Genetics Education

Innovations in Teaching and Learning Genetics

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Cats as an Aid to Teaching Genetics

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ABSTRACT

I have used an exercise involving domestic cats in the General Genetics course at the University of Nebraska-Lincoln for the past 5 years. Using a coherent set of traits in an organism familiar to the students makes it easy to illustrate principles of transmission and population genetics. The one-semester course consists primarily of sophomores and juniors who have either taken a one-semester introductory biology course, a one-semester cell biology course, or have a strong high school biology background. The students are given a handout and asked to determine the genotype at seven unlinked loci of at least one cat. To fill out the form, the students have to grasp such concepts as dominance, incomplete dominance, temperature-sensitive mutations, epistatic interactions, sex linkage, and variable expressivity. Completing the form reinforces these concepts as they observe the cat's phenotype and fill in the genotype. I then analyze the collected data and use it in my lectures on population genetics to illustrate the Hardy-Weinberg equilibrium, calculate allele frequencies, and use statistics. This allows the students to look at population genetics in a very positive light and provides concrete examples of some often misunderstood principles.

GENETICS is both more quantitative and more analytical than other areas of biology. The mathematical descriptions of Mendelian inheritance and population genetics are sometimes daunting, and students frequently have powerful misconceptions about population genetics. Good examples to illustrate principles of incomplete dominance, epistasis, and sex-linkage abound, yet these examples are often from organisms outside of the students' experience or interest (fruit flies, snapdragons, summer squash, roosters, etc.). Furthermore, if each example is from a different organism, the students can be distracted from the principles by the details. Common misconceptions by students about population genetics are that dominant alleles will take over a population, that the most abundant phenotype in a population represents the dominant trait, and that deleterious alleles will be eliminated quickly. One would expect that a clear understanding of the Hardy-Weinberg law would eliminate these misconceptions, but students are often unable to apply the principles to actual examples. Even though they may know how to calculate allele frequencies and test populations for Hardy-Weinberg equilibrium, their intuitions have not caught up with this knowledge. For example, many students can correctly answer question 1 in Table 1 but will incorrectly answer question 2.

I have attempted to find a coherent set of examples of Mendelian principles and to attack their misconceptions about populations. I have designed an exercise in cat genetics that helps me achieve both goals. The students are interested and engaged, and they also take home an increased knowledge of genetics. Many students have told of how they have interested family members and friends in genetics by discussing a pet cat. The process is simple and cat-friendly (the most intrusive part is determining the cat's gender). It is easy to carry out; many students use a family pet, others go to the Humane Society, pet shops, or use a friend's cat. Some have genotyped stray cats they have seen. Some students get so involved that they cannot seem to stop, even though they get no additional credit for additional cats—in the Spring of 1998 one student turned in the genotypes of 31 cats! Many students have given additional information or used a known pedigree to infer more detailed genotypes (*i.e.*, distinguishing *LL* from *Ll*). The data obtained by the class can be compared to published allele frequencies for cats in a variety of

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TABLE 1

Two Exam Questions, One Mathematical and the Other Intuitive

The first question is a simple Hardy-Weinberg calculation question that most students will get correct. The second is a problem that many students get wrong because their intuition about population genetics has not caught up with their ability to calculate allele frequencies.
Question 1. Given that *A* is dominant to *a*, assume Hardy-Weinberg equilibrium and calculate the allele frequencies for a population of 3000 *aa* and 1000 *A*_ individuals.
Correct answer: $p = 0.134$, $q = 0.866$.
Question 2. Cockroaches in the Biology building were sampled and 3000 with long wings were found along with 1000 with short wings. Which trait is dominant?
Correct answer: You can't tell.
Common answer: Long wings (sometimes this answer is accompanied by a detailed explanation of Mendelian monohybrid crosses).

geographic locations, and the students seem to find this interesting. When their data are used to teach population genetics they can focus on the underlying principles because they are already familiar with the genotypes and phenotypes, and the symbols for the loci and alleles are more meaningful.

THE EXERCISE

The exercise is defined very early in the semester, although the details and the handout are not distributed until after I have covered the topics of transmission genetics necessary for completing the assignment. I try to include examples of cat coat color genes as often as possible when covering Mendelian genetics. A good description of feline genes and phenotypes can be found in Robinson (1991). I have also collected a number of photographs of various cats and include them on the course web page (http://bs-biosci.unl.edu/GCMB/Christensen/cats.html) to illustrate various genotypes. The genes and associated concepts that need to be explained before the students are ready to collect data are as follows.

Long hair: Long hair is recessive, and is indicated by *ll*. Short hair is either *Ll* or *LL*. An explanation of this is appropriate at the very beginning of Mendelian genetics.

Agouti: An explanation of the *agouti* gene and its effect on hair pigmentation patterns is appropriate in the context of epistasis. Many genetics texts include examples of *agouti* and *black* in mice as an example of epistasis. In cats the explanation is complicated by the *Tabby* gene, which controls the pattern of expression of *agouti*. This concept is one of the more difficult ones for students. I generally use the example of mice to explain the pattern of pigmentation of each hair caused by the *agouti* gene, then introduce the idea that in cats the *Tabby* gene causes the *agouti* gene to be expressed for a different period of time during the hair growth cycle in the stripes, leading to the Tabby pattern. We do not score alleles of *Tabby* in the exercise because T^b (*Tabby-blotched*) and T^a (*Tabby-abyssinian*) are very rare in this area. In general it simplifies things for the students to use the Tabby pattern as an indicator of whether the cat is agouti (*A*_) or nonagouti (*aa*). If they can see a Tabby pattern in the fur, then the cat must be agouti, whereas if the colors are solid then the cat is nonagouti.

Dominant white: An all-white cat with nonpink eyes is likely to be *W*_ rather than albino. Albino cats are fairly rare; out of 1519 cats, my students have never reported one. Dominant white is an example of dominant epistasis as it is impossible to score any of the other color genes in the presence of *W*. Dominant white kittens often have one or more small pigmented spots on the forehead that usually fade by adulthood.

Siamese and Burmese: The c gene has two different temperature-sensitive alleles, c^s (Siamese) and c^b (Burmese). Both are recessive to *C*. The Burmese has more pigmentation in the warm parts of the body than the Siamese. I try to discourage students from genotyping Siamese and Burmese as the breeding of these cats is generally under close control by humans, thus the Hardy-Weinberg assumption of random mating is unlikely to be true. If students turn in the genotype of a Siamese or Burmese, I count the number of *C* and *c* alleles and calculate the allele frequencies, but do not include the other color genes from these cats in the population totals. If the class size were smaller, I would strongly discourage use of any fancy breeds.

Piebald spotting: This is a good example of incomplete dominance and variable expressivity. Simplified, *ss* cats have no white fur, *Ss* cats generally have $<50\%$ white fur, and *SS* cats generally have $>50\%$ white fur (cats who are 100% white are scored as dominant white and can't be scored for piebald spotting). The *S* allele is incompletely dominant, but variably expressed, so there is a more-or-less continuous gradient of white pigmentation in populations. The standard in the literature is to grade cats for piebald spotting on a scale of 1–10 (Robinson 1991); however, I have found that the

50% guideline works very well. Very few cats are close to the borderline, so the difficulties and inaccuracies caused by this approximation are few.

Orange: This is a good example to illustrate sex-linkage and dosage compensation. Students need to be told that the dominant *O* allele only changes the black pigment to orange, while the yellow pigments in the fur are unchanged. A Tabby pattern is still visible in an agouti, orange cat. Because the *O* gene is on the *X* chromosome, males are hemizygous and are either *O* or *o*. Females can be *OO* and completely orange, *oo* and have no orange, or are heterozygous, *Oo*, and are mosaics of orange and nonorange fur due to *X*-inactivation. The patch size of the mosaic can vary quite a bit, although it correlates with the size of the white spots produced by the piebald spotting locus (Norby and Thuline 1965). Students often ask about male calico or tortioseshell cats; these are rare and are usually *XXY*, the feline equivalent of Klinefelter's syndrome (Centerwall and Benirschke 1973; Moran *et al.* 1984).

Dilute: The final gene scored is dilute (*d*). This is a recessive modifier of pigmentation, which causes the black pigment to become gray (often with a bluish tint) and the orange pigment to be diluted to cream. Dilute can be scored in the presence of any of the other colors except dominant white, and is a good example of an epistatic interaction.

Color genes that are not scored include brown (*b*), which is found in the Havana brown or chocolate point Siamese and Burmese, but is otherwise very rare in the Midwest (only one Havana brown has been reported out of 1519 cats in five years), and silver (*I*), which alters the yellow pigments visible in the agouti cat to white. A few students have noticed the silver-tipped fur, but if they are instructed to only look at the darker pigments it will not cause confusion. Manx cats are are a good example of a single gene with two phenotypes: dominant tailless and recessive lethal. I use Manx cats as an example of a recessive lethal gene, and leave students space to describe it on the form, but it is rare in this area. Occasionally students report polydactyly, another example of variable expressivity and incomplete penetrance. In areas where these genes are common they could easily be added to the checklist.

Figure 1 shows the checklist that the students are given. A handout briefly describing the purpose of the exercise and reminding them of the genotypes and phenotypes is also distributed. One source of potential error is that it may not be possible for the student to accurately determine the cat's gender. It must be emphasized that they should not guess the gender, but just write unknown. Cats of unknown gender must not be used in the calculation of *Orange* allele frequencies. The first year that I did this exercise the results with *Orange* were not in Hardy-Weinberg equilibrium. In subsequent years I instructed them not to guess the gender if they were not completely sure, and the results with *Orange* have been in Hardy-Weinberg equilibrium since then. It is also important to emphasize to the students that they must record their data clearly, particularly taking pains to distinguish O from o and S from s. On the checklist I use a font for the lower case letters that helps distinguish them from upper case (see Figure 1) and I tell the students to write clearly.

RESULTS

During the past 5 years 766 students returned the form out of a total of 789 enrolled in the class (97%). This shows that it is an easy exercise to do, and clearly worth the 10 extra credit points (out of 500 possible for the course) they receive. Students get no additional credit for additional cats but there is room on the form for 5 genotypes and some students ask for additional forms and do large numbers of cats. The record so far is one student who turned in 31 cats, all from her family farm. Another student worked at a kennel and determined the genotype of 15 cats that were brought in for care while she was on duty. Many students bring photos or attach locks of fur to the forms. One student who wondered whether her cat was a male calico brought him into my office! The average number of cats per student is 2.1 (1644 cats reported by the 789 students), a reflection of their enthusiasm for the exercise. The numbers have been rising each year: in 1999 the average was 2.7 cats per student, and the return rate was 98%. This exercise is also a good way to interact with students one-on-one. With an enrollment of 120–200, this is the best opportunity for me to interact with students casually about genetics. Recently I started to require that the students meet with me individually when they turn in the form. This allows me to meet each student outside of lecture, correct misunderstandings, and catch errors in the forms.

Student accuracy is high, with $<5\%$ of the raw forms needing some form of correction. Discussing the cats with each student helps reduce the error rate. I ask the students where they found or saw the cats and try to be alert for duplicates (they are instructed to use different cats from other students). Once the forms are all in, I make a tally of the genotypes in the sample (I usually have one or two honors students help with the data analysis). We include only nonfancy breeds from our general geographic region. The instructions encourage local nonfancy cats and most of the students comply. Table 2 lists the numbers of cats of each genotype from 1998. Some of the totals do not quite agree due to incomplete forms (for example, a student may have been confused about the *A* locus and not remember the cat well enough for me to have confidence in the genotype at that locus, but the genotype at the *W* locus is clear and is therefore used in the table).

Name_____

If you can't determine a genotype, leave that square blank. Write the allele abbreviations in the boxes.

Phenotypic guide to genotypes	Cat #1	Cat #2	Cat #3	Cat #4	Cat #5
Cat's name (optional)					
Sex, m or f, (write "unknown" if you are not sure — **do not guess**)					
Long hair *ll*, short hair *L—*					
Dominant white *W—*, otherwise *ww*. If *W—*, you can not determine any of the other alleles, so leave the rest of the column blank.					
Agouti fur: if agouti, *A—*, if each hair is a solid color, *aa*.					
Orange: Male, completely orange: *OY* Female completely orange: *OO* Calico (mosaic of orange with other pigmented fur) is a female: *Oo* Males with no orange fur: *oY* Females with no orange fur: *oo* If unsure of the sex, write *o*? or *O*? Be sure to distinguish between *O* and *o* when you write it.					
Dilute color: if black is changed to blue-gray, or if orange is changed to light yellow or cream, write *dd*, otherwise, *D—*					
Piebald spotting: If less than half white, *Ss*, If more than half white, *SS*, if there is no white fur on the cat at all, *ss*. Be sure to distinguish between *S* and *s*.					
Siamese, $c^s c^s$ or Burmese, $c^b c^b$, otherwise *C—*					

Comments on location (specify the location if the cat was not seen in Lincoln), or comments on genotypes not listed in the table (i.e. Manx, silver, the various purebreds, fancy breeds, Cheshire, etc.):

Figure 1.—Checklist for cat genotypes. This checklist was handed out to the students to use in scoring cat phenotypes.

INTERPRETING THE DATA IN CLASS

I first introduce the concepts of the Hardy-Weinberg law in class by presenting the assumptions (infinite population size, random mating, and no migration, mutation or selection), and then the conclusions (allele frequencies do not change over time, and the phenotypic frequencies can be derived from the allele frequencies as p^2, $2pq$, and q^2). Next, I introduce the idea that if a population is in Hardy-Weinberg equilibrium the assumptions are likely to be true. I illustrate the ideas with the data they have collected on the *S* locus because the heterozygotes can be scored and alleles can be counted

TABLE 2

Number of cats of each genotype in 1998

Genotype	Number
Male	118
Female	128
Unknown	19
*L_*	168
ll	92
*W_*	26
ww	239
*A_*	100
aa	137
OY	30
oY	77
OO	9
Oo	37
oo	68
*D_*	175
dd	60
SS	18
Ss	104
ss	109
*C_*	235
cc	4

directly. Using the 1998 data, the allele frequency calculation for *S* is $p = ((2 \times 18) + 104)/(2 \times 231) = 0.30$. The allele frequency calculation for *s* is $q = (104 + (2 \times 109))/(2 \times 231) = 0.70$. Note that $p + q = 1$. We can then ask if the cat population is in Hardy-Weinberg equilibrium by calculating expected values from p and q, and using a χ^2 test. The expected values are $p^2 \times 231 = 21$ for the *SS* genotype, $2pq \times 231 = 98$ for the *Ss* genotype, and $q^2 \times 231 = 112$ for the *ss* genotype. A χ^2 analysis results in a P value of 0.65, thus the hypothesis of Hardy-Weinberg equilibrium can be accepted. The students have already learned the χ^2 test, but at this point they need to understand that there is only 1 d.f. in this analysis because the observations have been used once in deriving p and q and a second time to calculate the expected numbers using the total number of cats observed.

We can also directly count the alleles for the *Orange* locus, but it is complicated by the fact that the males only have one allele and the females have two. For the 1998 data, the calculation of p (for the *O* allele) is $(30 + (2 \times 9) + 37)/(107 + (2 \times 114)) = 0.25$. The allele frequency, q, of the *o* allele is $(77 + 37 + (2 \times 68))/(107 + (2 \times 114)) = 0.75$. Once again, $p + q = 1$. It must be emphasized to the class that the total number of alleles is the number of males plus twice the number of females, not twice the number of cats. This is an opportunity to explain once again why guessing the gender was discouraged. Calculating the expected values is also complicated by the sex-linkage of *Orange*. I prefer to use the observations as few times as possible in calculating expected values, so rather than using the actual numbers of males and females, I simply divide the total number of cats by 2 to get the expected numbers of males and females. The expected number of *OY* males is $p \times 221/2 = 28$, the expected number of *oY* males is $q \times 221/2 = 82$, the expected number of *OO* females is $p^2 \times 221/2 = 7$, the expected number of *Oo* females is $2pq \times 221/2 = 42$, and the expected number of *oo* females is $q^2 \times 221/2 = 62$. The χ^2 analysis gives a P value of 0.70 (3 d.f.), so the hypothesis of Hardy-Weinberg equilibrium can be accepted.

Every year since I began emphasizing that the students not guess the gender the population has been in Hardy-Weinberg equilibrium for *S* and *O*, with sample sizes of 200–300 cats each year. This suggests that the students have effectively sampled the cat population of Nebraska and some nearby areas (mainly Iowa and Kansas), and that the allele frequencies are relatively constant across this geographical area.

Having established that the collected cat population is in Hardy-Weinberg equilibrium I then use the Hardy-Weinberg law to estimate the allele frequencies of the other alleles. For example, the frequency of *aa* cats is 137/237, and is also equal to q^2. Solving for q gives a value of 0.76, and $p = 1 - q = 0.24$.

The allele frequencies can be compared to published allele frequencies of cats from various geographic locations. Several references include lists of allele frequencies found in a variety of locations in North America and Europe (Halpine and Kerr 1986; Klein *et al.* 1986; Dunn *et al.* 1989; Höger 1994). These comparisons allow the students to understand the forces that change allele frequencies, particularly migration and selection. Some of these references also discuss human migrations and the resulting cat migrations and allele frequencies.

Finally, I discuss some common misconceptions that people generally have about population genetics. All of these misconceptions are shown to be untrue by the Hardy-Weinberg law, but some practical examples from the class's data help reinforce the ideas. The first misconception is that dominant alleles will take over a population. The second misconception is that if a phenotypic ratio is 3:1, then the more abundant phenotype represents the dominant allele. Having memorized Mendel's ratios, students are apt to conclude that if three-quarters of a population shows a phenotype, then that is the dominant one. I use their cat data to show that this is only true for the progeny of a Mendelian monohybrid cross and has nothing to do with populations in equilibrium. A good example to use for both misconceptions is *W*, which is dominant but has a very low allele frequency of 0.05 and has not changed since the published work of Halpine and Kerr (1986). I try to use their data to show them how their intuitive answer to question

2 in Table 1 is incorrect. This is also an opportunity to challenge the assumptions they are making when they answer the question. The third misconception is that lethal or deleterious alleles will be wiped out quickly. Having seen Hardy-Weinberg at work, they can understand that although the allele frequency of a recessive lethal will drop quickly at first, the rate of loss declines as more and more of the lethal alleles are found in heterozygotes.

CONCLUSIONS

Students learn several genetic principles from this exercise and they have fun with it. They work with concepts such as dominance, incomplete dominance, variable expressivity, epistasis, sex-linkage, and *X* chromosome inactivation. They also learn about basic population genetics and the Hardy-Weinberg law. Most of the students enjoy the project and it increases their enthusiasm for genetics. I have spoken to several former students, who indicated that cat genetics remains one of the things they remember best from the class. The exercise helps tie together the transmission genetics and population genetics sections of the course. Although I use this exercise for a college level introductory genetics course I believe at least parts of it could be used at the high-school level as well. Cats provide excellent examples of several genetic principles at any level, and if the students can collect data from enough cats, the Hardy-Weinberg law can be illustrated using student-collected data.

This exercise was initiated following a conversation with Larry Harshman who told me that Tim Prout had once used a student exercise involving cat genotypes. Larry Harshman, John Osterman, Aleata Triplett, Patricia Pukkila, and two anonymous reviewers made helpful comments on the manuscript. Tony Joern did not. There were also helpful contributions by a number of teaching assistants through the years including Aleata Triplett, Maryanne Skavdahl, and Bill Shaffer. I also thank my Bios 301 students from 1995–1999 for their enthusiastic participation in this project.

LITERATURE CITED

Centerwall, W. R., and K. Benirschke, 1973 Male tortoiseshell and calico (T-C) cats. J. Hered. **64:** 272–278.

Dunn, T. B., K. K. Klein and S. J. Kerr, 1989 Mutant allele frequencies of domestic cats of Western Illinois and Eastern Iowa. J. Hered. **80:** 332–335.

Halpine, T., and S. J. Kerr, 1986 Mutant allele frequencies in the cat population of Omaha, Nebraska. J. Hered. **77:** 460–462.

Höger, H., 1994 Mutant allele frequencies in domestic cat populations in Austria. J. Hered. **85:** 139–142.

Klein, K., L. Wong, J. Olson and S. Amundson, 1986 Mutant allele frequencies in cats of Minneapolis-St. Paul. J. Hered. **77:** 132–134.

Moran, C., C. B. Gillies and F. W. Nicholas, 1984 Fertile male tortoiseshell cats. J. Hered. **75:** 397–402.

Norby, D. E., and H. C. Thuline, 1965 Gene action in the X chromosome of the cat (*Felis catus* L.). Cytogenetics **4:** 240–244.

Robinson, R., 1991 *Genetics for Cat Breeders*. Pergamon Press, London.

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