This is a single gene trait. The coloration of the flowers depends on the:
- production of the appropriate anthocyanin pigments
- presence of metal ions and co-pigments
- the vacuolar pH in epidermal cells

These wild-type (b) and mutant (a) morning glories produce exactly the same anthocyanin pigment in their petals. The phenotypic difference in the two plants is due to a single gene difference: the flower on the left has a recessive, loss-of-function mutation in a gene that codes for a Na\(^+\)/H\(^+\) exchanger. This mutation results in a decrease in the vacuolar pH of epidermal cells causing the petals to appear purple rather than blue.

Using genetical conventions, we would name the gene defined by this phenotypic variation the **purple gene** and assign the following allele symbols: \(p^+ = \text{blue} \quad p = \text{purple}\)

a. vacuolar pH = 6.6
b. vacuolar pH = 7.7
The art and genetics of color
in plants and animals
Are these examples of color variation single gene traits? In other words, can a single gene (perhaps with multiple alleles and complications to dominance) explain color variation in budgie parakeets or in bell peppers?
The table below shows the results of crossing true-breeding lines of green, blue, yellow and white budgies.

<table>
<thead>
<tr>
<th>parents</th>
<th>Green</th>
<th>Blue</th>
<th>Yellow</th>
<th>White</th>
</tr>
</thead>
<tbody>
<tr>
<td>Green</td>
<td>green</td>
<td>green</td>
<td>green</td>
<td>green</td>
</tr>
<tr>
<td>Blue</td>
<td>green</td>
<td>blue</td>
<td>green</td>
<td>blue</td>
</tr>
<tr>
<td>Yellow</td>
<td>green</td>
<td>green</td>
<td>yellow</td>
<td>yellow</td>
</tr>
<tr>
<td>White</td>
<td>green</td>
<td>blue</td>
<td>yellow</td>
<td>white</td>
</tr>
</tbody>
</table>

**Possibilities:**
- One gene: four alleles; dominance complete
- One gene: three alleles; some incomplete dominance
- Two genes: two alleles; dominance complete
- Three or more genes

Number of genes? Number of alleles?
P  true-breeding yellow X true-breeding blue

\[\downarrow\]

F1  green X F1 green

\[\downarrow\]

F2  9/16 green  3/16 blue  3/16 yellow  1/16 white

*How many genes involved?*

*Speculate about genotypes using elementary principles of combining colors*
**Additive Gene Effects**

- independent, additive contribution to phenotype: effects of the alleles of the two loci are essentially the sum of the independent gene actions
- unmodified Mendelian ratio: \( \text{AaBb} \times \text{AaBb} \rightarrow 9:3:3:1 \) (two genes; each gene has two alleles, complete dominance)
- essentially there is no gene interaction – the genotype at one gene locus doesn’t affect the expression/function of the alleles at a second gene locus

Yellow and blue pigments are synthesized in independent biochemical pathways. A (mutational) disruption in one pathway does not affect the other pathway
See also this beautiful example of additive gene effects in corn snakes (pg 240 in Chapter 6 of text):

Two genes independently controlling the synthesis of two different pigments; each gene has two alleles showing complete dominance
Polymorphic Determinants of Drug effects

- **Drug metabolizing enzymes, DMEs** (Phase I enzymes/Cytochrome P450 enzymes, e.g. CYP2D6; Phase II enzymes, e.g. N-acetyl transferases)
- **Drug transporters** (Solute Carrier (SLC)- and ATP Binding Cassette (ABC)-transporters, e.g. organic cation transporters, OCTs, as members of the SLC family)
- **Drug receptors** (ligand controlled ion channels or class 1 receptors, e.g. glutamate receptor; G-protein coupled receptors (GPCRs) or class 2 receptors, e.g. β-receptor; enzymatic receptors, e.g. insulin receptor; receptors regulating gene expression, e.g. steroid hormone receptor)
- **G-proteins**, e.g. GNAS1 or GNB3
In this hypothetical example (next page) there are two genes that influence the therapeutic effect of a particular drug.

Each gene has two alleles that show incomplete dominance.

**Gene Functions**

1. One gene is involved in **metabolizing the drug** (for eventual excretion) – see previous lecture notes on the CYP genes
2. The second gene codes for a **receptor protein** via which the drug exerts its therapeutic effect

**NOTE:** not addressed in the following example is the potential role of genetic polymorphisms in drug transporters. Although passive diffusion accounts for cellular uptake of some drugs and metabolites, increased emphasis is being placed on the role of membrane transporters in absorption of oral medications across the gastrointestinal tract; excretion into the bile and urine; distribution into “therapeutic sanctuaries,” such as the brain and testes; and transport into sites of action, such as cardiovascular tissue, tumor cells, and infectious microorganisms.
If the therapeutic effects of the two genes are strictly additive, we should see nine phenotype categories.

Note, though, the effects of the mm receptor genotype. It determines the % therapeutic effect independent of the metabolism genotype.
**Additive gene effects:**
- independent, additive contribution to phenotype: effects of the alleles of the two loci are essentially the sum of the independent gene actions
- unmodified Mendelian ratio: \(AaBb \times AaBb \rightarrow 9:3:3:1\)
- no interaction of the alleles – the genotype at one gene locus doesn’t affect the expression/function of the alleles at a second gene locus

**Gene Interactions:** Specific alleles of one gene mask or modify (enhance, suppress or in some way alter) the expression of alleles of a second gene
- complementary gene action
- epistatic gene interaction
- modifiers & suppressors
Coat color and type are essential characteristics of domestic dog breeds. Although the genetic basis of coat color has been well characterized, relatively little is known about the genes influencing coat growth pattern, length, and curl. We performed genome-wide association studies of more than 1000 dogs from 80 domestic breeds to identify genes associated with canine fur phenotypes. Taking advantage of both inter- and intrabreed variability, we identified distinct mutations in three genes, RSPO2, FGF5, and KRT71 (encoding R-spondin–2, fibroblast growth factor–5, and keratin-71, respectively), that together account for most coat phenotypes in purebred dogs in the United States. Thus, an array of varied and seemingly complex phenotypes can be reduced to the combinatorial effects of only a few genes.

See Figure on the next page: What type of gene interaction is seen here?
- represents ancestral allele (found in wolves)

+ = variant allele

3 genes, 2 alleles (complete dominance)

7 out of 8 combos are shown here

Which is missing?

<table>
<thead>
<tr>
<th>PHENOTYPE</th>
<th>FGF5</th>
<th>RSPO2</th>
<th>KRT71</th>
</tr>
</thead>
<tbody>
<tr>
<td>A Short</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>B Wire</td>
<td>-</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>C Wire and Curly</td>
<td>-</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>D Long</td>
<td>+</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>E Long with Furnishings</td>
<td>+</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>F Curly</td>
<td>+</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>G Curly with Furnishings</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
</tbody>
</table>

**Fig. 3.** Combinations of alleles at three genes create seven different coat phenotypes. Plus (+) and minus signs (−) indicate the presence or absence of variant (nonancestral) genotype. A characteristic breed is represented for each of the seven combinations observed in our data set: (A) short hair; (B) wire hair; (C) "curly-wire" hair; (D) long hair; (E) long, soft hair with furnishings; (F) long, curly hair; and (G) long, curly hair with furnishings. [Photos courtesy of M. Bloom (Copyright AKC)].