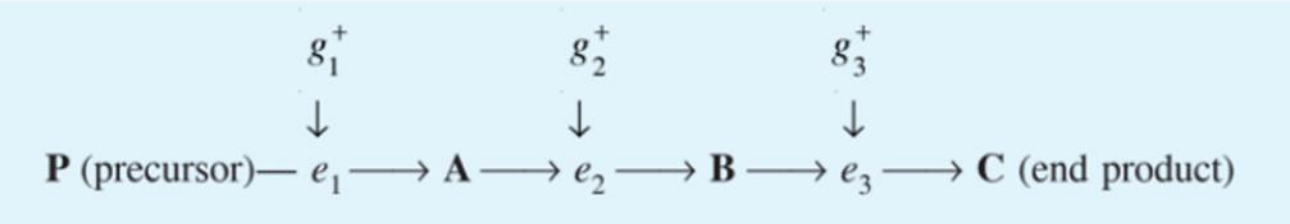
Genetic Interaction & Epistasis

The gene is a chemical determiner. Whereas a phenotypic trait results from the combined action of many genes and their products constantly interacting with the environment. The environment includes not only ecological factors such as temperature and the amount or quality of light but also internal factors such as hormones and enzymes. The enzymes are proteins and the specific molecular organization of protein is determined by genes. The enzymatic proteins perform a catalytic function in various cellular chemical (metabolic) reactions and causing the splitting or union of various molecules.

Each cellular chemical reaction involves a stepwise conversion of one substance called precursor into another, called end product. Each step is mediated by a specific enzyme. All the subsequent steps of a chemical reaction constitute the biosynthetic pathway. Thus, a simplest biosynthetic pathway includes various steps, each step is catalyzed by a specific enzymatic protein and each enzymatic protein in its turn depends on a specific gene for its production. For example, we may consider a simple biosynthetic pathway which transforms a precursor substance 'P' into the end product 'C' in the following three subsequent steps:



In this biosynthetic pathway, each metabolite (A, B, C) is produced by the catalytic action of different enzymes (e1, e2, e3, ... ex) specified by different wild type genes (g+1,g+2,g+3, ... g+x). When more than two or more genes become involved in the specification of enzymes for different steps of a common biosynthetic pathway, the phenomenon of genetic interaction occurs. If substance C is essential for the production of a normal phenotype and the recessive mutant alleles g1, g2, g3 produce defective enzymes, then a mutant or abnormal phenotype would result from a genotype homozygous recessive at any of the three loci. If wild gene g+3 becomes mutant, the conversion of metabolite B to C does not occur and substance B tends to accumulate in excessive quantity; if g+2 becomes mutant, substance A will

accumulate. Thus, the mutant genes caused “metabolic blocks” in the synthetic pathway.

An organism with a mutation only in gene g+2 could produce a normal phenotype if it was given either substance B or C, but an organism with a mutation in gene g+3 has a specific requirement for substance C for the production of normal phenotype. Thus, gene g+3 becomes dependent upon g+2 for its expression as a normal phenotype. If the genotype is homozygous for the recessive g2 allele, then the biosynthetic pathway ends with substance A. Neither g+3 nor its recessive allele g3 has any effect on the phenotype. Thus, genotype (g2g2) can hide or mask the phenotypic expression of alleles at the g+3 locus. Originally a gene or locus which suppressed or masked the action of a gene at another locus was termed the epistatic gene. The gene or locus which was suppressed by an epistatic gene was called the hypostatic gene.

Later studies revealed the fact that both loci or genes (i.e., epistatic and hypostatic) could be epistatic to one another. Presently, the term epistasis (Greek, standing upon) is used for almost any type of allelic genetic interaction.

Difference between dominance and epistasis:

The phenomenon of dominance involves intra-allelic gene suppression or the masking effect which one allele has upon the expression of another allele at the same locus, while the phenomenon of epistasis involves inter-allelic gene suppression or the masking effect which one gene locus has upon the expression of another.

The classical phenotypic ratio of 9 : 3 : 3 : 1 observed in the progeny of dihybrid parents becomes modified by epistasis into ratios which are various combinations of the 9 : 3 : 3 : 1 groupings.

Non-epistatic inter-allelic genetic interactions

In certain cases, two pairs of genes determine the same phenotype but assorted independently, produce new phenotypes by mutual non-epistatic interactions, and the F2 phenotypic ratio 9 : 3 : 3 : 1 remains unaltered.

Example: Combs in fowl (9 : 3 : 3 : 1). Two pairs of genes that interact to affect the size and shape of comb but are independently transmitted exist in chicken.

The classical case of genetic interaction of two genes is discovered by Bateson and Punnett (1905–1908) in fowls. There are many different breeds of domestic chicken. Each breed possesses a characteristic type of comb. The Wyandotte breed has a comb

called “rose”, the Brahmas breed has a comb called “pea”, and the Leghorns have a comb called ‘single’. Each of these types can be bred true.

A cross of chicken with a rose comb to one with a single comb produces in F2: ¾ rose and ¼ single, showing the dominance of rose over single. Another cross between pea combed and single combed chickens produce in F2: pea and single combed chickens in the ratio of 3 : 1, showing the dominance of pea over single. But, when a rose combed chicken crossed with that of pea combed, the F1 progeny was found with a different type of comb known as ‘walnut’ (Malay breed). When the F1 walnut combed chickens were bred together, in F2 all four types of combs, i.e., 9/16 walnut, 3/16 rose, 3/16 pea and 1/16 single appeared.

These peculiar results were interpreted by Bateson and Punnett as follows: The rose comb is caused by the combination of homozygous recessive genes “pp” and homozygous or heterozygous dominant genes ‘RR’ or ‘Rr’. The pea comb is supposed to be produced by a combination of a homozygous recessive condition (rr) and homozygous or heterozygous dominant condition (PP or Pp). While, the single type comb is produced by the double recessive, rrpp, genes. Thus, the R gene determines the shape of rose comb and P gene determines the shape of pea comb, but when both genes happen to come together in single individual due to cross between rose and pea combed chickens, they interact to produce a walnut comb in F1. In the cross of two walnut chickens, two genes interact variously and produce four types of offsprings in F2.

Thus, here two pairs of genes interact to produce comb size and shape in fowl. During the inheritance of combs in fowls, the genes themselves do not determine the development of a character (presence or absence of comb) and simply modify a character determined by a basic gene and, therefore, known as **supplementary or modifying genes**.

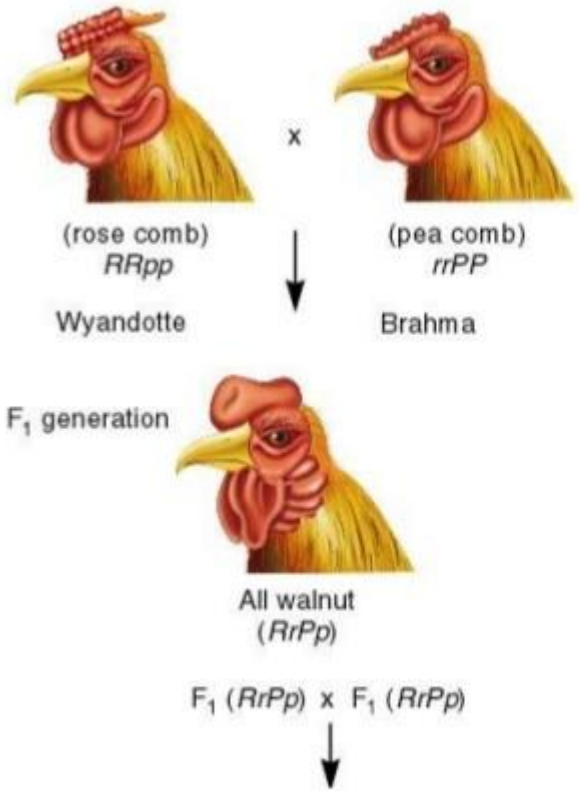


Figure 4.17*b*

The crosses of Bateson and Punnett

	RP	*Rp*	*rP*	*rp*
RP	*RRPP* Walnut	*RRPp* Walnut	*RrPP* Walnut	*RrPp* Walnut
Rp	*RRPp* Walnut	*RRpp* Rose	*RrPp* Walnut	*Rrpp* Rose
rP	*RrPP* Walnut	*RrPp* Walnut	*rrPP* Pea	*rrPp* Pea
rp	*RrPp* Walnut	*Rrpp* Rose	*rrPp* Pea	*rrpp* Single

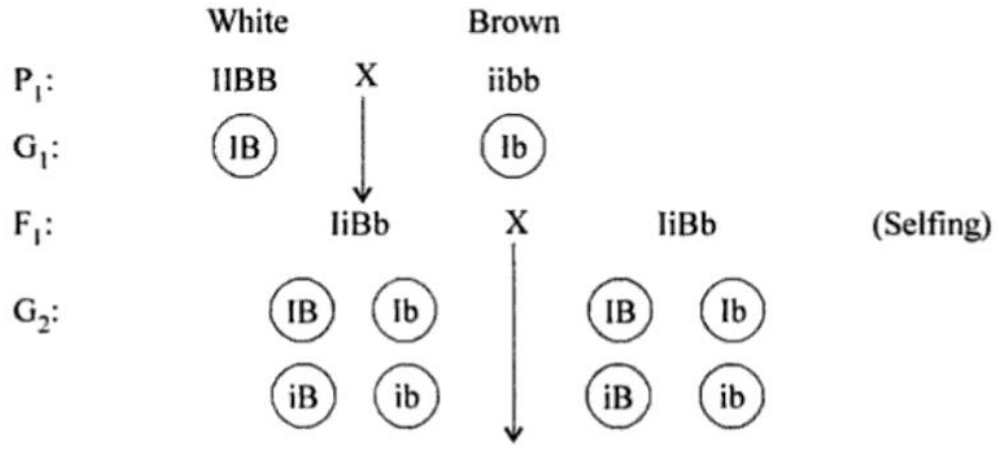
Kinds of Epistatic Interaction

When in dihybrid crosses, the epistatic interactions occur between two genes, less than four phenotypes appear in F2. Such bigenic (two genes) epistatic interactions may be of following six types:

1. Dominant Epistasis (12: 3 : 1)

When out of two genes, the dominant allele (e.g., A) of one gene masked the activity of alleles of another gene (e.g., B) and expressed itself phenotypically, then A gene locus is said to be epistatic to the B gene locus. Because, the dominant allele A can express itself only in the presence of either B or b allele, therefore, such type of epistasis is termed as dominant epistasis. The alleles of hypostatic locus or gene B will be able to express themselves phenotypically only when gene locus A may contain two recessive alleles (aa). Thus, the genotype AA BB or Aa Bb and AA bb or Aa bb produce the same phenotype whereas the genotype aa BB or aa Bb and aa bb produce two additional phenotypes. The dominant epistasis modifies the classical ratio of 9: 3: 3: 1 into 12: 3: 1 ratio.

Example: Dominant epistasis in dogs. Among dogs, the colours of coats depend upon the action of two genes. One gene locus has a dominant epistatic inhibitor allele (I) of coat colour pigment. The allele I prevents the expression of the colour allele at another independently assorting, hypostatic gene locus (B or b) and produces white coat colour. The alleles of hypostatic gene locus (BB, Bb, or bb) express only when two recessive alleles (ii) occur on the epistatic locus, i.e., ii BB or ii Bb produces black and ii bb produces brown individuals. When two such white coat colour dogs (Ii Bb) are crossed, the progeny will be:- 12 white : 3 black : 1 brown coat colours ratio.



F_2:

♀ \ ♂	IB	Ib	iB	ib
IB	IIBB	IIBb	IiBB	IiBb
Ib	IIBb	IIbb	IiBb	Iibb
iB	IiBB	IiBb	iiBB	iiBb
ib	IiBb	Iibb	iiBb	iibb

Ratio: I - B - → 9
I - bb → 3
} 12 → White

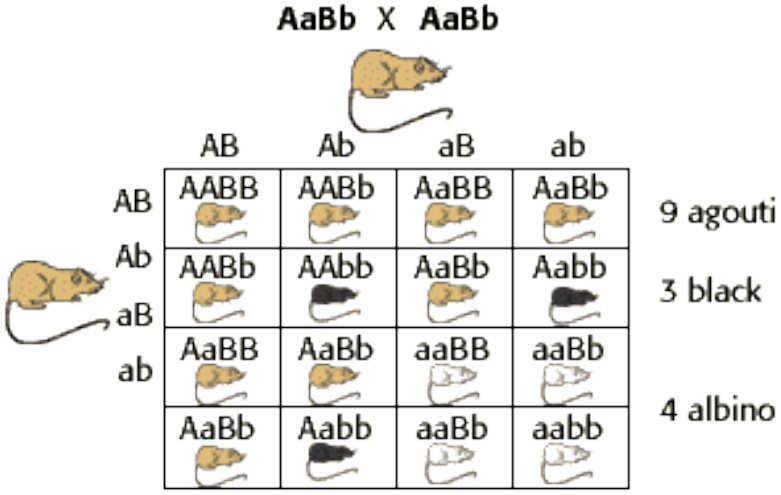
iiB - → 3 → Black

iibb → 1 → Brown

2. Recessive Epistasis (9 : 3 : 4)

Sometimes the recessive alleles of one gene locus (aa) mask the action (phenotypic expression) of alleles of another gene locus (BB, Bb or bb alleles). This type of epistasis is called recessive epistasis. The alleles of B locus express themselves only when epistatic locus has dominant alleles (e.g., AA or Aa). Due to recessive epistasis the phenotypic ratio 9: 3: 3: 1 becomes modified into 9: 3: 4 ratio.

Example: Recessive epistasis in mice. In mice, various types of epistatic genetic interactions have been reported. The most interesting case is of recessive epistasis in coat colours. The common house mouse occurs in a number of coats colours, i.e., agouti, black and albino. The agouti colour pattern is commonly occurred one (wild type) and is characterized by colour banded hairs in which the part nearest the skin is gray, then a yellow band and finally, the distal part is either black or brown. The albino mouse lacks totally in pigments and has white hairs and pink eyes.



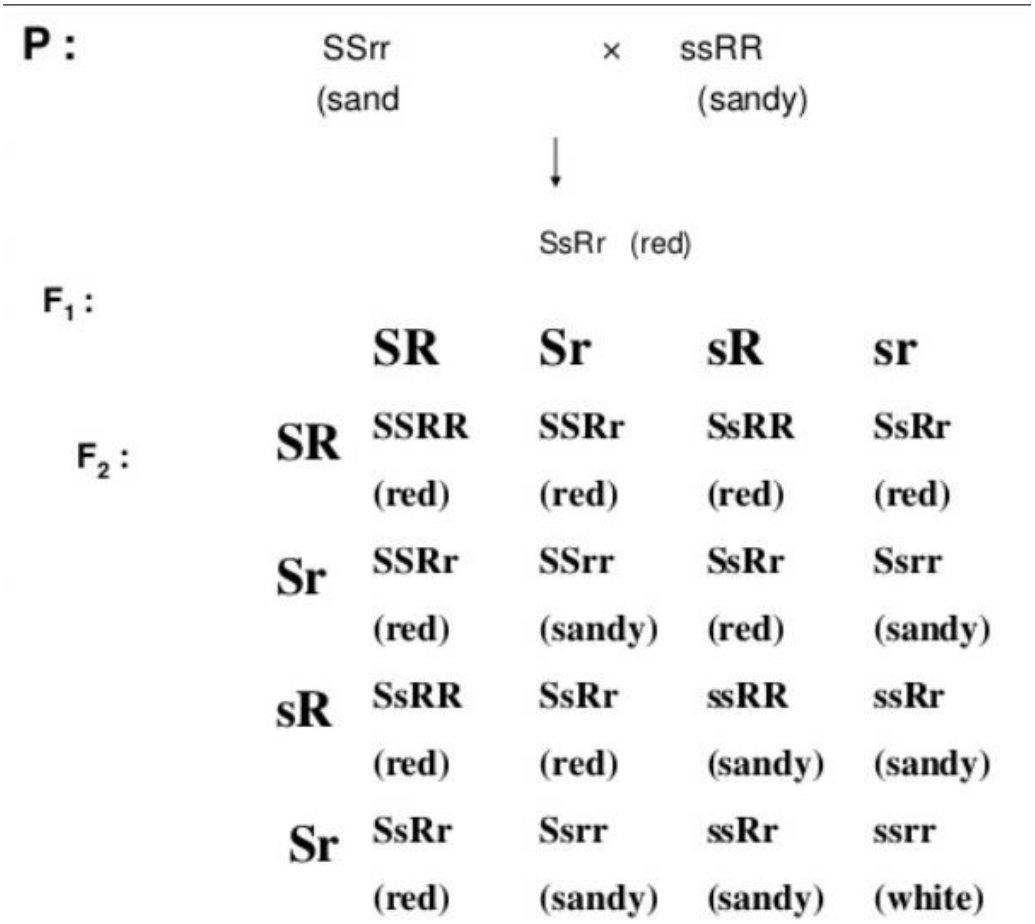
3. Duplicate Genes with Cumulative Effect (9: 6: 1)

Certain phenotypic traits (e.g., coat colouration) depend on the dominant alleles of two gene loci. When the dominant condition (homozygous or heterozygous) at either locus (but not both) produces the same phenotype, the F2 ratio becomes 9: 6: 1.

Example: The cumulative effect in the coat colour of pigs. In the Duroc-Jersey breed of pigs, coat colour is influenced by two pairs of genes that interact in a peculiar manner. Sandy coat colour results from a dominant gene S, and the homozygous recessive (ss) is white in colour. Sandy coat colour may also result from a non-allelic dominant gene R; it's homozygous recessive (rr) is also white.

Red (R- S-); Sandy (rr S- & R- ss); White (rr ss)

When a sandy pig (SS rr) is crossed with a second sandy pig (ss RR), the F1 offsprings were found with red coloured coats. Such interactions are said to be the result of mutually supplementary genes. When F1 red-coated pigs (Ss Rr) cross bred among themselves they produce red, sandy and white coats in the ratio of 9 : 6 : 1 .



4. Duplicate Recessive Genes (or Complimentary genes) (9: 7)

If both gene loci have homozygous recessive alleles and both of them produce identical phenotypes, the F2 ratio 9: 3: 3: 1 would become 9: 7. In such case, the genotypes aa BB, aa Bb, AA bb, Aa bb, and aa bb produce one phenotype (Table 4-7). Both dominant alleles when present together, complement each other and are called complementary genes and produce a different phenotype. A case of such complemental inheritance, resulting from the combined action of complemental genes is known in sweet peas.

Example: When a pure line variety of white-flowered sweet pea (*Lathyrus odoratus*) (CC ee) was crossed with another pure line variety of white-flowered sweet pea (cc EE), in F1 purple or red-flowered plants (Cc Ee) were produced. The F1 plants when self-pollinated or crossed among themselves, produced the F2 generation with the phenotypic ratio of 9 coloured and 7 white-flowered plants.

- Coloured (C- E-); White (cc E- , C- ee , cc ee)

Chromogen production due to complementation of C and E (i.e., dominant epistatic and hypostatic alleles).

These surprising results could be understood by analysing the mechanism of colour production in flowers. A given enzyme (genetically controlled as to absence or presence in a given individual) acts upon chromogen (a colourless colour base whose absence or presence is also genetically controlled) to produce the purple or red colour of flowers. The dominant allele or alleles (CC or Cc) of gene C are responsible for the presence of chromogen, while the homozygous recessive alleles (cc) of this gene are responsible for the absence of chromogen. Likewise, the dominant alleles of gene E in homozygous (EE) or heterozygous (Ee) conditions caused the production of an enzyme which is necessary for colour production from chromogen, while homozygous recessive (ee) condition does not produce any such enzyme.

CC ee X cc EE

White White

F1: Cc Ee (Coloured)

F2: 9 coloured and 7 white-flowered plants

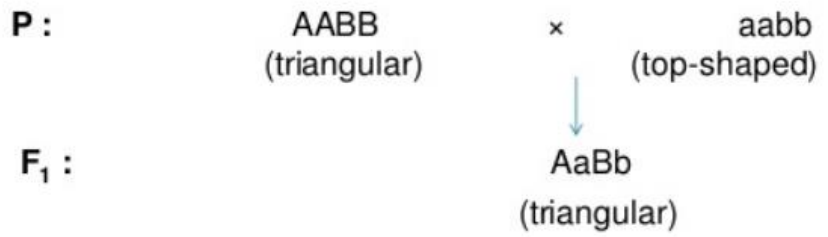
	CE	**Ce**	**cE**	**ce**
CE	CC EE Purple	CC Ee Purple	Cc EE Purple	Cc Ee Purple
Ce	CC Ee Purple	CC ee White	Cc Ee Purple	Cc ee White
cE	Cc EE Purple	Cc Ee Purple	cc EE White	cc Ee White
ce	Cc Ee Purple	Cc ee White	cc Ee White	cc ee White

5. Duplicate Dominant Genes (15: 1)

If the dominant alleles of both gene loci produce the same phenotype without cumulative effect, the 9: 3 : 3 : 1 ratio is modified into a 15 : 1 ratio .

Example: The seed capsules of shepherd's purse (genus Capsella) occur in two different shapes, i.e., triangular and top-shaped. When a plant with a triangular seed capsule is crossed with one having a top-shaped capsule, in F1 only triangular, the character appears. The F1 offsprings by self-crossing produce the F2 generation with

the triangular and top-shaped seed capsules in the ratio of 15: 1. Two independently segregating dominant genes (A and B) have been found to influence the shape of the capsule in the same way. All genotypes having dominant alleles of both of these genes (A and B) would produce plants with triangular-shaped capsules. Only those with the genotype aa bb would produce plants with top-shaped capsules.



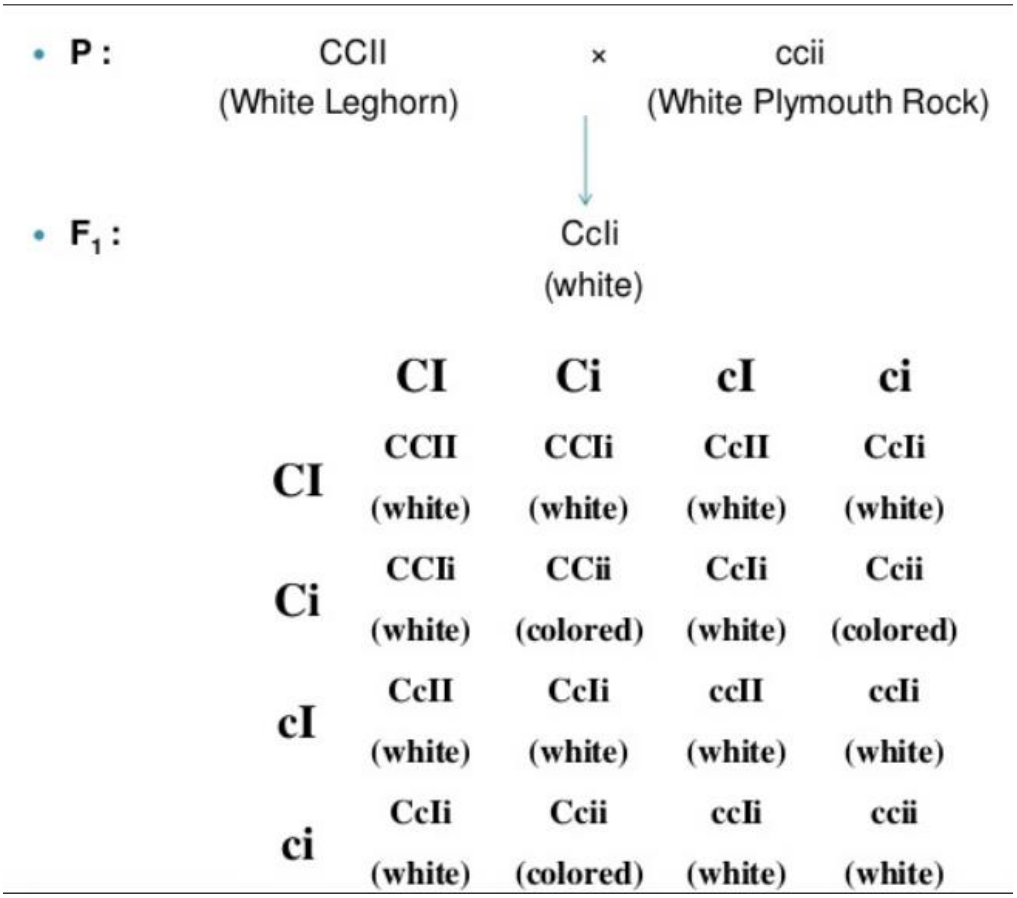
	AB	Ab	aB	ab
AB	AABB (triangular)	AABb (triangular)	AaBB (triangular)	AaBb (triangular)
Ab	AABb (triangular)	AAbb (triangular)	AaBb (triangular)	Aabb (triangular)
aB	AaBB (triangular)	AaBb (triangular)	aaBB (triangular)	aaBb (triangular)
Ab	AaBb (triangular)	Aabb (triangular)	aaBb (triangular)	aabb (top-shape)

6. Dominant and Recessive Interactions (13: 3)

Sometimes, the dominant alleles of one gene locus (A) in homozygous (AA) and heterozygous (Aa) condition and the homozygous recessive alleles (bb) of another gene locus (B) produce the same phenotype, the F2 phenotypic ratio becomes 13: 3 instead of 9: 3 : 3 : 1. In such case, the genotype AA BB, AABb, Aa BB, Aa Bb, AA bb and Aa bb produce same phenotype and the genotype aa BB, aa Bb and aa bb produce another but same phenotype.

Example: In Leghorn type of fowl, the white colour of the feather is caused by the dominant genotype CC II, similarly, the white colour of feathers of Plymouth Rock breed is caused by the recessive genotype cc ii. When both white varieties of fowl are crossed, in F1 white coloured hybrids appear. The F1 hybrids in F2 produce the white and coloured offsprings in the ratio of 13: 3.

The pigment produces by allele C. While allele I inhibit of the feather colouration. Thus, only the genotype C- ii has a coloured feather.



Summary of various epistatic ratio

Genotype	**A- B-** **(AA BB, Aa BB, AABb, AaBb)**	**A- bb** **(AA bb, Aa bb)**	**Aa B-** **(aa BB, aa Bb)**	**aa bb**
Classical ratio	**9**	**3**	**3**	**1**
Dominant epistasis	**12**		**3**	**1**
Recessive epistasis	**9**	**3**	**4**	
Duplicate Genes with Cumulative Effect	**9**	**6**		**1**
Duplicate Recessive Genes	**15**			**1**
Duplicate Dominant Genes	**9**	**7**		
Dominant and Recessive Interactions	**13:3**			