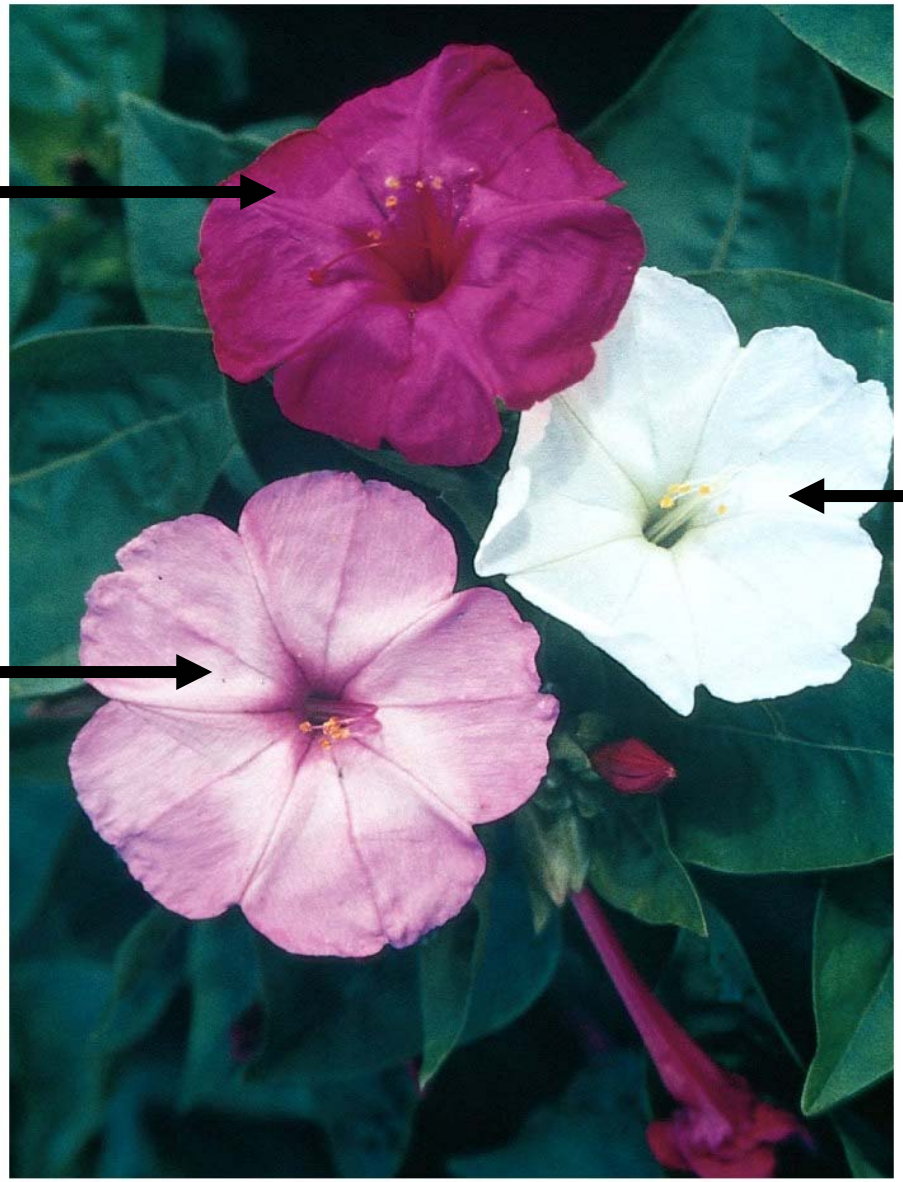
Incomplete dominance for flower colour in *Mirabilis jalapa*



R_1 Red pigment

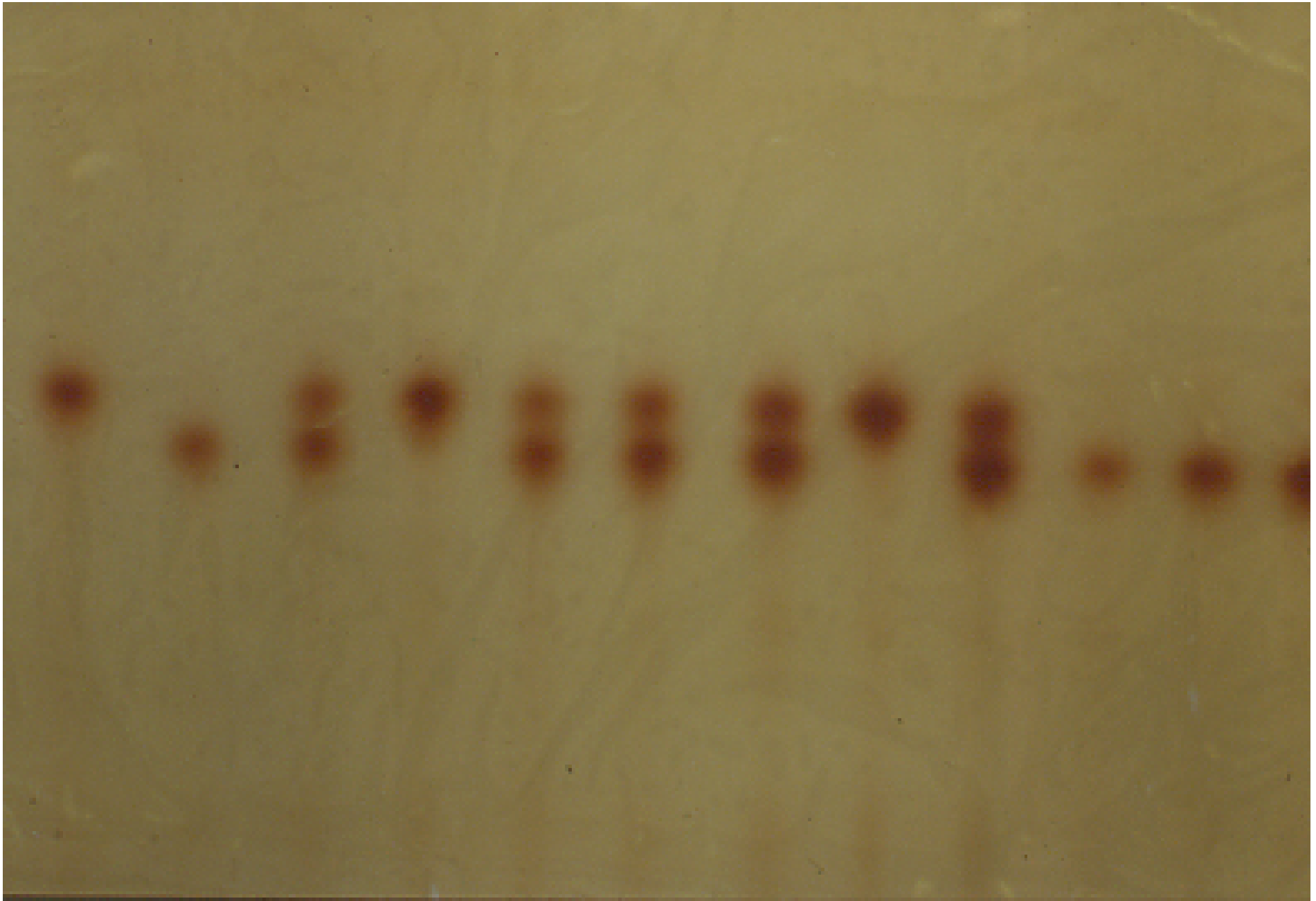
R_2 No pigment

Figure 6-4
Introduction to Genetic Analysis, Ninth Edition

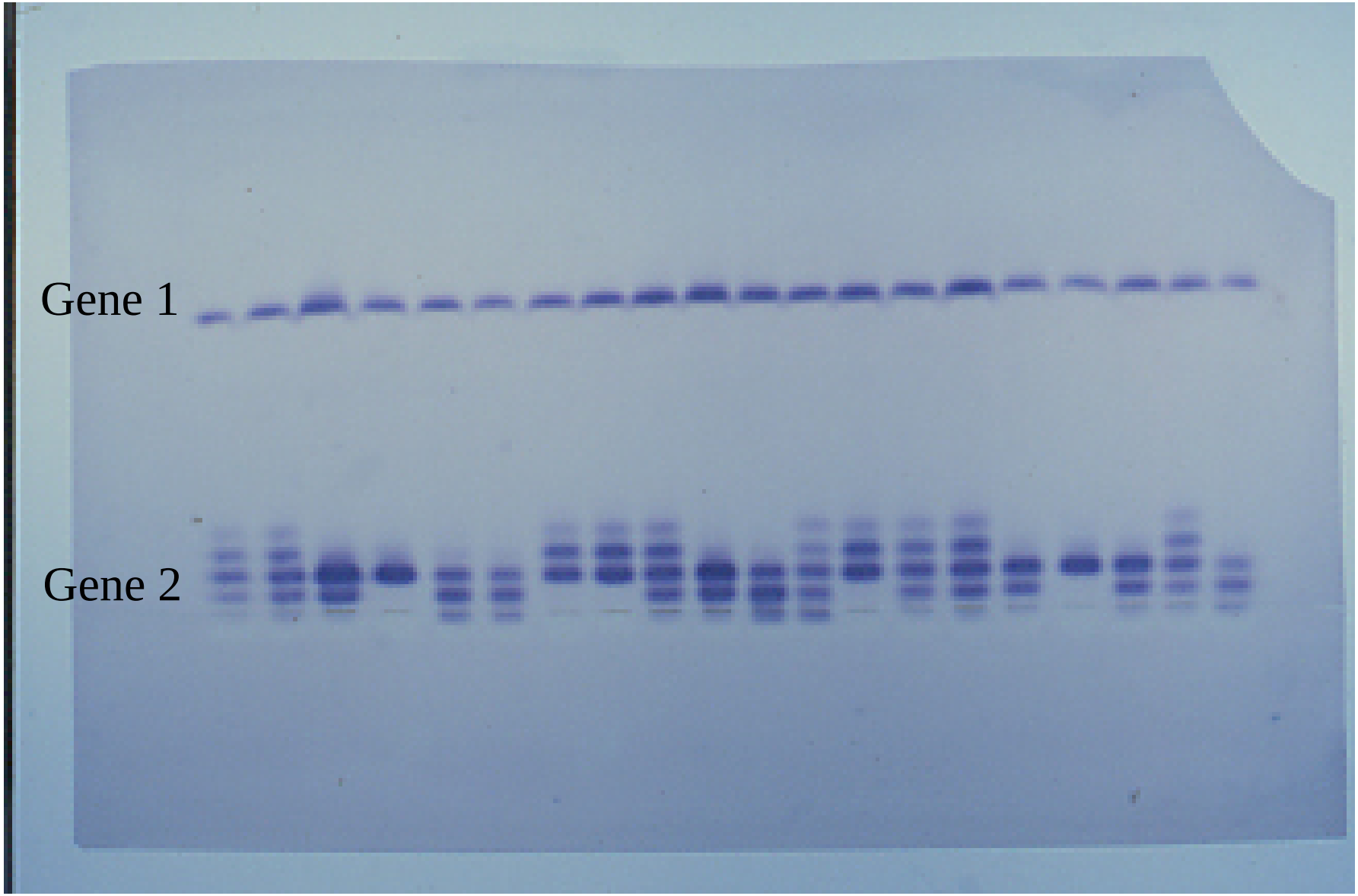
Co-dominance at an isozyme locus (gene for an enzyme)

Alcohol dehydrogenase in pollen of *Asclepias syriaca* (milkweed)

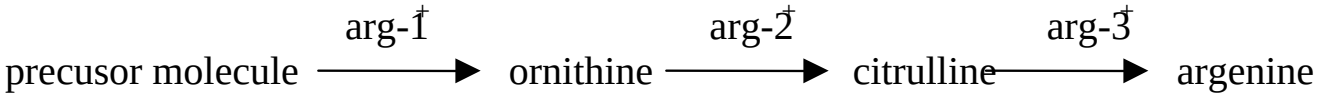
Co-dominance for two alleles for an esterase locus with two alleles



Co-dominance for 3 alleles for a dimeric enzyme,
Glucose phosphate isomerase in autotetraploid *T. subulata*



From this analysis Beadle and Tatum proposed the following biochemical pathway would lead to the correct interpretation of there results:



arg-1 mutant can’t make ornithine
arg-2 mutant can’t make citrulline
arg-3 mutant can’t make argenine

Inferring Gene Interactions

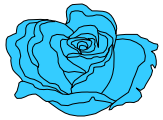
The approach to using a genetic analysis to infer gene interactions involves the following steps:

1. Generate mutants (xrays, uv, EMS etc) for the property you are interested in studying. Use crosses to show that each mutant exhibits single gene inheritance. Describe the phenotypic effect of the mutation.

2. Test these mutants to determine which ones are alleles of the same gene, or represent different genes. Determine the total number of genes affecting the property of interest.

3. Combine the mutations in pairs using crosses to generate double mutants to see if the genes interact. Gene interaction is inferred from the phenotype of the double mutant and the ratios of phenotypes in crosses. Essentially any departure from the simple combination of each single mutant phenotype suggests gene interaction. If the mutant genes interact, then we assume this is also true of the non-mutant or wild type genes.

Complementation test for flower colour

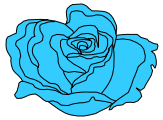
Wild type  Generate 3 independent mutants

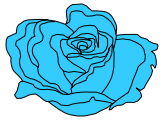
Mutant 1  Mutant 2  Mutant 3 

Crosses reveal each white mutant results from single gene.
That is, if you cross the mutant to wild type, all the F1s are blue.
The F2 all show 3 blue : 1 white ratios.

Now do the complementation tests to determine whether the mutants results from alleles of the same or different genes

Mutant 1  X Mutant 2  → All white 

Mutant 1  X Mutant 3  → All blue 

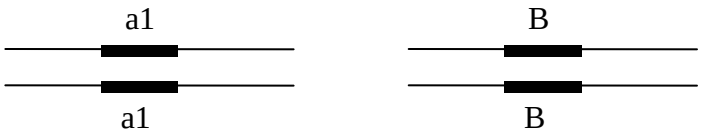
Mutant 2  X Mutant 3  → All blue 

Complementation of flower colour genes in C. rotundifolia

So let's consider our mutant1 and mutant 3.

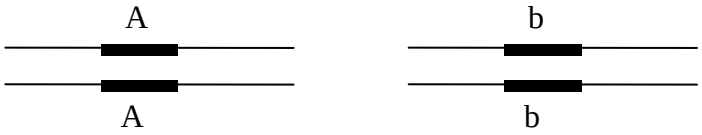
Mutant 1 has a mutation in a gene A making it recessive a1.
Mutant 3 has a mutation in a different gene B, making it a recessive b.

Genotypically our true breeding mutant 1 is a1a1BB (assuming unlinked mutations).



Mutant 1

Genotypically mutant 3 AAbb

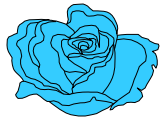


Mutant 3

Now what is the F1 between them?

It is Aa1Bb. Since both mutants are recessive, there is in essence a "functional" copy of each gene so purple pigment and purple flowers are produced.

F1



Lack of complementation for mutants 1&2 indicate mutations are alleles of the same gene

What about mutant 2?

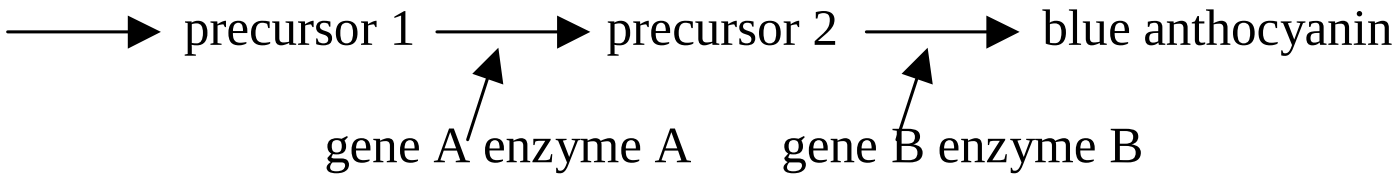
Well the lack of complementation indicates it is an allele of the same gene as mutant 1. So we'll call the mutation a2a2

For it is genotypicall a2a2BB

Mutant1 x Mutant 2 then gives an F1 that is: a1a2BB and is white-flowered.

we presume that both alleles a1 and a2 do not function to produce some product necessary for blue flower colour.

Hypothetical pathway for blue pigment production



The mutations a1, a2, and b all result in a non-functional enzyme so that no blue pigment is formed.

Analyzing double mutants

Once it is established (for example using the complementation test) that two genes are involved we can look for gene interaction by performing and analyzing F2 ratios.

Departures or really, modifications of the 9:3:3:1 ratio provide evidence that the genes interact.

Eg. ratios of 9:7, 12:3:1, 9:3:4

Skin pigmentation in corn snakes

Two genes involved in colour. O- orange; oo no orange pigment

B- black pattern; bb no black

To determine if the genes interact, construct an F2 cross

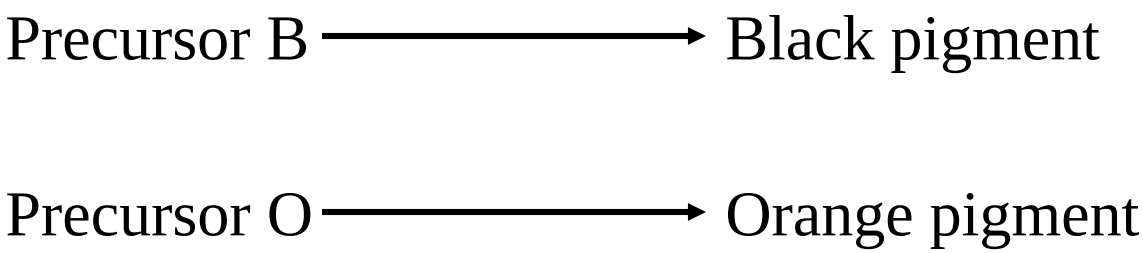
F1 OoBb phenotypically Orange with black colouration called camouflaged

F2

9 O-B- camouflaged
3: O- bb orange with no black patches
3: oo B- no orange with black patches
1: oo bb no black or orange

The 9:3:3:1 ratio indicates genes don’t interact. They colours from each gene **add** up to giving the final colour.

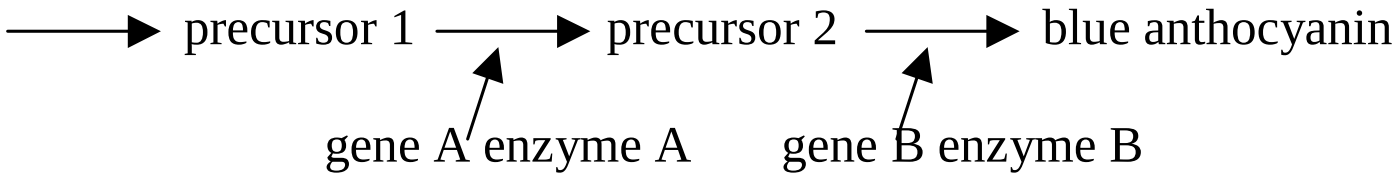
Here the pathways to snake skin colour are independent



If a mutation “knocks out” the black pigment production it doesn’t at all effect orange pigment production, and vice versa

If we return to our flower colour pathway previously

Hypothetical pathway for blue pigment production



The mutations a1, a2, and b all result in a non-functional enzyme so that no blue pigment is formed.

Constructing an F2 between white mutant 1 (a1a1BB and white mutant 3 AAbb

F1 Aa1Bb

F2 Aa1Bb X Aa1Bb

F2 ratios

9 A- B- blue

3 A- bb white

3 a1a1 B- white

1 a1a1 bb white

} 7 white

So here we have gene interaction indicated by 9:7 ratio.
The results are consistent with our linear biochemical pathway for pigment production.

Similar results can emerge for genes with regulatory function.

Regulatory gene R, encodes a protein that binds upstream of a target gene A. The binding results in expression of gene A, which produces a functional protein.

Imagine you had two recessive mutants. In one, the regulatory gene is non-functional, rr. In the other, the target gene is non-functional aa.

Cross RRaa x rrAA, F1 are RrAa and are phenotypically normal.

9 R-A- functional protein - Phenotype normal

3 R-aa no functional protein - Phenotype mutant

3 rrA- no functional protein - Phenotype mutant

1 rraa no functional protein - Phenotype mutant

} 7

Recessive Epistasis: Characterized by an F2 of 9:3:4

One of the recessive mutations (when homozygous) overrides the effect of the mutant allele of the other gene when homozygous.
e.g. Flower colour in *Collinsia parviflora*
Wild type plants are blue flowered WWMM

white mutant wwMM and magenta mutant WWmm

F1 WwMm blue flowered

F2 9 W-M- blue
3 W-mm magenta
3 wwM- white
1 **wwmm white**

} 4

Pathway underlying flower colour may be as follows:

A mutation in gene W knocking out function will not result in formation of the intermediate magenta pigment and hence, no blue pigment can be produced even if there is a functional M gene present.

If the M gene is knocked out, then no blue can be produced

Tristyly in Oxalis. An example of dominant epistasis

short-styled S- --

mid-styled ssM-

long-styled ssmm

F2 gives 12 short : 3 mid : 1 long

Suppressors

A suppressor is a mutant allele of a gene that reverses the effect of a mutation at another gene. That is, a suppressor will restore the normal phenotype

Suppressor mutations can be produced by applying chemical mutagens to a mutant you have already created. You would screen numerous progeny for the restored normal phenotype.

Some of the normal progeny will be the result of the reversion to the normal allele of the original mutation. You don't want those, and can distinguish them using crosses.

You want the non-allelic mutants

In flys, pp gives purple eye colour
ss, at another gene, has no effect alone on eye colour

cross purple eyed fly (ppSS) to normal with the suppressor mutation, PPss (red eyed)

ppSS x PPss
F1 PpSs (red eyed)

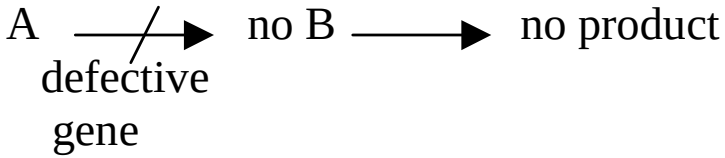
F2 gives 13 : 3 ratio
9 P-S- red
3 P- ss red
3 pp S- purple
1 ppss red due to effect of suppressor

Note, in suppression there are two phenotypes as opposed to 3 for epistasis. Suppressors can be dominant, and can act on dominant mutations, giving different ratios

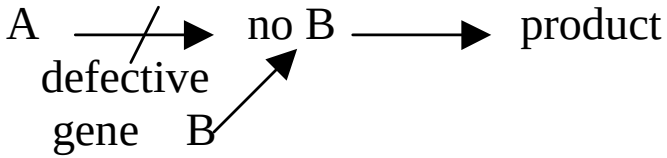
Two possible molecular mechanisms for suppression are as follows:

1. Bypass of block in a biochemical pathway.

No suppressor



With suppressor



Here the suppressor provides the intermediate product B via perhaps a different pathway so that the final product is produced, thus restoring the wild type phenotype.

A second possible mechanism involves mutations first eliminating and then restoring the direct binding of the allele of one gene with the suppressor gene.

Modifiers

As the names implies, these genes modify the phenotype caused by genes at another locus.
They don't cause a new phenotype but
they might make the mutant phenotype more or less severe.

One possible mechanism is a the modifier is a regulatory gene that doesn't completely shut down expression but causes a lower level of expression.

Leaky mutation aa causes low level of expression causing a mutant phenotype
mm mutation in a regulatory gene causes a reduction in expression levels causing a more severe phenotype

aaMM (leaky mutant) x AAmm (inefficient or down- regulation)

A-M- ("normal" phenotype)

A-mm defective due to low transcription showing mutant-like phenotype

aaM- defective due to defective protein produced by leaky a-allele giving mutant phenotype

aamm more defective due to both leaky a allele and low transcription giving a more severe phenotype

SYNTHETIC LETHALS

When two mutants on their own are viable, but when combined together they result in lethality, they are called synthetic lethals.

Yield F2 ratios of 9:3:3 since the double homozygous recessive results in lethality.

Mechanistically, if one mutation is leaky providing sufficient product to be viable, and the second gene is in the same pathway and is also leaky.
However, if the mutations are put together, not enough product is produced and this results in lethality .

PENETRANCE AND EXPRESSIVITY

Incomplete penetrance

This describes the situtation where an individual of an appropriate genotype does not show the associated phenotype

E.G. Imagine the genotype, pp, has some phenotype it causes, but only 70% of individuals with the pp genotype show this phenotype. Then we'd say there is incomplete penetrance or that the p allele exhibits 70% penetrance.

The causes of incomplete penetrance are complex.
1. It could be the expression is environmentally determined.
2. Other interacting genes may be involved.
In part, it might reflect our incomplete knowledge of the genetics of the particular system, or its environmental determinants.

Variable Expressivity

This measures the degree to which some allele is expressed at the phenotypic level. So, there could be various shades of light to dark blue flower colour. Again the causes of the variability are unknown and may be environmental or genetically determined (or both).