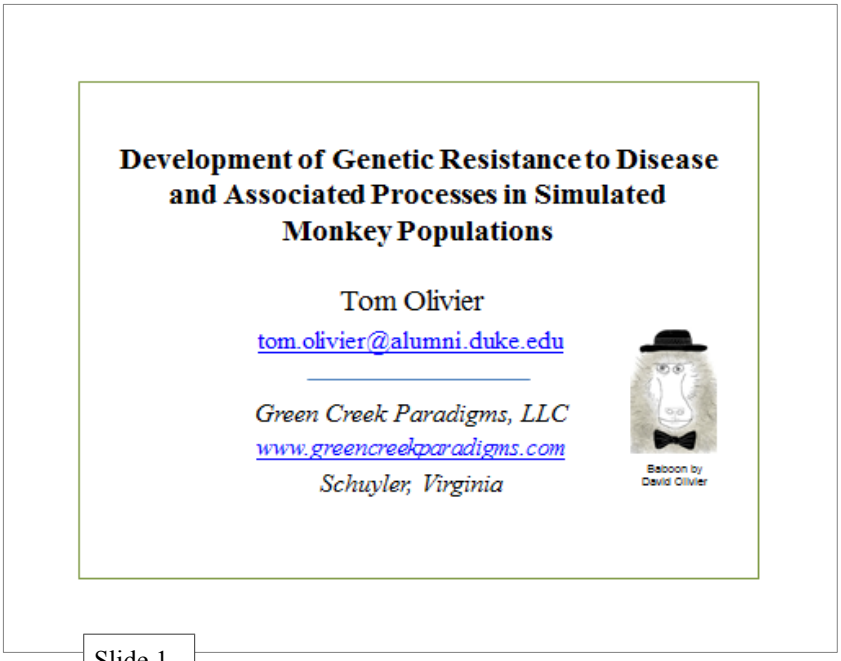


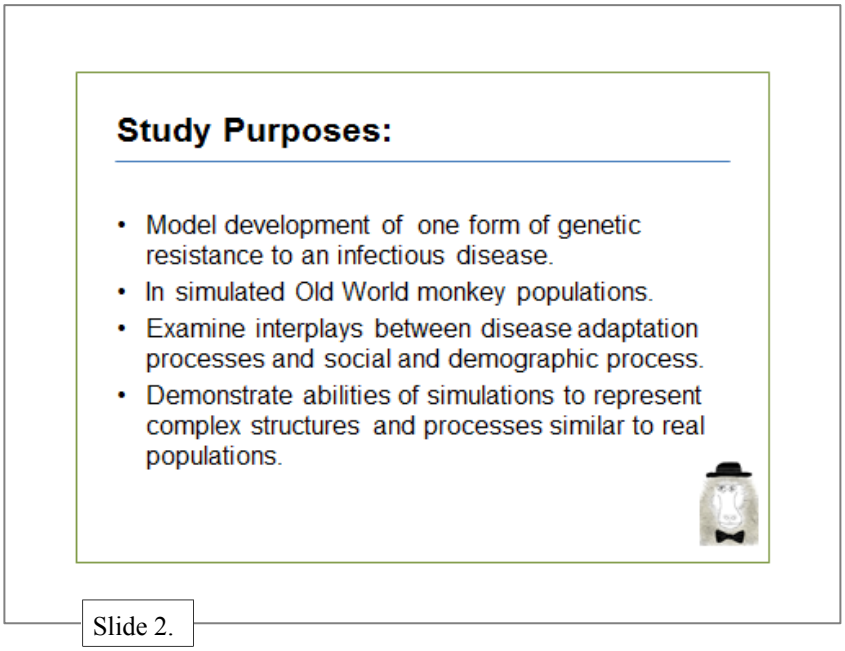
Slide 1.

ABSTRACT

This study contrasts infectious disease dynamics and related social and demographic processes in simulated Old World monkey populations with and without selection for genetic resistance to infection. Simulated populations were spatially and socially subdivided, with subpopulations resembling cercopithecine multimale groups. Simulations were built with the CRITTRZ population modeling library. Starting populations contained 653 animals, divided into 29 social groups, with 448 infected. An uninfected individual's risk of becoming infected was directly related to the number of infected neighbors and, in one series, genetic makeup. The initial frequency of an allele at a diploid autosomal locus potentially contributing to resistance was 0.49. Infected individuals were exposed to an additional risk of dying in each time period. In both series, population size declines were accompanied by spikes in numbers of group fusions. In the series without selection for resistance, infected individuals remained common. In the series with selection for resistance, numbers of infected individuals declined rapidly and often reached zero. In those populations, frequencies of the allele conferring resistance rose in early time periods, while the disease still was common. Some features of the series with selection for resistance to infection contrast with results from a recent simulation study that examined genetic selection for reduced disease virulence in monkey populations. Implications of these findings to known diseases of nonhuman primates, such as yellow fever, are considered.

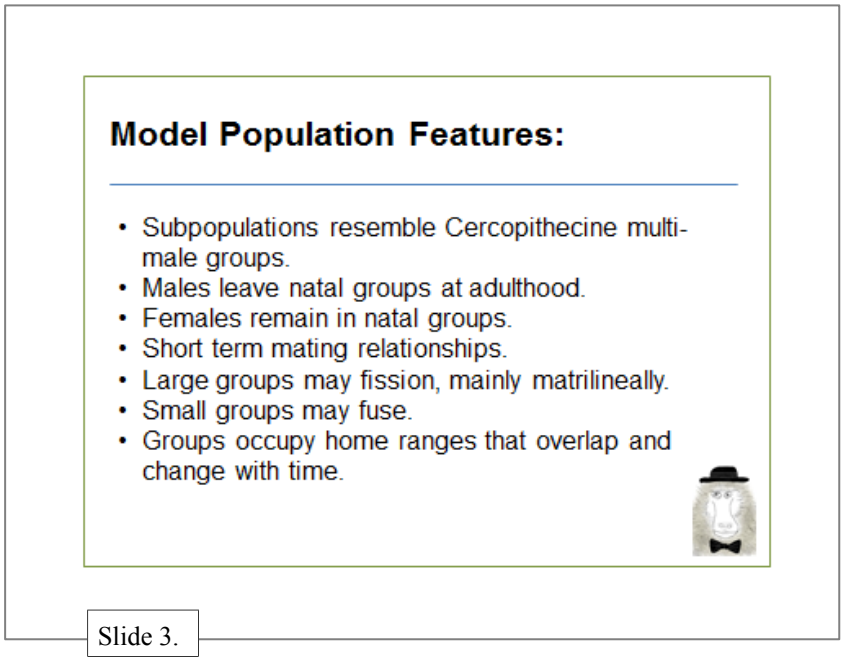
Good afternoon. I'm Tom Olivier. I will be speaking today about the development of genetic resistance to disease and associated processes in simulated monkey populations.

I began working on population genetic studies of Old World Monkeys, namely troops of Kenya olive baboons, in the 1960's. I worked with John Buettner-Janusch. In the 1970's I continued work on Kenya baboon genetics and then began work on studies of genetic dynamics of the Cayo Santiago rhesus colony with Don Sade and others. In the 1970's, we began using computer simulations to explore the apparently rich genetic dynamics of monkey groups. The work I report on today is an outgrowth of earlier studies. The addition of disease modeling here in part reflects the importance of disease processes to anyone engaged in mammalian population conservation.



Slide 2.

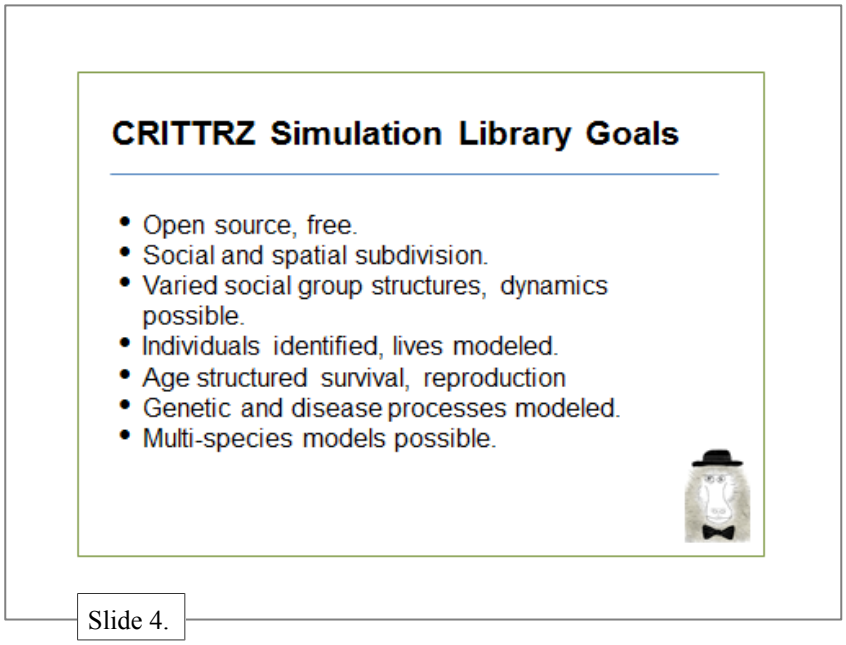
The purpose of this study is to examine interplays between one form of genetic adaptation to disease and social and demographic processes. The study also aims to further demonstrate abilities of simulations to represent complex structures and processes resembling those seen in real primate populations. In particular, this study examines development of genetic resistance to infection in simulated Old World Monkey populations. In contrast, at the 2011 American Society of Primatologists (ASP) meeting I presented a related paper in which simulated monkey populations adapted to disease exposure by selection for an allele that reduced the impacts of disease on infected individuals. Many of the other conditions in simulations in these two papers are similar.



Slide 3.

This slide sketches major features of simulated populations.

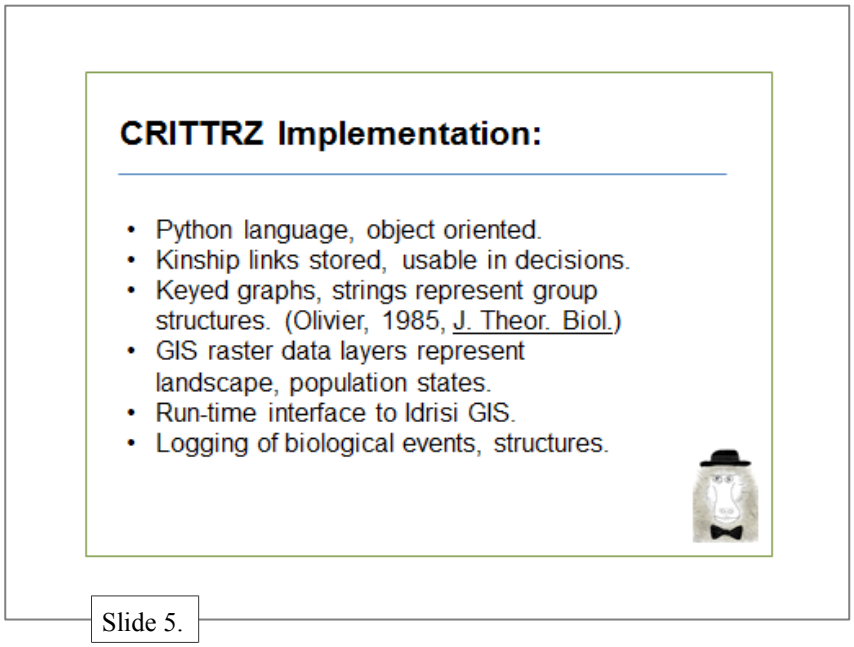
Subpopulations resemble Cercopithecine multi-male groups. Males leave their natal groups around adulthood and join other groups as adult males. They may subsequently migrate to one or more other groups while adults. Females remain in their natal groups (or fission-product groups). Mating relationships are short term. Large groups may fission. In fissions, natal subsets of groups divide matrilineally. Groups that become small may fuse with a nearby group. Groups occupy home ranges that can overlap and change with time. Home range changes are driven largely by availability of resources on the model landscape.



Slide 4.

The simulations reported here were conducted using the CRITTRZ simulation library. I began developing CRITTRZ in 2002. Goals for the package incude:

1. The code is open and freely available.
2. Social and spatial subdivisions are represented.
3. Modeling of varied social structures and dynamics is possible.
4. Individuals are identified. Their births, deaths, movements and reproduction are modeled and can be individually recorded.
5. Age-structured survival and reproduction are incorporated.
6. Modeling of genetic and disease processes is supported. Genetic traits modeled include linked and unlinked autosomal loci, mitochondrial DNA and Y-linked loci.
7. Multi-species models are possible. The species can interact. For example, one sample application included with the full CRITTRZ distribution simulates spread of a disease initially in one monkey population into a second, partially sympatric monkey population



Slide 5.

This slide lists some implementation features of CRITTRZ:

1. It is written in Python, a highly object-oriented scripting language. This methodology eases extensions and other model customizations.

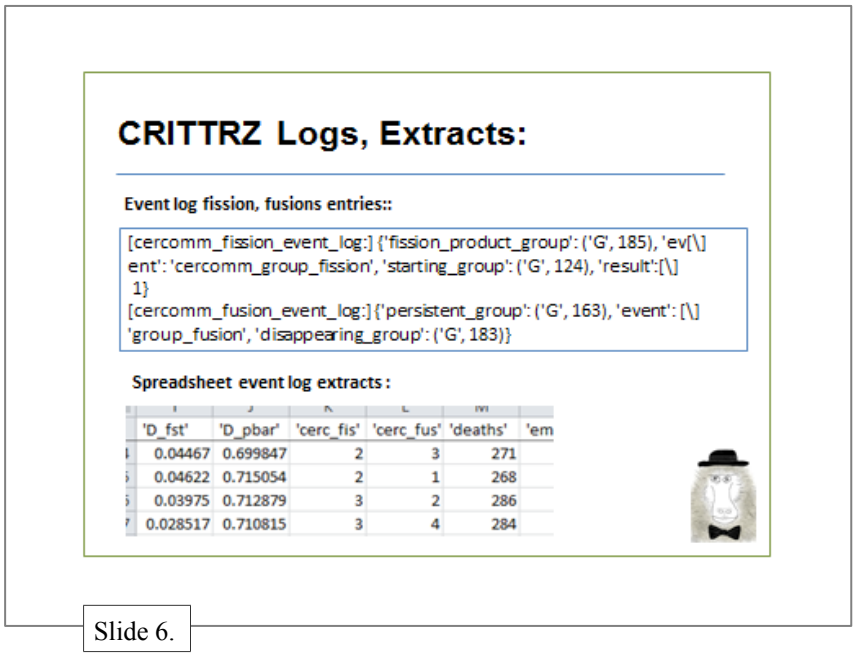
2. Kinship links of simulated animals are stored and available in process decision-making (for example in lineal group fissions).

3. Keyed strings and graphs are used to represent group structures. These data structures and operators on them facilitate modeling many aspects of group dynamics. (T.Olivier, Journal of Theoretical Biology, 1985).

4. Geographic information system raster layers represent many landscape and population states. For example rasters can represent resource distributions, costs of animal movement in different places, home ranges of groups and population gene frequency surfaces.

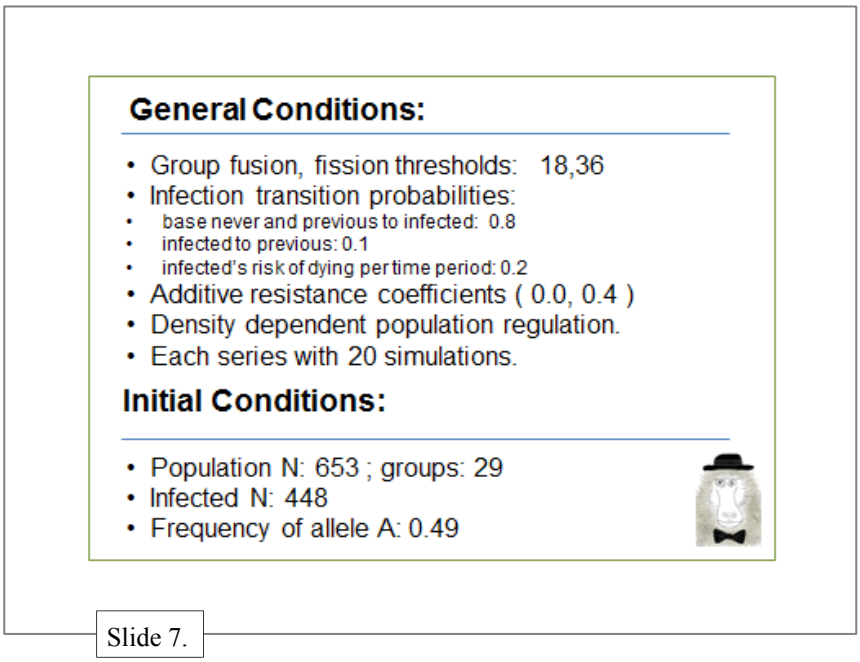
5. CRITTRZ provides a programming interface to the Idrisi GIS. You can issue commands to the GIS during simulations and use the results in subsequent steps of the models.

6. Detailed logging of biological structures and events is optionally available. For example, an input setting allows you to turn on group fission logging. With this on, every group fission, including identifications of parent and derived groups is logged.



Slide 6.

The usefulness of detailed demographic and other population data at Cayo Santiago inspired inclusion of extensive logging facilities in CRITTRZ. In this slide, in the event log entry at the top, we can see example entries during one time period in one simulation run of fission and fusion events. Using entries such as these, one could, for example, construct the historical fission-fusion relationships of all groups present in population at the end of a simulation run. However, simpler summaries of events and structural conditions are probably most broadly useful. To that end, CRITTRZ includes a log summarization utility that can read logs and summarize a wide range of structural conditions (gene frequencies, group numbers) and event counts (fissions, natal male emigrations, adult male migrations) for each time period in each simulation run. The image at the bottom of the slide illustrates a section of a spreadsheet showing such summaries. These log summaries provided most of the basis for analyses in this paper.



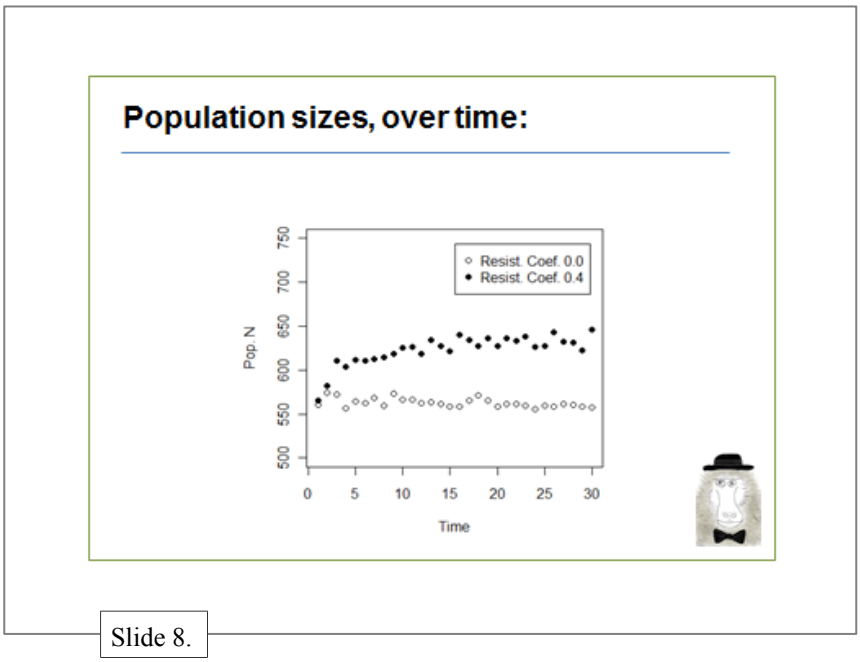
Slide 7.

In these models, small groups may fuse with neighbors or fission. Threshold sizes for these processes in these simulations are 18 and 36. Mean group sizes normally are between fusion and fission thresholds.

The base, maximum probability of uninfected or previously infected individuals becoming infected in one time period is 0.8. The effective probability is this base probability multiplied by the proportion of surrounding animals that are infected. If half your neighbors are infected, in this case your effective probability is half of 0.8 or 0.4. If zero neighbors are infected, your risk becomes zero. The probability of an infected individual becoming uninfected is fixed at 0.1 per time period. Infected individuals have an additional risk of dying in each time period of 0.2

In addition, in this study, the final probability of an uninfected becoming infected is influenced by the number of A alleles from a polymorphic autosomal locus that are possessed by the uninfected individual. In the series with a resistance coefficient of 0, final infection probabilities equal effective probabilities. For the series with a resistance coefficient of 0.4, final probabilities of uninfected individuals becoming infected are 1, 0.6 or 0.2 times the effective infection probability, depending on the number of 'A' alleles possessed by the uninfected individual.

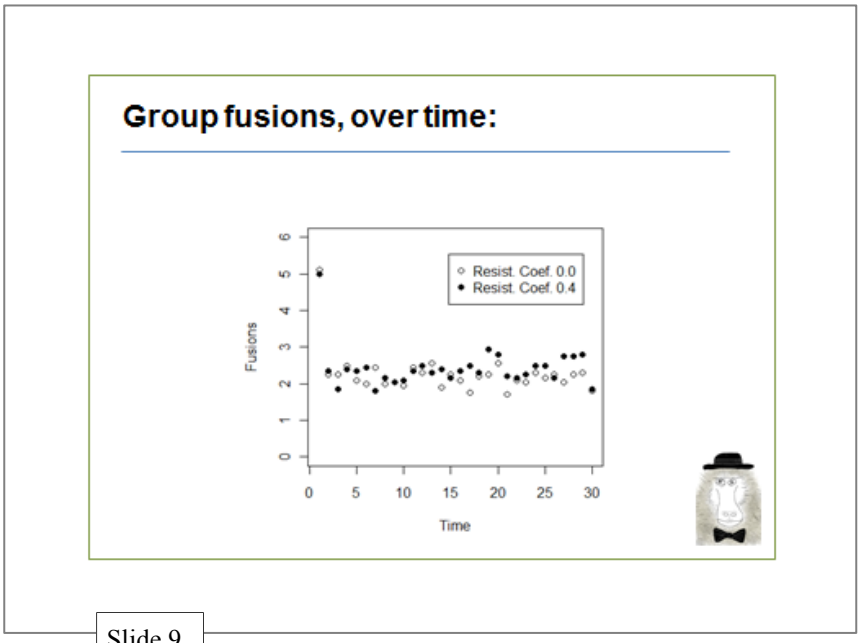
The simulations employ density-dependent population regulation. Twenty simulations are run for two series. Conditions in the series vary only in infection resistance values. The initial population size is 653, divided into 29 social groups. Initially, 448 animals are infected. The starting frequency of the A allele, the one conferring resistance, is 0.49. Simulated animals can live for a maximum of five time periods.



Slide 8.

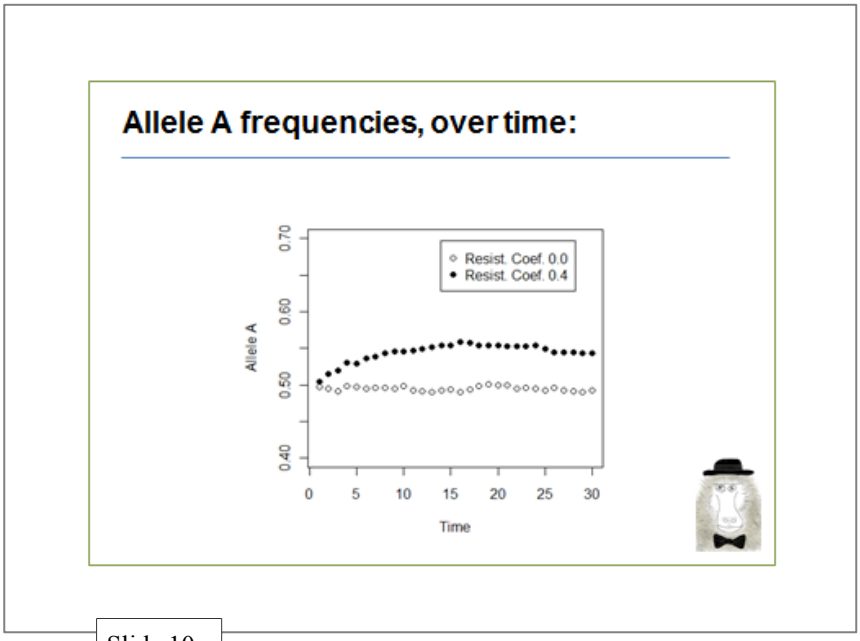
This slide shows mean population sizes at each time period in the two simulation series. In this and following graphs, open circles represent mean values for simulations in the series with zero resistance coefficient. Dark circles represent values for the series with resistance coefficients of 0.4.

The initial population contained 659 members. We can see that in both simulation series, there is a drop in mean population sizes down to around 560 individuals. In the series with zero genetic resistance, mean population number remain near this level for the subsequent time periods. In the series with genetic resistance, we see mean population sizes rise then nearly level.



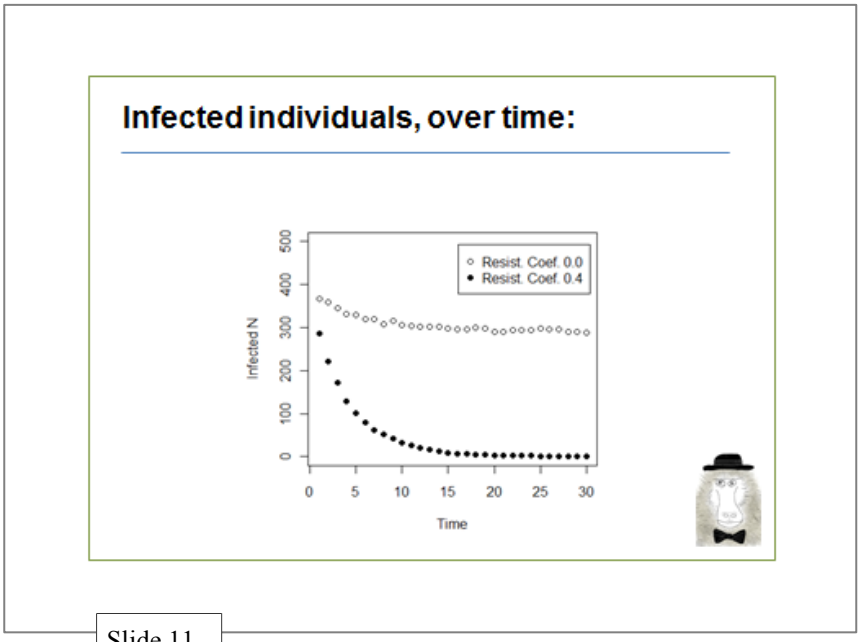
Slide 9.

The strong early drop in population sizes, suggests that we could see a spike in group fusions early on in that series. We can see in this slide that in the first time period, about five group fusions occurred on average in both simulation series. This is well above values seen later.



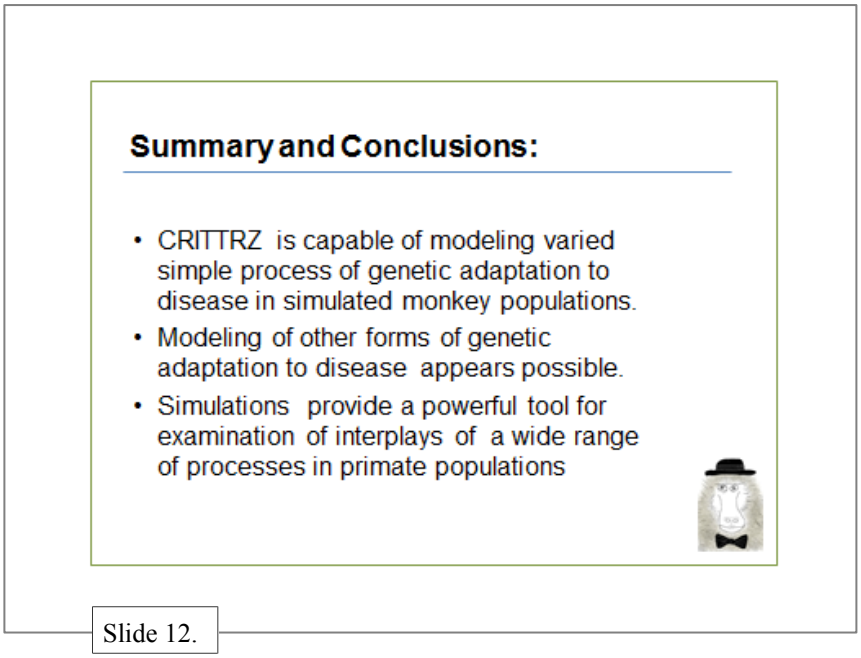
Slide 10.

Here we see the frequency of the A allele holding roughly steady in the series where it confers zero resistance to infection. In the series with the 0.4 genetic resistance coefficient, we see the frequency of the A allele, the one conferring resistance, rise early in the simulation series and then level, with some late decline.



Slide 11.

In this slide, the number of infected individuals drops early in the series without genetic resistance and then nearly stabilizes. In contrast, there were rapid declines in numbers of infected individuals to zero or near zero in the populations with genetic resistance.

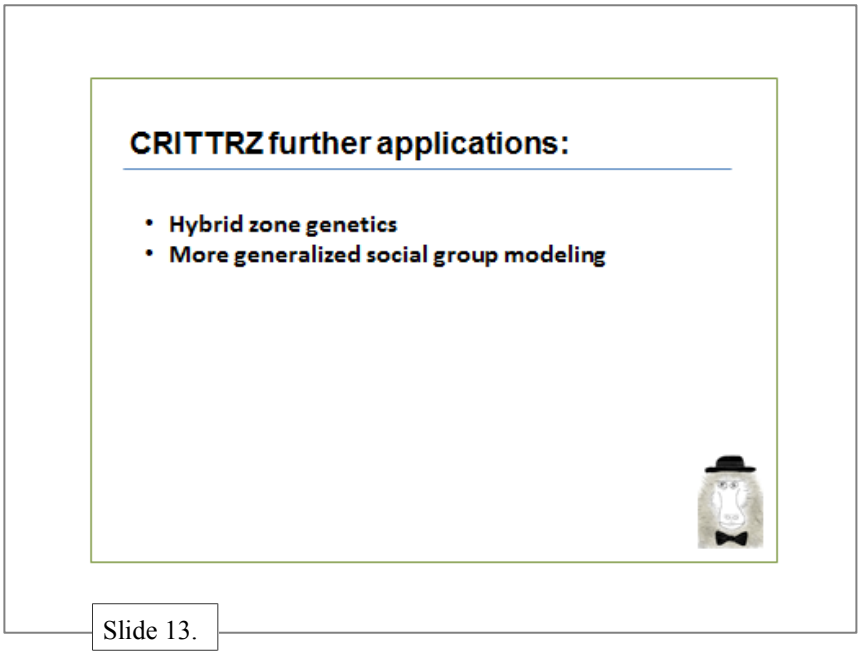


Slide 12.

In this study we saw an early drop in mean population sizes, coupled with a spike in group fusions. Presumably groups that have been reduced by disease are fusing. In the series with one allele conferring strong resistance to infection, the allele conferring resistance became more common for a while but then no longer increased. The average number of infected individuals in the population dropped to around zero. Presumably, there was a decline in selection on the allele conferring resistance with the reduction in infected individuals in the population.

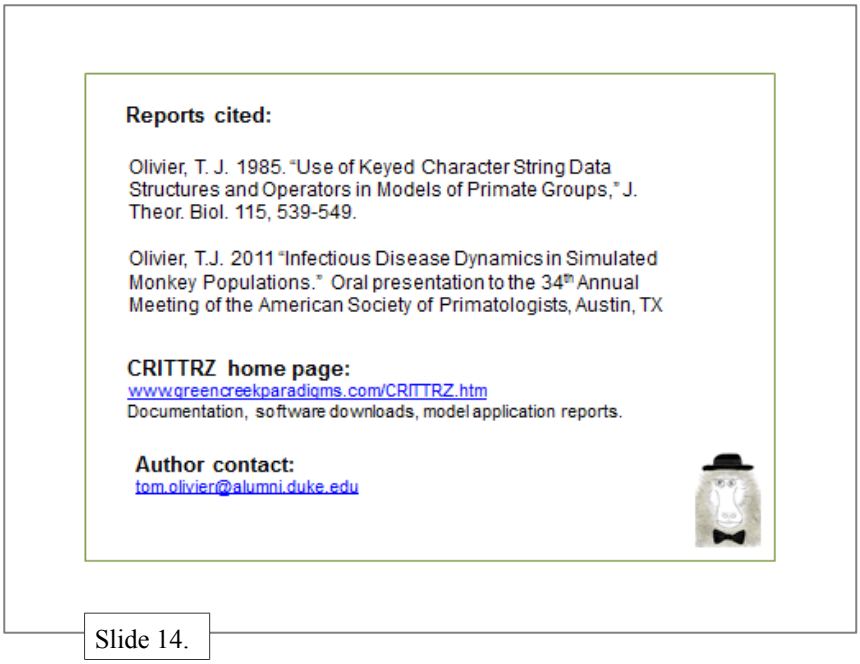
In my ASP 2011 simulations, a favored allele acted to reduce consequences of infection, not resistance to infection. Early drops in population sizes and spikes in fusions were observed there also. However, in the series with strong selection, the favored allele became fixed or nearly so and infected individuals remained widespread.

These studies suggest that CRITTRZ can be used to explore a variety of simple genetic adaptations to diseases in monkey populations. Examinations of more complex cases should be possible.



Slide 13.

Areas in which I aim to apply CRITTRZ in the next year are 1) monkey hybrid zone genetics, with Jeff Rogers and 2) generalization of social system modeling capabilities.



Slide 14.

This slide provides additional information on research cited, the CRITTRZ home page and my email.