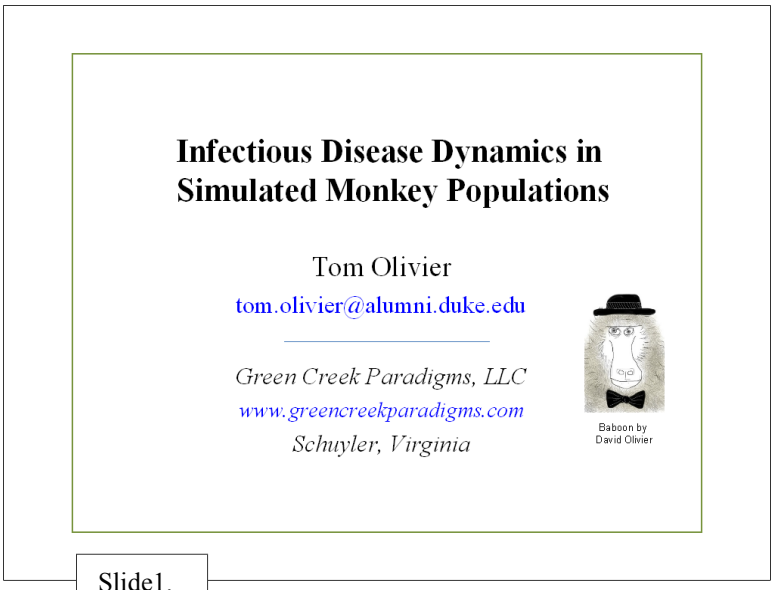


Slide1.

ABSTRACT

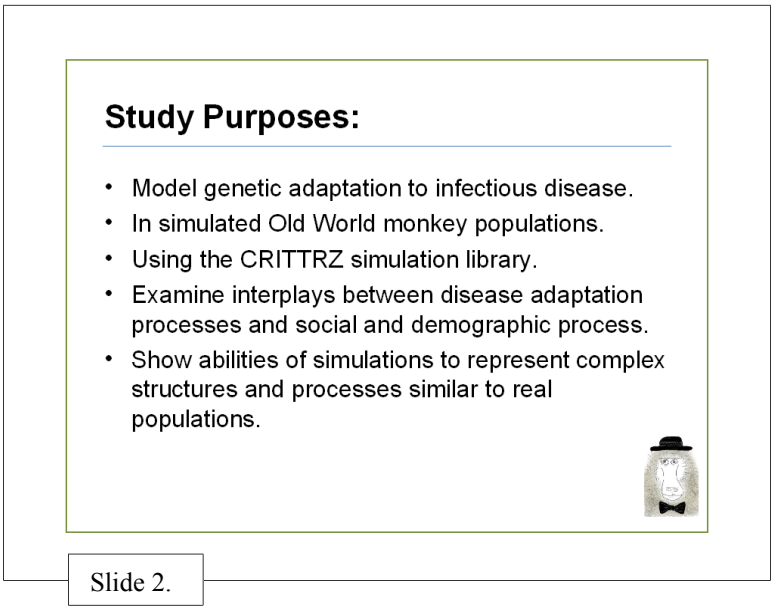
This study examines infectious disease dynamics and associated genetic, demographic and social processes in simulated monkey populations. It models gene frequency changes that reduce impacts of the disease on infected individuals. Simulations were built using CRITTRZ, a simulation library developed by the author. An interface to the Idrisi geographic information system (GIS) allowed use of GIS data layers for representation of model landscapes. Simulated populations contained subpopulations resembling cercopithecine multimale groups. Reproduction and survival rates were density-dependent. Starting populations contained 659 individuals divided into 28 social groups, with 280 members infected. The genotype at an autosomal locus potentially affected likelihood of survival of infected individuals. The risk of dying from disease in one time period for infected individuals heterozygous for a selected-against allele equaled a specified selection coefficient. Infected individuals homozygous for this allele had a risk of dying twice the selection coefficient. Initial frequency of the selected-against allele was 0.68. Simulation series employing selection coefficients of 0, 0.2 and 0.4 were conducted. In the series with selection, population sizes and group numbers dropped noticeably in early time periods. Group fusions were common then. Over time, population sizes and group numbers recovered. Frequencies of the selected-against allele declined. Infected individuals remained widespread. This study shows that genetic adaptations of natural populations to disease may entail shifts in their social and demographic states.

INTRODUCTION

In the 1970's, I was involved population genetic studies of troops of Kenya savanna baboons and social groups of rhesus monkeys at Cayo Santiago, Puerto Rico. The research employed electrophoretic variants of blood proteins as genetic markers. My colleagues in much of this work were Donald Sade, John Buettner-Janusch and Carole Ober.

We began using computer simulations to model aspects of the genetics of these Old World monkey groups, including stochastic male migration between troops (Ober et al., 1978), gene distributions among matrilines within rhesus groups (Olivier et al., 1981), and genetic lineal effects in social group fissions (Buettner-Janusch et al., 1983).

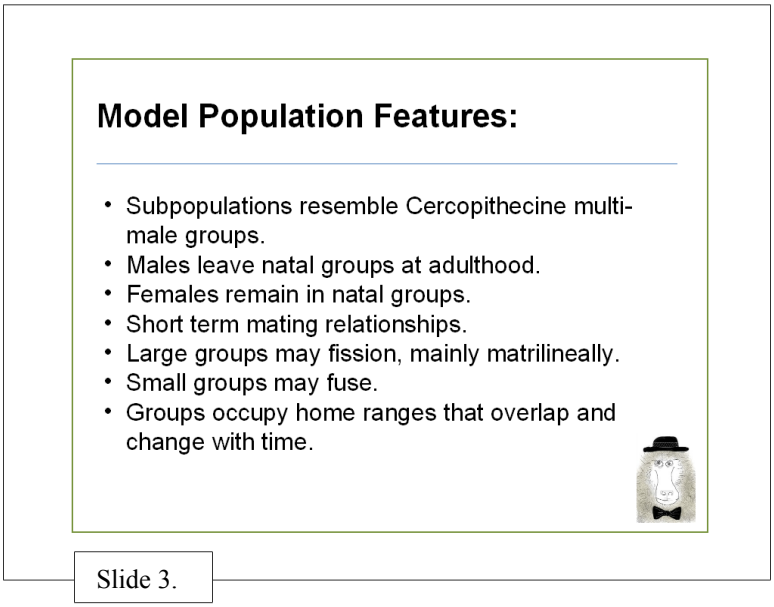
The research I present today uses the CRITTRZ simulation package, a successor I developed to those early models.



Slide 2.

Today, I will be presenting the results from a study that explores genetic adaptation to infectious disease in simulated Old World monkey populations. This study examines some interplays between genetic adaptations to disease and social as well as demographic processes.

In part, my goal is to demonstrate the abilities of computer simulations to represent complex structures and processes similar to those in real primate populations.



Slide 3.

Slide 3 presents some features of the 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.

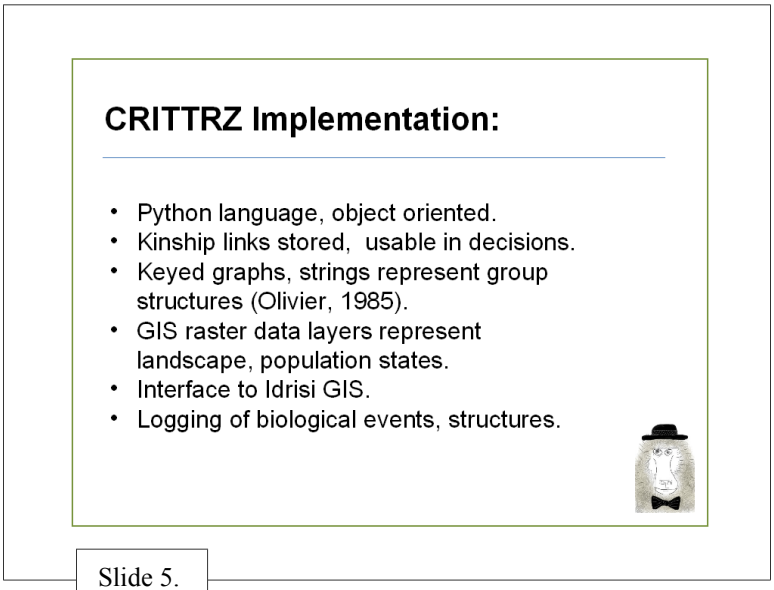
Females remain in their natal groups (or fission-product groups). Mating relationships are short term. Large groups may fission. In fissions, natal subsets of groups divide matrilineally. Groups that become small may fuse with nearby groups.

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.

Slide 4 presents some design goals for CRITTRZ:

1. The code is readily and freely available.
2. Modeling of genetic and disease processes is supported.
3. Age-structured survival and reproduction are incorporated.
4. Social and spatial subdivisions are represented.
5. Individuals are identified. Their births, deaths, movements and reproduction are modeled and can be individually recorded.
6. Modeling different kinds of social structures, dynamics supported.
7. Multi-species models are possible. The species can interact. For example, in one of the standard models included with CRITTRZ, two monkey species occupy the same model landscape. Initially, an infectious disease is present in one, but can jump to the second. In simulations, spread of the disease from one population to the other can be observed.



Slide 5.

Slide 5 lists some implementation features of CRITTRZ:

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

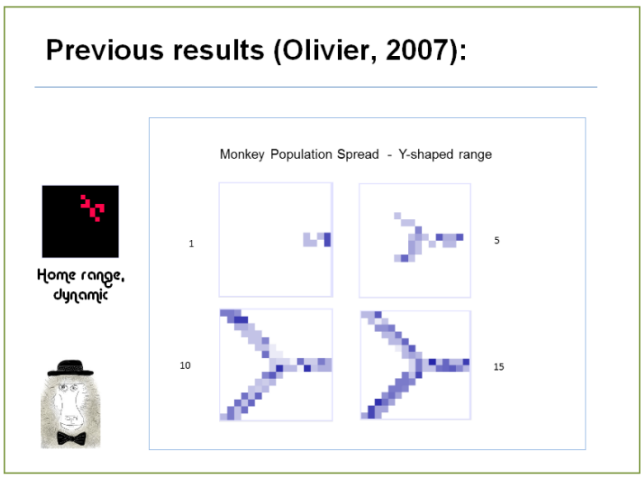
2. Kinship links of simulated animals are stored and available in process decision-making (for example in lineal group fissions).

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. They're discussed in a paper I published in the Journal of Theoretical Biology in 1985 and elsewhere.

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.

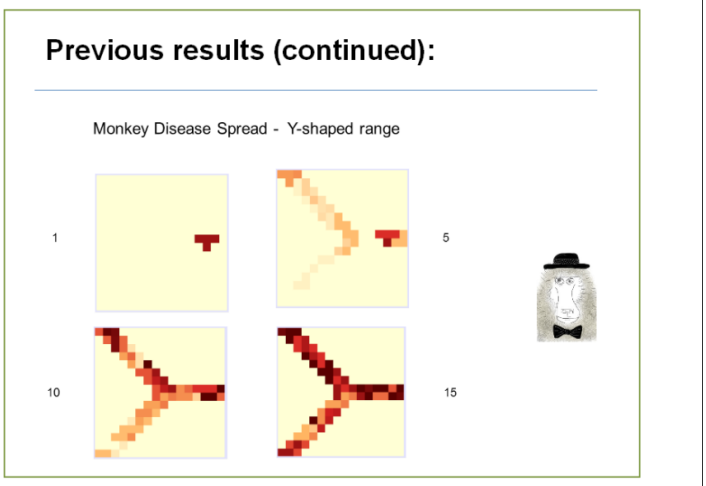


Slide 6.

I want to show two slides from a previous report (Olivier, 2007) that relate to the study I'm presenting today.

The small black and red square in Slide 6 is the raster representation of the home range of one group at one point in time. Range sizes and shapes vary over time as neighboring groups pursue and compete for resources specified by a population resource raster layer.

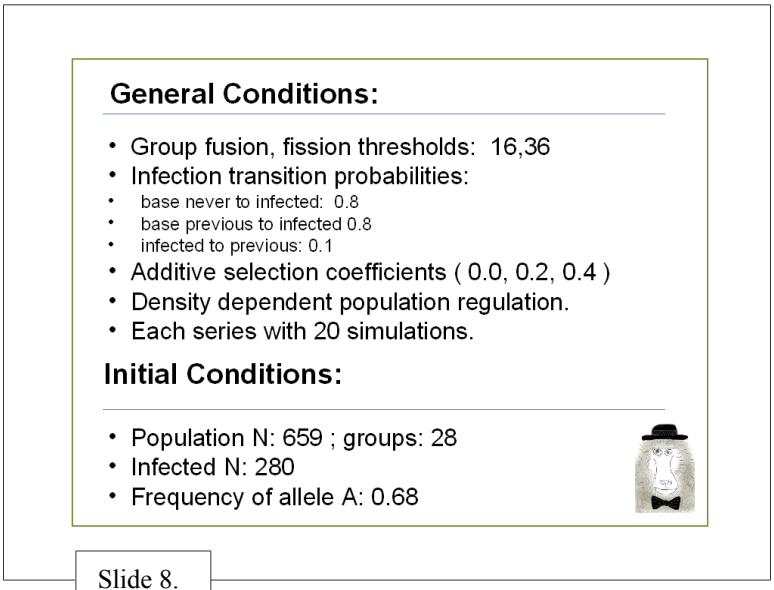
The figures in the large box of this slide illustrate the spread into a nearly empty Y shaped habitat by a monkey population initially composed of two groups. Purple represents population densities, with darker purple indicating higher density. As we move ahead from time period 1 we see the population expand to approximately fill the available habitat.



Slide 7.

Slide 7 represents spread of an infectious disease through a monkey population already occupying a Y-shaped habit. Parameters affecting disease propagation are set to promote rapid spread. The brown color represents infected animals, with darker brown indicating higher infection level.

In time period one, infected individuals are present in only one group. As we proceed through time periods, we see the infection spreads throughout the population.



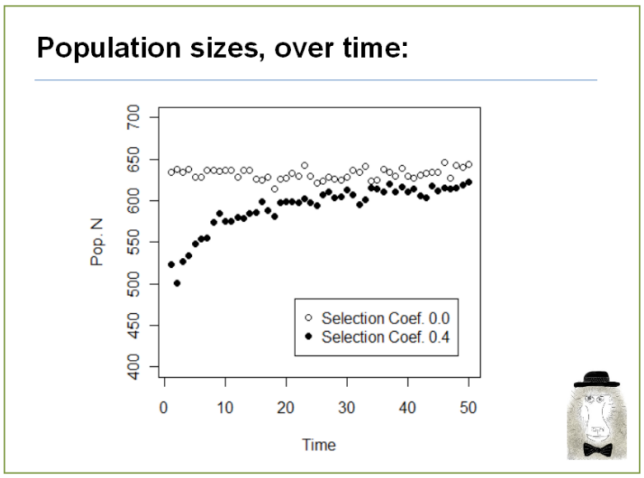
Slide 8.

In these models, small groups may fuse with neighbors or fission. Threshold sizes for these processes in these simulations are 16 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 final, effective probability is the 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.

Augmenting separate age and sex specific survival modeling, in each time period, each infected animal is exposed to a risk of dying from disease. The risk is influenced by the genotype at an autosomal genetic locus. Two alleles are present, capital A and lowercase a, with selection potentially against the capital A allele. Three selection coefficients are used, one for each of three simulation series. These coefficients are: 0.0, 0.2 and 0.4. Fitness effects are additive. If the selection coefficient in a simulation series is 0.2, then in that series the additional risk of dying of an infected heterozygous individual (i.e. Aa) simply 1*.2 or 0.2. For homozygous, AA individuals, the risk is 2 times 0.2 or 0.4. For aa homozygotes, there is no additional risk of dying. The infection, in essence, is benign.

The simulations employ density-dependent population regulation. Twenty simulations are run for three series. Conditions in the series vary only in selection coefficient values. The initial population size is 659, divided into 28 social groups. Initially, 280 animals are infected. The starting frequency of the A allele is 0.68. Simulated animals can live for a maximum of five time periods.



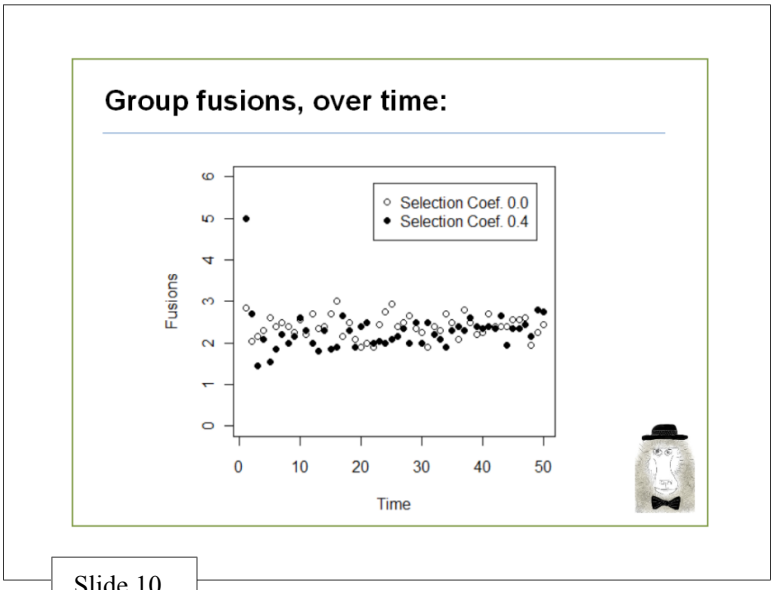
Slide 9.

In both simulation series with selection against the A allele, similar kinds of effects were observed. For simplicity, in the following graphs I am contrasting results from the unselected series (that is, with selection coefficient of 0) with the series with strongest selection (coefficient of 0.4).

Slide 9 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 selection coefficient. Dark circles represent values for the series with selection coefficients of 0.4.

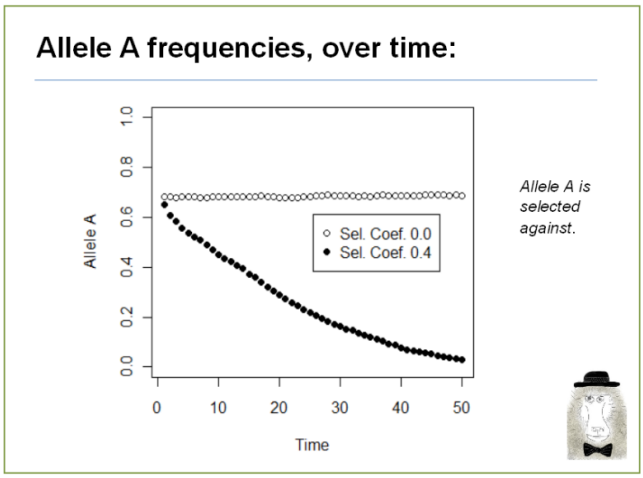
The initial population contained 659 members. Hence, can see that in the first time period for the zero selection series there is a modest drop in population sizes to a mean of around 640 individuals. Population size means then fluctuate for the rest of the time periods, without a strong time trend.

In the selected series, we see a strong early drop in population numbers and then a recovery near to values seen in the unselected series by time period 50.



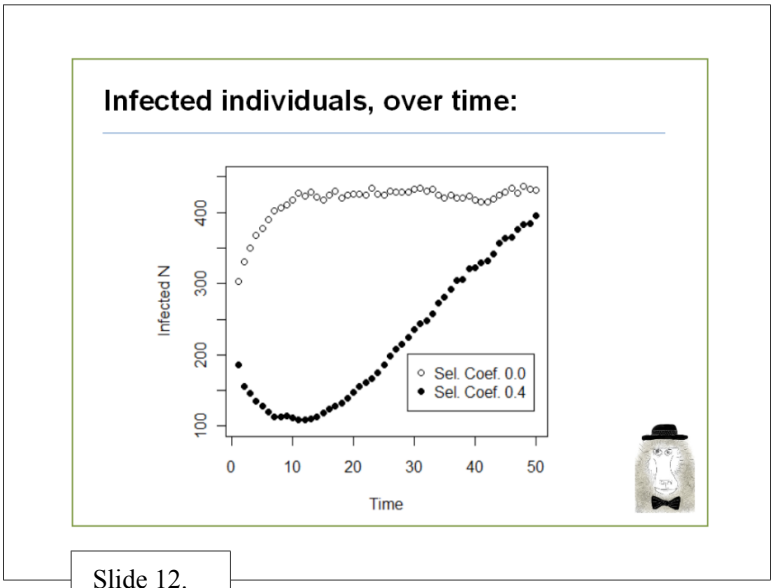
Slide 10.

The strong early drop in population sizes seen in the selected series, suggests that we could see a spike in group fusions early on in that series. We can see in Slide 10 that in the first time period, five group fusions occurred on average. This is well above values seen later.



Slide 11.

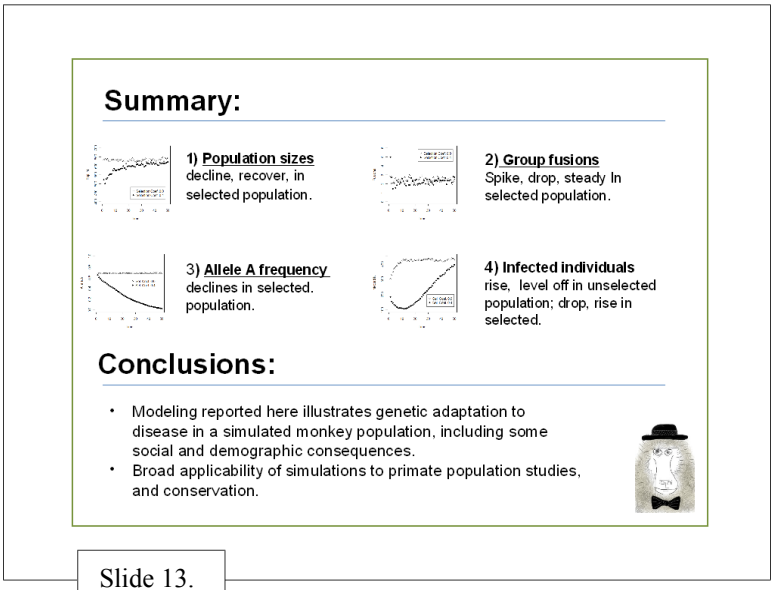
In Slide 11 we see mean frequencies of the A allele in the zero selection population holding nearly steady over time. In contrast, and probably unsurprisingly, we see the A allele frequency drop steadily in the series in which it is strongly selected against. In some simulations with selection, the A allele was completely eliminated.



Slide 12.

In the initial populations, 280 individuals were infected. We see in Slide 12 that in the unselected series the numbers of infected individuals rise quickly for a while. That number then fluctuates with an average of 400 plus individuals infected at any point in time. This number, 400 plus, may be a function of the infected state transition probabilities presented in one of the early slides.

In contrast, we see the number of infected individuals drop initially in the heavily selected population. Presumably, this is caused by deaths of the many individuals with selected-against genotypes. Over time, as the less fit allele A becomes rare, we see an increase in infected individuals. At the end of simulations, the number of infected individuals is near the number of infected individuals in the unselected series.



Slide 13.

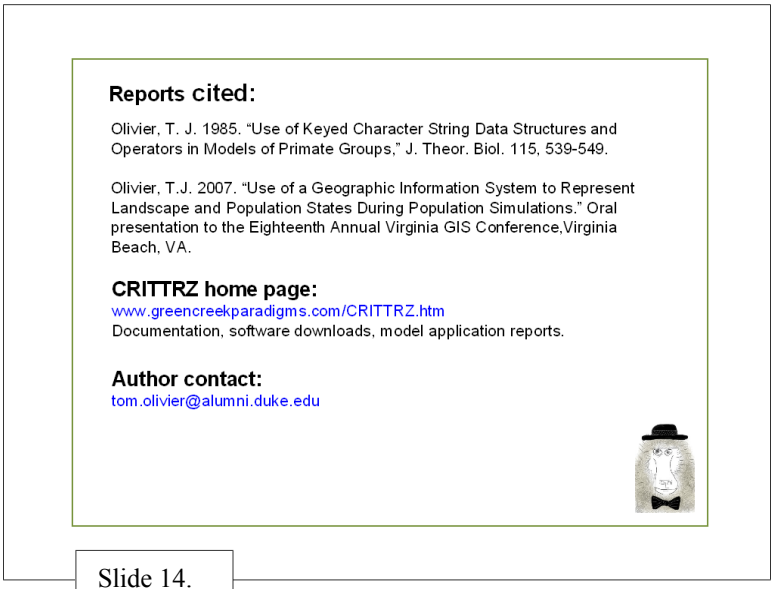
SUMMARY:

In the simulations reported here we saw:

1. A decline and recovery of population size in the heavily selected populations.
2. An early spike in group fusions in the heavily selected population, presumably related to the early declines in sizes of those populations.
3. Steady declines over time of the frequency the selected against allele in populations with heavy selection.
4. A rise then leveling of numbers of infected individuals in populations without selection. In contrast, in populations with heavy selection, numbers of infected individuals dropped early and then increased to levels near those seen in unselected populations.

CONCLUSIONS:

1. Modeling reported here illustrates genetic adaptation to disease in a simulated monkey population, including some social and demographic consequences.
2. Broad applicability exists for computer simulations in primate population research and conservation.



Slide 14.

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