EXPERIMENT 19 APPLICATION OF PROBABILITY TO PROBLEMS IN GENETICS

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19.1 INTRODUCTION

One of the effective tools for a geneticist and a genetic counsellor to assess the possible occurrence of a trait in a family is the application of probability theory. A probability is the ratio of the number of times a particular event occurs *to* the number of trials during which the event could have happened. Assuming a man and his wife seek advice of a genetic counsellor on a genetic problem, the counsellor analyses the pedigree of the couple's family, establishes the genotypes of the couple and then makes calculations relating to the probability of the appearance of the trait in question in the children to be born to them in future. In this lab. exercise, you will learn some of the basic rules of probability theory. You should try to apply them to problems in genetics.

Objectives

At the end of this lab. exercise, you should be able to:

- describe the basic principles of probability,
- make use of the principles of probability to solve genetic problems,
- apply the formula for the binomial expansion to determine the probability of any combination of events,
- comprehend the Pascal's triangle to determine the coefficient of binominal expression that tells how many ways a particular combination may be obtained.

19.2 THE BASIC PRINCIPLES OF PROBABILITY THEORY

The probability theory, it can be said, helps you to make a proper and meaningful guess of the occurrence of an event. The probability P of the occurrence of an event is the number of favourable cases a divided by the total number of possible cases n.

$$P = \frac{a}{n}$$

In determining the probability of an event, one way is to observe a large number of cases and record the number of times an event occurs or does not occur. But this is an empirical method. A better way of determining the probability is the one that is generally used by the geneticists for making predictions on the occurrence of an event. The probability obtained by this method is *a priori* probability. You look into the following example that explains the calculation of probability before we take up specific examples from genetics.

Take a die (plural = dice) with six faces numbered 1 to 6. When the die is rolled, the probability P of any one face showing up is 1/6.

$$P = \frac{a}{n} = \frac{1}{6} = 0.167$$

The probability of picking up the nine of spades from a deck of 52 cards is

$$P = \frac{1}{52} = 0.0192$$

And the probability of drawing any one club from a deck of cards is

$$P = \frac{13}{52} = \frac{1}{4} = 0.25$$

Now let us cite one or two examples from genetics. The probability of an offspring to be of recessive genotype when a monohybrid is self-fertilised is

$$P = \frac{1}{4} = 0.25$$

and the probability of an offspring to be of dominant phenotype for both traits on self-fertilisation of a dihybrid is

$$P = \frac{9}{16} = 0.5625$$

When we say that the probability of the occurrence of an event is P, the combined probability of occurrence of all the other events is Q = (1 − P). Thus when the P of occurrence of dominant phenotypes = 9/16, the combined probability of occurrence of other phenotypes = Q = 1 − 9/16 = 7/16 and P + Q = 9/16 + 7/16 = 1. P + Q is always equal to 1. In fact all probabilities must lie between 0 and 1. A probability of 1 means that the event is certain to occur; a probability of zero indicates that the event cannot occur.

Now, let us look into situations where we consider the occurrence of two events. By two events, we moan the occurrence of either one of the two events or both the events simultaneously. Essentially in such cases we will be combining the probability of occurrence of the two events. There are three rules under which the combining of the probabilities can be done.

19.2.1 Addition Rule

When the occurrence of one event precludes the possibility of the occurrence of another event, the two events are said to be **mutually** exclusive. Essentially it means that when one event occurs, the other does not. And the probability of occurrence of one of several mutually exclusive events is the sum of the probabilities of individual evcuts. For instance, when a die is thrown what is the probability that it shows either a two or a three?

P of getting a two = 1/6 = 0.167
P of getting a three = 1/6 = 0.167

Therefore, the two events are mutually exclusive. The probability of getting either a two or a three = 1/6 + 1/6 = 2/6 = 113 = 0.33. Since the probability of occurrence of mutually exclusive events is summed up, the rule is called addition rule.

19.2.2 Product Rule

Product rule is used when the occurrence of one event is not dependent on the occurrence of another event; in other words we are dealing with independent events. For instance, when two dice are thrown simultaneously the probability of getting a two and a three in that order are

P of getting a two = 1/6 = 0.167
P of getting a three = 1/6 = 0.167

Probability of getting a two and a three = 1/6 x 1/6 = 1/36 = 0.028. Since the probability of occurrence of independent events is the product of their separate probsbilities, this rule is called the **product rule.**

Look into this example,

What is the probability of getting a head and a tail, when two coins are tossed simultaneously? This procedure as we are going lo demonstrate to you, requires the use of both addition and product rules. For each coin the probability of getting a head H or tail T is

P (H) = 1/2 = 0.5
P (T) = 1/2 = 0.5.

When the coins are tossed one at a time, there are two ways of getting a head or a tail.

First head and then tail (HT)
First tail and then head (TH)

The results of each of the two tosses in a sequence are independent events.

The probability of getting HT arid TH = 1/2 x 1/2 = 1/4 = 0.25

At the same time, the two sequences are mutually exclusive. The probability of getting either of two sequences of a set of mutually exclusive events is

$$\frac{1}{4} + \frac{1}{4} = \frac{1}{2} = 0.5$$

Thus when events are unordered, the probability can be obtained by combining addition and product rules.

19.2.3 The Binomial Theorem

The probability of unordered events can be determined by using binomial theorem. This theorem defines the probability of the occurrence of some arrangement of two mutually exclusive trials where the final order is not specified. According to this theorem the frequencies or the probabilities of the occurrence of various combinations correspond to the terms of the binomial expansion. The first three binomial expressions are as follows.

$$(a + b)^2 = a^2 + 2ab + b^2$$

$$(a + b)^3 = a^3 + 3a^2b + 3ab^2 + b^3$$

$$(a + b)^4 = a^4 + 4a^3b = 6a^2b^2 + 4ab^3 + b^4$$

The symbol ! is read as factorial. 5! or factorial 5 = 5 x 4 x 3 x 2 x 1.

A simple formula based on l binomial theorem would help you to calculate the probability by a short-cut method. According to this formula:

$$P = \frac{n!}{s!t!} \times p^s q^t$$

Where n is the total number of events, p is the probability of the occurrence of an event (X), q is the probability of the occurrence of an alternate event (Y), s is the number of times the event X will occur and t is the number of times the event Y will occur out of n number of trials. Here, $s + t = n$ and $p + q = 1$.

Let us look into the previous example. When

$n = 2$

Probability of getting a head = $p = \frac{1}{2}$

Probability of getting a tail = $q = \frac{1}{2}$

and $s = t = 1$.

Substituting the above data in the formula,

P = the probability of getting a head and a tail when two coins are tossed simultaneously = $\frac{2}{1!1!} \cdot \left(\frac{1}{2}\right)^1 \cdot \left(\frac{1}{2}\right)^1$

$$= \frac{2 \times 1}{1 \times 1} \cdot \frac{1}{2} \cdot \frac{1}{2} = \frac{1}{2}$$

$$= 0.5$$

Let us now look into more specific examples from genetics. What is the probability that a family with five children will have 3 boys and 2 girls?

The probability of a child to be a boy = $p = \frac{1}{2}$

The probability of a child to be a girl = $q = \frac{1}{2}$

Applying the formula

$$P = \frac{5!}{3!\,2!} \cdot \left(\frac{1}{2}\right)^3 \cdot \left(\frac{1}{2}\right)^2$$

$$= \frac{5 \times 4 \times 3 \times 2 \times 1}{3 \times 2 \times 1 \times 2 \times 1} \times \frac{1}{2} \times \frac{1}{2} \times \frac{1}{2} \times \frac{1}{2} \times \frac{1}{2} = 0.312$$

Assuming the parents want the 5 children to be born in a specific order—say 2 boys, 1 girl 1 boy and a girl. Essentially this would mean that you have to apply the product rule; in which case the probability would be

$$\frac{1}{2} \times \frac{1}{2} \times \frac{1}{2} \times \frac{1}{2} \times \frac{1}{2} = \frac{1}{32} = 0.312$$

Thus you can see from the two answers, that when an order is specified, the probability is 10 times less than when no order is specified. In other words, while there is only one way of getting 2 boys, 1 girl, 1 boy and 1 girl, there are 10 different ways of getting 3 boys and 2 girls.

1	2	3	4	5	6	7	8	9	10
B	B	B	B	B	G	G	G	G	G
B	B	B	G	G	G	B	B	B	G
B	G	G	G	B	B	G	B	B	B
G	B	G	B	G	B	B	G	B	B
G	G	B	B	B	G	B	B	G	B

[B = boy; G = Girl]

Assuming a couple is heterogygous (Aa) for albinism, what is the probability that 4 children out of 6 born to them are normal?

Let A = allele for normal skin

a = allele for albinism

Aa x Aa

AA Aa Aa aa

normal albino

Since the ratio of normal to albino is 3 : 1, the probability of a normal son being born is $\frac{3}{4}$ and an albino is $\frac{1}{4}$.

The probability of 4 children being normal is

$$\frac{3}{4} \times \frac{3}{4} \times \frac{3}{4} \times \frac{3}{4} = \frac{81}{256} = 0.316$$

What is the probability of 4 children being normal and 2 children albinos?

In this case,

$$P = \frac{6!}{4!\,2!}$$

$$= \frac{6 \times 5 \times 4 \times 3 \times 2 \times 1}{4 \times 3 \times 2 \times 1 \times 2 \times 1} \times \frac{3}{4} \times \frac{3}{4} \times \frac{3}{4} \times \frac{3}{4} \times \frac{1}{4} \times \frac{1}{4}$$

$$= \frac{1215}{4096} = 0.297$$

Assuming you specify the order in which the normal and albino children are born say the first 3 children are normal, 1 albino, 1 normal and 1 albino, then the probability would be

$$\frac{3}{4} \times \frac{3}{4} \times \frac{3}{4} \times \frac{1}{4} \times \frac{3}{4} \times \frac{1}{4} = \frac{81}{4096} = 0.0198$$

You can again observe that once the order is specified, the probability assumes a lower value. In other words, if no order is specified, the probability is fifteen times larger than when it is specified.

19.3 PASCAL'S TRIANGLE

We earlier said that in the formula $P = (n!/s!t!)\, p^s q^t$, $(p+q) = 1$ and $(s+t) = n$. This formula essentially separates the binomial equation $(p+q)^n = 1$ and gives the probability of one of the terms. The binomial expansion of $(p+q)^n$ contains (n+1) terms. A device called Pascal's triangle is useful to get the coefficient of the terms. The coefficients tell you the number of ways by which one can obtain a particular combination of events. The following is the Pascal triangle upto n = 7.

1.	n	=	0	$(p+q)^0$	1
2.	n	=	1	$(p+q)^1$	1 1
3.	n	=	2	$(p+q)^2$	1 2 1
4.	n	=	3	$(p+q)^3$	1 3 3 1
5.	n	=	4	$(p+q)^4$	1 4 6 4 1
6.	n	=	5	$(p+q)^5$	1 5 10 10 5 1
7.	n	=	6	$(p+q)^6$	1 6 15 20 15 6 1
8.	n	=	7	$(p+q)^7$	1 7 21 35 35 21 7 1

The above triangle is built out of the coefficient of binomial expansion. You may observe that any given row begins with 1, then proceeds by the addition of two adjacent coefficients from the preceeding row and finally ends in 1. For example, take the 7th row, $(p+q)^6$.

$$(p+q)^6 = (1)p^6 + (1+5)p^5q + (5+10)p^4q^2 + (10+10)p^3q^3 + (10+5)p^2q^4 + (5+1)pq^5 + (1)q^6$$

Let us get back to our earlier problems. What is the probability of 4 normal and 2 albino children born to a couple heterozygous for the albino allele?

$$n = 6;\ s = 4\ t = 2\ p = \frac{3}{4} \text{ and } q = \frac{1}{4}$$

The problem is completely described by the expression of $(p+q)^6$. In the equation $(p+q)^6$ (remember n = 6), the term that is of interest to us is $15p^4q^2$, since s = 4 and t = 2.

$15p^4q^2 = 15\ (3/4)^4\ (1/4)^2$

$$= 15 \times \frac{3}{4} \times \frac{3}{4} \times \frac{3}{4} \times \frac{3}{4} \times \frac{1}{4} \times \frac{1}{4}$$

$$= \frac{1215}{4096} = 0.297$$

This is the same answer that we obtained using the formula. But when **the** order of the binomial increases, its expansion to get all the terms becomes difficult. **In** such cases we can readily use the formula.

19.4 MULTINOMIAL EXPRESSION

The formula has one more advantage. It could be expanded to include more than two events. The multinomial expansion $(p+q+r\ ...)^n$ can **be** represented as the general formula for calculating the probability.

$$p = \frac{n!}{s!\ t!\ u!} \times p^s q^t r^u .....$$

Where p+q+r..... = 1 and s+t+u.... = n.

Assuming a couple were told by the genettic counsellor that each of them carry an allele for albino trait. The couple wants,to have six children. What is the probability that of the six children, two will be normal daughters, two normal sons, one albino son and one albino daughter?

In this problem, you first apply the product rule to know the probability for each item and then apply the formula to get the probability for the entire event. For example,

Probability of getting a normal son p = (314) (112) = 318

Probability of getting a normal daughter q = (314) (1/2) = 3/8

Probability of getting a albino son **r** = (114) (1/2) = 1/8

Probability of getting a albino daughter k = (1/4) (1/2) = 1/8

Probability of getting **2** normal sons (s), 2 normal daughters (t), 1 albino son (u) and 1 albino daughter (v) =

$$p = \frac{n!}{s!\ t!\ u!\ v!} \cdot p^s q^t r^u k^v$$

$$p = \frac{6!}{2!\ 2!\ 1!\ 1!} \cdot (3/8)^2 \cdot (3/8)^2 \cdot (1/8)^1 \cdot (1/8)^1$$

$$= \frac{6 \times 5 \times 4 \times 3 \times 2 \times 1}{2 \times 1 \times 2 \times 1 \times 1 \times 1} \cdot 3/8 \times 3/8 \times 3/8 \times 3/8 \times 1/8 \times 1/8$$

$$= \frac{14580}{262144} = 0.0556$$

19.5 SAQ

1. Assuming a sex ratio of 1:1, what is the probability that a family of 4 children will consist of

   i) 3 daughters and 1 son

   ii) all daughters

   iii) alternating sexes

   iv) all sons

   v) atleast two daughters

2. In lab exercise 8, we discussed about phenylthiocarbamide tasters. PTC tasting, as you are aware is dominant to non-tasting. A taster man whose mother is a non-taster marries a taster woman who in a previous marriage had a non-taster daughter. What would be the probability of the couple having

   a) their first child a taster?

   b) their first child a non-taster boy?

   c) 7 children with 4 tasters and 3 non-tasters?

   d) 5 children, of whom 2 taster bodys 1 taster girl 1 non taster body and 1 non taster girl in that order.

3. Two parents have genotype Mm and suffer from migraine headache. What is the probablity that

   a) their first child will be a girl with migraine and their second a boy without the disorder.

   b) 4 children are born to them with 3 children born without migraine and one child with it.