USING AGENT-BASED SIMULATION TO UNDERSTAND POPULATATION DYNAMICS AND COEVOLUTION IN HOST-PATHOGEN RELATIONSHIPS

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ABSTRACT

The development of anti-biotic resistant strains of bacteria and the nearly annual emergence of new strains of influenza virus are evidence of the rapid adaptation of pathogens to environmental pressures. The ability to predict the outcome of a long-term host-pathogen interaction could significantly improve public health decisions. Starting from the premise that all interactions between hosts and pathogens are stochastic in nature, we developed a generic agent based simulation of a population of hosts infected by a population of pathogens. Our simulation suggests that a host population is not intrinsically stable absent negative feedback loop mechanisms. We show that even in the face of a specific pathogen pressure, the outcome of a given initial host-pathogen community can be expressed only as a set of probabilities, unlike the prediction of traditional mathematical models constructed in the language of differential calculus.

1 PREVIOUS WORK IN COEVOLUTION THEORY

Previous theoretical work in coevolution has focused on host-pathogen interactions at the genetic level, see Anderson and May (1982), or at the transcriptional level, see Zhu, S. (2012). However, quantitative predictions of host-pathogen interaction outcomes at the population level are lacking.

2 A STOCHASTIC AGENT-BASED SIMULATION OF PATHOGEN MOVEMENT IN A HOST POPULUATION

To investigate the parameters that may contribute to the stability of a host-pathogen community, we developed an agent-based simulation of an isolated human population. In our simulation, the outcome of an infection in a given individual could result in one of four outcomes: recovered but susceptible to reinfection, recovered but now a chronic carrier, immune from further infection, and death. We assigned to the population as a whole a probability of developing clinical disease as a result of exposure to the pathogen, but each individual within the population was assigned a specific probability based on a Gaussian distribution around the population average. Exposure to the pathogen occurs through "contact" with an infected individual. Each individual was randomly assigned the number of contacts each day, based on a Gaussian distribution about a mean specific to each individual. We also included a "distance" parameter, which we could vary between runs of the simulation. This "distance" parameter allowed us to simulate typical social interaction patterns: each individual has repeated contact with a small set of other individuals, with progressively less contact with individuals who are "far" from the circle of frequent contacts. We found that even under highly infective conditions, some individuals would not be infected by the pathogen. A population that was highly gregarious suffered more extensively than a population in which social interaction was more limited.

3 A STOCHASTIC AGENT-BASED SIMULATION OF A HOST POPULATION SPANNING MANY GENERATIONS: ALL POPULATIONS EITHER EXPLODE OR DIE

To understand the impact on the host population by a set of pathogens, we first developed a simulation of an isolated host population. The simulation included assumptions about the fertility rate, expressed as the

probability of a pregnancy occurring as a function of the age of the individual female, and the mortality rate, expressed as a probability of death occurring as a function of the age of the individual. We found that it is possible to find combinations of fertility rates and mortality rates that will create a more or less stable population over many generations. However, we found that extremely small changes in mortality rates, particularly in infancy (as small as 0.1%) could result in the population either exploding or collapsing in a large fraction of simulation runs.

4 STOCHATIC VARIATION IN THE HOST-PATHOGEN INTERACTION CAN LEAD TO MULTIPLE OUTCOMES

We introduced pathogens into our host population simulation by providing for each individual in the host population a probability that on any given day the individual would become infected by one of two strains of a pathogen. Each individual in the host population was also randomly assigned a "resistance" to each strain. The "resistance" was captured in the simulation as a decrease in the probability that the individual would develop clinical disease as a result of exposure to the pathogen. To capture the effect of inheritance, for each new born individual, the "resistance" to each pathogen was assigned based on the "resistance" of one of the parents, to which was added a small random variation. Multiple runs of the simulation were carried out, with each run starting with the same initial conditions. We found that over the span of many generations, the host population would develop a decreased resistance to one strain of the pathogen and an increased resistance to the second strain of the pathogen.

5 SUMMARY:

Here we have demonstrated that agent-based simulation can be an effective and informative tool for understanding population dynamics, pathogenicity, and pathogen evolution. Importantly, we have demonstrated that for a wide range or parameters, we can expect divergent outcomes over the span of many simulations having the same initial conditions and dynamic parameters.

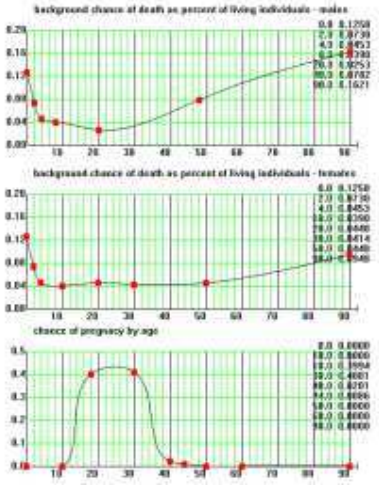

Figure 1: assumed mortality and fertility, by year of age

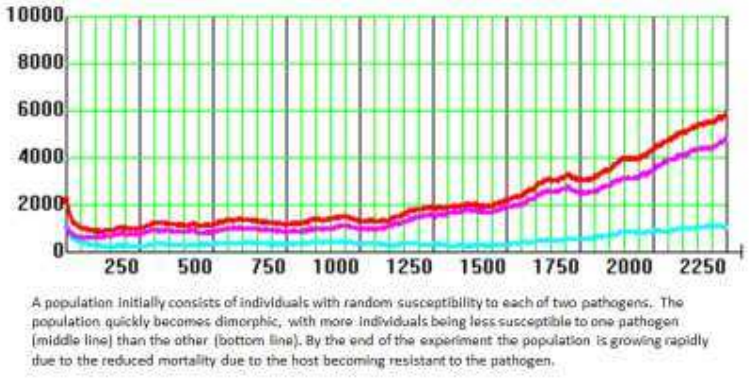

Figure 2: representative output of one simulation run covering 2200 years

REFERENCES

Anderson, R. M. and May, R. M. 1982 "Coevolution of hosts and parasites" Parasitology 85, 411-426

Zhu, S., et al (2012) "A quantitative model of transcriptional differentiation driving host-pathogen interactions" Briefings in Bioinformatics 14(6) 713-723