,10));
hold on;
plot3 (us2(b,1)+us2(b,6)+us2(b,7), us2(b,2)+us2(b,3)+us2(b,8)+us2(b,9),
us2(b,4)+us2(b,5)+us2(b,10), 'r');
axis vis3d
a =1:1:numel(ts1);
b =1:1:numel(ts2);
plot3 (us1(a,1)+us1(a,6)+us1(a,7), us1(a,2)+us1(a,3)+us1(a,8)+us1(a,9),
us1(a,4)+us1(a,5)+us1(a,10));
plot3 (us2(b,1)+us2(b,6)+us2(b,7), us2(b,2)+us2(b,3)+us2(b,8)+us2(b,9),
us2(b,4)+us2(b,5)+us2(b,10), 'r');
xlabel('susceptible');
ylabel('infectious');
zlabel('recovered');
hold off;

figure;
hold on;
plot (us1(a,1)+us1(a,6)+us1(a,7), us1(a,2)+us1(a,3)+us1(a,8)+us1(a,9));
xlabel('susceptible');
ylabel('infectious');
hold off;

figure;
plot(ts1,us1);title('1e-9 acc +ve'); axis([0 130 -1e3 1e3])
hold on;
```

```
plot(ts2,us2);

figure;
plot(ts1, log(sqrt(sum((us1-us2).^2,2))));
```

Second code is an adaptation of the first one, for plotting a graph of Lyapunov exponent against the parameter φ :

```
%Searching for Chaos in the MSEIR model for infectious diseases
%Jonathan Wills, Fall 2009

%Dengue fever is a multi-strain system that can be modeled by a
permutation
%of the SIR model: here are the differential eqns.

%Constants:
N = 100;          %puts values in percentages of total population
M = (1/65);       %years^(-1)    %average life span/death rate
Y = 52;           %years^(-1)     rate of recovery from infection, In-
>Rn, where n=1 or n=2
B = 2*Y;                         %infection rate from either of groups
I1 or I2
A = 2;            %years^(-1)    %rate of loss of cross immunity from
R1->S1
Q = 0.9;

steps = 15;      %increase to get more lyapunov exponents to average
for a single Q
lyap = zeros(10,50); %different starting values for each calculation of
the lyapunov exponent for a single Q
lyap(:,1)=uo;
h = zeros(1,steps); %list of lyapunov exponenets for a single Q to
average
h2 = zeros(1,10); %list of average lyapunov exponents to plot

figure;
hold on;

for Q2 = 1:30;    %vary this to get more accurate graphs of Q vs.
lyapunov exponenet
    Q = Q2/10;


eps = 0.1;
F = @(t,u) [-B/N*u(1)*(u(2)+Q*u(9))-B/N*u(1)*(u(3)+Q*u(8))+M*(N-u(1));
B/N*u(1)*(u(2)+Q*u(9))-(Y+M)*u(2); B/N*u(1)*(u(3)+Q*u(8))-(Y+M)*u(3);
Y*u(2)-(A+M)*u(4); Y*u(3)-(A+M)*u(5); -B/N*u(6)*(u(3)+Q*u(8))+A*u(4)-
M*u(6); -B/N*u(7)*(u(2)+Q*u(9))+A*u(5)-M*u(7); B/N*u(6)*(u(3)+Q*u(8))-
(Y+M)*u(8); B/N*u(7)*(u(2)+Q*u(9))-(Y+M)*u(9); Y*(u(8)+u(9))-M*u(10)];
% below are a variety of initial conditions i used throughout the
% investigations
%uo = [27;16;14;12;10;8;6;4;2;1];
%uo = [35.6932; 0.0005; 0.0068; 0.0622; 0.0731; 19.0647; 14.3795;
0.0036; 0.0002; 30.7162];
uo = [35.8207; 0.0001; 0.0074; 0.0196; 0.0768; 19.0634; 14.3108;
0.0040; 0.0000; 30.6972];
```

```
for z=1:steps;
    uo = lyap(:,z);
uo2 = uo + 1e-4 * [1; zeros(8,1); -1];
%uo2 =
[18.3877;0;0.0119;0.0048;0.0538;13.5421;9.0077;0.0088;0;58.9834];
%[ts,us] = ode45(F,[0 500],uo);

T = 500;
s1 = ode45(F,[0 T],uo,odeset('abstol',1e-9,'nonnegative',1:10));
ts = 1:0.5:T;
us1 = deval(s1,ts)';

s2 = ode45(F,[0 T],uo2,odeset('abstol',1e-9,'nonnegative',1:10));
us2 = deval(s2,ts)';
disp(Q2);   %indicator of progress

if 0
%plot for each calculation of lyap exp
figure;
plot(ts, log(abs(us1(:,1)-us2(:,1)))); xlabel('time');
ylabel('log(distance between two trajectories)');

end

dist = sqrt(sum((us1-us2).^2,2));
ff = find(dist>1);
fg = numel(ff);
if fg > 0
gg = ff(1);
end
if fg <1
    gg = 250; %an approximation for slope when lyapunov exponent is
less than zero (any stopping point should work because there will be no
plateau)
end
lyap(:,z+1) = us1(gg,:);

h(z)=(1/(gg-10)*((log(dist(gg)))-log(dist(10))));

end


avgh = sum(h)/numel(h); %averages h for a single Q

h2(Q2) = avgh; %records the average h for this value of Q, makes a list

end

plot(0.1:0.1:3, h2);  %plots Q vs. h
```