Student Handout

Basic Probability and *Chi*-Squared Tests

The goal of this activity is to improve your familiarity and confidence with basic probability and *chi*-squared tests. These skills are used extensively for genetic analysis.

In the following exercises, we will be working with the following phenotypes:

Gender (male or female)
Month of birth (Jan - Dec)

Part 1 – Probability

The multiplication "AND" rule:

If you want to know the probability of two independent events BOTH happening, then multiply the individual probabilities together.

Note that gender and month of birth are independent events.

Example: The probability of drawing a heart from a well-shuffled deck is ¼. The probability of drawing a 10 is 1/13. The probability of drawing a 10 AND drawing a heart (i.e., the 10 of hearts) is 1/4 * 1/13 = 1/52.

The addition "OR" rule:

If you want to know the probability of ONE OR THE OTHER of two mutually exclusive events happening, then add the individual probabilities together.

Note that the two traits of interest, gender or month of birth ARE NOT mutually exclusive (e.g., you can be a female born in January), but that the possible phenotypes within each trait (e.g., born in January or born in February) ARE mutually exclusive events.

Example: The probability of drawing a heart from a well-shuffled deck is ¼. The probability of drawing a spade is 1/4. Hearts and spades are mutually exclusive "phenotypes" because it's impossible for a card to be both hearts and spades. The probability of drawing a heart or a spade is ¼ + ¼ = ½.

In your group

Use the class data (from all groups, compiled by your instructor) to calculate the frequency of students in each group (male or female, month of birth) and write it down. For example, p(male) = X or p(January) = Y. You should have a frequency for each gender and each month of the year, for a total of 14 different frequencies.

Write three probability questions about these data as follows:

1. The first question must use ONLY the multiplication (or product) rule and ask about independent events.
2. The second question should use ONLY the addition (or sum) rule and should ask about mutually exclusive events.

3. The third question must use BOTH the multiplication and addition rules and ask only about independent and mutually exclusive events.

On a separate piece of paper, write an answer key for each of the questions. Let the instructor know when you are finished. You will be asked to exchange questions with another group and solve the questions written by the other group.

Part 2 – *Chi*-squared tests

Chi-squared tests are used to evaluate whether data are consistent with a null model. You will use the data collected about gender and birth month phenotypes to evaluate null hypotheses about enrollment in this class.

The *null hypothesis* is defined by the experimenter and can differ from test to test. It usually reflects the simplest or most common assumption(s). For example, the null hypothesis for a series of coin flips is that heads and tails will appear with equal frequency. In genetic analysis, the null hypothesis is often used to predict the number and kinds of offspring expected if certain conditions (for example, Mendelian inheritance of alleles) are true.

A *chi-squared test* is used to determine how likely the observed data are if the null hypothesis is true. For example, in the coin flip example, the null hypothesis predicts that heads will appear 50% of the time and tails will appear 50% of the time. So if a coin is flipped 10 times, we "expect" to see 5 heads and 5 tails. But, what if we observe 6 heads and 4 tails? Is this consistent with the null hypothesis? What if we observe 7 heads and 3 tails, or 8 heads and 2 tails? A chi-squared test allows us to answer these questions.

The chi-squared test statistic is calculated by comparing the observed data (O) to the data expected (E) under the null hypothesis. Briefly, for each group (e.g., heads or tails), we calculate $(O-E)^2/E$ and sum these values for all groups. We then determine the degrees of freedom (*df*) for the test, which is often simply the number of groups minus 1, and use these values with a chi-square table to determine the probability (p-value) of the observed data occurring by chance if the null hypothesis were true.

In your group

Use the class data (from all groups, compiled by your instructor) and *chi*-squared tests to evaluate the following two null hypotheses:

1. an equal number of males and females are enrolled in this class.

2. an equal number of people in this class were born in each quarter of the year.

In each case, you must (1) calculate the *chi*-squared value, (2) determine the proper degrees of freedom for the test, (3) use the table below to determine the approximate p-value, and (4) decide whether or not the class data is consistent with the null hypotheses shown (i.e. should you accept or reject the null hypothesis in each case). The instructor is there to provide help and guidance when you need it.

When you finish with the tests, discuss the following questions:

- Why did (or could) the class data cause you to reject the null hypothesis used in each case?
- How could we have made more accurate null models to test the idea that students in the class have the expected distribution by gender and month of birth?

Part 3 – Genetics application

After crossing true-breeding yellow and green pea plants, Mendel allowed the F_1 plants to self. He observed 6022 yellow and 2001 green pea plants resulting from this F_1 self-cross. He used these data to develop his law of segregation.

Write the genotypes for the true-breeding yellow and green plants, the F1 hybrids, and the green and yellow progeny from the F_1 self-cross. Be sure to indicate which allele is dominant with your notation.

Using a chi-squared test, determine if the 6022 yellow and 2001 green pea plants Mendel observed are consistent with his law of equal segregation. Be sure to set up a table of observed and expected data and record the chi-squared value, degrees of freedom, approximate p-value (use the table above), and indicate whether the null hypothesis should be rejected.

***Chi*-square table:**

					P					
df	**0.995**	**0.975**	**0.9**	**0.5**	**0.1**	**0.05**	**0.025**	**0.01**	**0.005**	**df**
1	.000	.000	0.016	0.455	2.706	3.841	5.024	6.635	7.879	1
2	0.010	0.051	0.211	1.386	4.605	5.991	7.378	9.210	10.597	2
3	0.072	0.216	0.584	2.366	6.251	7.815	9.348	11.345	12.838	3
4	0.207	0.484	1.064	3.357	7.779	9.488	11.143	13.277	14.860	4
5	0.412	0.831	1.610	4.351	9.236	11.070	12.832	15.086	16.750	5
6	0.676	1.237	2.204	5.348	10.645	12.592	14.449	16.812	18.548	6
7	0.989	1.690	2.833	6.346	12.017	14.067	16.013	18.475	20.278	7
8	1.344	2.180	3.490	7.344	13.362	15.507	17.535	20.090	21.955	8
9	1.735	2.700	4.168	8.343	14.684	16.919	19.023	21.666	23.589	9
10	2.156	3.247	4.865	9.342	15.987	18.307	20.483	23.209	25.188	10
11	2.603	3.816	5.578	10.341	17.275	19.675	21.920	24.725	26.757	11
12	3.074	4.404	6.304	11.340	18.549	21.026	23.337	26.217	28.300	12
13	3.565	5.009	7.042	12.340	19.812	22.362	24.736	27.688	29.819	13
14	4.075	5.629	7.790	13.339	21.064	23.685	26.119	29.141	31.319	14
15	4.601	6.262	8.547	14.339	22.307	24.996	27.488	30.578	32.801	15

MENDELIAN GENETICS PROBLEMS

The following problems are provided to develop your skill and test your understanding of solving problems in the patterns of inheritance. They will be most helpful if you solve them on your own. However, you should seek help if you find you cannot answer a problem. Most of these problems are fairly simple, yet mastering their solutions will provide the background to solve many genetic puzzles and will strengthen your understanding fundamental principles of genetics.

A. PROBABILITY

1. You and your spouse have no children. You stand to inherit a sizeable fortune from your crazy Uncle Irving if you can produce three daughters in your family of three children. What is the probability of doing just that?

2. If you could convince Uncle Irving that simply having three children all of the same sex would do, then what would be the probability of your receiving the inheritance?

3. In quest of the family stipulated in #2 above, you produce a boy as your first child. Now what is the probability of inheriting the fortune?

4. Why are the answers to #2 and #3 the same?

5. Finally, you have convinced Uncle Irving that you will agree to try for at least three girls out of four children. How likely are you to become wealthy given those conditions?

B. MONO-, DI-, AND POLYHYBRID CROSSES; DOMINANCE AND RECESSIVENESS

In all of the following problems, capital letters will be used to denote a dominant trait, and lower-case letters will be used for the recessive trait.

6. In peas, seeds may be round (R) or wrinkled (r). What proportion of the offspring in the following crosses would be expected to be wrinkled?

   a. RR x rr b. Rr x Rr c. Rr x rr

7. In peas, seeds may be yellow (Y) or green (y). What proportion of the offspring in the following crosses would be expected to be yellow?

   a. YY x Yy b. Yy x Yy c. yy x yy

8. In peas (again), the stem length may result in a tall (T) or dwarf (t) plant. What proportion of the offspring in the following crosses would be expected to be tall, and what proportion dwarf?

   a. TT x tt b. TT x Tt c. Tt x Tt d. tt x Tt

9. What proportion of the plants from the following crosses would be tall with yellow, wrinkled seeds?

   a. TtYYRr x ttYYrr b. TTYyRr x TtYyRr
   c ttYyrr x ttyyRr d. TtYyRr x TtYyRr

10. From the crosses TTYyRr x TtYyrr, what proportion of the offspring would be expected to be

    a. tall plants with round, yellow seeds
    b. tall plants with round, green seeds
    c. dwarf plants with round, green seeds
    d. tall plants with yellow, wrinkled seeds
    e. tall plants with green, wrinkled seeds

11. For the purpose of this problem assume that in humans the gene for brown eyes is dominant to that for blue eyes.

    a. A brown-eyed man marries a blue-eyed woman, and they have eight brown-eyed children. What are the genotypes of all the individuals in the family?
    b. What is the probability that the first child produced in parents who are both heterozygous for brown eyes will be blue-eyed?
    c. If the first child is a brown-eyed girl (same parents as in b), what is the probability that the second child will be a blue-eyed boy?
    d. Again referring to the marriage in b, what is the probability that the first three children will be blue-eyed girls and the fourth a brown-eyed boy?

12. Eye color in certain species of flies is controlled by a single pair of genes. A white-eyed fly, both of whose parents had white eyes, was crossed with a red-eyed fly, and all of their offspring (both male and female) were red-eyed.

    a. Is the gene for red eyes or that for white eyes dominant? Proof?
    b. What was the genotype of the white-eyed parents?
    c. What was (were) the genotype(s) of the red-eyed offspring?
    d. If one of the red-eyed offspring was mated with the white-eyed parent, what would be the expected ratio of offspring, with respect to eye color?
    e. If two of the red-eyed offspring are mated, how many genetically different kinds of zygotes, with respect to eye color, will be formed, and what will the proportions be?

13. In cattle, the gene for hornless (H) is dominant to the gene for horned (h), the gene for black (B) is dominant to that of red (b), and the gene for white face (or Hereford spotting) (S) is dominant to that for solid color (s). A cow with the genotype BbHhSs is inseminated by a bull of the genotype bbhhSs. What is the probability of the calf's being:

    a. a black, hornless cow with Hereford spotting
    b. a red, horned bull with solid color
    c. a red, hornless bull with Hereford spotting

(Hint: the sex of the calf is part of the phenotype)

14. Assume that D, E, F, G, H, and I are autosomal genes on different chromosomes. From the mating DdeeFfGGHhIi x DdEEFFGgHhii:

    a. What is the probability that one of the offspring will have the genotype DdEeFFGghhIi?
    b. What is the probability that one of the offspring will be heterozygous for each allele?
    c. What is the probability that one of the offspring will have the genotype DDEEFfGGhhii?

C. INCOMPLETE DOMINANCE

15. In cattle, RR = red, Rr = roan, and rr = white. What are the predicted color phenotypes and their frequencies for the offspring from crosses between:

    a. a red bull and a white cow
    b. a red bull and a roan cow
    c. a roan bull and a roan cow

16. Given the following information about the inheritance of characteristics in pea plants, answer the questions below:

    Y (yellow) is dominant to y (green)
    R (round) is dominant to r (wrinkled)
    B (bitter) is dominant to b (sweet)
    S (smooth) is dominant to s (hairy)
    L (long pod) shows incomplete dominance to l (short pod) (Ll is medium in length)

    Given this cross: (P_1) Yy Rr Bb SS Ll (male) x yy RR Bb Ss Ll (female)

    a. How many different gametes can be formed by the female plant?
    b. How many different genotypes are possible in the F_1 offspring?
    c. How many different phenotypes are possible in the F_1 offspring?
    d. What percent of the F_1 individuals will be
        - green, bitter, and smooth _____
        - hairy, medium, and sweet _____
        - round, bitter, and long _____

D. MULTIPLE ALLELES

17. In humans, the ABO blood groups are controlled by three alleles (only two of which occur in any one individual): the alleles for A and B type blood are co-dominant toward each other, and both are dominant to the allele for O type blood.

    a. If a person with type AB blood marries someone with type O blood, what are the possible phenotypes of their offspring?

    In the following, determine the genotypes of the parents:

    b. One parent has type A and the other has type B, but all four blood groups are represented in the children.
    c. Both parents have type A, but 3/4 of the children are A and 1/4 are O.
    d. One parent has type AB and the other has type B, but of the children 1/4 have type A, 1/4 have type AB, and 1/2 have type B.

18. In the following cases of disputed paternity, determine the probable parent.

    a. Mother is type B, child is type O. Father #1 is A; father #2 is AB.
    b. Mother is type B, child is type AB. Father #1 is A; father #2 is B.
    c. Mother is type O and bears non-identical twins, one type A and one type B. Father #1 is type A; father #2 is type B.

19. Two babies in a maternity ward have lost their identity bands, and there is some confusion about their footprint records. Baby #1 is type A; baby #2 is type B. If you are one of the mothers and your blood type is O, which one of the following statements applies.

    a. Neither baby could be yours.
    b. The type A baby is yours.
    c. The type B baby is yours.
    d. Either baby could be yours.

20. A woman with type A blood has parents who are both type AB and a husband who is a type B. What is the probability that their first child will be a son with type O blood?

21. In a local court, a woman is suing a male acquaintance for financial support of her recently born child. If the woman is blood type B, Rh+, and the baby is type O, Rh-, and the man is blood type AB, Rh-, what are her chances of success in the lawsuit?

22. In the organism under consideration, r* acts like r allele, except when homozygous (r*r*). From the information given below, work out the phenotypic and genotypic ratios for each of the crosses.

    Given: RR (red) x rr (white) $\rightarrow$ Rr (pink); and
    rr* x rr* $\rightarrow$ 3/4 white, 1/4 dead zygotes

    a. Rr x Rr b. Rr x rr c. Rr* x Rr* d. Rr* x rr*

23. In rabbits, fur color is determined by a set of multiple alleles at one locus (gene) that have the following relationship:

    C^{-} (agouti) is dominant to all other alleles
    c^{h} (himalayan) is dominant to c^{a} (albino)
    c^{u} (chinchilla) shows incomplete dominance with regard to c^{h} and c^{a}

    The genotypes $c^{u}c^{h}$ and $c^{u}c^{a}$ are light-grey phenotypes

    a. What breeding stock (parents) would you select if you wished all of the offspring to be chinchilla?
    b. In one of the matings of rabbits, the litter contained 4 grey bunnies, 2 albino bunnies, and 2 himalayan bunnies. What were the genotypes of the parents?
    c. In another mating, the litter contained 3 agouti bunnies and 3 light-grey bunnies. What were the genotypes of the parents of this litter?

E. MULTIPLE GENES

24. In cocker spaniels, the following genotypes and phenotypes are found:

AABB = white A-bb = red aabb = lemon AaB- = black aaB- = liver AABb = grey

a. A red female is mated with a liver-colored male, and one of the pups produced is lemon-colored. What are the genotypes of the parents?
b. What proportion of these offspring would be expected to be black?
c. A black male is mated with a liver-colored female, and they produce the following pups:

3/8 black	1/8 red
3/8 liver-colored	1/8 lemon-colored

What are the genotypes of the two parents?

25. If two cocker spaniels of the genotypes below are mated, and eight pups are born, what is the most likely distribution of coat colors in that litter?

P_1 AaBb x AABb

_____white _____red _____lemon _____black _____liver _____ grey

26. A dominant gene, A, causes yellow color in rats. The dominant allele of another independent gene, R, produces black coat color. When the two dominant genes occur together (A-R-), they interact to produce grey coat color. Rats of the double recessive genotype are cream-colored. If a grey male and a yellow female are mated and produce approximately 3/8 yellow, 3/8 grey, 1/8 cream, and 1/8 black, what were the genotypes of the parents?

F. SEX LINKAGE

27. In humans, dark hair (B) is dominant over blondness (b), and color blindness (c) is a sex-linked recessive trait. A women has a blond brother, a blond mother, and a dark-haired father. Her brother and her parents have normal vision. She bears the following three children by her blond, normal-visioned husband:

a dark-haired son with normal vision
a dark-haired daughter with normal vision, and
a dark-haired color-blind son

a. Make a pedigree of the entire family showing the probable genotypes of all individuals.
b. What is the probability that her next (fourth) child will be a color-blind boy?
c. If her fourth child is a boy, what is the probability that he will have dark hair?
d. What is the chance that her next four children will all be girls?

28. Your research in hematology has led you to the discovery of a new type of inherited anemia, which exists in two forms--mild and severe. The information you have gathered on the familial patterns for the disease is summarized below. From these data determine a mechanism for the inheritance of these traits that is consistent with all of the information.

a. normal female x normal male = all normal children
b. normal female x anemic male = 1/2 mild females
= 1/2 normal males
c. mild female x normal male = 1/4 normal males
= 1/4 anemic males
= 1/4 normal females
= 1/4 mild females
d. mild female x anemic male = 1/4 normal males
= 1/4 anemic males
= 1/4 mild females
= 1/4 anemic females
e. anemic female x normal male = 1/2 mild females
= 1/2 anemic males
f. anemic female x anemic male = all anemic children

29. In chickens and other birds, the chromosomal basis of inheritance is the opposites of that in man; i.e., in birds, XX individuals are males, and XY individuals are females.

    In chickens, barred plumage is dominant to nonbarred plumage; the gene is sex-linked.

    Suppose that you were a poultry breeder and that you needed large numbers of barred males and nonbarred females. Describe a breeding stock that you could assemble for this purpose, which would produce only barred males and nonbarred females.

    Be certain that you show the genotypes of both the roosters and the hens in your breeding stock and also the genotypes of all the offspring that this stock will yield.

30. The inheritance of color blindness in humans is due to a recessive gene located on the X chromosome (X linked).

    X^+ (normal) > X^c (color blind)

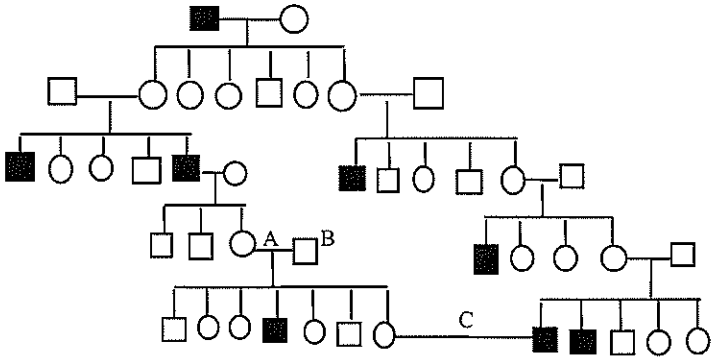
    a. If a color-blind boy is born to parents both of whom have normal vision, what are the genotypes of the three individuals?
    b. What is the probability that the second child born to that couple will be a color-blind daughter?
    c. If this couple has four children, what is the probability that the first two children will be color-blind boys and the last two children will be girls with normal vision?

31. A particular inherited abnormality in humans has been shown to be an X-linked recessive trait. In one family seeking professional help from a genetic counselor, the following information is known:
    1. The mother shows the abnormality.
    2. Their only child is a daughter who is normal.

    a. If their next child is a son, what is the probability that he will show the abnormality?
    b. What is the probability that the next child born will be a daughter showing the abnormality?

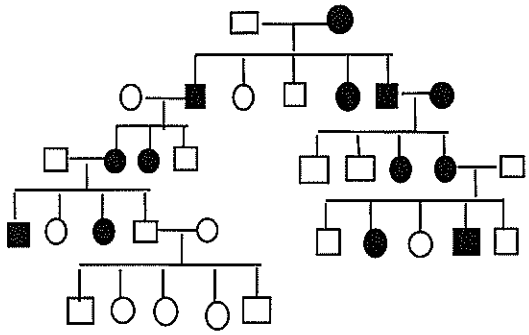
G. HUMAN GENETICS

32. Research has shown that a particular eye defect is represented in a family pedigree as follows:

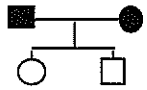


    a. On the basis of this data, which of the following mechanisms of inheritance are POSSIBLE? autosomal dominant, autosomal recessive, sex-linked dominant, sex-linked recessive, Y-linked.
    b. What is the most PROBABLE mechanism of inheritance?
    c. What is the genotype of female A?
    d. What is the genotype of male B?
    e. What is the probability that a child from marriage C will show this eye defect?

33. The following pedigree shows the presence of individuals bearing extra fingers and toes--exhibiting "polydactyly." Explain the genetic mechanism for the inheritance of this trait in the family.

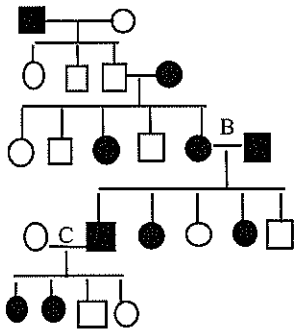


34. Given the family history below for the inheritance of a skin abnormality in humans, what is the correct mechanism of inheritance for this abnormality?



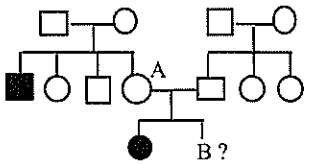
a. X-linked dominant
b. x-linked recessive
c. autosomal dominant
d. autosomal recessive
e. y-linked

35. The inheritance of a particular facial hair pattern in a given family is indicated below. Answer the following questions about this family tree.



a. Which is the correct mechanism of inheritance?
   autosomal dominant autosomal recessive y-linked
   x-linked dominant x-linked recessive
b. Using the symbols "F" and "f" to indicate dominance and recessiveness, show the genotypes of the parents at B.
c. In the marriage at C, what is the probability that the next child born will show the trait?

36. Because you have some basic knowledge of genetics, a young woman (A, below) has come to you for help. She has a brother who is mentally retarded, but her parents and all of her husband's family are normal. She has a two-year-old daughter who shows the retardation of her brother. She is now pregnant and is considering a therapeutic abortion because of her fear that the next child will also be retarded. Can you help her by answering the questions below?



a. What is the probability that her second child will be mentally retarded?
b. If the second child is a boy, what is the probability that he will be mentally retarded?

H. GENERAL REVIEW QUESTIONS

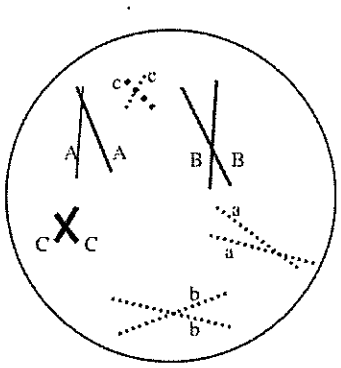
37. In domesticated cats, the following genetic patterns have been described as independently assorting. Normal ears (T) is dominant to tufted ears (t); curved whiskers (C) is dominant to straight whiskers (c); the presence of six toes (S) is dominant to five toes (s); and the gene for hair length is an X-linked codominant. The three phenotypes for hair length are long (X^HX^H), medium (X^HX^h), and short (X^hX^h); medium is the heterozygous condition. Sex determination in cats is the same as for humans (XX = female).

    Given two parent cats:

    $$Tt\ cc\ SS\ X^HX^h\ \times\ Tt\ Cc\ Ss\ X^HY$$

    a. How many different gametes could be formed in the female cat with respect to these four traits?
    b. How many phenotypes are possible in the offspring from this mating?
    c. What fraction of the offspring will have tufted ears, curved whiskers, six toes, and long hair?
    d. In a litter of 10 kittens, six are male. How many of the males would be expected to have tufted ears, six toes, straight whiskers, and medium-length hair?

38. Assume that the cell below is from an insect testis and is about to undergo spermatogenesis (gamete production by meiosis). The letters represent dominant or recessive alleles at particular gene positions on each chromosome.



    a. What is the haploid chromosome number of the insect?
    b. How many genetically different kinds of gametes could be formed from this cell (assume no crossing over)?
    c. How many pairs of homologous chromosomes would you observe in a muscle cell from this insect?
    d. What is the probability that a gamete produced by this cell will be completely recessive for the alleles shown?
    e. Which of Mendel's laws tells us that a gamete containing a chromosome with an "A" allele will not necessarily contain a chromosome with a "B" allele?
    f. Which of Mendel's laws tells us that a gamete cannot contain both an "A" allele and an "a" allele?

I. LINKAGE AND CROSSING OVER

39. In the common bluebell, two linked, autosomal genes control flower color and plant height, as follows:

    B (blue flowers) > b (white flowers)
    T (tall plants) > t (dwarf plants)

    If the crossover frequency between these two loci (genes) in 26%, what will be the expected F_1 phenotypes and their frequencies from the following cross:

    P_1 BT//bt x bt//bt

40. Genes A and B are located 20 map units apart on the X chromosome in humans. Thus they are X-linked. The two genes show simple dominance to their recessive alleles, a and b, respectively. Given the following genotypes for the parents:

$$X^{AB}//X^{ab} \times X^{Ab}//Y$$

a. What will be the frequency of offspring that are male and show both dominant traits (A and B)?
b. What will be the frequency of offspring that are female showing both dominant traits (A and B)?

41. In the fruit fly, Drosophila melanogaster, crossing over is absent in the males. Suppose you are interested in the relationship between two linked genes on chromosome 2. The genes are for black body (b) and for curved wings (c), each of which is recessive to the normal (B) body color and normal (C) wing shape. In your laboratory, females that are heterozygous at the body color and wing shape loci are mated with a black-bodied male with curved wings. The offspring of these matings were counted, with the following results:

367 normal body, curved wing
131 normal body, normal wing
139 black body, curved wing
363 black body, normal wing

a. What is the cross-over frequency between these two loci?
b. How many map units separate these two loci?
c. Show the pattern of linkage (coupling or repulsion) in the female flies of this mating?