Gene Inheritance and Transmission

Class 3

SLE254 Genetics and Genomics

Chapter 3 Concepts of Genetics (12th edition)

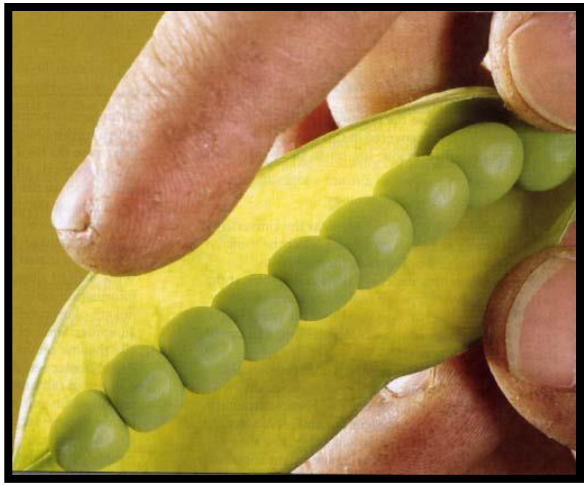
Pp 73-96

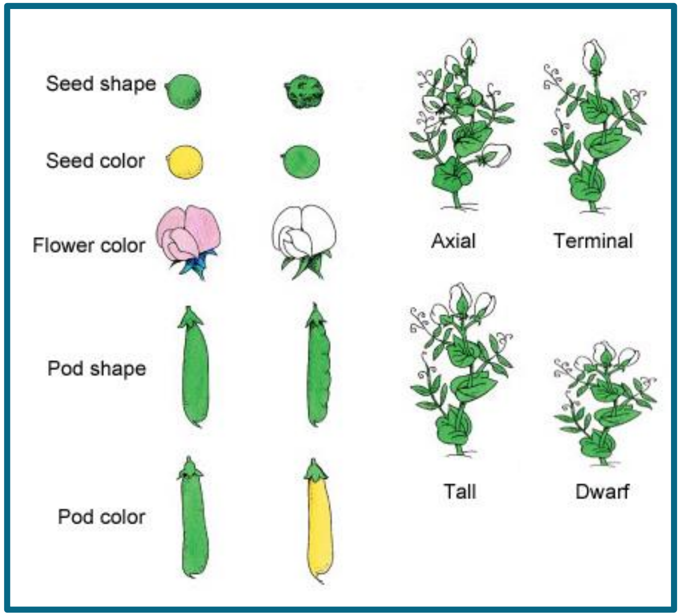
Gregor Mendel 1822-1884

The father of Genetics

Mendel’s breeding experiments

- 1856 – performed hybridisation experiments of pea plants (*Pisum sativum*)
  - Easy to grow and cross-breed experimentally
  - Reproduces well and grows to maturity in a season
- Mendel created “**pure breeding***” strains for various traits

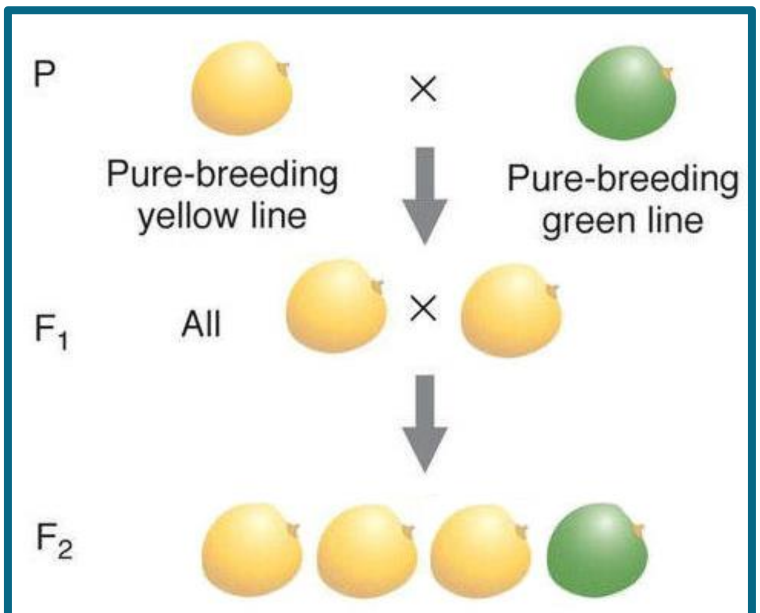




Mendel's observations

- He noted that in 1st generation (**F_1**) cross of these strains, certain (recessive) traits disappeared

- However, in the F2 crosses they reappeared!!!



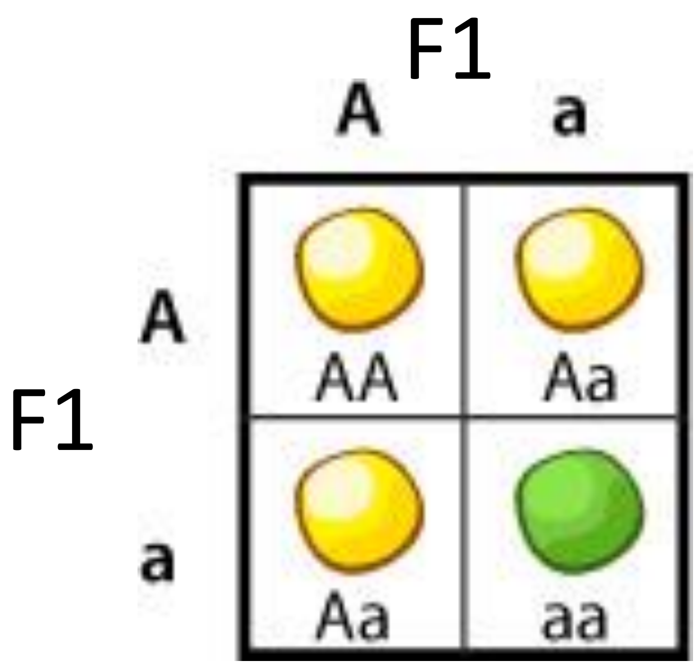
The ¾ to ¼ ratio in Mendelian inheritance

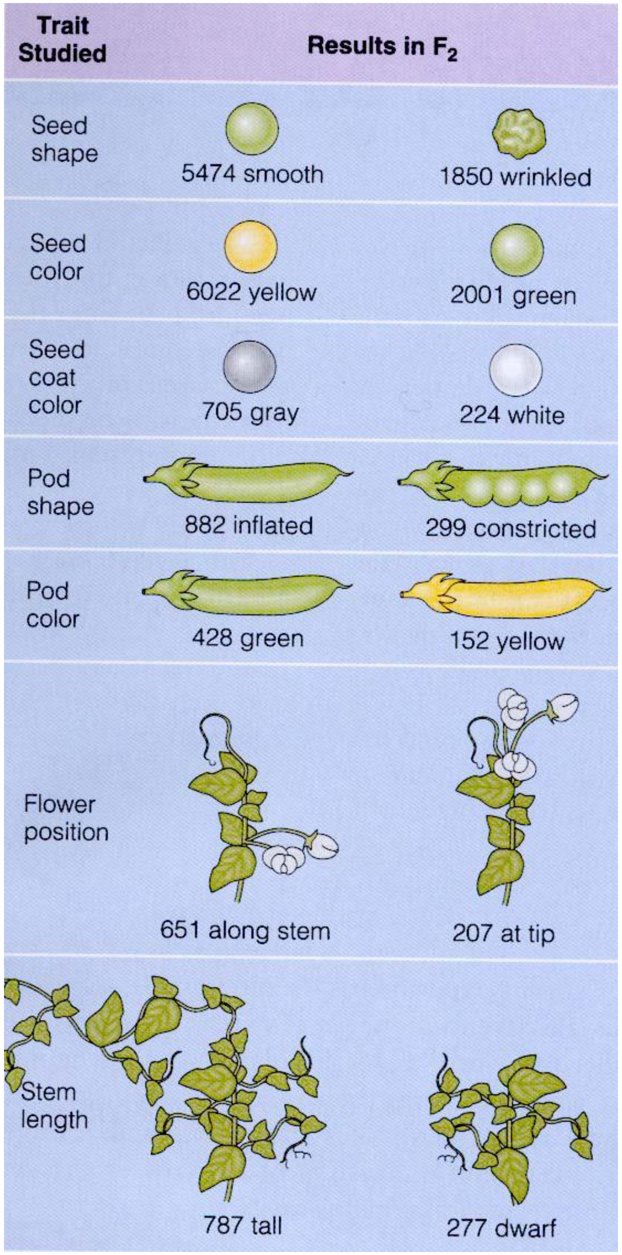
Mendelian inheritance

Monohybrid cross

- A **Punnett Square** shows how the traits are inherited (A=dominant trait; a=recessive trait).

All possible fertilization events





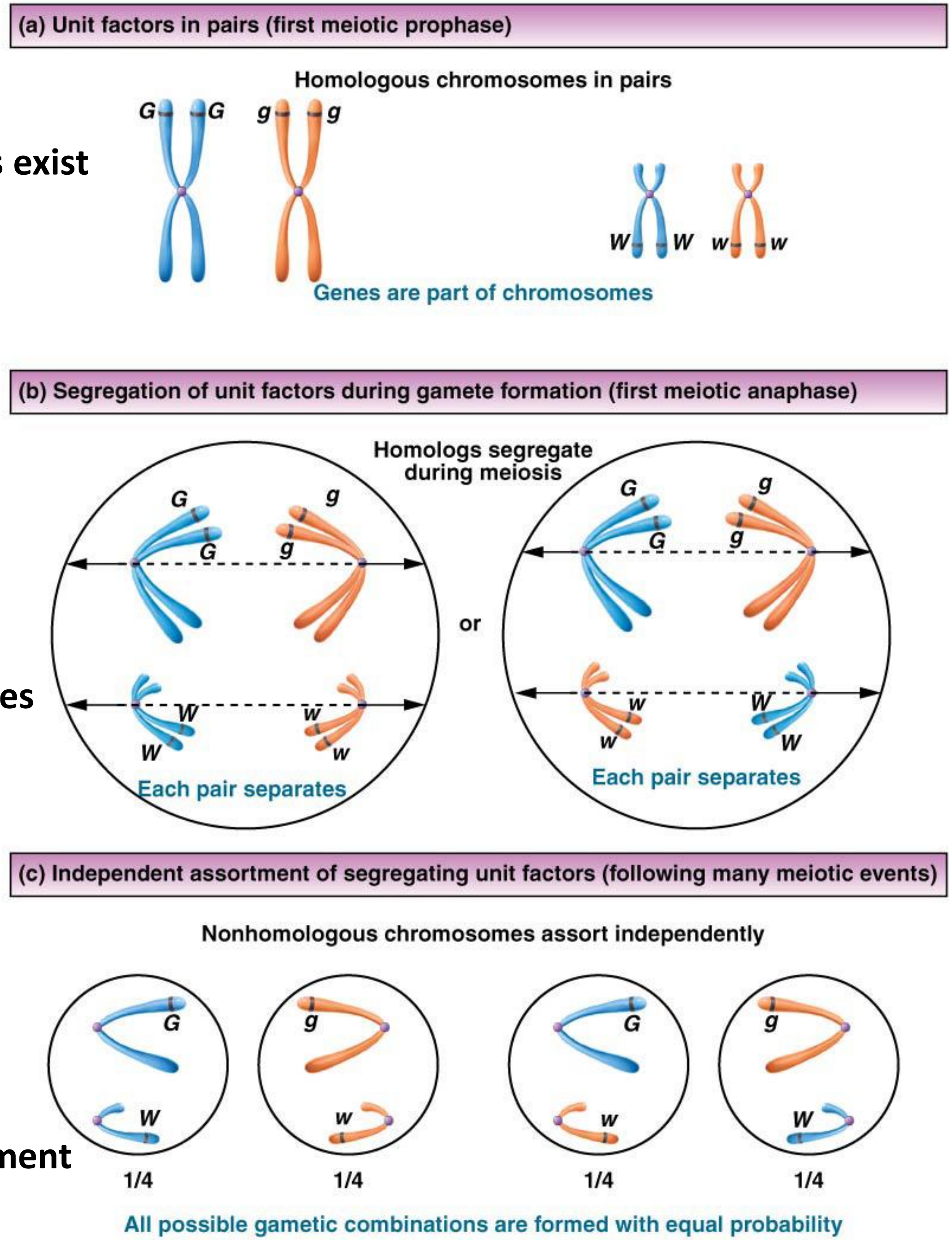
Mendel's postulates

1) Hereditary factors (we now know them as **genes**) exist in **pairs** in individual organisms and determine traits
2) Traits can be present but not always expressed – **dominant** and **recessive**
   - Difference between appearance (**phenotype**) and genetic constitution (**genotype**)
3) Each parent contributes only **one copy** of their unit factors to each offspring
   - **Law of segregation**
4) During gamete formation, segregating pairs or unit factors sort independently
   - **Independent assortment**

1. Heredity factors exist in pairs

3. Each parent contributes one copy to each offspring

4. Independent assortment



Pearson Education, Ltd.

Figure 3.10

Law of Independent assortment

Dihybrid cross- relationships between two different genes

While Mendel's experiments with mixing **one trait** always resulted in a 3:1 ratio between dominant and recessive phenotypes, his experiments with mixing **two traits** (dihybrid cross) showed 9:3:3:1 ratios

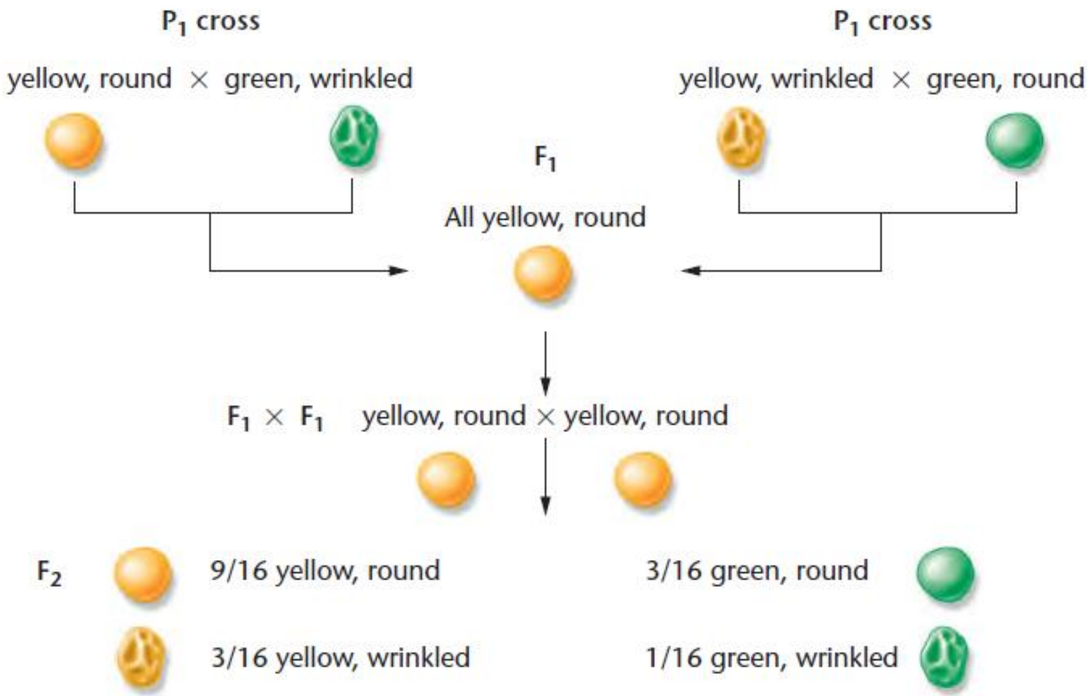


Figure 3.5

Dihybrid cross – Punnett square

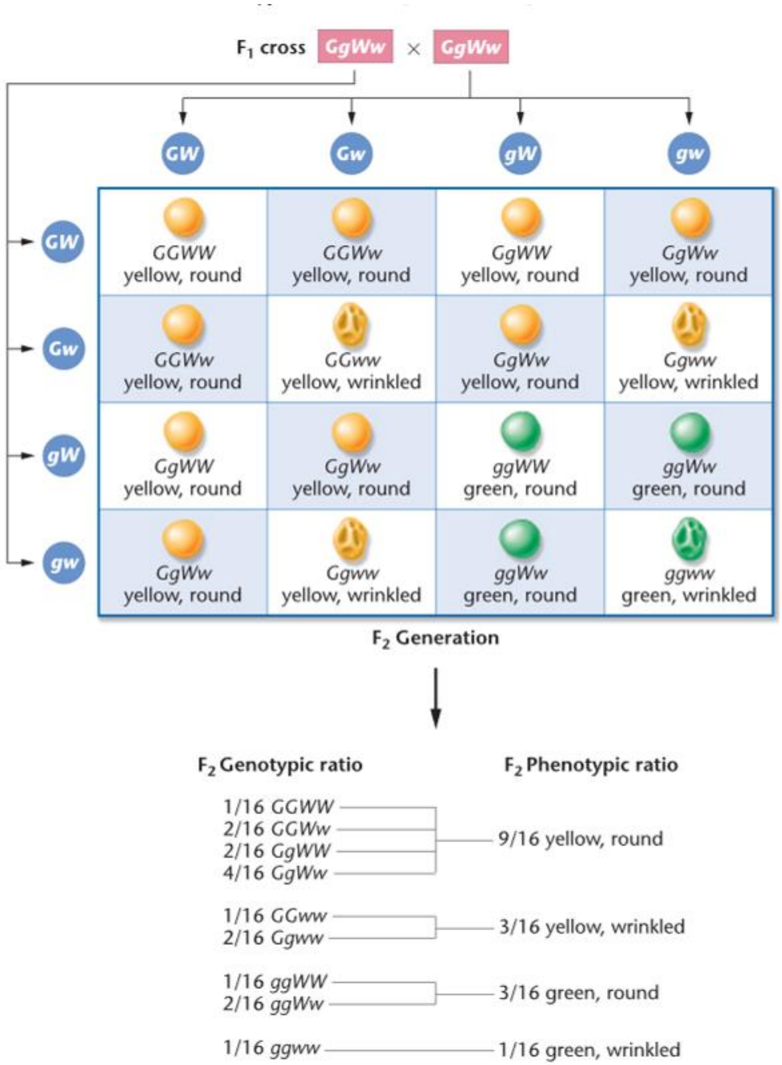


Figure 3.7

We can use probability to **predict** the outcome of Mendelian crosses

- **Punnett Square Method** – useful for beginners but has limitations ***beyond a two gene situation***
  - E.g. In a cross between AaBbCc x AaBBCC what is the probability that the offspring will be AaBbCC?
  - This trihybrid cross would be a complicated Punnet square

	ABC	ABc	AbC	Abc	aBC	aBc	abC	abc
ABC	AABBCC	AABBCc	AABbCC	AABbCc	AaBBCC	AaBBCc	AaBbCC	AaBbCc
ABC	AABBCC	AABBCc	AABbCC	AABbCc	AaBBCC	AaBBCc	AaBbCC	AaBbCc
ABC	AABBCC	AABBCc	AABbCC	AABbCc	AaBBCC	AaBBCc	AaBbCC	AaBbCc
ABC	AABBCC	AABBCc	AABbCC	AABbCc	AaBBCC	AaBBCc	AaBbCC	AaBbCc
aBC	AaBBCC	AaBBCc	AaBbCC	AaBbCc	aaBBCC	aaBBCc	aaBbCC	aaBbCc
aBC	AaBBCC	AaBBCc	AaBbCC	AaBbCc	aaBBCC	aaBBCc	aaBbCC	aaBbCc
aBC	AaBBCC	AaBBCc	AaBbCC	AaBbCc	aaBBCC	aaBBCc	aaBbCC	aaBbCc
aBC	AaBBCC	AaBBCc	AaBbCC	AaBbCc	aaBBCC	aaBBCc	aaBbCC	aaBbCc

The probability method

- The most *flexible and applicable* method
- A dihybrid cross is a situation in which two monohybrid crosses are involved and problems can sometimes be more easily solved by considering the two crosses independently (**if the loci are unlinked**) and then combining the results
  - The same principal applies, no matter how many gene loci are involved
- **There are two rules of probability you need to understand – Multiplication (one trait AND another) and Addition (one trait OR another)**

Multiplicative rule (Product law)

- If two events are **independent** of each other then the probability of them occurring at the same time is the product of their independent probabilities.

p(A **and** B) = p(A) **X** p(B)

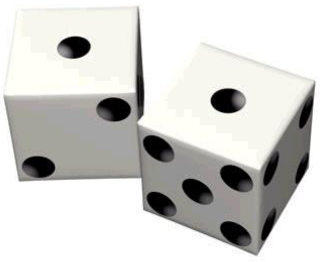
- E.g. What is the probability of flipping a coin five times **and** getting tales on every flip?

$\frac{1}{2} \times \frac{1}{2} \times \frac{1}{2} \times \frac{1}{2} \times \frac{1}{2} = \mathbf{1/32}$

Multiplicative rule – more examples

- Rolling “snake eyes” on pair of dice: getting one **AND** one

$$1/6 \times 1/6 = 1/36$$

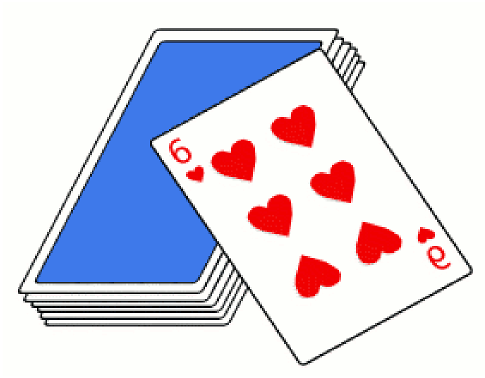


- Picking an ace out of a deck of cards, **returning it AND** picking a six out of the deck.

$$4/52$$

$$\downarrow$$

$$1/13 \times 1/13 = 1/169$$



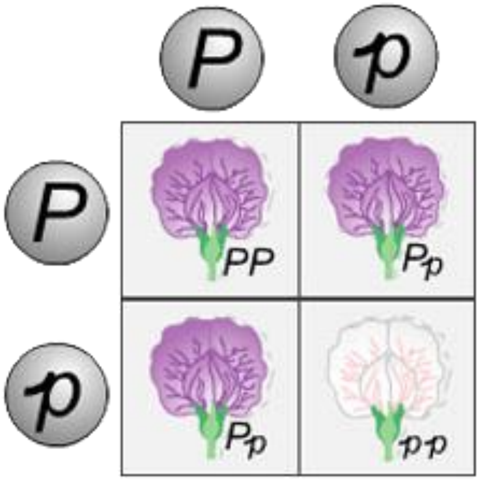
Multiplicative rule in genetics

- In a cross between pea plants that are heterozygous for purple flower colour (Pp), what is the probability that the offspring will be homozygous recessive **(p AND p)**?

Pp x Pp

1/2 x 1/2 = 1/4

pp



Multiplicative rule in genetics

- In a cross between AaBbCc x AaBBCC what is the probability that the offspring will be AaBbCC?

What is the probability Aa x Aa will give Aa?

	A	a
A	AA	Aa
a	Aa	aa

1/2

x

What is the probability Bb x BB will give Bb?

	B	b
B	BB	Bb
B	BB	Bb

1/2

x

What is the probability Cc x CC will give CC?

	C	C
C	CC	CC
c	Cc	Cc

1/2

= 1/8 Aa **AND** Bb **AND** CC

Additive rule (Sum law)

- If two events are <u>**mutually exclusive**</u> then the probability that at least one of them occurs is the sum of their individual probabilities.

$$p(C\ \textbf{OR}\ D) = p(C) + p(D)$$

- E.g. What is the probability of flipping *one* coin, *one* time and getting either a head **OR** a tail?

$\frac{1}{2} + \frac{1}{2} = 1$ (or 100% of the time)

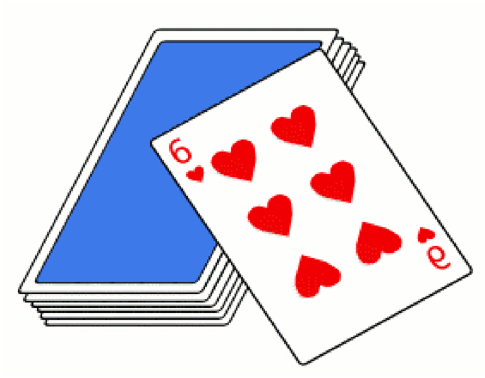
Additive rule – more examples

- Rolling a three **OR** a two on **ONE** six-sided die

$$1/6 \quad + \ 1/6 \quad = 2/6 = 1/3$$

- Picking a six **OR** a two out of a deck of cards.

$$4/52 \quad +4/52 \qquad = 8/52$$

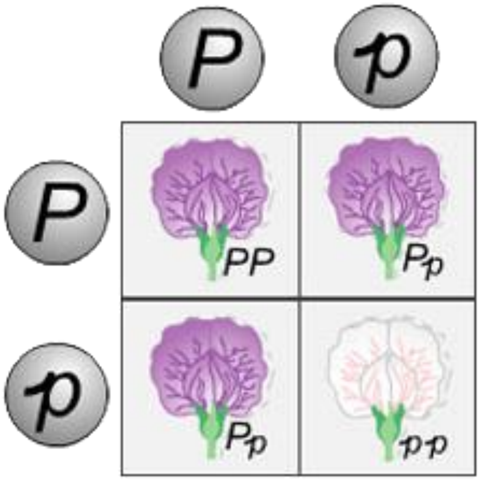


Additive rule in genetics

- In across between pea plants that are heterozygous for purple flower colour (Pp), what is the probability of the offspring being a heterozygote?

Pp x Pp

Pp Pp



$1/2 \times 1/2 \quad 1/2 \times 1/2$

$1/4 + 1/4 = 1/2$

Which rule to use?

AND/OR Rule

Probability of A **AND** B

Independent = multiplication

AaBbCC

Probability of A **OR** B

Mutually exclusive = addition

Additive rule in genetics

- In a cross between AaBbCc x AaBBCC what is the probability that the offspring will be AABbCc **OR** AABBCC?

	What is the probability Aa x Aa will give AA?		What is the probability Bb x BB will give Bb?		What is the probability Cc x CC will give Cc?	
AABbCc	1/4	x	1/2	x	1/2	= 1/16
	What is the probability Aa x Aa will give AA?		What is the probability Bb x BB will give BB?		What is the probability Cc x CC will give Cc?	
AABBCC	1/4	x	1/2	x	1/2	= 1/16

$$1/16 + 1/16 = 2/16 = 1/8$$

Try this one

- You have freckles and a widow's peak (heterozygous for both) and no dimples. Your partner has freckles and dimples (heterozygous for both), but a continuous hairline.
  - Question: What is the probability your darling child would have all three recessive phenotypes: no freckles (ff), no dimples (dd) and a continuous hairline (ww)?

You
FfddWw

Partner
FfDdww

Child
ffddww

NOTE: none of these are actually single gene traits!

Try this one

Are each of these independent events? Which rule?

Freckles: Ff
Widow's peak: Ww
Dimples: Dd
No freckles: ff
No dimples: dd
continuous hairline: ww

You
FfddWw

Partner
FfDdww

Child
ffddww

	F	f
F	FF	fF
f	Ff	ff

¼ ff

x

AND

	d	d
D	dD	dD
d	dd	dd

½ dd

x

AND

	W	w
w	Ww	ww
w	Ww	ww

½ ww

ffddww = 1/16

The Binomial Theorem

- The binomial theorem can be used to calculate probability where there are **alternative ways to achieve a combination of events**.
- Rule: the sum of the probabilities for alternative events equals one

$$(p + q) = 1$$

p = probability of occurrence of **particular** event A

q = probability of occurrence of **alternative** event B

Example: you have 6 kids, what's the probability of having 5 girls and one boy

The Binomial Theorem

- The general expression for a single term is

$$\frac{n!}{x!\,(n-x)!}\; p^{x}\, q^{(n\,-\,x)}$$

where **n** = total number of events

x = number of times event **A** occurs = **5 girls**

(**n – x**) = number of times event **B** occurs = **1 boy**

n! = **factorial** n = n(n - 1)(n – 2) …….1

6!= 6x5x4x3x2x1 = 720

The factorial is used to determine the possible number of combinations of birth outcomes- that is boy girl girl girl girl girl and all the different orders the children could be born

The Binomial Theorem

- E.g. In a family of 6 children what is the probability of having 5 girls and 1 boy

  Step 1: Calculate the individual probabilities
  - p = ½ (probability of occurrence of particular event – girl)
  - q = ½ (probability of occurrence of alternative event – boy)

  Step 2: Determine the number of events
  - n = 6 (total number of children)
  - x = 5 (event A – girls)
  - n-x = 1 (event B – boys)

$$\frac{n!}{x!\,(n-x)!}\; p^{x} q^{(n-x)}$$

n = total number of events

x = number of times event A occurs

(n – x) = number of times event B occurs

n! = factorial n = n(n - 1)(n – 2) …….1

The Binomial Theorem

- Step 3: Substitute the values for p, q, x, and n in the binomial expansion equation
  - The symbol **!** denotes a factorial, which is the product of all the positive integers from 1 through some positive integer
    - E.g. 5! = (5)(4)(3)(2)(1) = 120

6!= 6x5x4x3x2x1 = 720

We use a factorial to determine the possible number of combinations of birth outcomes- e.g. boy girl girl girl girl girl and all the different orders the children could be born

- Back to the example problem…

$$\frac{n!}{x!\,(n-x)!}\; p^{x}\, q^{(n-x)}$$

The Binomial Theorem

- Step 3: Substitute the values for p, q, x, and n in the binomial expansion equation

$$\frac{n!}{x!\,(n-x)!}\; p^{x} q^{(n-x)}$$

- Back to the example problem…
  - $P = (6!/5!x1!)(1/2)^5(1/2)^1$
  - $P = 6x(1/2)^5(1/2)^1$
  - $P = 6x\ 0.015625 = 0.09375 = 3/32$

n = 6 (total number of children)
x = 5 (event A – girls)
n-x = 1 (event B – boys)

p = ½ (prob. of occurrence of particular event – girl)
q = ½ (prob. of occurrence of alternative event – boy)

6! = 720
5! = 120
(6!/5!x1!) = 6
$1/2^5 = 0.03125$
$(1/2)^5(1/2)^1 = 0.015625$

So in families with 6 children, on average, 3 out 32 will have 5 girls and 1 boy.

Try this one

Two heterozygous brown-eyed (Bb) individuals have five children. What is the probability that three will have blue eyes?

Step 1: Calculate the individual probabilities

(Punnett square will help here)

- P(blue eyes) = p = 1/4
- P(brown eyes) = q = 3/4

Step 2: Determine the number of events

n = total number of children=5

x = number of blue eyed children=3

n-x = number of brown eyed children = 2

Try this one

Step 3: Substitute the values for p, q, x, and n in the binomial expansion equation

$$\frac{n!}{x!\,(n-x)!}\; p^{x} q^{(n\,-\,x)}$$

$5! = 120$
$3! = 6$
$2! = 2$
$3!\ X\ 2! = 12$

$$P = (5!/3!x2!)(1/4)^3(3/4)^2$$

$1/4^3 = 0.015625$
$3/4^2 = 0.5625$
$(1/4)^3(3/4)^2 = 0.00878$

$$P = 10 \text{ x } (1/4)^3(3/4)^2$$

$$P = 0.0878 = 8.78\%$$

$(1/4)3 = ¼ \text{ x } ¼ \text{ x } ¼ = 1/64$
$(3/4)2 = ¾ \text{ x } ¾ = 9/16$

The Chi-Square Test in Genetics

- An important question to answer in any genetic experiment is how can we decide if your data fits Mendelian ratios?
- The **chi-square test** compares your expected values to your observed (experimental) values
- A judgement can then be made as to whether we accept or reject the deviation as being significant
- We therefore have a statistical means of testing the validity of a hypothesis that formed the basis for an experiment

The Chi-Square Test

observed result

sum

Chi squared

$$\chi^2 = \sum \frac{(o - e)^2}{e}$$

expected result

The Null Hypothesis

- When we assume data will fit a given ratio we establish a null hypothesis – **H_0.**
- The null hypothesis assumes there is no difference between measured values and the predicted values
- We cannot perform a statistical test without first establishing **H_0.**

- The point of the Chi-Square test is to either **REJECT** or **ACCEPT** our null hypothesis

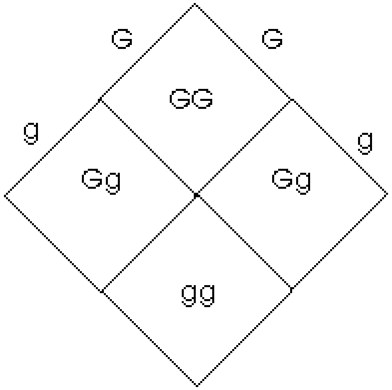
The Chi-Square Test in genetics

- A cross between two pea plants yields a population of 880 plants, 639 with green seeds and 241 with yellow seeds. You are asked to propose the genotypes of the parents.

- Step 1: State the hypothesis being tested and the predicted results
  - **Hypothesis**: the allele for green is dominant to the allele for yellow and that the parent plants were both heterozygous for this trait

The Chi-Square Test in genetics

- If your hypothesis is true, then the predicted **phenotypic** ratio of offspring from this cross would be 3:1 (based on Mendel's laws) as predicted from the results of the Punnett square



- Step 2: Determine the expected numbers for each observational class
  - If the ratio is 3:1 and the total number of observed individuals is 880, then the expected numerical values should be 660 green and 220 yellow

The Chi-Square Test in genetics

- Step 3: Calculate χ^2 using the formula

O	639	241
E	660	220

$$\chi^2 = \Sigma \frac{(o-e)^2}{e}$$

$(639 - 660)^2/660$ $\quad$ $(241 - 220)^2/220$

$$0.668 + 2 = 2.668$$

The Chi-Square Test in genetics

- Step 4: Determine degrees of freedom and locate the value in the appropriate column
  - There are two categories (green and yellow); therefore, there is 1 degree of freedom

The Chi-Square Test - example

	Probability (p)					
	0.90	0.50	0.20	0.05	0.01	0.001
1	0.02	0.46	1.64	3.84	6.64	10.83
2	0.21	1.39	3.22	5.99	9.21	13.82
3	0.58	2.37	4.64	7.82	11.35	16.27
4	1.06	3.36	5.99	9.49	13.28	18.47
5	1.61	4.35	7.29	11.07	15.09	20.52
6	2.20	5.35	8.56	12.59	16.81	22.46
7	2.83	6.35	9.80	14.07	18.48	24.32
8	3.49	7.34	11.03	15.51	20.09	26.13
9	4.17	8.34	12.24	16.92	21.67	27.88
10	4.87	9.34	13.44	18.31	23.21	29.59
15	8.55	14.34	19.31	25.00	30.58	37.30
25	16.47	24.34	30.68	37.65	44.31	52.62
50	37.69	49.34	58.16	67.51	76.15	86.60

χ^2 values

*The relative standard commonly used in biological research is $p < 0.05$

*The p value is the **probability that you would get your χ^2 value** if the null hypothesis was true

0.05 = 1/20 probability of Type I error (false positive)
0.01= 1/100
0.001= 1/1000

The Chi-Square Test in genetics

- Step 5: Use the chi-square distribution table to determine significance of the value.
  - Locate the value closest to your calculated χ^2 on that degrees of freedom df row
  - Move up the column to determine the p value

	Probability (p)					
	0.90	0.50	0.20	0.05	0.01	0.001
1	0.02	0.46	1.64	3.84	6.64	10.83
2	0.21	1.39	3.22	5.99	9.21	13.82
3	0.58	2.37	4.64	7.82	11.35	16.27
4	1.06	3.36	5.99	9.49	13.28	18.47
5	1.61	4.35	7.29	11.07	15.09	20.52
6	2.20	5.35	8.56	12.59	16.81	22.46
7	2.83	6.35	9.80	14.07	18.48	24.32
8	3.49	7.34	11.03	15.51	20.09	26.13
9	4.17	8.34	12.24	16.92	21.67	27.88
10	4.87	9.34	13.44	18.31	23.21	29.59
15	8.55	14.34	19.31	25.00	30.58	37.30
25	16.47	24.34	30.68	37.65	44.31	52.62
50	37.69	49.34	58.16	67.51	76.15	86.60

χ^2 values

$$\chi^2 = 2.668$$

$$p > 0.05$$

Try this one

- A large ear of corn has a total of 433 grains, including 271 Purple & Smooth (A in picture), 73 Purple & Shrunken (B in picture), 63 Yellow & Smooth (C in picture), and 26 Yellow & Shrunken (D in picture).

Your null hypothesis:

This ear of corn was produced by a dihybrid cross (PpSs x PpSs) involving two pairs of heterozygous genes resulting in a theoretical (expected) ratio of 9 purple, smooth:3 purple, shrunken:3 yellow, smooth:1 yellow, shrunken.

Notice how detailed and specific this is!

Test your hypothesis using chi square and probability values.

Work out expected ratios with a Punnett square

PpSs x PpSs				
	PS	Ps	pS	ps
PS	PPSS (purple smooth)	PPSs (purple smooth)	PpSS (purple smooth)	PpSs (purple smooth)
Ps	PPSs (purple smooth)	PPss (purple shrunken)	PpSs (purple smooth)	Ppss (purple shrunken)
pS	PpSS (purple smooth)	PpSs (purple smooth)	ppSS (yellow smooth)	ppSs (yellow smooth)
ps	PpSs (purple smooth)	Ppss (purple shrunken)	ppSs (yellow smooth)	ppss (yellow shrunken)