Can evolutionary principles explain “man flu”?

Evolutionary genetics

January 23, 2018

Abstract

Do males typically suffer worse flu symptoms than females, or are they just complainers? In this exercise we will ask several questions about sex differences in immunity, and hopefully get to the bottom of this (obviously tongue-in-cheek) question. We will explore field and laboratory data pertaining to a new species, propose evolutionary hypotheses to explain these observations, and discuss how these hypotheses could be tested. Through this exercise, we hope that students will be able to 1) explain what it means for a trait to evolve, and 2) develop evolutionary hypotheses to explain data collected from field and laboratory experiments.

What is evolution?

We are all familiar with the concept that species can evolve. But how does evolution proceed in nature, and what types of changes in a species’ characteristics should we consider to be evolutionary? We will investigate this question through a series of “experiments” that you and your peers will design and carry out.

Reptile traits

You and your colleagues have discovered a new reptile species! Congratulations!

Figure 1: Two reptiles that are representative of the light and dark morphs of your new species.

Interestingly, you discover two broad coloration patterns among the reptiles that you sample, with both light-colored and dark-colored individuals (Fig. 1). You record the trapping location for each individual, and find an intriguing pattern (Fig. 2). Individuals with light coloration tend to be discovered in areas where the surface rock is light in color, while dark colored individuals tend to be discovered in areas with dark substrate. What could explain this association between reptile characteristics and geographic characteristics of the sampling locations?

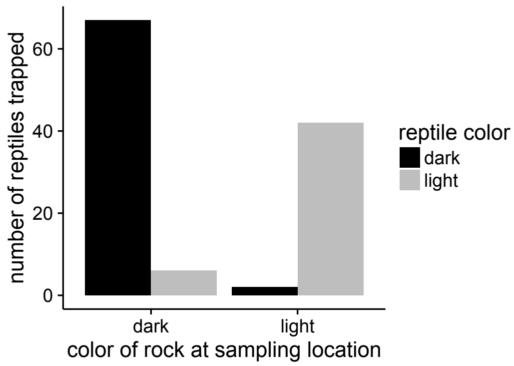


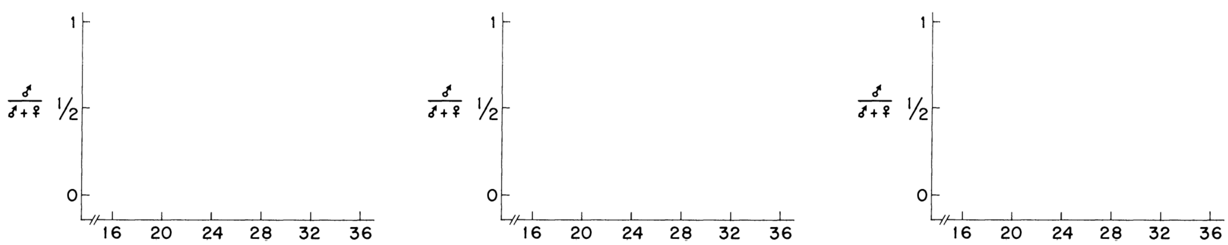
Figure 2: The number of reptiles captured on light rock and dark rock, separated by the coloration of the reptile.

Discuss the following questions

1. What biological or evolutionary processes could explain the variation in color (Fig. 1) among the reptiles you have sampled? (*hint: think about whether coloration is permanent/impermanent in species you are familiar with*).
2. How can the association between background color and reptile coloration (Fig. 2) be explained? Provide at least 2 hypotheses.
3. Suppose that you obtain additional funding to sequence a gene that is known to contribute to color variation in another reptile species. You record the various alleles that you discover in the population, and how they relate to the color phenotype. You discover that all of the light colored individuals are homozygous for a one allele (denoted AA), while all the dark individuals are homozygous for a different allele (denoted aa). What do these data suggest about the biological basis of the color phenotype in your newly discovered reptile species?
4. You perform a genetic cross experiment where you now mate AA individuals with aa individuals. You discover that the Aa individuals, which you did not observe among the samples you collected, are viable and have an intermediate color. Provide a hypothesis for why these individuals are not observed in nature.

Sexual dimorphism in reptiles

As an herpetologist, you are aware that there are a variety of sex determination systems in reptiles. In some species, sex is determined by genetics, while in other species it is determined by environment, often the temperature experienced by the embryo during the development period. To investigate how sex is determined in this new species, you design an experiment. You sample 10 female and 10 male individuals, breed them, and record the sex of the offspring under a variety of conditions. You test three hypotheses: *H0*) sex is determined by genetics alone, *H1*) sex is determined by temperature alone, and *H2*) sex is determined by genetic factors under a threshold temperature, but above this threshold sex is determined by a combination of temperature and genetics.



(a) *H0* (b) *H1* (c) *H2*

Figure 3: The proportion of males ($\frac{♂}{♂+♀}$) as a function of temperature corresponding to three hypotheses.

With your group,

1. Sketch your expectation of the proportion of male offspring as a function of temperature under each hypothesis (*note that there may not be a unique answer for each hypothesis*).
2. Discuss why these sex determination systems (genetic and temperature-dependent) may have evolved.
3. Once you have completed the previous two items, ask Professor Parr or Dr. Uricchio for the "results" of your experiment for your new reptile species. Given your discussion of the sex determination mechanisms, what do these data tell you about your species? What can you conclude about the environment experienced by embryos in this reptile?

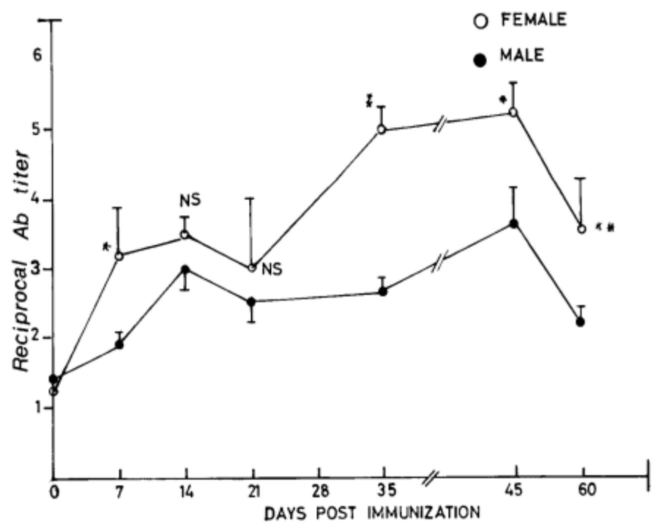


Figure 4: Time course of antibody titer (*i.e.*, the amount of antibody produced by infected individuals in response to infection).

4. Through a series of additional experiments, you observe that males born at high temperature have higher fitness than males born at low temperature, while the opposite is true for females. Can this additional data help clarify your answer to question 2?

Sexual dimorphism of immunity

Having discovered the mechanism for sex determination in your newly discovered species, you are now curious if there are any interesting differences in male and female traits. You inoculate a set of individuals with a pathogen of interest, and monitor their immune responses. You discover that females have an elevated immune response, as determined by a laboratory experiment (antibody titer, Fig. 4).

The results of this experiment are exciting! They suggest that infection may be more "costly" to males, because it may take longer for them to clear infection. However, they also raise an important question: why does this pattern exist?

With your group, complete the following questions:

1. Suppose that this pathogen often kills infected individuals. How will evolution act to shape immune responses to the infection?
2. If evolution is acting to shape the immune response, why haven't males evolved an immune response equal to that of females? Provide at least one hypothesis.
3. Can you propose a biological mechanism for the difference in immune responses of males and females?
4. Now suppose that the infection that we are studying is rarely a primary cause of mortality for infected individuals. What does this suggest about the evolutionary cost of the the infection? Can the immune response to the infection still impact the organism's fitness?

How will sexual dimorphism in immunity continue to evolve in the context of modern medicine?

Humans are a sexually dimorphic species. While many traits are not substantially differentiated between human males and females, some traits (*e.g.*, levels of hormones such as testosterone and estrogen) are differentiated between the sexes. Suppose that evolution has acted to promote sexually dimorphic immune response to the flu in humans, with males having a weaker response. In the context of modern medicine, do we expect this trait to continue to evolve? Supposing that humans persist for millions more years, do we expect generations in the distant future to maintain this sexual dimorphism in immune response?