Modelling the Spread of Influenza A H1N1

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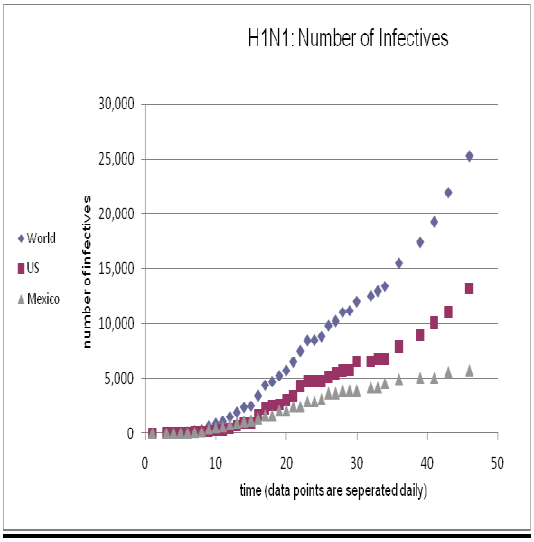
June 19, 2009

Introduction

Recently there has been (and in fact continues to be) a scare of a possible pandemic due to the spread of the influenza A H1N1 virus. This virus is associated with the disease that is commonly known as "swine flu". The H1N1 virus is considered particularly dangerous because of its high mutation rate. There are two biological processes behind this elevated mutation rate: (1) the genome of the H1N1 virus consists of eight separate RNA segments resulting in the mixing and swapping of entire RNA segments (for example, the H1N1 virus has been found to be composed of genetic elements from influenza viruses most common in birds, pigs, and humans); and (2) RNA proofreading enzymes are absent. The graph shown below demonstrates how the spread of "swine flu" has progressed. The last data point corresponds to the information as available on June 8, 2009.



The Spread of H1N1

My 2009 summer research activity will be dedicated to the development of a simple realistic model that is in agreement with the data from the above diagram and that might be used to explain certain trends observed in the complexity of the spread of the H1N1 virus.

It is interesting to notice the geographic variation in the spread of the H1N1 virus. From the *World Health Organization* website, one may obtain daily updates of the number of the laboratory confirmed cases of influenza A (H1N1) for most countries. According to this source, as of June 17, 2009, there were 39620 confirmed cases in the world, 17855 cases in the United States, and 6241 cases in Mexico. In particular, for the United States one can obtain the number of confirmed cases for each individual state. From the *Centers for Disease Control and Prevention* website, one can readily find that as of June 5, 2009, there were 2217 cases in Wisconsin, 858 cases in the New York state, and 247 cases in Florida. One of the goals of my model is to provide a realistic explanation for this geographic variation in the spread of the H1N1 virus.

In the mathematical biology literature, several mathematical models have been proposed for modeling the spread of infectious diseases. In particular, the *compartmental models* subdivide a population into certain classes that are characterized and distinguished by the infectious properties of their constitute individuals. Mathematically speaking, these compartmental models belong essentially to the same model class as they differ only in terms of the particularities of the disease and when considering the nature of the population class under study. In other words, when modeling the spread of an infectious disease, it is the *biological* factor that determines what particular model should be considered.

The *SIR Model* illustrated below has been proven a relatively good predictor for infectious diseases such as measles, mumps, and rubella. Under this model, when an individual becomes infected, he/she becomes immediately infectious and is able to infect other individuals. However, the infected individuals may recover from the disease and therefore move to a recovered class, where they will be no longer infectious while acquiring immunity to the disease.

SIR Model

The *SIR Model* described above translates symbolically into

$(S1)\ S + I \xrightarrow{i} I + I$

$(S2)\ I \xrightarrow{r} R$

where *S* denotes the susceptible class of individuals, *I* the infectious class, and *R* the recovered class; *i* and *r* are the two (constant) transition rates respectively.

The above symbolic equations imply the following system of ordinary differential equations:

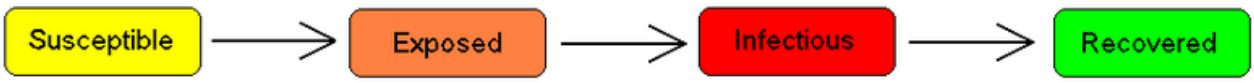
$$(E1)\ \frac{dS}{dt} = -iSI$$

$$(E2)\ \frac{dI}{dt} = iSI - rI$$

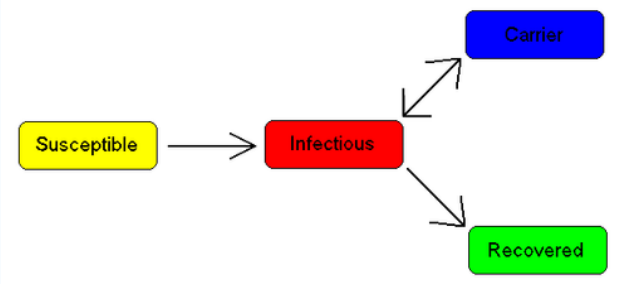
$$(E3)\ \frac{dR}{dt} = rI$$

(E1), (E2), (E3) represent the mathematical translation of the *SIR Model,* allowing us to use mathematical analysis tools for answering certain question of interest for the biological phenomenon.

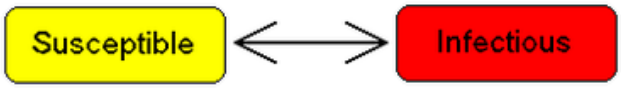
There are several different types of *compartmental models*, and as has already been mentioned they differ only in the nature of the classes involved. It is often difficult to determine accurately what model will best describe the biological phenomenon under study. This is in fact one of the challenges of my summer research project. Several compartmental models are summarized below. Together with other types of modeling, they will inspire my search for a simple realistic model that will best describe the spread of the H1N1 influenza.



SEIR Model



Carrier State Model



SIS Model

Analyzing the spread of an infectious disease not only requires mathematical knowledge and computational skills but also a good understanding of the biological processes behind the disease under study.

Methods

One of the objectives of my summer research project is to develop my ability to apply techniques from the *Qualitative Theory of Ordinary Differential Equations* to a concrete biological problem of significant importance and interest, and to further extend my understanding when a *stochastic factor* is added to the model. These two mathematical fields lie at the foundation of many applications in C*omputational Biology.* For this reason, I will study them intensively while keeping an eye on other possible applications in the infectious diseases field.

When describing qualitatively the structure of the solutions set of a system of ordinary differential equations that involve one or more parameters, we rely on terms and concepts such as steady-states, stability analysis, periodic solutions and oscillations, simple bifurcations of saddle-node, transcritical, pitchfork, or Hopf type, and possibly the chaotic behavior that arises when dealing with the spread of an infectious disease such as the H1N1 virus. Under this theoretical frame, I will look for a model and for results that are both mathematically and biologically meaningful.

In addition, I will also employ certain stochastic techniques. Stochastic systems are a counterpart of deterministic systems as they incorporate randomness as a phenomenological factor. Stochastic processes are a very modern tool for modeling biological systems because of their ability to better incorporate the complexity that is often associated with the biological systems in a computationally manageable manner.

Research Plan

Timeline

1) Learn and understand the concepts and methods associated with the qualitative descriptions of systems of ordinary differential equations as they pertain to modeling biological phenomena. (1.5 weeks)
2) Learn and understand how to apply the concepts of stochastic methods to modeling biological phenomena. (1.5 weeks)
3) Propose several models that describe the spread of the H1N1 virus and account for geographic variation. (1 week)
4) Determine which of the proposed models most accurately explains the trends observed and which is in agreement with the data. Make any necessary adjustments to the proposed models. (2 weeks)

References

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