

Ewald (1996) Ch. 1 & 2  
and  
Otto and Day (2007) Ch. 2 & 3.

January 25, 2007

## Questions

## Modeling

1. In many scientific programs/projects, objectives may change as information is gathered, what effect can that have on establishing a mathematical model?
2. I am skeptical of modeling...how is it possible to really account for all the variables and how accurate are most models? 99% accurate? more? less??
3. What are the "real life" applications of these models? Are they actually used as a basis for implementing things like vector control measures or vaccines?
4. There are many, many variables in biological phenomena,—most of which are either poorly or not understood by humans... How can we possibly construct an accurate model of something that we don't fully understand?

5. Since models can make several assumptions that may not hold true in nature, what practical purpose do they serve?
6. Frequently, the world is more complex than we account for, how often do unknown variables effect a model? If the variable is unknown how would you correct for it?
7. Although it is easy to become overly enamored with mathematical models, what are the alternatives? Isn't all science based on some kind of model?
8. Discrete time models assume changes that cannot be compounded in a unit of time. In which cases can this model be used for a long unit of time? Does the number of variables affect the dynamic model one should choose?
9. In the second chapter of 'How to Construct a Model,' the author says that the variables in an ecological model are not continuous. How could you construct a model when you have these kinds of variables? How could the error in the result could be minimized since it is more difficult to treat them mathematically? Could this model then still be used for calculating rates of changes?
10. Why are simple statistical models so readily accepted by empiricists but more explicit and complex models viewed with great skepticism?
11. Ewald stats that "A sloppy educated guess is better than a random guess." But aren't 'mis-educated' guess likely worse than a random guess?
12. Given Ewald's strong criticism of previous 'educated' and that 99% of our previous hypotheses about how things work (e.g. protein was the material that encoded genetic information), how can he be confident that his 'educated' guess is better than his predecessors?

# Disease Evolution & Ecology

1. Do all pathogens have a greater potential for rapid evolution than all hosts?
2. Ewald cites the evolution of antibiotic resistance as a major bridge between medical and evolutionary sciences. Why don't viruses work the same way (or do they??) For example, the flu vaccine is given to a large subset of the human population each year—are we facilitating the evolution of vaccine resistant viruses because there presumably exists 1) a reservoir of genetic diversity of flu viruses within the non-vaccinated population (some of which may be resistant to the vaccine) and 2) a plethora of vaccinated people who would weed out non-resistant strains thereby increasing the prevalence (i.e., the evolutionary fitness) of resistant flu strains?
3. The author talks about how the current theory on lethal epidemics is that the right mutation has to occur and he mentions that that mutation has to be more beneficial to the agent's over survival. Can we realistically hope that if bird flu does mutate that this mutation will not be more beneficial - i.e. it will be competed out by the current bird flu virus.
4. Can we predict when when a mutation that is harmful to the host will invade/evolve?
5. Much of Ewald's arguments assume there are trade-offs between various aspects of the host's response. Is this a safe assumption to make? Are there always trade-offs? Or do we only notice situations where trade-offs exist?
6. The author describes that *V. cholerae* submits a toxin that is detrimental to other bacteria that normally infest the gut, but this toxin is not produced after the initial colony is established. Would a potential therapy be one that includes giving the patient back their normal intestinal flora through ingestion?

## Disease Symptoms

1. What characteristic properties enable certain pathogens to trigger fever in the host body while the others cannot?
2. Does a high replication rate within a host necessarily cause more detriment to the host? Couldn't a virus evolve to replicate rapidly but not harm the host, thereby having the best of both worlds (e.g., prolonged, high rates of transmission)?
3. Fever can enhance the control of some viruses. Do you think that this is because either the high temperature denatures the envelope protein or the DNA/RNA of the virus? Could it be that some of the mutations, like changing the nucleotide sequence to express different proteins, would give more stability to them under these conditions?
4. How do host characteristics influence parasitic virulence?
5. According to the book, diarrheal and febrile illnesses are associated with anorexia. Is anorexia a defense or a manipulation or a side effect?
6. How does a virus cause symptoms in a host? For example: which of the following would/could cause a host to sneeze more when infected by an air-transmitted virus: 1) evolution of the virus which somehow causes greater sneezing, 2) higher replication rates of the virus within the host (thereby increasing whatever the virus was doing to make the host sneeze), or 3) is this something that is moderated entirely by the host reaction to the virus?

# Evolutionary Medicine

## Validity

1. 'Drugs that reduce the inflammatory response without reducing fever and pain (e.g., phenylbutazone) would allow for evaluation of synergistic negative effects of reducing fever and pain in addition to inflammation' (pg 22). Phenylbutazone and Aspirin are both cyclooxygenase inhibitors that reduce prostaglandins and thromboxanes, therefore both of these drugs have analgesic, anti-inflammatory and antipyretic properties. Phenylbutazone also is a uricosuric substance and, therefore, has the same (if not more) 'side effects' as Aspirin. Why would this drug even be suggested for use in evaluation?
2. In stating that "the evolution of human characteristics is relatively slow", is Ewald actually being negligent of human cognizance as a major factor in the evolution of infectious disease?
3. With reference to evolutionary success (p5 para 1-2) The author asks "How could the less harmful, slower reproducers compete..." Why does the author assume that all invading organisms are in acute competition? (i.e. . pathogens have different receptors, environmental and host requirements, etc that may not lead to direct competition regardless of the pathogens "speed")
4. In my opinion Ewald's two chapters are a game of semantics. From the perspective of 'intuitive/informed veterinary clinician' I conclude, from the examples cited that disease is truly a "temporary state of imbalance" (p.12, paragraph 2) It confounds me that the author does not acknowledge "symptomatic treatment", in and of itself, as resulting in selective pressure.

## **Adoption by the Medical Field**

1. In what ways can modern medicine use the application of evolutionary thinking to determine the appropriate treatment for disease?
2. This article discusses using different parasites for biological control of grasshoppers depending on such things as species and temperature range. Are these forms of control commonly used and are the people implementing such programs really "up" on this information?
3. From the standpoint of development of secondary immune response by the host body, is an immediate suppression of disease symptoms by powerful medicines always the best solution or should we let them run their course?
4. How often is the general public informed about the negative effects of taking drugs like 'Tylenol' to alleviate cold symptoms?
5. Ewald talked about several studies that looked at treatment of the common cold and found that some can actually worsen nasal congestion, increase the duration of infectiousness, etc. I know these results were obviously published in a journal or article because they were cited in this book but is this information every directly released to the public through family physicians or pharmacists?
6. What percentage of the medical field should be focused on the evolution and natural selection of diseases, and what percentage should be focused on host immune systems, preventative measures, and direct treatment of symptoms?

## **Public Knowledge/Education**

1. "From secondary school through medical school, the fundamental relevance of evolution to all of human life often has been ignored or even suppressed." p 7 Ewald. Is this

changing in our schools today? What kind of evolutionary education did you grow up with?

## **Implications/Implementation**

1. It is stated in Evolution of Infectious Disease that ‘treating the symptoms ’ is not always the best method of care for many diseases. What impact do you think the use of antibiotics ‘prophylactically’ by medical professionals has had on the duration and impact of many diseases?
2. Is there any pharmacological or other methods to reduce fever without majorly messing about with other physiological and immunological aspects of the animal, like- pain or inflammatory response?
3. The author reported that acetaminophen, aspirin and ibuprofen all have the same result on rhinoviruses “it prolongs the period of viral multiplication.” Is it possible but that the COX-1 inhibition that is common to all 3 types of drugs is causing some other mechanism that is beneficial to viral replication?
4. How does neutralization of allergic components of the immune system lead to increased rates of cancer and other mutation-induced diseases?
5. If a symptom is a correct defense against an invading organism, but happens to be ‘hyper-responsive’ (exaggerated), would controlling/reducing the response instead of eliminating it still be considered treating a symptom? Would this type of control of the response not potentially allow the organism to overcome the disease?
6. Taking the approach of not controlling a fever because it is a defensive host mechanism and you do not want a pathogen to benefit from its reduction seems dangerous to the

host. What about the effects of long duration, high temperature states? Should the fever not be controlled and then the pathogen dealt with?

7. "It is best to avoid anti-inflammatory drugs during viral infections" p 23 Ewald. Is this common knowledge? It sounds like it would often be better to let the illness run its course.

## **Others**

1. How common is Reye's syndrome; is it hereditary?
2. What exactly is a "sieve of natural selection"...is that, like, a Class VI tree-trunk strainer?
3. Ewald brings up several ideas and examples of how we look at health and wellness today. One example was the "beneficial effects of...severely restricted amounts of food." p 10. If you are interested in reading more on this topic (because it is an interesting way to look at food, nutrition, health and wellness) check out articles on google and [www.calorierestriction.org](http://www.calorierestriction.org).