Massimo A. Picardello
Universita' di Roma "Tor Vergata"
Dipartimento di Matematica
00133 Roma, Italy

Feline Genetics: a Combinatorial Approach with a few genomic insights
Massimo Picardello

Introduction: combinatorial models for feline genetics. These notes, originally written before the genoma mapping, are aimed to give a simplified and synthetic account of feline genetics, where biological and biochemical prerequisites are reduced to a minimum. Since most of our approach is combinatorial, we take the liberty of choosing our own names for the genes, often different from the choice made by the geneticists – indeed, we need large tables, and they cannot be fitted in a page unless we choose short names for the genes. Only in a few instances, related to scientific findings subsequent to the genoma mapping and correcting some previous combinatorial approaches, we'll give some (very sketchy and inaccurate) biochemical hints, namely, for the action of the white (KIT), agouti, albino, tabby, ambe (Extension), golden (Corin) and sphynx/rex (KRT71) genes. In these instances we shall also include the scientific names of the genes and loci, and some mention of the bibliographic reference; on the other hand, we shall also include bibliographic references to old papers or books that go back to the euristic, phenotypical studies of the pre-genoma mapping times.

Our combinatorial goal is achieved by systematically using Mendelian models of genetic transmission, based on one or few "principal" genes acting sharply instead of gradually: their effect shows up completely or not at all, according to which variant *(allele)* of the gene is considered. So, rather than DNA proteins, we shall have the combinatorics of symbols, standing for genes. Please be warned that the mathematical models are aimed to explain the Mendel tables: the symbols may or may not correspond to real genes (and often, as already remarked, they do not correspond to the names usual in scientific literature), and in all cases lead to oversimplification of the true biological complexity, which relies not only on principal genes, but also on a multitude of modifying genes. Each modifier has a minor effect which piles up with the others, yielding a more gradual combined result than a unique gene could account for. Sometimes we shall present two alternative mathematical models to explain the same effect. If the two models give the same effect in all cases, they are mathematically equivalent, although not biochemically, and it will be irrelevant to us which of them is "biologically true" (probably none: biology tends to be more complex!). On the other hand, sometimes different models are not quite equivalent, because the statistical frequency of their effects after many generations may not be the same. This is usually the case when comparing a model based on a single Mendelian gene with another based on a group of modifiers. In order to choose the one which has a better fit with experimental evidence one needs an extensive database of experimental results. We shall limit our attention to simplified models which do not claim a refined overall precision, but are simple to discuss and work well within reasonable levels of approximation.

The following hints are our only biological prerequisites. Each cell contains a nucleus, enclosed in a membrane. The nucleus carries inheritance information, codified biochemically in certain helicoidal protein filaments called chromosomes. Suitable segments of these filaments

carry individual genetic traits, and are called *genes*. The position of a gene in its chromosome is called *locus*. The cat has 19 pairs of chromosomes, for a total number of 38. The two chromosomes in a pair are said to be *homologous* (that is, similar). The gene at corresponding loci in homologous chromosomes act on the same genetic trait. If they are identical, then their action is the same; otherwise, it may be different. Different genes at the same locus in homologous chromosomes are called *alleles*.

There are two ways in which a cell can duplicate. In the first, called mitosis, the membrane of the nucleus breaks, the chromosome align themselves at the center of the cell and each of them creates an equal copy of itself same (except rare errors of biochemical transcription, important to explain mutations and genetic recombinations). Each identical pair then separates, and the two constituent chromosomes migrate to the opposite heads of the cell. This gives rise to two identical groups of 38 chromosomes at the opposite sides of the cell. Now the cell separates into two new cells identical to the starting one. This is the mechanism of duplication with which biological tissues grow.

But the interesting mechanism of duplication is another, tied up to fertilization. Here cells undergo a different duplication process, called meiosis, that transforms it in two new cells, not equal and not identical to the original. They are called germinal cells. Each germinal cell is endowed with only 19 chromosomes, one for each homologous pair: half of the genetic patrimony. Meiosis works in the following way. Also in this case the starting point is the breakup of the nucleus' membrane, and the alignment of the 38 chromosomes at the center of the cell. Now, however, homologous chromosomes keep close (so close that they may exchange chemical fragments, an important process which gives rise to genetic recombinations). At this point, one of the two chromosomes of each pair migrates to an end of the cell and the other to the opposite end: which goes where is random. When this process is completed, at one end there are 19 chromosome and at the other there are their homologous chromosomes, but the selection is random. Now, as in the mitosis, the cell splits in two cells, each of which possesses only 19 chromosome. They are germinal cells: they can merge with those of a partner after mating, to give rise to an usual cell with 38 chromosome in 19 pairs. The resulting cell is called fertilized: it is the first cell of a new kitten. Therefore each pair of chromosomes of the fertilized cell consists of a chromosome from the germinal fatherly cell and one from the maternal one.

This leads to the fundamental principle of genetic inheritance: the hereditary transmission of each genetic trait is due to the fact that the fertilized cell is endowed with a pair of alleles, one from each parent. The expression of the genetic trait depends on which alleles are transmitted to the fertilized cell, and if they are equal *(homozygosis)* or different *(heterozygosis)*. Often, among two alleles known to produce different effects on the same genetic trait, one predominates on the other and imposes its effect: it is called a *dominant* gene, while the other is called *recessive.*

Eumelanistic colors without maltese dilution (black, chocolate, cinnamon). We start by introducing the **B** gene, responsible for black pigmentation of the coat. More precisely, the **B** gene forces the pigment-producing cells at the root of the hairs to release a pigment called eumelanin, consisting of spherical molecules whose physical effect is to paint the hair black. The rate of eumelanin production depends on temperature: at lower temperature, the coat will be painted with more intense black. This is why in many long-haired blacks the color is paler at the base (in the warmer region closer to the body), and in blacks with very short hair (Devon Rex for instance) the color is darker on the *points* (face, ears, tail and legs), areas far away from the large heat-producing muscle bundles.

The **B** gene has a recessive b allele. This allele induces a deformation of the pigment

particles, which become longer and oval. The result is chocolate pigmentation. There is another allele, $\mathbf{b^l}$, which produces an even paler color: cinnamon. The gene **B** is dominant over the other alleles, and b is dominant over $\mathbf{b^l}$. Consider mating a cat which is homozygote **BB** to another which is homozygote **bb**. Let us fill a table whose rows correspond to the possible genes in the sperm cell, and the columns correspond to the ovulus genes. Each entry in the table determines a possible phenotype of the offspring (all equally likely). It is readily seen that all the kittens are phenotypically black, but carriers of chocolate:

	B	*B*
b	Bb	Bb
b	Bb	Bb

Let us now consider the cats obtained by the previous mating: what happens when they breed? In the second generation one has:

	B	*b*
B	BB	Bb
b	Bb	bb

Therefore, the new kittens are homozygotic black with probability 1/4, heterozygotic black (carriers of chocolate) with probability 1/2, and chocolate with probability 1/4. This does not mean that each litter will consist of 75% blacks and 25% chocolates: however, this is the most likely statistical distribution after many litters.

Finally, let us consider the case **Bb** x $\mathbf{Bb^l}$

	B	*b*
B	BB	Bb
b^l	Bb^l	bb^l

With the same probability (25%) the kittens are homozygotic blacks, blacks carrying chocolate, blacks carrying cinnamon or chocolates carrying cinnamon.

>   ***Problem.***   *1. A black queen has a chocolate kitten. What are the possible colors of the sire? (Do not consider colors which have not been introduced yet)*
>   *2. If the kitten is black and the queen chocolate, what are the possible colors of the sire?*

Diluted eumelanistic colors (blue, lilac, fawn). All the colors considered so far exist in a diluted version, caused by the action of the maltese dilution gene, which is denoted by **d**. The dominant allele **D** does not yield any dilution, but the recessive allele **d** gives rise to a different distribution in space of the pigment particles, whose visual effect is a lower color intensity. Then black is transformed into blue (that is, gray with bluish hue), chocolate becomes lilac and cinnamon becomes fawn (a very pale color, vaguely resembling cream, but without any rufousing).

The **d** gene changes the pigment particles' arrangement, not their shape. Therefore, it acts upon a genetic trait different from shape (spherical or elongated). Indeed, it is at a locus different from **B**. Therefore these two genes, **B** and **d**, interact as independent genes. The next table shows the outcome of a breeding of a blue cat **BBdd** to a black carrying dilution (**BBDd**; we shall often

use the expression *black carrying blue*). Statistically, half of the kittens are black carrying blue, the others are blue.

	BBd	*BBd*
BBD	BBDd	BBDd
BBd	BBdd	BBdd

In general, the interaction of two independent genes may need tables with four rows (corresponding to the genetic content of the mother's gametes) and four columns (for the father's gametes). For instance, let us consider the breeding of a black carrying chocolate and blue (**BbDd**) to a blue carrying fawn (**Bb^{l}dd**):

	BD	*Bd*	*bD*	*bd*
Bd	BBDd	BBdd	BbDd	Bbdd
Bd	BBDd	BBdd	BbDd	Bbdd
b^{l}d	Bb^{l}Dd	Bb^{l}dd	bb^{l}Dd	bb^{l}dd
b^{l}d	Bb^{l}Dd	Bb^{l}dd	bb^{l}Dd	bb^{l}dd

As we can see, 3/8 of the kittens have black phenotype (carrying various colors), 3/8 blue, 1/4 chocolate, 1/4 lilac, but no cinnamon or fawn.
Please observe that in this table the four rows are pairwise identical. Therefore, a two by four table (one with two rows and four columns) would have been enough.
This is so because the blue is chosen to be homozygotic with respect to the d allele. A full 4 by 4 table is required for the breeding of two blacks both carrying chocolate and blue (**BbDd**). We leave this case to the reader.

> **Problem.** *A blue queen has a lilac kitten. What are the possible colors of the sire, and which colors may he carry? (Please disregard any color not discussed yet).*

> **Problem.** *1. What are the possible colors of the kittens of a black carrying only blue and of a homozygotic blue, and what are their probabilities?*
> *2. What are the possible colors of the kittens of a homozygotic blue and a homozygotic chocolate, and what are their probabilities?*

Note. The last problem shows that the kittens of a blue and a chocolate may be black. At first glance, this is surprising, because black is dominant over both blue and chocolate. But there is no mistake: the chocolate gene and the maltese dilution gene are at different loci, and so they interact as independent genes.

Pheomelanistic colors (red, cream) and sex-linkage (tortie, blue-cream). Mendel's laws of genetics deal with genes with sharp effect: either the genetic trait shows up completely or not at all. The color genes considered so far behave this way.
A typical sharp genetic trait is sex: either male or female. However, gender cannot be determined by only one gene. If so, one sex would be genetically dominant over the other (a partial dominance would cause all individuals to be hermaphrodite). Therefore, after just one generation, all individuals would belong to the same gender, and the species would be extinguished.
Indeed, the genetic root of gender is not one gene, but a whole chromosome. One of the pairs of

chromosomes may consist of two chromosomes not quite similar. One is larger, and approximately shaped as an X. The other, smaller, lacks a leg of the X: it is shaped roughly as a Y. The chromosomic patrimony of a male contains a pair XY. In a female there are two X chromosomes: XX. Thus, the genetic effect is sharp but without dominance of one gender over the other. Moreover, the following table shows that another necessary requirement for species survival is satisfied: the probability that an individual be male or female is the same.

	X	Y
X	XX	XY
X	XX	XY

females males

On the other hand, since the Y chromosome lacks a leg of the X chromosome, in a male the genes whose locus is on this leg do not come in pairs, that is, lack their allele. This facts changes their hereditary transmission scheme. These genes are said to be *sex-linked.*

One of the color genes is sex-linked. It is the orange gene, **O**, which transforms the black pigment (eumelanin) particles, approximately spherical, into different pigment particles (phaeomelanin), much more elongated. This pigment is responsible of the deep intense red color of show cats (and several yellowish variants in cats whose lines did not undergo any selection, like stray cats for instance). Its allele **o** does not change eumelanin into phaeomelanin (it does nothing). In principle, the genotypes **BO**, **bO** e **b^{l}O** might produce three different hues of red, paler and paler, and sometimes one can perhaps distinguish among their phenotypes. But the difference is so slight that one prefers not to make this distinction: all these variants of red will be jointly denoted as "red". Similarly, the corresponding maltese dilutions are merged into one color, cream.

The orange gene is somewhat peculiar. It is sex-linked: a male can be either **o** (eumelanistic phenotype) or **O** (red or cream), but not both. However, a female may be **oo** (eumelanistic), **OO** (red or cream) or **Oo**. It is in the last case that the second peculiar aspect shows up. The **O** allele is not dominant over **o**. The genotype **Oo** does not yield red or cream females. Instead, in the pigment producing cell (melanocyte) at each hair's base only one of the two orange alleles belonging to the two X chromosomes is activated. The other is disactivated, and produces no effect. Therefore, the **Oo** females have some red/cream hairs and some black/blue hairs (or their lighter versions). Which of the two alleles is activated is determined at random; but once the choice is made for a melanocyte in the embryo, subsequent duplications of the same cell are likely to yield the same choice. It follows that, if the color information in the embryo stops at an early phase of the growth, there will be distinct wide patches of black and red (or their diluted versions). In other words, activation in all the somatic cells takes place in a short period of time during early development. If this period of time is very early, when there are still few somatic cells, then the following duplications of a cell where the **O** allele is activated preserve the same choice, and similarly for **o**. The typical gene responsible for stopping the flow of information along the neural crest at early phases of embryo growth is the White gene (also responsible for white spotting: see the chapter on Epistasis later on). Therefore torties with white we usually see large red and black patches (or their various dilutions). But if activation of some melanocytes takes place later, typically if there is no white spotting gene, then the two colors are finely mingled. These phenotypes are called *black tortoiseshell* (or *tortie*), or chocolate tortie, or cinnamon tortie; the diluted versions are called blue tortie, lilac tortie or fawn tortie (in some associations the latter colors are called blue cream, lilac cream and fawn cream, respectively).

We have already pointed how that the hereditary transmission of sex-linked genes is different. Indeed, the independent interaction scheme of the two alleles is changed, as we now

show. The usual table,

	O	O
O	O O	O O
o	O o	O o

is now *wrong.* Instead, one has

	O	-
O	O O	O -
o	O o	o -

because males do not have the **OO** genotype. A red male has just one allele, **O**. For the sake of clarity, we replace the missing allele by a dash. Thus, if there are no maltese dilution nor chocolate/cinnamon lighter alleles, a tortie female mated to a red male produces, with equal probability, red or tortie female kittens and red or black male kittens. We can summarize this as a rule: for sex-linked traits, male kittens get the trait (in this case, color) only from their dam, but female kittens get it from both parents in equal proportions.Here is a complex example: a breeding of a black sire carrying chocolate and maltese dilution (**BbDdo-**) to a bluecream dam carrying fawn (**Bb^{l}ddOo**):

	BDo	Bdo	bDo	bdo	BD -	Bd -	bD -	bd -
BdO	BBDdOo	BBddOo	BbDdOo	BbddOo	BBDdO-	BBddO-	BbDdO-	BbddO-
BdO	BBDdOo	BBddOo	BbDdOo	BbddOo	BBDdO-	BBddO-	BbDdO-	BbddO-
b^ldO	Bb^{l}DdOo	Bb^{l}ddOo	bb^{l}DdOo	bb^{l}ddOo	Bb^{l}DdO-	Bb^{l}ddO-	bb^{l}DdO-	bb^{l}ddO-
b^ldO	Bb^{l}DdOo	Bb^{l}ddOo	bb^{l}DdOo	bb^{l}ddOo	Bb^{l}DdO-	Bb^{l}ddO-	bb^{l}DdO-	bb^{l}ddO-
Bdo	BBDdoo	BBddoo	BbDdoo	Bbddoo	BBDdo-	BBddo-	BbDdo-	Bbddo-
Bdo	BBDdoo	BBddoo	BbDdoo	Bbddoo	BBDdo-	BBddo-	BbDdo-	Bbddo-
b^ldo	Bb^{l}Ddoo	Bb^{l}ddoo	bb^{l}Ddoo	bb^{l}ddoo	Bb^{l}Ddo-	Bb^{l}ddo-	bb^{l}Ddo-	bb^{l}ddo-
b^ldo	Bb^{l}Ddoo	Bb^{l}ddoo	bb^{l}Ddoo	bb^{l}ddoo	Bb^{l}Ddo-	Bb^{l}ddo-	bb^{l}Ddo-	bb^{l}ddo-

The left half of the table contains the genotypes of female kittens (two orange alleles!). It is readily seen (in the bottom of this half of the table) that 3/16 are black (carrying various colors), 3/16 blue, 1/16 chocolate, 1/16 lilac, but none is cinnamon or fawn. In the top part, one has the corresponding tortie colors: 3/16 are black torties, 3/16 blue torties, 1/16 chocolate torties, 1/16 lilac torties, but none are cinnamon torties or fawn torties. The right half of the tables contains the genotypes of male kittens. Again, the bottom part yields the probabilities of eumelanistic male kittens: 3/16 black (carrying various colors, as above), 3/16 blue, 1/16 chocolate, 1/16 lilac. The top part yields the same proportions for thepheomelanistic males. However, we identify the different red (or cream) genotypic variants, and this fact now yields equal proportions: 1/4 red, 1/4 cream.

Problem. *A tortie kitten has a black sire. What can be the color of the dam, and which color genes can she carry? (Please disregard any color not discussed yet).*

Modifiers of maltese dilution: caramel and apricot colors. Evidence coming from Birman

breeders reveals the existence of a gene that modifies the maltese diluted colors, making them rufoused and giving them a metallic sheen (particularly visible on tabbies). There is no genetic evidence of these color variants, only phenotypic: in other words, these principal genes may not exist at all, and their phenotypes may be color variants due to the pile-up action of several modifier polygenes. This phenotype appears to be the consequence of a dominant gene **Dm** at a different locus than the maltese dilution locus (hence acting independently). When it acts upon eumelanistic diluted colors (blue, lilac and fawn), **Dm** produces the corresponding caramel colors; on pheomelanistic, it produces apricot. The recessive allele **dm** does not modify the usual colors. Presumably the gene acts both on the shape of the pigment particles and on their packing.

Caramel lynx point Birman based on blue

For many photographs of caramel and apricot colors in Birmans, Burmese, Devon Rex, Oriental Shorthair, Siamese, Australian Mist and household pets, see http://www.catagility.com/Dm.htm, by Lesley Morgan Blythe.

Clearly, the combinatorics is analogous to the maltese dilution: for instance, the breeding of two cats with genotype **BBddDmdm** yields 75% of caramel based on blue and 25% blue.

Problem: *show that from two cats of genotype **BbddDmdm** we obtain 9/16 caramel based on blue, 3/16 caramel based on lilac, 3/16 blue and 1/16 lilac.*

Epistasis: white and white spotting. In section 2 we studied an instance of dominance: the black gene **B** is dominant over its chocolate allele **b**. Dominance means that, among two alleles of the same gene, one imposes its effect on the other in the phenotype. On the other hand, we encountered some genes that modify phenotypic traits usually controlled by other genes at a different locus. For instance, the orange gene **O** transforms black color into red, and the maltese dilution gene d transforms black into blue and red into cream. Sometimes, one says that black is dominant over blue, but this is not quite right: the gene that is dominant over d is not **B**, it is **D**. The effect of d overlaps and changes that of **B**. This phenomenon is called *epistasis.* Similarly, the epistatic action of **O** over **B** and its alleles is the transformation of eumelanin into phaeomelanin.

The white gene

Transmission of white is due to the **W** gene, which produces complete depigmentation of all the body. This results into entirely white coat, with pink nose leather and paw pads. Eye color may be affected. If so, then one or both eyes are blue or pale blue, and the cat might be deaf on the corresponding side. The fully recessive allele **w** does not cause depigmentation, it allows full color. There is another allele **w^m** recessive to **W**, that gives rise to colors with white spots: various combinations of **w^m** and **w** yield wider or smaller areas of white. Once again, these symbols are not the usual choice of geneticists: the locus responsible for white is normally called

KIT – but this name is too long for our tables. The gene **W** is epistatic over all color genes. Since **W** is epistatic, all kittens of a homozygotic white are white. On the other hand, a heterozygotic white mated to any solid colored cat other than white has white and non-white kittens with equal probabilities, as can be seen from the following table that shows the offspring of a heterozygotic white **Ww** and a solid **ww**:

	W	*w*
w	Ww	ww
w	Ww	ww

whites

Previously, the piebald spotting was thought to be the consequence of a gene **S** at a different locus. This view was changed by genetic research on the DNA of cats, specifically at the so-called KIT locus, published in 2014 in <u>G3 (Bethesda).</u> 2014 Aug 1;4(10):pages 1881-91, by M.A. David, M. Menotti-Raymond and several other authors.

Let us consider an example in full detail: the breeding of a heterozygotic white male carrying homozygotic black and heterozygotic white with genotype **Ww BB o- DD** to a tortie and white female heterozygotic for piebald spot and carrying maltese dilution (**wᵐw BB Oo Dd**). We skip the **B** locus in the table because it is irrelevant: both parents are homozygotic **BB**, and so all their kittens are like that. The left half of the table contains the genotypes of the white kittens (50%). The upper part of the right half and the left half of the remaining quarter contain the genotypes of the white spotted kittens (37.5%). The remaining 4 by 2 block in the lower right corner refers to the kittens without white: half of them are black, 1/4 are red and 1/4 are tortie (females).

	WSoD	*WS - D*	*WsoD*	*Ws - D*	*wSoD*	*wS - D*	*wsoD*	*ws - D*
wSOD	WwSSOoDD	WwSSO-DD	WwSsOoDD	WwSsO-DD	wwSSOoDD	wwSSO-DD	wwSsOoDD	wwSsO-DD
wSOd	WwSSOoDd	WwSSO-Dd	WwSsOoDd	WwSsO-Dd	wwSSOoDd	wwSSO-Dd	wwSsOoDd	wwSsO-Dd
wSoD	WwSSooDD	WwSSo-DD	WwSsooDD	WwSso-DD	wwSSooDD	wwSSo-DD	wwSsooDD	wwSso-DD
wSod	WwSSooDd	WwSSo-Dd	WwSsooDd	WwSso-Dd	wwSSooDd	wwSSo-Dd	wwSsooDd	wwSso-Dd
wsOD	WwSsOoDD	WwSsO-DD	WwssOoDD	WwssO-DD	wwSsOoDD	wwSsO-DD	wwssOoDD	wwssO-DD
wsOd	WwSsOoDd	WwSsO-Dd	WwssOoDd	WwssO-Dd	wwSsOoDd	wwSsO-Dd	wwssOoDd	wwssO-Dd
wsoD	WwSsooDD	WwSso-DD	wWwssooDD	Wwsso-DD	wwSsooDD	wwSso-DD	wwssooDD	wwsso-DD
wsod	WwSsooDd	WwSso-Dd	WwssooDd	Wwsso-Dd	wwSsooDd	wwSso-Dd	wwssooDd	wwsso-Dd

By now, the reader should be able to complete the tables for typical breedings of cats with **S** and **W** genes, as in the following problems. Hopefully, he should also be able to find the answers without explicitly writing down the full tables.

Problem. *The litter of a fawn dam consists of a white and two bicolors, lilac/white and fawn/white respectively. What are the possible colors of the sire, and which color genes can he carry? (Please disregard any color not discussed yet).*

Problem. *1. What are the colors of the kittens (and their probabilities) when a*

blue/white homozygotic for blue and heterozygotic for piebald spotting is mated to a lilac/white homozygoic for lilac and heterozygotic for piebald spotting?

2. How would you answer the previous question if the blue/white cat, instead of being homozygotic for blue, carries also lilac?

The piebald spotting gene (in reality, an allele of the white gene)

We shall now study two other instances of epistasis. The first is related to the piebald pot gene **S**, which was believed to exist until 2010, to give rise to complete lack of hair pigment in specific areas of the body. In 2014, Victor David and others published an article in G3 (Genes|Genomes|Genetics), that presented their genetic research that proves that the White gene and the Piebald Spotting gene are actually variants at the same locus, called the KIT locus. In the next pages, the piebald spotting gene can be identified with what we denoted by $\mathbf{w^m}$ in the previous Section. But, in order to keep attention focused onto the white spotting, in this Section we abuse of notation and adopt a different symbol, **S**, for the piebald spotting gene. This allows us to stress the fact that this gene is dominant over the allele **S** that produces no white (by using a capital letter as symbol), although it is not the fully dominant allele at the KIT locus (indeed, this is the White gene **W**)

The allele **S** is epistatic over all color genes that we have studied so far, and to all the others that we shall introduce later with the only exception of the white gene **W** explained in the previous Section, which produces complete hair depigmentation over all of the body. Actually, if the areas where the piebald spot gene **S** acts are covered by coat, then the coat is white, but also the skin is depigmented there. Therefore, if these areas have no hair, as in the case of the nose leather or the paw pads, then the leather is depigmented, that is, pink. Moreover, if in the beginning phase of somatic cell duplication the gene **S** acts on the cells which give rise to the eye tissue, then depigmentation may yield blue or pale blue eye color when the eye growth is completed. Of course, it may happen that one eye is blue while the other is normally colored. Near the eye tissue cells there are the ear tissue cells: often the ear on the side of the blue eye is malfunctioning, up to deafness. The recessive allele **s** does not cause depigmentation, it allows full color everywhere.

The following table applies, for instance to a breeding of a black cat to a black and white heterozygotic **Ss**. Half of the kittens are black and white, half are black. The reader should complete the table by taking into account the **B** gene.

	S	*s*
s	Ss	ss
s	Ss	ss

The **S** gene has a wide range of effects, from a tiny white spot *(white button, locket)* to white almost all over the body, as in the harlequin and van distributions. The range of action is gradual, and it is partially due to polygenes. But recent studies show that homozygotic **SS** cats have more white than heterozygotic **Ss**, for instance the Van pattern. We shall return to this soon, when we introduce other alleles of **S**, in order to explain the different white patterns of Ragdolls.

The Birman gloved pattern gene

It is important to observe that the **S** gene controls the genetic transmission of white spots, but not their sizes and positions. It is not clear if the position of the spots is entirely controlled by genetic transmission. Undoubtedly, some common white spot distributions are often passed to the kittens. This happens, for instance, to the mitted pattern of the Birmans and Ragdolls, and to the inverted V shape on the face of the cats with bicolor distribution. Indeed, geneticists have debated if the mitted pattern is caused by a specific gene, either an allele of **S** or a completely different gene at a different locus. In the latter case, should this new gene be dominant? If it is dominant, then there would exist cats heterozygotic for mitted pattern. The kittens of two cats with this genotype would have 25% likelihood of having no white whatsoever. But there does not seem to be any record of solid pointed kittens in litters of Birmans! On the other hand, for many generations Birmans have always been mated to Birmans, so they might be all homozygotic for this hypothetical mitted pattern piebald gene.

But later articles (J.P. Maas, *Introduction into the Heredity of the Albino Series, Piebald Spotting and Epistatic White,* 1995), based upon evidence from Dutch breeders of Birman cats, claim that experimental breedings of Birman to solid pointed cats (without white) lead to litters of solid pointed kittens only (no white spots). If so, then a Birman gloved pattern gene does really exist: call it s^b (the *b* stands for *Birman*). Indeed, if the Birman gloved pattern were only a consequence of piebald spotting (dominant), at least half of the first generation kittens would have white spots. More than that: the gloved pattern gene s^b must be recessive!

On the other hand, we mention the fact that the french Club of the Sacred Cat of Burma (M.A. Taranger, private communication) claims that this evidence is faulty, and that the first generation kittens may be either gloved or colorpoint. If so, then the most plausible theory would be that the gloved pattern of Birmans is caused by a piebald spotting genotype (either heterozygotic **Ss**, which yields a reduced amount of white, as we shall see soon, or homozygotic **SS**), and to the superimposed action of a control gene at a different locus. This second gene would have the effect to reduce the expression of white to the gloves and gauntlets only, and to draw the shape of the white areas: we could call it **mit**, from *mitted.* Since the shape of white gloves in Birmans is distinctive and is consistently similar, the control gene **mit** would likely be recessive, so that all Birmans would be homozygotic **mit mit**. Then, all kittens of the mating of two Birmans of genotypes **SS mit mit** are Birman. However, the mating of two Birmans of genotypes **Ss mit mit** would yield 75% Birman kittens and 25% colorpoints (without white). But this probability distribution of kitten color does not appear to be found in real life. As we mentioned above, this discrepancy might be explained only by assuming that, due to inbreeding, all Birmans are homozygotic **SS**: but mating Birmans to colorpoints (solid pointed) would clearly produce heterozygotic Birmans, so we cannot explain the discrepancy, which leads us to drop the theory suggested by the french Club of the Sacred Cat of Burma. Other discrepancies with everyday's evidence are readily obtained: when mating a **SS mit mit** Birman to a **ss Mit Mit** colorpoint, all kittens would turn out to be pointed with white in bicolor pattern (not mitted, hence not Birmans). So, we believe that no shaping control gene **mit** exists.

But even the sounder model proposed by J.P. Maas has some drawbacks. Indeed, be warned that the existence of a specific recessive Birman gloved gene yields some queer genetic consequences. Indeed, there would be at least two different principal genes producing white spots (one for the Birman gloved pattern and the other for the various white spots). Their overlapping might yield entirely white cats whose kittens would have low probability of being entirely white (although one must admit that this event would be rather unlikely). This conflicts with statistical evidence of hereditary transmission of white, as we shall see later.

The piebald spotting allelic series: genetics of the Ragdoll patterns

Mitted patterns exist in other breeds too, for instance in Ragdolls. It is very likely that the Ragdoll pattern is not due to the same mitted gene: there is some additional piebald spotting action, which is responsible for the white strip on the belly of mitted Ragdolls. Because of this mixing of its action with the typical piebald spotting, the Ragdoll's mitted pattern gene appears to be at the same locus of the piebald spotting gene S.

In recent years, the genetics of the Ragdoll's white patterns has been well understood (see, for instance, the papers by Robin Pickering, pg. 73-86, and Roy Robinson, pg. 93-95, in *The definitive Guide to Ragdolls,* L. Wallace, R. Pickering & D. Pollard, editors, Ragdoll World U.K., 1995). This understanding has been made possible by the fact that matings between bicolor, mitted and pointed Ragdolls (without white) are frequent. The first generation kittens of the mating of a mitted and a colorpoint Ragdolls may be pointed without white or mitted. So, the mitted pattern in Ragdolls is due to a gene which is epistatic over color without white. When the mitted parent is heterozygotic, statistically half of the kittens do not have white spots. When homozygotic, then all kittens are mitted. We shall now see that the Ragdoll mitted pattern gene, which could be denoted by s^m, appears to be partially recessive with respect to S. Partial dominance of S over s^m can be used to explain the various degrees of white spotting in Ragdolls. In addition to the colorpoint Ragdolls (without white), which are homozygotic ss, there are five genotypes. The mitted Ragdolls have the genotype $s^m s$ (heterozygotic for the mitted allele!) Their phenotype has considerably more white than in Birmans: typically, not only on the feet, but also up to the hocks of the back legs, and on a narrow strip on the underside, from the chin to the base of the tail. The genotype Ss gives rise to the ideal bicolor pattern, with no more than 1/3 of white on the back, white legs and the underbody almost entirely white with white extending to the face in the shape of an inverted V. The genotype $s^m s^m$ produces a reinforcement of the mitted pattern, which has been called *high mitted* pattern: it is close to the bicolor pattern (these cats are entered in shows as bicolors), with possibly less than 1/3 white on the back, occasional breakthrough spotting on limbs, and white in the underbody which often extends to an inverted V shape on the face. All the remaining genotypes produce Ragdolls with larger amount of white, which are entered in shows as bicolor Ragdolls, although their pattern is not ideal in terms of the standard. The Ss^m Ragdolls have the so called *mid-high white* pattern, with usually more than 1/3 white on the back, inverted V on the face, white limbs and underbody with occasional breakthrough spotting on limbs. Finally, the SS Ragdolls have *high white* pattern, which is nothing but the Van pattern. Indeed, the piebald spotting alleles act not only on Ragdolls, but on all other breeds, and their phenotypes can be seen in all breeds where white spotting is recognized (except Birmans, where they are undesired because a different type of mitted pattern is requested). The reason for which it has been studied more extensively in Ragdolls is that this breed's standard has detailed description of the various recognized patterns. But it is extremely likely that the Van pattern of other breeds, like Turkish Vans, is obtained by precisely the same genotype.

Problem.   *Prove that the probabilities of white patterns in matings of Ragdolls are as follows:*
- *no white x no white:*   *100% no white (that is, colorpoint)*
- *no white x mitted:*   *50 % no white, 50% mitted*
- *no white x bicolor:*   *50% no white, 50% bicolor*
- *mitted x mitted:*   *50% mitted, 25% colorpoint, 25% high mitted*
- *bicolor x bicolor:*   *50% bicolor, 25% colorpoint, 25% high white*

- mitted x bicolor:	*25% colorpoint, 25% mitted, 25% bicolor, 25% mid-high white*
- no white x high mitted:	*100% mitted*
- no white x mid-high white:	*50% bicolor, 50% mitted*
- no white x high white:	*100% bicolor*
- mitted x high mitted:	*50% mitted, 50% high mitted*
- mitted x mid-high white:	*25% mitted, 25% bicolor, 25% high mitted, 25% mid-high white*
- mitted x high white:	*50% bicolor, 50% mid-high white*
- bicolor x high mitted:	*50% mitted, 50% mid-high white*
- bicolor x mid-high white:	*25% mitted, 25% bicolor, 25% mid-high white, 25% high white*
- bicolor x high white:	*50% bicolor, 50% high white*
- high mitted x high mitted:	*100% high mitted*
- high mitted x mid-high white:	*50% high mitted, 50% mid-high white*
- high mitted x high white:	*100% mid-high white*
- mid-high white x mid-high white:	*50% mid-high white, 25% high mitted, 25% high white*
- mid-high white x high white:	*50% mid-high white, 50% high white*
- high white x high white:	*100% high white*

Tabby patterns: the classic theory. So far we considered solid color or particolor genes. Let us now turn our attention to the genetics of tabbies. In this chapter we present the classic theory, based on one Tabby locus. The modern theory involves at least two tabby loci, and has also to do with the Extension locus and several modifiers: we shall present it later, after the chapters on Silver and Extension. Most readers interested in deriving offspring probabilities may skip the modern theory unless they are interested in predicting more accurately the probabilities of specific tabby patterns and the occurrence of multiple patterns in the same litter.

Each tabby (or, as we usually say, agouti) hair carries several color bands. While each hair grows, the pigment producing cells at its base alternately undergo two phases. In one phase, pigment of intense color -that is, of nearly spherical shape- is produced. In the other phase, the pigment is more elongated, and it looks lighter and more reddish. This phenomenon is activated by the agouti gene, **A**. Its recessive allele, **a**, does not allow agouti hairs, and is therefore the genetic reason of solid coat colors. The tabby cat should be regarded as the natural expression. Actually, the non-agouti allele (**a**) reinforces intense color production, thereby filling up the agouti bands with full color. So, the **A**. allele allows the natural agouti pattern to show up. There is a more recent allele at the agouti locus, A^{pb}, that reinforces the black pigmentation and produces thicker and darker tabby markings. It is recessive to **A** but partially dominant over **a**. The heterozygotic A^{pb} **a** are tabbies with strong, dark, thick marks but well separated and distinct, also on the face: these are the charcoal tabbies. The homozygotic $A^{pb}A^{pb}$ are less distinct charcoals, a darker version where often on the flanks and the head the marks tend to glue together giving an impression a bit closer to solid.

Biochemistry of the agouti bands. The coat (and skin) pigmentation is due to variants of the melanin pigment, synthesized in the melanocytes (pigment producing cells). As observed above, there are two such variants, eumelanin (rounded shape, giving rise to black-based colorations) and phaeomelanin (more elongated shape, that yields red-based colors).
The production of melanin is a consequence of the binding of an appropriate hormone (the

melanocyte stimulating hormone, MSH) to its specific receptor, the *melanocortin receptor* MC1R): this receptor is genetically coded by genes at a specific locus, the extension locus. When binding occurs, the melanocyte synthesizes eumelanin. So far we have seen two primary loci responsible for phaeomelanin production: the sex-linked Orange locus, that permanently stops production of eumelanin in favor of phaeomelanin, and the Agouti locus, that induces periodic transitions from (production of) eumelanin to phaeomelanin. The Agouti gene (and the associated wide-band modifiers) achieve this effect by coding the *agouti signal protein* ASP, a protein that is antagonist of MSH: indeed, it binds to MC1R, thereby preventing the binding of MSH. If this binding occurs, then the melanocyte does not produce pure eumelanin, and shifts towards producing pheomelanin, that is, reddish pigment. The rate of production of pheomelanin depends on the level of a specific enzyme, called *tyrosinase*, that is coded at the albino locus (responsible for the Burmese and Siamese colors, see later the chapter on Pointed colors), and also controlled by the Extension locus (see later the chapter on Amber colors). The level of tyrosinase is subject to periodic fluctuations. Therefore the production of pheomelanin occurs at a time dependent rate, causing agouti (pheomelanistic, orange) bands. The action of tyrosinase is heat-dependent: more pheomelanin is produced if the temperature is higher. Therefore, the first band in each tabby hair, closer to the skin hence warmer, is reddish. The exception is the Orange gene **O**, that switches off production of eumelanin in each hair and gives rise to red or cream colors: but even when the color is red or cream, the periodic fluctuation of the tyrosinase level stimulates higher or lower production of the pigment, hance many red or cream solid cats show some ghost markings.

If the Orange gene is not present, then which parts of the body show tabby markings is determined not by the Agouti gene, but by the Tabby genes.
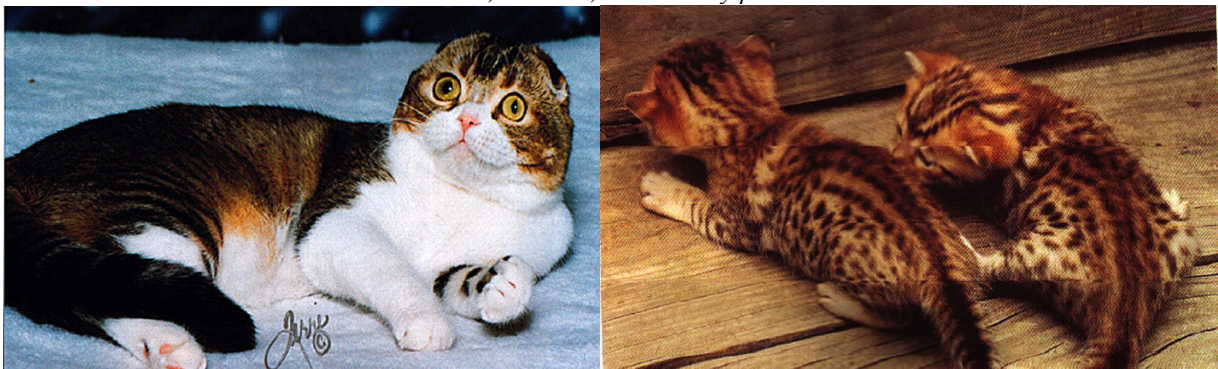
The tabby genes.

In specific body areas, the pattern makes the hairs agouti. In the remaining parts the hairs' agouti bands are filled up with full color (exactly what happens everywhere on non-agouti, solid-colored cats). The latter areas are the so called tabby markings. There are three main tabby patterns: ticked, mackerel and classic (or blotched, in the terminology of some associations). All three have the same face and forehead markings. The ticked pattern, as in the Abyssinian, has no markings except on the head (and occasionally on legs and tail, in less than ideal ticked patterns): all other hairs have agouti bands (at least where pigmentation is heavy enough to make this noticeable –the hair on the belly is often too pale to make agouti bands visible). The mackerel pattern has thin parallelel lines on body, legs and tail. The classic pattern has thicker markings, arranged on the sides as spirals, bull's eyes or butterfly shapes. These three patterns are produced by three alleles of the tabby gene, whose (partial) dominance order is as follows. Ticked (T^a) is dominant. Mackerel (**T**) is recessive with respect to ticked but dominant over classic. Classic (t^b) is recessive. There are two other patterns. One is the spotted pattern, where the lines become spots, often arranged along ideal mackerel lines. The dominance levels of spotted and mackerel are the same, and they are believed to be produced by the same tabby allele **T**, under the action of a group of modifiers (polygenes). Some breeds (for instance the Bengal, thanks to its unusual gene pool inherited by its wild ancestor, the asian leopard cat or *Felis Bengalensis*) show characteristic spotted patterns, with larger, rosette shaped spots not in a mackerel arrangement. It is likely but not yet clear that also these atypical spotted patterns are produced by the **T** gene modified by polygenes. A second pattern, that originally appeared in the American Shorthair and then in the Bengal, is the marbled pattern, reminiscent of classic but with very elongated and irregular bull's eyes and spirals, and thicker, often closed lines. This pattern may be

produced by the classic tabby gene t^b under the action of modifier, or maybe by another allele t^m with partial dominance: indeed, the kittens of marbled tabbies bred to spotted tabbies show breaking of the marbled pattern into rosettes and irregular spots partially distributed according to the marbled design. Then there is the agouti pattern, very close to ticked and produced by the same gene, but with necklaces and tabby bars (rings) on the legs and tail (as in the Singapura). With the possible exception explained in the next paragraph, in eumelanistic cats the agouti gene acts not only on coat, but also on the nose leather, which becomes brick red (in brown tabbies) or various shades of pink, all with a rim colored with the base color.

Blotched, marbled, ticked tabby patterns

Mackerel and spotted tabby patterns
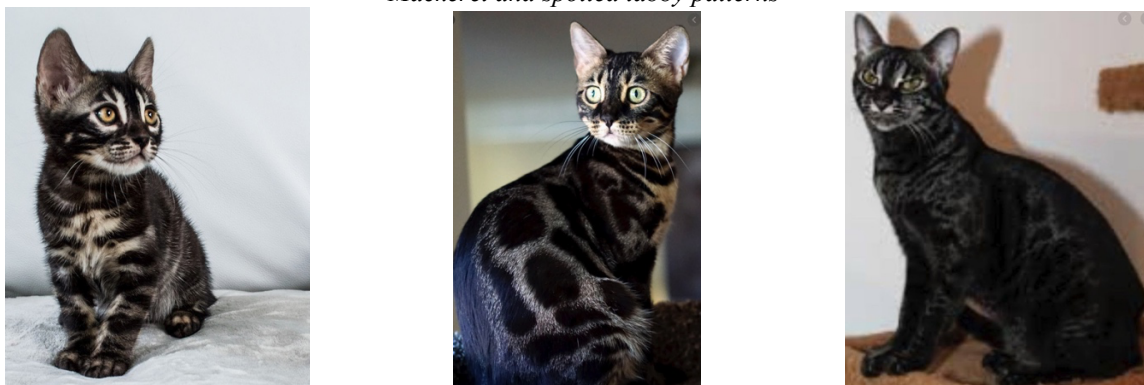
Charcoal spotted tabby patterns (the last is homozygotic $A^{pb}A^{pb}$)

Finally, another pattern appeared recently in the Chausie, perhaps due to the inheritance of tabby genes from its wild ancestor, the Jungle cat: the grizzled pattern. This pattern, so far seen only on eumelanistic cats (the only colors accepted in the Chausie!), usually leads to fully colored

legs and face (even the nose leather is black, contrary to what happens in general on tabbies: see the next paragraph). The hairs on the body have agouti bands (up to five) that under the microscope show pale yellow color, but not very warm, and so at first glance give the impression of silver tips, although they are not a consequence of the silver genes.

The same grizzled jungle cat as a young adult and a mature adult

Grizzled Chausie

It is not yet clear if this phenotype is a consequence of a new dominant allele at the tabby locus (a "grizzled tabby" allele), or of the action of an epistatic gene at a different locus, the Extension locus E, as seen on other species, as for instance the rabbit, where the E^S "steel" allele at the Extension locus generates a steel pattern rather similar to the grizzled pattern in cats. We shall outline the genetics and phenotypes due to the Extension locus in cats later in this presentation. The fact that the nose leather of grizzled cats does is not brick red with a black rim leads to conjecture that the grizzled pattern is a consequence of an allele at the epistatic Extension locus instead than at the tabby locus. Anyway, even in the hypothesis that its genetics is not the consequence of an epistatic action but of a new tabby allele, the grizzled pattern alleles dominant over all the others.

The agouti and tabby genes are at different loci. The fill-up caused by the **a** allele at the agouti locus is epistatic over the action of the tabby genes. That is to say, a solid colored cat carries its tabby pattern, and can transmit it genetically. It is easy to witness this: visible tabby markings are often seen on black (or smoke, see later) kittens before their pigmentation reaches full intensity. Even after pigmentation is complete, a black cat under radent light shows a different reflectance in the areas which have been filled up by the a gene, hence it shows its underlying pattern.

Dominance of a tabby allele over another is only partial. For instance, a $\mathbf{T^a t^b}$ cat has a ticked pattern superimposed to a classic pattern. The resulting pattern is ticked, but it may have

poor uniformity of ticking, and markings on legs, tail and breast, close to the classic pattern. Before full pigmentation, kittens with this genotype may show the underlying classic pattern very clearly. Something similar happens, for instance, to shaded silver T^aT or T^at^b kittens, often showing well defined markings which disappear with growth (disuniformities in their adult ticking are masked by the inhibitor gene, see the chapter on silvers later on.

The genetics of red and cream tabbies is the same. However, the non-agouti gene is much less effective on pheomelanistic than on eumelanistic colors. It is therefore unlikely that tabby markings of red or cream cats be canceled by its action. Some genetist claim that the a gene does not act at all on pheomelanistic colors, and the (partial) cancellation of markings on solid red or cream is only due to polygenes. In any case, a very tough selection is necessary to reduce or cancel pheomelanistic tabby markings. Therefore, it is clear that to produce these markings is more important the cumulative action of many genes (polygenes) than the sharp action of a principal gene. To realize how much weaker the non-agouti gene acts on red, it is enough to look at the torties (or dilute torties), where almost always there are markings in the red patches which disappear in the black ones.

The next table refers to the offspring of a brown classic tabby sire which is heterozygotic for agouti ($\mathbf{Aa\ BB\ o\text{-}\ DD\ t^bt^b)}$ and a tortie dam carrying maltese dilution and ticked and mackerel patterns ($\mathbf{aa\ BB\ Oo\ Dd\ T^aT}$). Since the sire has only two heterozygotic genes, the table has only four columns. But the dam is heterozygotic on three genes: the table needs eight rows.

	At^boD	At^b - D	at^boD	at^b - D
aT^aOD	AaT^{a}t^{b}OoDD	AaT^{a}t^{b}O - DD	aaT^{a}t^{b}OoDD	aaT^{a}t^{b}O - DD
aT^aOd	AaT^{a}t^{b}OoDd	AaT^{a}t^{b}O - Dd	aaT^{a}t^{b}OoDd	aaT^{a}t^{b}O - Dd
aT^aoD	AaT^{a}t^{b}ooDD	AaT^{a}t^{b}o - DD	aaT^{a}t^{b}ooDD	aaT^{a}t^{b}o - DD
aT^aod	AaT^{a}t^{b}ooDd	AaT^{a}t^{b}o - Dd	aaT^{a}t^{b}ooDd	aaT^{a}t^{b}o - Dd
$aTOD$	AaTt^{b}OoDD	AaTt^{b}O - DD	aaTt^{b}OoDD	aaTt^{b}O - DD
$aTOd$	AaTt^{b}OoDd	AaTt^{b}O - Dd	aaTt^{b}OoDd	aaTt^{b}O - Dd
$aToD$	AaTt^{b}ooDD	AaTt^{b}o - DD	aaTt^{b}ooDD	aaTt^{b}o - DD
$aTod$	AaTt^{b}ooDd	AaTt^{b}o - Dd	aaTt^{b}ooDd	aaTt^{b}o - Dd

The left half of the table shows the genotypes of agouti kittens. Please note that these kittens are not classic tabbies, as a consequence of the tabby allele transmitted by the dam -ticked or mackerel- which is (partially) dominant over classic. This tabby pattern is genetically transmitted by the dam even though it is not visible in her non-agouti phenotype. Partial dominance may give rise to imperfect pattern in these kittens.

Problem. *1. What are the colors (and their probabilities) of the kittens of a brown classic tabby $Aa\ t^bt^b\ BB\ DD$ and a blue mackerel tabby $Aa\ Tt^b\ BB\ dd$?*
2. How would you answer the question if the brown classic tabby is heterozygotic for maltese dilution?

The silver colors (smoke, shaded, silver tabby). Let us now come to the silver colors: smoke, silver tabby, shaded silver and chinchilla (and their pheomelanistic equivalents, called cameos in some associations). In these color classes, the coat is depigmented at the base, silver white without any rufousing. But in some silver tabbies, the hairs are pigmented all the way up to the root in the tabby markings' areas. The agouti areas of a silver tabby are pale silver, with high

contrast to the markings. An ideal chinchilla has no trace of tabby markings, only the hair tips are colored *(tipping)*. The same descriptions holds for shaded silvers, but the tipping extends for approximately one third of the hair's length (sometimes a bit less). The smokes' coat has a silver base covering between one third and one half of the hair (approximately); the remainder is colored.

The genes responsible for these colors have not been identified yet. Therefore, we'll give a purely combinatorial outline, stressing many fine details (for instance, about the length of the first depigmented band of the hairs) that are not very important: we do this as an instance of how a purely combinatorial modelcould be developed to account for many minute details. The reader can skip this analysis with no damage to her/his understanding of the full view.

The one-gene theory

Time ago, a unique principal gene was thought to give rise to all silver colors. This gene was called the *inhibitor* gene, denoted by **I**, and thought to inhibit pigment production and also to cancel rufousing (the reddish color shades of eumelanistic cats, particularly in the agouti areas of brown tabbies). Here is how a single gene can yield so many different colors.

Smokes are non-agouti cats whose coat color fades and disappears at the hairs' base because of the action of the **I** gene. The base color is silver white, uniformly all over. Pigmentation is inhibited on one third of the hair's length, in some cats on one half.

All other silvers are agouti. Shaded silvers and chinchillas have ticked pattern. The **I** gene turns the hair color into silver at its base, but without its action, the hair would still have lighter agouti bands with less intense pigmentation. However, the **I** gene cancels all reddish tones from these bands, making them silver too. These two silvering effects overlap, and make the hair silver for approximately two thirds of its length if the **I** gene acts mildly (shaded silvers), and all over it except on the tip (the last full-color agouti band) if it acts strongly (chinchillas). The fact that eumelanistic chinchillas and shaded silvers are agouti is also evident by their brick red (or deep pink) nose leather, sorrounded by the dark rim typical of tabbies.

Finally silver tabbies are agouti with classic or mackerel/spotted pattern. Of course, the **I** gene acts much more effectively on the agouti areas than on tabby markings. This yields a very sharp tabby pattern, with full contrast to the ground color areas.

But now we see that the genetic model for silver tabbies cannot be satisfactorily explained in terms of a unique gene. Indeed, if only one gene were responsible for silver colors, then not only the smokes, but also the tabby markings of silver tabbies should be discolored at the hairs' base. Sometimes we see silver tabbies like that, but many others' tabby markings are fully colored up to the root. The geneticist Roy Robinson, in its well known book *Genetics for Cat Breeders* (Cambridge, 1972, 2nd edition), suggests that the fill-up with color that occurs in the tabby markings overcomes the inhibition action of the **I** gene. but this is not convincing, because the contrary is true in the smokes, where the non-agouti fill-up action occurs all over the body. At any rate, Robinson's theory does not explain why the tabby markings are silver at the base in some silver tabbies.

The two-gene theory

More recent theories -see the articles by J. Jerome, TICA Trend vol. 13 n. 6 (dec. 1992/jan. 1993), pg. 14 and TICA Yearbook 12 (1991), pg. 218- state that silver colors result from the combined action of two genes, one of which*(eraser)* inhibits pigmentation at the hair's base, while the other *(bleaching)* cancels rufousing. We shall call the latter "silver gene", and denote it by **Sv**. The eraser gene will be denoted by **I**, but the reader should be warned that some recent books denote by **Sh** the mild form of the gene **I**, which gives rise to shaded silvers, and by **Ch**

its strong form, which gives rise to chinchillas. There is not enough evidence that these two expressions of **I** are due to two different alleles rather than to a group of polygenes. (Indeed, the transition from shaded silver to chinchilla is more gradual than sharp. Therefore, we do not make use of two different alleles **Sh** and **Ch**, and do not distinguish between the genotypes of shaded silvers and chinchillas (as far as principal Mendelian genes are concerned). But the reader can easily adapt our results to the **Sh/Ch** notation, if so desired.

It is now easy to fill up the list of genotypes of the various silver colors in the two-gene theory:

Smoke: $\qquad\qquad\qquad\qquad\qquad$ ***aa I- Sv -***

Shaded silver and chinchilla: ***A- T^{a}T^a I- Sv -***

Silver tabby mackerel/spotted:
$\qquad\qquad\qquad$ ***A- TT I- Sv -*** $\qquad$ if the hairs' base in the tabby markings is silver (silver tabby shell or shaded, according to the higher or lower amount of silver)
$\qquad\qquad\qquad$ ***A- TT ii Sv -*** $\qquad$ if the hairs' base in the tabby markings is fully colored, not silver

Silver tabby classic:
$\qquad\qquad\qquad$ ***A- t^{b}t^b I- Sv -*** $\qquad$ if the hairs' base in the tabby markings is silver (silver tabby shell or shaded, according to the higher or lower amount of silver)
$\qquad\qquad\qquad$ ***A- t^{b}t^b ii Sv -*** $\qquad$ if the hairs' base in the tabby markings is fully colored, not silver.

In this list of genotypes, the tabby genes are assumed homozygote in shadeds and chinchillas and in silver mackerel/spotted tabbies because the dominance of the tabby genes is only partial. For instance, the genotype **T^{a}T** produces a partially hybrid pattern, with diffuse ticking partially superimposed to mackerel (particularly on legs and tail, but often also on the flanks to some extent). The result is likely to be poor uniformity of tipping on shaded silvers and chinchillas. These cats are still registered as shaded silvers or chinchillas, but their color is not ideal.
A silver tabby can have an excllent contrast between ground color and tabby markings even without the eraser gene **I**. Indeed, the bleaching gene **Sv** transforms the readdish agouti bands in the ground color areas into pale silver white. Therefore these areas look silver and very light and clear. moreover, if **I** is not present, then the tabby markings are intensely colored all the way to the root. This further enhances contrast, particularly on black silver tabbies, where the absence of rufousing makes black more intense.

Other colors predicted by the two-genes theory; goldens
Consider what happens if in the shaded or chinchilla genotype the eraser gene is discarded. The genotype becomes **A- T^{a}T^a ii Sv-**. Phenotypically, we should have silver ticked tabbies which are not shaded, that is, which have a colored band near the skin. As far as we know, cats like these have never been seen (see further comments below). If we do the same exercise for smokes, then we get **aa ii Sv-**, which phenotypically corresponds to non-agouti unrufoused cats (that is, without reddih tones in eumelanistic colors, and without warm tones in phaeomelanisitic ones). These cats may result from matings of silvers which are heterozygotic for the gene **I**. In the sucond generation the offspring may have genotype **ii sv sv**. In this way we obtain solid-colored cats from a breeding line of smokes (non-agouti), and ticked tabbies from a line of shaded silvers

or chinchillas (let us say, homozygotic agouti **AA T^{a}T^a**). The latter are colored as Abyssinians. However, one cannot expect to get ticked tabby kittens with the warm rufoused color shades of Abyssinians from heterozygotic **Ii Sv sv** shaded or chinchilla parents. Indeed, all shaded silvers and chinchillas are selected against rufousing, that is, in favor of unrufousing polygenes.

But, by breeding together chinchilla or shaded silvers heterozygotic for **Sv** and endowed with the eraser gene **I**, we can obtain kittens with genotype **I- sv sv**. These are ticked tabbies with a paler coat's base, but without the cold tones produced by the sv allele (still, without very warm reddish shades, as a consequence of polygenic selection against rufousing in breeding lines of shadeds or chinchillas). The base color shade is gold rather than reddish brown. In the eumelanistic versions, these color classes are called *shaded golden*. The corresponding pheomelanistic versions are phenotypically too close to red (or cream) ticked tabbies, and are not recognized as color classes on their own. (Note: here we refer to the golden colors of Persians, determined by genes that have not been identified yet, whence they are treated here in a combinatorial manner. For other breeds, Siberians, Kurilean Bobtails, British, the "golden" genes have been identified: we shall separately present the scientific findings later on).

Similarly, we can have *golden tabbies* by breeding together silver tabbies heterozygotic for the **Sv** allele. Let us compare the golden and brown tabby genotypes:

Shaded golden and chinchilla golden (golden shell):　　　**A- T^{a}T^a I- sv sv**

Golden mackerel/spotted tabby:　　**A- TT I- sv sv**　　(here the hairs' roots in the tabby markings are depigmented: golden tabby shell or shaded, according to the lower or higher amount of pigmentation)

Brown mackerel/spotted tabby:　　**A- TT ii sv sv**　　(the hairs' roots in the tabby markings are not depigmented)

Golden classic tabby:　　　　**A- t^{b}t^b I- sv sv -**　　(here again the hairs' roots in the tabby markings are depigmented: golden tabby shell or shaded, according to the lower or higher amount of pigmentation)

Brown classic tabby:　　　　**A- t^{b}t^b ii sv sv**　　(the hairs' roots in the tabby markings are not depigmented).

Unsatisfactory consequences of the two-gene theory

The reader should be warned that the two-gene theory is not completely satisfactory. Indeed, it predicts some phenotypes never seen so far. For instance, the genotype **aa I- sv sv** should be a "golden smoke", that is, a smoke with golden instead of silver base color. But nobody has ever seen a non-agouti golden. To be consistent with the two-gene theory, one might assume that the sv allele is inactivated in non-agouti cats. If so, however, observe that the genotypes of eumelanistic solid color cats without rufousing differ from the corresponding rufoused cats only because of polygenes.

We have already encountered another dubious consequence for silvers (not goldens). The genotype **A- T^{a}T^a ii Sv -** should correspond to silvers which are not shaded . That is, to silvers without pigment inhibition at the hairs' base, and with ticked pattern. We have seen that the **I** gene transforms the agouti bands into silver bands. One can easily see several alternating silver and black bands in the agouti areas of black silver mackerel or classic tabbies which are not depigmented at the base. But ticked tabbies should have these alternating bands all over the

body. Such cats have not been observed, as far as we know. Perhaps we could assume that the **Sv** allele is active only in the presence of the **I** gene, and actually modifies and reinforces the effect of the **I** gene.

The two additional assumptions made above in order to "save" the two-gene theory amount to say that the allelic series **Sv/sv** is activated by the **I** allele. Not enough experimental research has been performed so far to support this conjecture.

The epistatic golden modifier theory

Under the assumption of the previous section, the two-gene theory becomes mathematically equivalent to another genetic model which has been introduced time ago. This model explains goldens by assuming an epistatic action over **I** of a second gene **g** (similarly to what is done to explain maltese dilution by the epistatic action of the allele d over the **B** gene and its allelic series). The other allele **G** has no action (no golden pigmentation at the hair's base).

Finally, it is important to realize that the **Sv** gene cancels rufousing in eumelanistic colors, much less in pheomelanistic ones. The tipping of some red smokes and red shaded silvers is rather warm (particularly in the red smokes).

The [golden = brown ticked tabby] theory

Another genet)c model which has been considered simply identifies shaded goldens with ticked tabbies (actually, we should say "agouti tabbies", which is the official TICA name for the version of the ticked pattern without stripes on the legs, but we shall agree to use the term "ticked tabby" here, which is more reminiscent of the name of the tabby allele giving rise to this pattern, and more often used in all other Associations. Because pigmentation is heat-dependent, the coat color is usually lighter near the skin. This is true for all cats, including ticked tabbies (open the coat of an Abyssinian!). Therefore the golden and the ticked tabby phenotypes are often very similar. This theory is very attractive, because it answers many of the questions unexplained by the one-gene theory and the two-gene theory. The only fact that this theory does not explain is why some ticked tabbies are only a little depigmented at the coat's base while others (namely, the goldens) are more depigmented. But this could be the result of a group of polygenes. Indeed, the goldens are bred from shaded silver and chinchilla lines, and these cats are certainly selected for the greatest possible amount of depigmentation, not only from the inhibitor gene but also from depigmenting polygenes. Therefore, two chinchilla or shaded silvers heterozygotic for the inhibitor gene would produce ticked tabby kittens depigmented at the base, just like goldens. Still, we shall adhere to the two-gene theory, because it is the most satisfactory in explaining the existence of the two types of silver tabbies: the silver tabbies with markings colored all the wa9 to the root and those with markings depigmented at the base. But for every other phenotypic trait, the genetic model which identifies goldens with ticked tabbies yields the same probabilities of the two-gene theory, and is a very sound and interesting model (the fact that goldens have different eye color from the usual ticked tabby is explained later at the end of this chapter).

The wide-band gene theory

Let us continue this presentation of different genetic models for silvers and goldens by introducing an alternative model which makes use of two genes, but with a different action than in the two-gene theory (see the contributions of H. Lorrimer on the *Internet Fancier's List,* in march and april 1995). Actually, one of the to genes is still the silver gene which cancels rufousing. The other is a dominant gene which makes the agouti bands wider, denoted by **Wb** (wide-band). However, the gradual variation in tipping's length seems to suggest that wide-banding is the effect of a group of polygenes. This theory plainly solves the problem of non-

existing golden smokes (the wide-band gene only acts on agouti cats, of course!), but cannot explain the phenotype of the smokes, that are not only unrufoused, but also depigmented at the base, and still not agouti. However, there is a very interesting variant of it which works very well: we describe it next.

The [golden = brown ticked tabby + wide-band modifiers] theory: we finally have a comprehensive genetic model for smokes, silvers and goldens!

Let us return to the theory which identifies the shaded golden coat color with the ticked tabby pattern (agouti tabby in TICA). So far, this is the most convincing theory that we have seen so far, except for the crucial fact that it does not allow for partial depigmentation at the hairs' base, a crucial feature in the golden's phenotype. But cats registered as goldens show varying levels of depigmentation, and some have almost inexistent depigmentation... This leads to consider the possibility that depigmentation in goldens is not the consequence of a principal gene, whose action is sharp (either depigmented or full color). Instead, goldens' depigmentation might be the result of the action of a set of polygenes, with gradual effect (and sometimes, alas, almost null...). But then, we have already a beautiful candidate for this group of polygenes: the wide-band modifiers introduced in the previous section. Now, shaded goldens should be nothing but ticked tabbies with wide-band enhancing (except for eye color: we'll come to it later). If so, then everything works out: all goldens must be tabbies (no golden smokes!), and partially depigmented at the base (with amount of depigmentation which varies on different cats according to the pile-up of the wide-band polygenes' effect). Of course, this assumes that perfect shaded goldens will arise from matings of shaded silvers which are heterozygotic for silver and homozygotic for the ticked tabby pattern. What if the shaded silvers are heterozygotic for the ticked tabby gene too? For instance, they may carry mackerel. Then, if the parents were not shaded but brown tabbies instead, we should see tabby stripes on their legs, because the ticked allele is incomplete dominant over mackerel. But they are shaded silver, and their markings will be there, but will be faint. Indeed, some shaded silvers do show faint tabby stripes on the legs. But their golden kittens are brown tabbies! Those kittens carrying the mackerel factor will have rather visible tabby stripes on the legs, a very undesirable feature on shaded goldens, but frequently observed. On the other hand, the wide-band modifiers transform the other tabby patterns (spotted, mackerel and classic) into golden tabby colors, respectively golden spotted tabby, golden mackerel tabby and golden classic tabby. In these color varieties, the agouti areas are partially depigmented at the base and have warm apricot colors.

So, at this stage, we have a convincing theory for goldens. But we must review and change our theory for silvers! Rather than two genes for silvers, one for depigmentation and the other for silvering, we now must use only one gene, which produces silvering and a consequent depigmentation, as observed, for instance, in smokes. We do not introduce a separate principal gene (eraser) responsible for depigmentation but not silvering, otherwise, as already seen, the theory would predict the inexistent golden smokes, that is, non-agouti non-rufoused colors depigmented at the coat's base. On the other hand, it seems at first glance that we lose the beautiful explanation that the two-gene theory provides for the fact that the tabby markings of some silver tabbies are depigmented at the hairs' base and those of others are not depigmented in those areas. But this is not so: the varying amount of depigmentation in the markings can be explained as a consequence of modifiers similar to (or maybe just the same as) the wide-band modifiers, whose gradual action is confined to tabby cats. By abuse of notation, let us say that these additional modifiers belong to the same group of polygenes of the wide-band modifiers (although, in principle, we should not, because they act on the markings areas, while the wide-band modifiers act on the agouti areas: but we have seen plenty of goldens where the wide-band

depigmentation was also on the tabby marking areas...). Under this viewpoint, it is clear that this new genetic model consists of keeping the eraser, or inhibitor, gene **I** (now considered again responsible of erasing and of silvering, as in the one-gene theory) and of replacing the silvering gene **Sv** with a group of polygenes, that we shall denote by **Wb** (for wide-band). What is particularly nice is the fact that the gradual action of the wide-band modifiers may be thought responsible also for the difference between the shaded silver and chinchilla phenotype! However, these are polygenes, and therefore they are not subject to the simple Mendelian laws of principal genes: in order to follow the mathematics of this model, we need some statistics, whose subtle results are not easily seen in the phenotypes. Therefore we shall not be able to explain all results by means of simple tables.

Silver versus goldens

It is worth observing that the refinement of the one-gene theory presented in the last section, as well as all the others presented previously, rules out the genetic possibility of cats being at the same time silver and golden: silver occurs as a consequence of the inhibitor gene, that goldens do not have. Both shaded silvers and goldens have eraser genes in the form of wide-band alleles or modifiers. In the last version of the theory that we just presented, the golden pattern is due to the suppression action of the wide-band genes over an already banded hair due to the agouti gene: if the tabby pattern is ticked then we have the perfect golden, uniformly colored all over, but if the pattern is mackerel, spotted or (even worse) classic, then more or less large areas of fully pigmented markings are evident, and are orange at the base. These patterns could be classified as golden tabbies (mackerel, spotted or classic, respectively). Because of the fact that the areas where the wide-band alteration of the natural pigmentation are smaller, these golden tabby colors are more difficult to determine with certainty, particularli in kittens, and even more so if they arise as ghost patterns in young cats as a consequence of heterozygous tabby genotypes with only one ticked allele, and some stud books (for instance, TICA's) do not accept them.
Finally, observe that the action of the wide-band genes create long agouti bands, whose color is pheomelanistic: therefore, they might be difficult, if not impossible, to determine on already pheomelanistic cats. If the wide bands are not long then this is easier, exactly as in the case of the tortie ticked tabby pattern.

Eye color of shaded silvers and goldens: an example of persistence?

We remarked that goldens and ticked tabbies are very similar. However, the usual eye color in ticked tabbies is copper (Persians) or gold, or hazel or green (Abyssinians). In eumelanistic chinchillas and shaded silvers the eye color is emerald or blue-green, while it is copper or gold in the phaeomelanisitic ones. With suitable breedings and selection copper eyes have been introduced in eumelanistic chinchillas and shaded silvers. The corresponding standard, called pewter, is recognized in most european cat associations, but not yet in TICA.
The difference between the golden and eumelanistic ticked tabby standards is slight in the coat color, but obvious in the eye color (emerald versus copper). Silver tabbies have green or yellow-green eyes, green preferred (most european associations accept also copper). pheomelanistic shaded silvers and silver tabbies have copper eyes, and the corresponding torties have either copper eyes or emerald (in shaded torties) or green (in silver torbies) eyes, copper preferred.
Pewters prove that the emerald eye color of shaded silver is not produced by the silver genes. To a large extent, eye color is controlled by a principal Mendelian gene (although polygenes are certainly involved). nevertheless, eumelanistic shaded silvers with copper eyes do not arise frequently. Therefore, even though eye and coat colors are controlled by independent genes, their probabilities are not independent. A persistent link between eye and coat color takes place

in shadeds and chinchillas. A possible explanation of this link can be given by assuming that the main genes responsible for silver and for emerald eye color are located in the same chromosome, and so both or neithert are genetically transmitted. This set-up is called persistence, and changes the joint probability of hereditary transmission. To break the link an unlikely event must occur: genetic recombination (that is, molecular exchange) between the chromosome carrying the two genes and its paired chromosome, during the close contact phase before meiosis. However, we should keep in mind that the recombination probability becomes higher and higher when we consider two loci of the same chromosome that are more and more distant: past a certain distance they may be considered to be inherited virtually independent. So, persistence of eye color as explained here would suggest that the silver and eye color loci are quite close in the same chromosome. A rather satisfactory alternative explanation is based on the eye color being controlled by group of polygenes that have nothing to do with silver, but have been dramatically selected towards uniformity in the shaded silvers.

Examples of combination tables (Punnet diagrams) for silvers

The **I** gene (and, for those who choose to adopt the two-gene theory, also the **Sv** gene) is epistatic over the **B** allelic series, the orange gene and their maltese dilutions. That is, silver is epistatic over solid colors (both eumelanistic and pheomelanistic), but not over white (**W**) and piebald spotting (**S**). Indeed, both **S** and **W** are epistatic over silver. For instance, in the phenotype corresponding to **W- B- A- T^aT^a I- (Sv-)** white masks shaded silver, but eye color can be blue (because of the action of the **W** gene) or emerald.

Let us consider a typical breeding. Let us first make up its table under the viewpoint of the two-gene theory. The sire, **Ww aa BB T^aT ii sv sv**, is heterozygotic white, non-agouti, carrying homozygotic black and a ticked pattern heterozygotic to mackerel. The dam, **Aa BB T^aT Ii Sv sv**, is a shaded silver heterozygotic for agouti, bleaching and eraser, and carrying mackerel (rather unusual in real life, because, as already remarked, a hybrid tabby pattern does not produce the best shaded silver color). As usual, in the table we disregard the homozygotic **BB** genes common to both parents.

	$W\ a\ T^a\ i\ sv$	$W\ a\ T\ i\ sv$	$w\ a\ T^a\ i\ sv$	$w\ a\ T\ i\ sv$
$w\ A\ T^a\ I\ Sv$	WwAaT^{a}T^{a}Ii Sv sv	WwAaT^{a}TIi Sv sv	wwAaT^{a}T^{a}Ii Sv sv	wwAaT^{a}TIi Sv sv
$w\ A\ T^a\ I\ sv$	WwAaT^{a}T^{a}Ii sv sv	WwAaT^{a}TIi sv sv	wwAaT^{a}T^{a}Ii sv sv	wwAaT^{a}TIi sv sv
$w\ A\ T^a\ i\ Sv$	WwAaT^{a}T^{a}ii Sv sv	WwAaT^{a}Tii Sv sv	wwAaT^{a}T^{a}ii Sv sv	wwAaT^{a}Tii Sv sv
$w\ A\ T^a\ i\ sv$	WwAaT^{a}T^{a}ii sv sv	WwAaT^{a}Tii sv sv	wwAaT^{a}T^{a}ii sv sv	wwAaT^{a}Tii sv sv
$w\ A\ T\ I\ Sv$	WwAaT^{a}TIi Sv sv	WwAaTTIi Sv sv	wwAaT^{a}TIi Sv sv	wwAaTTIi Sv sv
$w\ A\ T\ I\ sv$	WwAaT^{a}TIi sv sv	WwAaTTIi sv sv	wwAaT^{a}TIi sv sv	wwAaTTIi sv sv
$w\ A\ T\ i\ Sv$	WwAaT^{a}Tii Sv sv	WwAaTTii Sv sv	wwAaT^{a}Tii Sv sv	wwAaTTii Sv sv
$w\ A\ T\ i\ sv$	WwAaT^{a}Tii sv sv	WwAaTTii sv sv	wwAaT^{a}Tii sv sv	wwAaTTii sv sv
$w\ a\ T^a\ I\ Sv$	WwaaT^{a}T^{a}Ii Sv sv	WwaaT^{a}TIi Sv sv	wwaaT^{a}T^{a}Ii Sv sv	wwaaT^{a}TIi Sv sv
$w\ a\ T^a\ I\ sv$	WwaaT^{a}T^{a}Ii sv sv	WwaaT^{a}TIi sv sv	wwaaT^{a}T^{a}Ii sv sv	wwaaT^{a}TIi sv sv
$w\ a\ T^a\ i\ Sv$	WwaaT^{a}T^{a}ii Sv sv	WwaaT^{a}Tii Sv sv	wwaaT^{a}T^{a}ii Sv sv	wwaaT^{a}Tii Sv sv
$w\ a\ T^a\ i\ sv$	WwaaT^{a}T^{a}ii sv sv	WwaaT^{a}Tii sv sv	wwaaT^{a}T^{a}ii sv sv	wwaaT^{a}Tii sv sv
$w\ a\ T\ I\ Sv$	WwaaT^{a}TIi Sv sv	WwaaTTIi Sv sv	wwaaT^{a}TIi Sv sv	wwaaTTIi Sv sv
$w\ a\ T\ I\ sv$	WwaaT^{a}TIi sv sv	WwaaTTIi sv sv	wwaaT^{a}TIi sv sv	wwaaTTIi sv sv
$w\ a\ T\ i\ Sv$	WwaaT^{a}Tii Sv sv	WwaaTTii Sv sv	wwaaT^{a}Tii Sv sv	wwaaTTii Sv sv
$w\ a\ T\ i\ sv$	WwaaT^{a}Tii sv sv	WwaaTTii sv sv	wwaaT^{a}Tii sv sv	wwaaTTii sv sv

Let us now write up the same table under the viewpoint of the comprehensive theory with one silvering-eraser gene, the inhibitor gene **I**. Of course, we cannot include in the table the effect of polygenes, particularly those responsible for wide-bands on agouti cats.

The left half of the table contains the genotypes of white kittens. In the third column, the first cell consists of shaded silvers, the second of shaded goldens, the third to silvers not depigmented at he coat's base (not actually encounterd: see the comments above on the unsatisfactory aspects of the two-gene theory), the fourth to ticked tabbies (we ignore eye color here). The next four cells yield the same colors, but the ticked pattern is actually partially a hybrid of ticked and mackerel (the overall look is closer to ticked, because of partial dominance of T^a over T). The ninth cell consists of smokes, the tenth of the mysterious "golden smokes", never seen but predicted by the two-gene theory (see above again for the difficulties in this theory). The eleventh cell yields unrufoused solid blacks, and the twelfth to solid blacks which could have some traces of rufousing. The last four cells correspond to the same colors; only the tabby pattern genes are different, but they have no influence on the kittens' looks because the pattern is masked by the non-agouti genes **aa**.

Let us now discuss the last column. The first four cells yield the same colors of the corresponding cells in the third columns, except a partial hybridization of the ticked pattern with mackerel, and the same is true for all the cells in the lower half of the fourth column, where, on the other hand, hybridization is not visible because these kittens are non-agouti (indeed, the last four cell at the bottom yield mackerel genotypes rather than hybrid, but nevertheless not visible in the phenotypes). Finally, the fifth cell of the fourth column consists of silver mackerel tabbies, the sixth of golden mackerel tabbies, the seventh to silver mackerel tabbies which are not shaded (these too were never observed) and the eigth to golden mackerel tabbies which are not shaded (never seen, either).

	$W\,a\,T^a\,i$	$W\,a\,T\,i$	$w\,a\,T^a\,i$	$w\,a\,T\,i$
$w\,A\,T^a\,I$	WwAaT^{a}T^{a}Ii	WwAaT^{a}TIi	wwAaT^{a}T^{a}Ii	wwAaT^{a}TIi
$w\,A\,T^a\,i$	WwAaT^{a}T^{a}ii	WwAaT^{a}Tii	wwAaT^{a}T^{a}ii	wwAaT^{a}Tii
$w\,A\,T\,I$	WwAaT^{a}TIi	WwAaTTIi	wwAaT^{a}TIi	wwAaTTIi
$w\,A\,T\,i$	WwAaT^{a}Tii	WwAaTTii	wwAaT^{a}Tii	wwAaTTii
$w\,a\,T^a\,I$	WwaaT^{a}T^{a}Ii	WwaaT^{a}TIi	wwaaT^{a}T^{a}Ii	wwaaT^{a}TIi
$w\,a\,T^a\,i$	WwaaT^{a}T^{a}ii	WwaaT^{a}Tii	wwaaT^{a}T^{a}ii	wwaaT^{a}Tii
$w\,a\,T\,I$	WwaaT^{a}TIi	WwaaTTIi	wwaaT^{a}TIi	wwaaTTIi
$w\,a\,T\,i$	WwaaT^{a}Tii	WwaaTTii	wwaaT^{a}Tii	wwaaTTii

The left half of the table consists of heterozygotic whites, carrying agouti (top half) or not (bottom half), and ticked, mackerel or hybrid patterns. The rows correspond, alternatively, to carriers of silver or not. The right half of the table contains the same genetic informations for cats without white. The top half consists of agouti cats. In the first row, the second last column yields shaded silvers (or chinchillas), and the last column yields shaded silvers (or chinchillas) with hybrid tabby pattern (and therefore, in all likelihood, with some undesirable tabby markings on legs and tail). The corresponding cells of the second row are the same colors without silver: that is, ticked tabbies (goldens, if the eye color is blue-green); beware of the goldens with tabby markings of the last column. In the third row, the same cells give, respectively, shaded silvers with hybrid pattern and silver mackerel tabbies. In the next row, we'll have (poor) ticked tabbies or goldens, and mackerel tabbies, respectively. The bottom right quarter of the tables refers to

non-agouti cats. The rows yield, alternatively, smokes and solid cats. One immediately sees that this description is simpler and does not introduce unexpected color descriptions.

   Problem.   *What are the colors (and their probabilities) of the kittens of a silver tabby* **Aa $t^b t^b$ Bb o- Ii Sv Sv** *and a tortie smoke* **aa Tt^bBB Oo Ii Sv sv**?

The Extension locus and amber colors. This section gives an outline of the genetics of amber color, that is colors due to the genes at the Extension locus. For a deeper introduction to most of the contents of this section the reader is referred to the presentation given by Dr. Adriana Kajon, *The Extension Locus – or – An Intro to X-Colors*.

Review of the biochemistry of eumelanin-phaeomelanin production, the Agouti locus and the Extension locus

We have seen, in the chapter on the Agouti and Tabby genes, that the coat (and skin) pigmentation is due to variants of the melanin pigment, synthesized in the melanocytes (pigment producing cells) when they are stimulated by the Melanocortic Stimulating Hormon MSH, and that the production of melanin can be disactivated, or reduced, by Agouti gene **A**, that achieves this effect by coding the agouti signal protein ASP, a protein that is antagonist of MSH: indeed, it binds to MC1R, thereby preventing the binding of MSH. The production of pheomelanin occurs at a time dependent rate, proportional to the level of an appropriate enzyme, tyrosinase: its fluctuation gives rise to pheomelanistic bands: when the level of tyrosinase decreases in the melanocyte, phaeomelanin is produced. The genes at the extension locus do not code for tyrosinase, but control the level of tyrosinase in the melanocyte.

In most mammals, the dominant allele **E** at the extension locus yields high levels of tyrosinase, hence eumelanistic pigment. Instead, the recessive allele **e**, in its homozygotic genotype **ee**, yields low levels of tyrosinase and pheomelanistic pigmentation. In humans there exist several different alleles at the Extension locus, responsible for various shades of red hair and fair skin color. An interesting instance of different alleles at this locus occurs in the rabbit, where a dominant allele, **E^S**, distributes the pigmentation in the hair shaft by stopping it at the hair tips. This gives rise to grizzled colors (silver tips). This allele is dominant over the full color Extension allele, that in the rabbit is denoted by **E^D**. Both are dominant over some other alleles that give rise to phaeomelanin production or to the separation of color in the hair shafts of different body areas.

The action of the recessive and dominant Extension alleles is independent of the Agouti locus, and so it may appear in the genotype of non-agouti animals.

British steel rabbit

Grizzled jungle cat

Grizzled Chausie

First instances of amber colors in cats

New colors produced by the Extension locus probably appeared in cats long ago, but were first observed and studied in a consistent way in the last decade of the last century, in breedings of Norwegian Forest Cats in Scandinavia. Several cats were seen to change their colors with growth, from black or blue to something like red or cream, respectively. Something like these colors but not quite them, because the paw pads remained black or slate gray. This was observed both in solid cats and tabbies. Several enlightening photographs can be seen in *The Extension Locus – or – An Intro to X-Colors*, by Dr. Adriana Kajon. The breeders performed experimental matings to determine the genetics of these colors. Outcross to chocolate point Birmans gave rise to brown tabbies and blue tabbies only: so the x-color genotype is not due to alleles at the B locus as chocolate, cinnamon, lilac and fawn (or recessive to them), or to alleles at the Albino locus as siamese (or recessive to it: the Albino locus will be explained in the next chapter). Other experimental matings were performed between solid x-colored and solid non-x-colored cats: no tabbies were born. This shows that the x-colors are not due to agouti genes.

Evolution of the same amber cat

As already remarked, it would be difficult or impossible to spot the action of the Extension locus (which turns black-based colors to reddish ones) on purely pheomelanistic cats. On the other hand, it is easy to distinguish between fully colored x-colors (black at birth, then gradually evolving towards red) and their maltese dilution (blue at birth). These two colors are now called *amber* and *light amber*, respectively. No case of chocolate, cinnamon, lilac or fawn amber colors have been observed yet, but this is probably due to the fact that in Scandinavia the Norwegian Forest cat is not recognized in chocolate, cinnamon, lilac or fawn (in other species chocolate x-colors exist).

The genetics of amber colors

Now it is clear how to model the combinatorics of amber color genetics. The dominant allele **E** gives rise to normally colored cats, the recessive homozygotic **ee** genotype produces amber colors.

Problem.

1. *What is the probability of amber kittens from two amber parents?*
2. *What is the probability of amber kittens from a mating of an amber to an amber carrier (non-amber) ?*
3. *If two of the non-amber kittens of part 2 are mated together (when adults!), what is the probability of amber kittens in their offspring?*

The grizzled pattern: a new dominant allele at the Tabby locus or at the Extension locus?

We have introduced the grizzled pattern in the chapter on the Agouti and Tabby loci. A possible explanation for this pattern is to consider it a consequence of a new dominant allele at the Tabby locus. We recall that some grizzled cats are black on the face (where the tabbies normally have visible markings or tipping), and without a black or dark rim around a red nose (another typical characteristic of tabbies). Nevertheless, microscope observation of the grizzled hairs reveals agouti bands (phaeomelanin bands in between the eumelanistic ones).

A possible alternative explanation of the grizzled color is to assume that in the cat there may be another dominant allele at the Extension locus, like the allele **E**^{S} responsible of the steel color in rabbits (see the first section of this chapter), dominant over both **E** and **e**, whose action consists in redistributing the color pigment along the hair shaft. The fact that several bands of "agouti" have been seen in grizzled cats indicates that, anyway, this action would be not quite the same

as that of the $\mathbf{E^S}$ allele in the rabbit, that depigments only the tips.

In order to decide which one between the Extension model and the Agouti model might be correct in this analysis, the suitable experiment consists of mating grizzled to amber colored cats. Very few amber cats exist at present: this leads to assume that most cats are not heterozygotic for the recessive amber allele **e** at the Extension locus. Therefore, if the grizzled pattern is due to the $\mathbf{E^S}$ allele, that is if the grizzled parent has genotype $\mathbf{E^S E}$ or $\mathbf{E^S E^S}$, some or all kittens would be grizzled, none amber, but all would carry the amber gene. In second generation one would have some ambers and some grizzled, but no kitten simultaneously amber and grizzled. Instead, if the grizzled pattern is due to a grizzled allele at the Tabby locus, then we can assume that the grizzled parent is "normal" at the Extension locus, that is **EE**: no kitten would be amber but some would carry amber, and some kitten would be grizzled. In second generation one would have kittens that are simultaneously amber and grizzled. (Of course, spotting silver tips on amber colored hairs would be more difficult than spotting them on black hairs, but certainly possible, particularly before the amber colored hairs have become fully reddish.)

Since the phenotype of the Norwegian Forest Cat (where amber cats are usually found) is considerably different from that of the Chausie (that has the grizzled colors), and in most respect quite opposite, no breeders has been interested in carrying out this program yet.

The modern theory of tabbies – and a recapitulation on silvers

How many Tabby loci?

The classical explanation of tabby genes, that we explained in a previous chapter, claims that the tabby pattern is a consequence of the action of different alleles at the same locus, with partial dominance in the order $\mathbf{T^a}$, $\mathbf{T}$, $\mathbf{t^b}$. If this is so, then two cats with ticked pattern must have only ticked kittens if one of them is homozygote, or else, if both are heterozygote, their kittens can only have two patterns: ticked with probability 75%, and one between mackerel-spotted or classic with probability 25% (mackerel-spotted if one of the parents carries this allele, classic if both carry classic). Of course, on young kittens the effects of partial dominance may be gradual and the identification of the final pattern is difficult, but on mature cats it is not. So we should expect this rule to hold on them. But numerous observations revealed that all three patterns may occur in the same litter. For more details on these observations, we refer to the article *Genetics of the silver tabby and shaded patterns, in particular in the American Shorthair*, by Dr. Carol Johnson, that is also an important reference for the rest of this chapter; for additional insight, see the article *Tabby pattern inheritance*, by Dr. Heather Lorrimer. The scientific article that gave full genetic evidence on the fact that at least three different loci are involved with the tabby patterns was published in the journal Genetics by Eduardo Eizirik and others in 2010.

So we must argue that the ticked allele is at a different locus, and is partially epistatic to the mackerel-spotted and classic alleles that are at the usual locus. Therefore there must be (at least) two Tabby loci. The hereditary transmission of the tabby pattern does not change very much with respect to the simpler classical theory (which is why we started by introducing it), except that now we can have all patterns in the same litter.

But there is another, subtler change. Very often we see ticked cats with bars on torso, neck, legs and tail and markings on head. Consider the opposite cases of the Abyssinian, that has no bars, and the Singapura, who has bars on the back hocks and the inside of the front hocks and on the tail. The cat association TICA does even include in its Uniform Color Description two different

tabby patterns to distinguish these two: *ticked*, where all hairs (except on the belly) are ticked, with no bars, and *agouti*, with bars on legs and tail. In the classic theory of tabbies, explain the ticked pattern with residual bars, that is the agouti pattern, as the consequence of heterozygotic **TᵃT**, with a (partially) recessive mackerel allele. But this cannot be, for two reasons. First, the partial dominance of ticked over mackerel becomes more and more dominant with age, whereas in old Singapuras the bars do not fade. Second, if it was so the transmission probability of the agouti pattern would always be 50%, with 25% purely ticked (no bars) and 25% purely mackerel. But nobody has ever seen purely ticked Singapuras, and even less mackerel Singapuras.

So, the explanation of the agouti pattern (ticked with residual, genetically stable bars on the legs and tail) is different: there must be a separate allele for this, or more probably, to fit the observed statistics of the transmission probabilities, a relatively small group of poligenes. If it is a single allele, the natural place for it would be the second Tabby locus, that is the locus for the ticked allele, or else a third Tabby locus; instead, if we are dealing with a group of polygenes, then obviously we should assume the existence of enough appropriate loci for them. So, we now have quite a number of Tabby loci! For simplicity, in the following we shall assume two main loci plus polygene loci.

For consistency with the classic notation, we still denote by **Tᵃ** the ticked tabby gene at the new Tabby locus. However, please observe that this allele causes ticking in all hairs (except the belly), thereby removing or muting the partially unmasked tabby pattern determined by the mackerel-spotted or classic genes at the old Tabby locus (except for residual markings on legs, tail and head). For this reason, and to avoid confusion at the expense of introducing a backward-incompatible notation, Dr. Johnson in *Genetics of the silver tabby and shaded patterns, in particular in the American Shorthair* calls this allele **U** (for Unstriped), and she calls **u** its recessive allele at the same locus: the allele **u** does nothing to mute the pattern, in other words it does not induce ticking on the hairs belonging to the tabby marks. We shall instead denote this recessive allele by **tᵃ**. So we have the following genotypes:

Tᵃ –	**t –**	ticked pattern, partially or totally masking mackerel-spotted
Tᵃ –	**tᵇ tᵇ**	ticked pattern, partially or totally masking classic
tᵃ tᵃ	**t –**	mackerel or spotted pattern
tᵃ tᵃ	**tᵇ tᵇ**	classic

How the ticked genes masks the mackerel or classic patterns

The new tabby pattern theory that we just presented requires further reflection, along the guidelines explained above. In the old theory, the ticked allele was partially dominant over the others (mackerel-spotted and classic). The action of the recessive allele was supposed to be partially or fully visible at birth, to fade away with growth. If there was no recessive allele, that is for homozygotic ticked (**TᵃTᵃ**) , then of course the kittens would be completely ticked already at birth, since there was no genetic coding for other patterns.

But with the new theory there is always genetics coding for the other patterns, since their alleles are present at another Tabby locus. How does the masking happen now? Is the masking action more pronounced when the new Tabby locus is homozygotic for **Tᵃ** (as, for instance, in the Abyssinians, that breed true for the ticked pattern without stripes, and therefore must be homozygotic for **Tᵃ**)? Or even for homozygotic **TᵃTᵃ** should we expect some visible underpattern on the flanks, with residual stripes or butterfly markings? It appears that this latter answer is the correct one: all Pixiebobs are heavily muted, and therefore they must be homozygotic for **Tᵃ**, but they all show visible spots, at least before they become old.

But then, some homozygotic **TᵃTᵃ** cats don't show any residual stripes or spots and some do.

Therefore the presence or absence of these residual ghost markings are not completely determined by the new Tabby locus: here again, the conclusion is that they must be regulated by other genes, or more probably groups of polygenes.

To understand the masking action better, in the next sections we consider how the tabby pattern appearance can be changed. This may happen by modifying the distribution of tabby bands in individual hairs or the localization of agouti hairs in the coat. Appropriate genes must be introduced to account for these changes.

But first, let us mention the fact that genomic studies proved the existence of multiple loci for the tabby genes. As we inferred in the sections above, there is indeed a locus for the ticked pattern and another locus for the mackerel/classic(=blotched) pattern. The homozygotic cats for the ticked allele are ticked, the homozygotic for non-ticked are not ticked, but the heterozygotic are ticked on the body but with mackerel stripes on legs, tail and face (the agouti pattern in TICA). The mackerel allele is dominant over blotched. The ticked pattern is epistatic over mackerel/blotched, that is, it masks the mackerel or blotched pattern. However, the heterozygotic cats at the ticked gene often have a progressive masking with age: at young age the underlying mackerel/blotched pattern is still well visible (we say it is muted). The localization of these loci in the chromosome was found in the paper by E. Eizirik et al., "Defining and Mapping Mammalian Coat Pattern Genes: Multiple Genomic Regions Implicated in Domestic Cat Stripes and Spots", Genetics, vol. 184 (2010), pp. 267-275. However, there are two important additions in this paper. The first is just terminologic: instead of using the old names T^a, T, t^b for the allelic sequence, these authors use new names. At the Ticked locus, responsible for the ticked pattern, they call the two alleles Ti^A and Ti^+, the first allele being partially dominant over the second (as we just mentioned, the heterozygotic combination $Ti^A Ti^+$ gives rise to the ticked pattern with underlying stripes on the points). At the other locus, thereafter called the Tabby locus, the sequence is Ta^M, Ta^b: the first allele produces the mackerel pattern and is dominant over the second, that produces the classic (=blotched) pattern. Therefore the table above should now be rewritten as

Ti^A –	Ta^M –	ticked pattern, partially or totally masking mackerel-spotted
Ti^A –	$Ta^b Ta^b$	ticked pattern, partially or totally masking classic
$Ti^+ Ti^+$	Ta^M –	mackerel or spotted pattern
$Ti^+ Ti^+$	$Ta^b Ta^b$	classic pattern

The second point to be explained in the above mentioned paper is the explanation of the spotted pattern, that comes from a group of polygenes that modify the stripes of the mackerel pattern into spots (several other loci). One additional locus would probably not suffice, because of the wide variety of spots, in packing (from sparse to tightly packed), arrangement (vertically aligned hinting stripes, or randomly distributed, or aligned along bull's eyes) and shape (spots, rosettes, marble design). If we would want to model all this as depending only on one locus, we would need many alleles! So, this is the first example pf polygenes associated to the tabby patterns (we are going to introduce a few more in the next sections). But, for the purpose of simplifying the calculations, we can do so, that is, assume only one locus for spotted pattern modification, where we could restrict attention to three alleles, that, in the order of dominance (dominant to recessive) should be: Ts^{sp}, Ts^{ma}, ts. The first allele changes mackerel to spotted, the second to marbled, the third does not give rise to any spotting. But, as already mentioned, only in rare cases the modern theory gives rise to different predictions from the old one-locus theory. As already observed, the difference are related to the fact that the same litter can contain kittens with more tabby patterns than possible in the old

theory, given the tabby patterns of father and mother. For instance, in the one locus theory, a litter of two ticked tabbies can contain kittens ticked and mackerel/spotted, or kittens ticked and blotched, but not kittens ticked, mackerel/spotted and blotched in the same litter. This is so because, in the one locus theory, a ticked cat must have at least one ticked allele T^a, and the other allele can be again T^a, and if so all kittens are ticked, or T or t^b, but of course not both. In case the parents are both heterozygotic, that is, have only one allele T^a, then we expect 25% of the kittens to be non-ticked. If both parents' genotype is $T^a t^b$, then the non-ticked kittens are $t^b t^b$, blotched. If both parents' genotype is $T^a T$ then the non-ticked kittens are TT, mackerel. If one parent is $T^a T$ and the other $T^a t^b$, then the non-ticked kittens are Tt^b, mackerel, since T is dominant over t^b. But in the multiple loci theory this is not so. For instance, if both parents have genotype $Ti^A Ti^+ Ta^M Ta^b$, then as before 75% of the kittens are ticked (even though two out of three of these kittens will be heterozygotic at the ticked locus, hence may have tabby marks on the points). Of the remaining 25%, non-ticked, one fourth will be homozygotic for Ta^b, blotched, one fourth homozygotic for Ta^M, mackerel, and one half heterozygotic $Ta^M Ta^b$, mackerel carrying blotched. So the same litter can include ticked, mackerel and blotched kittens. In addition, on the basis of the presence of spotted/marbled modifiers at the spotted loci, we can also have spotted and/or marbled kittens in the same litter.

But apart from this, all the conclusions of the one-locus theory are still correct. Therefore, in the rest of this paper, for the sake of simplicity and for greatly reducing the size of tables, we shall henceforth use the old terminology.

Polygenes for agouti band distribution: band frequency and wide-band genes, as for instance in the shadeds

Every hair in the agouti areas has alternate bands of the full genetic color (eumelanistic or pheomelanistic) and agouti bands. The agouti bands are pheomelanistic, and are the consequence of the action of the agouti signal protein ASP (antagonist of the melanocyte stimulating hormone) on the melanocortic receptor, as explained in the previous chapter. For instance, let us consider an eumelanistic hair. When sufficiently high levels of this protein are reached, the pigment production in its pigment cell shifts from eumelanin to phaeomelanin, but after this happens the protein level decreases and after some time the pigment production reverts to eumelanin. So the hair tip is always eumelanistic, and the rest of the hair has alternating bands. The frequency of the bands is inversely proportional to the time needed to the ASP protein level to exceed the transition level and to fall back below it. This time is not the same for each hair, and not even for each band in the same hair, and this gives rise to a possibly irregular distribution of bands (length, position and number) from hair to hair. The wide-bands introduced to explain the goldens are an example: the agouti band near the skin is long, that is its pigmentation period is long, or we can say that the frequency is low. (However, the evidence for inheritance probabilities appears to indicate that the wide-band genes may be at a different locus than the band frequency genes that we are about to discuss in this section, so that they transmit independently.)

The masking effect of the ticked pattern over the other tabby patterns is related to the frequency of banding. The important aspect of it is not, in this respect, the length of the agouti bands (that, instead, is so important for smokes and for goldens). The important aspect is the coherence of the bands. If the pigment follicles of adjacent hairs are well synchronized in their ASP levels,

then these hairs have bands at the same places and of the same length. When this happens, the ticking appears more uniform and generally darker. This is the case for Abyssinians. Ayssinians have a very uniform ticking: all hairs in large areas have more or less the same number of bands, and the corresponding bands in different hairs have more or less the same length. The base of the hair in non-silver Abyssinians has a markedly rufoused and relatively wide band, that creates a beautiful apricot base color in ruddies and cinnamons, and a clear base with beautiful contrast in blues. The overall effect is to have a uniform ticking and color all over the flanks, all the way down to the beginning of the belly, where ticking stops and all of a sudden the hair changes color and becomes paler. In blue Abyssinian the belly color has a rosy hue, and this effect of color contrast is astonishing. It is very interesting to notice that a similar effect often occurs in shaded silver Abyssinians, although the selection for this color variety has been shorter because this variety has been accepted more recently in some large associations, for instance the american associations: several shaded silver Abyssinians show a relatively uniform ticking aver the flanks, due to coherence of the band frequency, with strong contrast to the candid white belly.

The converse happens for American Shorthairs and Persians, for instance. In these breeds the preferred shaded silver pattern, in most association, should have a sparkling appearance. This is achieved by selecting for very non-uniform frequency of agouti bands. The lack of coherence in the bands makes the silver emerge more randomly and more effectively, and this helps greatly to create the sparkling look (in Persians, the long hairs help further, by giving rise to a possibly larger spreading of the band distribution and a certainly wider spread of alignment of bands due to gradual overlapping of hairs).

There must be a gene that controls the band frequency, because the effect is genetically transmitted. More likely, since the localization and number of agouti bands varies over a considertably huge range, instead of one gene there should be a family of poligenes, but probably not many, because the inheritance is relatively predictable (large groups of polygenes have transmission probabilities that follow a more complex statistics, that gives rise to more gradual effects: see, for instance, Roy Robinson's book, *Genetics for Cat Breeders*, 2nd edition, Chapter 4, or its outline given by the present author in *Inbreeding for closed stud systems*). As a consequence of the need to select for more genes, selection and inbreeding for groups of polygenes takes more generations (and, for large groups, considerably more) than for a simple principal gene.

Although here we are likely to have a small group of polygenes (or a group of alleles), we shall pretend to deal with just one gene, for the sake of simplicity. Dr. Johnson in *Genetics of the silver tabby and shaded patterns, in particular in the American Shorthair* calls this gene *Confusion*. To make notation shorter, we shall call it **F** (for *frequency*). The dominant allele **F** yields coherence of the band frequency distribution; the recessive allele **f** creates disorder.

Observe that the action of **f** is a powerful tool to mask a striped, spotted or classic pattern. Indeed, the tabby markings gain their contrast by the coherence with which the full color bands of adjacent hairs are aligned. For instance, a perfect classic pattern should be associated with full coherence (**F-** or better **FF**) to enhance the tabby markings; the same is true for the spots of Bengals (this is the genetic reason for the Bengal breeder to prefer lack of ticking:this simply means lack of disordered short bands of high frequency superimposed to the low frequency of the bands inside the spots). In particular, here are four breeds where the classic pattern is selected for complete contrast, and therefore full coherence (**FF**): Persians, Exotics, American Shorthairs and (marbled) Bengals.

In particular, let us see what this means if we want to select for excellent shaded silvers after having performed an outcross to a brown or silver classic tabby (a question of interest to breeders of American Shorthairs, that has been considered for this breed in the above mentioned paper

by Dr. Johnson, but has been answered there without a precise computation of probabilities). The problem is how many generation we should wait before being able to recover the perfect shaded silver pattern by selection. Here we give a more accurate explanation by computing probabilities. To save space we shall never write full tables of combinations Punnet diagrams): the probabilities will be obtained by muliplying results of partial tables. The reader who feels uneasy with this method should read the last chapter of this paper before proceeding.

The mating of a cat with a fully disordered band frequency distribution **ff**, for instance a shaded silver American Shorthair or Persian, to another cat with orderly, coherent distribution **F-** (or better **FF**), for instance a brown classic tabby or silver classic tabby American Shorthair, typically yields all kittens of uniform, coherent tipping in the first generation, bur all carriers of **f**. Mating these together, in the second generation we can expect 25% of the kittens to be disordered in banding frequency, that is sparkling shaded silvers instead of dark, heavily tipped if they are shaded silvers. Of course, if we start with a very good shaded silver to begin with, this ancestor should be homozygotic ticked (**T^{a}T^a**), as we explained in the chapter on silvers: indeed, this is how the masking effect of the ticking to the recessive striped, spotted or classic patterns is at the fullest. Then in the first generation of the above mating all kittens are heterozygotic ticked (**T^{a}t^a**), that is, if silvers, they are shaded with poor pattern,with residual ghost bars and markings. All kittens in the first generation are heterozygotic **Ff**, that is rather good classic tabbies or else too dark ticked tabbies or shaded silvers with heavy tipping.

In the second generation 25% of the kittens should be non-ticked **t^{a}t^a**, for instance silver classic tabbies, 50% heterozygotic ticked **T^{a}t^a**, that is poorly tipped shaded silvers or brown ticked tabbies with some residual ghost markings, and 25% homozygotic **T^{a}T^a**, that is shaded silvers or brown ticked tabbies of excellent pattern. If we are selecting for excellent shaded silvers we should restrict attention to these 25%: but they cannot be all excellent, because to be excellent, sparkling shaded silvers they must have disorder in the band frequency distribution, that is they must be homozygotic **ff**, and this happens only 25% of the times. So, in the second generation, only 25% times 25%, that is one out of 16, of the kittens have the desired pattern.

In the first generation of the mating of a shaded silver heterozygotic for silver to a brown classic tabby, half of the kittens are expected to be silvers and the other half brown tabbies, and all the silvers must be heterozygotic silvers, whereas, if the shaded silver is homozygotic, then all kittens are heterozygotic shaded silvers *(why? We leave all this to the reader as an exercise)*. Therefore, by mating two silver shadeds from the first generation, in the most unfavourable case we still can expect only 75% of silvers among their kittens. If our goal is to recover a beautiful sparkling shaded silver pattern, by piling up these probabilities we see that our chances are only 25% times 75%, that is 3 out of 16, in the second generation: but to have these kittens in the second generation we must restrict the matings among cats of the first generation to silvers only: they are all silvers only if the shaded silver ancestor is homozygotic for silver (**II**), otherwise this constraint reduces the chance to 50%: the fact that we need to chose two such cats for the next mating reduces all possibilities further down of a factor ¼. But even not counting this possibility (that is, limiting the shaded ancestor to be homozygotic for ticking and for silver), we still are expecting chances of the order of 1/16 times 3/16, that is 3/256, a number of the order of one over 85. But a queen does not give birth to 85 kittens in a lifetime! True, we can use several different couples of first generation siblings for the matings, but we have just observed.that the expected number of appropriate first generation cats to choose from is severely limited.

If the original mating of the shaded silver is made to a silver classic tabby, then all or some of the first generation kittens are homozygotic for silver, and this increases these slim chances to find good cats to mate again, but it is clear that a reasonable hope of recovering a good shaded

silver pattern must lead us at least to the third generation and most probably to the fourth, and actually may possibly never work if we are not lucky and insist in performing inbreeding within the same closed line group. To make the project work, of course, we should mate a cat of the first generation to a cat not from the same parents: we should use an excellent silvers, and to increase our chances this cat should be as homozygotic as possible: **II TᵃTᵃ ff**. Then the mating of this cat to those form the first generation of genotype **I- Tᵃtᵃ Ff** yields one probability over 8 to achieve the desired result: that is, we have to divide by 8 the already slim probability of success of the first generation (1/16), and the probability of having a good second generation kitten is 1/16 times 1/8 = 1/128: it is virtually impossible to succeed in our goal in the second generation even with a second generation outcross to a perfect shaded silver.

Of course this estimate of three to four generations in order to recover the perfect shaded pattern with a second and third generation outcross to a perfect shaded, after outcrossing to a silver or brown classic tabby in the first generation, takes into account the band frequency coherence only, and is valid under the assumption that this coherence is due to a simple Mendelian gene, not a group of polygenes. If we refer to a group of polygenes, as explained expect to wait more generations before we recover the pattern.

But unfortunately, this is not quite true. We have forgotten two problems: the persistence of stripes and bars on torso and neck and legs and tail, that we mentioned above, and the need of wide-band genes for perfect shaded silvers, explained in the chapter on silvers. We must erase these pattern faults by further selection. To understand how, we need to consider another appropriate gene. We do this in the next sections.

Observe also that, if we start with an outcross to a brown classic tabby instead than a silver classic tabby, we induce tarnishing (that is, rufousing) on the silver base. Tarnishing is due to a group of polygenes, and requires at least two generations to be erased, if in the second generation we outcross to a perfect, untarnished shaded silver (by selection only within the same closed group we might never erase the tarnishing unless we are very lucky).

Polygenes for agouti hair distribution: area coherence

The other important genetic factor in establishing a clear, stripeless shaded silver pattern is the lack of area coherence of the agouti hairs. To understand this point, consider a perfect silver classic tabby or brown classic tabby. The markings are intensely colored of the full genetic color, say black; the agouti areas, instead, consist of agouti hairs only, either pale (for silver tabbies) or rufoused (for brown tabbies). The transition from the markings to the agouti areas is sharp. In a less perfect classic tabby this transition is not sharp: the markings are muted by some agouti hairs. We have already discussed, in the chapter on silvers, the occurrence of a silver band at the base of the hairs in the markings; the same happen for brown tabbies. The base band is not visible without opening the coat and therefore does not disrupt the pattern; agouti hairs with many bands, however, are visible and mute the pattern. This muting is what Bengal breeders call ticking, a bit inappropriately, because Bengals, being tabbies, always have ticked hairs in the agouti areas. By ticking the Bengal breeders mean the presence of banded agouti areas inside the black spots.

Contrarily to the case of brown spotted or marbled Bengals, this intrusion of agouti hairs inside the markings is often desirable to obtain a perfect shaded silver: it helps destroying the remaining stripes in the torso. Again, this amounts to have a lack of order in the area distribution of agouti hairs: a lack of area coherence. We must introduce a new gene to account for the genetic transmission of area coherence. Again, due to the wide range of area distributions of agouti hairs,

we should assume to have a group of polygenes, but for the sake of simplicity we only introduce one simple Mendelian gene, that we call **Ad** (for agouti area distribution): Dr. Johnson in *Genetics of the silver tabby and shaded patterns, in particular in the American Shorthair* calls this gene *Chaos*. The dominant allele **Ad** yields lack of coherence (disorder), the recessive allele **ad** yields order, that is unmuted stripes or spots or butterflies. Because of this dominance, in the mating of a clear shaded silver to a silver tabby, all kittens in the first generation are likely to have no stripes in the torso (on the contrary, the lack of coherence for the frequency distribution is given by the recessive gene **f**: therefore all such kittens are likely to have rather uniform ticking, that appears heavy). This of course is accurate only under our oversimplification that assumes that these two factors are controlled by simple Mendelian genes and not by several polygenes.

With the introduction of this new factor, the breeding project outlined above, that starts with the mating of a clear sparkling shaded silver to a classic tabby and is aimed to recover an excellent shaded pattern, becomes more difficult. The shaded has genotype **Ad –** but the classic tabby has genotype **ad ad**. In the first generation all kittens are **Ad ad** or **ad ad** if the shaded parent is heterozygotic: **Ad ad**, as already observed, is ok for a good muting of stripes on the torso, but we must discard the **ad ad** kittens from the breeding line. So we keep two **Ad ad** cats and marry them to obtain a second generation that, of course, will give rise to 25% **ad ad** kittens, not useful for our purposes, 50% **Ad ad**, good but perhaps not perfect, and anyway undesirable for continuing the line because they would give rise to some **ad ad** kittens in the next generation and so would not breed true, and finally 25% **Ad Ad**, that is what we want. This introduces a further decrease in the expected probability of success of the order of ¼. Therefore the number of generations that we should expect necessary to recover the perfect shaded pattern increases: it was four (three only if an outcross to a perfect clear sparkling shaded silver outside of the closed line group was made in the second and third generation): now it increases to four or five (four is likely enough if outcrosses to perfect clear sparkling shaded silvers outside of the closed line group are made in the second and also the third generation, and the line breeding is repeated with as many couples of first generation siblings as possible). Quite a long wait!

The Area Distribution locus controls the erasing of stripes from the torso. Leg and tail bars, and also necklaces, are more persistent, and are likely to be controlled by genes at yet another locus, therefore acting independently (or by different genes in this group of polygenes, located at different loci).

This fact makes the goal of the breeding project outlined above (the recovery of the perfect shaded pattern) still longer to achieve. Actually, it is even longer than expected so far, because we still have to reintroduce the wide-band genes, already introduced in the chapter on silvers. We reconsider them in in the next section, that is just a recapitulation on silvers on the basis of the updated tabby theory.

A recapitulation on shaded silvers: the inhibitor gene and band distribution

Let us go back to the conclusion of the previous chapter on silvers, with the aim of relating them to the present theory and analyzing further the line breeding of a clear sparkling shaded silver pattern. We have just introduced a ticked tabby gene responsible for muting all stripes except on legs, tail, neck and spine, plus band frequency genes and area distribution genes responsible for making the pattern clear and sparkling and disrupting these residual tabby markings, respectively. All this, however, applies equally well to brown ticked tabby patterns, where, often, we do not want too much clarity: we like intense rufousing but visible, coherent brown ticked tabby patterns, as in the Abyssinian, that has plenty of disordered area distribution, that is the incoherence induced by the area distribution gene, but no band frequency variation.

On the other hand, to have a silver ticked tabby, this is not enough, we need the silver gene **I-** that inhibit pigmentation (no rufousing, unless partially induced by secondary polygenes). Still, this is not enough to have a perfect shaded silver color, because the overall silver ticked tabby look is too dark. A perfect shaded silver must have a long clear hair base: the result of the wide-band polygenes. The base becomes white for a long stretch, and the colored bands closer to the hair base disappear: the color becomes not only sparkling (salt and pepper) but also confined to the tips (or maybe with an additional short band or two near the tip). In brown tabbies, non silver, the action of these wide-bamd polygenes gives rise to goldens.

Returning to the line breeding of shaded silvers, the hope to recover the perfect shaded silver pattern after an outcross to a silver tabby or to a brown tabby now must take into account the transmission probabilities of the wide-band polygenes, that are a bit more complex as always when we deal with groups of genes instead of a simple mendelian one. The silver tabby or brown tabby may not have significant wide-band action (it might, in which case we would have a silver tabby with really pale base areas or a golden tabby; because of the difficulty in distinguishing at birth a golden tabby from a non-golden brown tabby with large areas of markings, some associations, notably TICA, do not register golden tabbies except in the ticked variant, that is golden shaded). If the ancestor used for outcross does not have wide-banding, chances to recover the perfect shaded pattern are even lower, and we may have to wait one more generation for this goal. Of course, if many breeders cooperate in this program and so enough kittens are born in each generation, it is likely that simultaneous selection may be more effective and reduce the number of generations that we must wait before success to four instead than five or six. Again, this holds under the assumption that more or less always, after the first outcross, we avoid to inbreed the cats generation after generation but instead apply line breeding on the original perfect shaded silver ancestor, that is we use descendants of him, with enough consanguineity, but no disruption of the shaded silver pattern brought in by the classic tabby ancestor).

Burmese and siamese modifications (sepia, mink, pointed colors); the Ojos Azules gene. All the coat colors introduced so far are fully colored (possibly with silver or golden depigmentation). There is a family of genes, called the *albino* family, which act on color distribution and give rise to various shades of color intensity. The albino family consists of a dominant one, the full-color allele **C**, and several more: the burmese allele c^b, the siamese c^s, the blue-eyed albino c^a and the pink-eyed albino **c**. The burmese allele is partially dominant over the siamese allele. They are both dominant over c^a, which is dominant over **c**. The last two genes are rare, and experimental evidence is not sufficient to ascertain if dominance of c^a over **c** is partial or total.

The action of the genes at the albino locus consists in coding for the hormone tyrosinase, that activates the melanocytes. Therefore these *pointed* genes yield some degree of depigmentation. This hormone is heat-dependent, hence, when these depigmentation genes are fully active, the corresponding colors are darl on the parts of the body that are less warm: face, tail, ears, feet.

The c^b allele makes the pigmentation lighter: the pigment cells become longer, and the resulting color has reddish tinges. In the ideal cat, the points (head, ears, legs, tail) should be of the same color shade of the body, but since pigmentation is temperature related, the points are often slightly darker. This group of colors (in the various eumelanistic, pheomelanistic or tortie variants) are called *sepia.* We do not say "black sepia" but "seal sepia", or also "sable". Breeds

where the accepted colors are only sepia are the Burmese (sable, blue sepia, chocolate sepia, and so on) and the Singapura (sable ticked tabby). Eye color is also affected by c^b. For instance, Burmese have gold eye color, or chartreuse (green-gold to yellow-green), but neither copper nor green.

The c^s allele gives rise to pointed colors, as in the Siamese or the Himalayan. The body is light (typically, warm ivory in the dark eumelanistic colors, and cream-white in the light eumelanistic or pheomelanistic ones). The points are intensely colored, but their color has reddish shades. The points of a genetically black pointed cat are seal rather than black. All colors have a pointed counterpart. Eye color is also changed: it is blue.

The genotype $c^b c^s$ gives rise to an intermediate phenotype, where points are intensely colored with reddish shades and body is paler with similar shades. The overall color is paler than burmese and has less contrast than siamese. These colors are called *mink,* and are typical of Tonkinese. The eye color is aquamarine (between blue-green and green-blue).

The last two alleles are called albino. The c^a allele stops pigmentation completely on body and points (which become white), and makes eyes blue. The c gene completely stops pigmentation everywhere: points and body are white, and eyes are transparent with pink hue due to the blood vases in the retina.

Genetic transmission related to the albino group is straightforward. Here are a couple of tables, rather obvious. By breeding two solid colored cats, one carrying burmese and the other siamese, we obtain 25% homozygotic fully colored kittens, 25% solid kittens carrying burmese, 25% solid kittens carrying siamese and 25% mink.

	C	c^b
C	CC	Cc^b
c^s	Cc^s	$c^b c^s$

In the second example, we breed a homozygotic siamese with a burmese carrying siamese, and obtain 50% pointed kittens and 50% mink (of course, if the body and head types of the parents are siamese and burmese, the kittens have intermediate types, which might result in poor tonkinese).

	c^b	c^s
c^s	$c^b c^s$	$c^s c^s$

Finally, homozygotic pointed cats mated to homozygotic sepias produce all mink kittens.

Concerning blue eye color, it is worth observing that blue eyes are produced not only by the genes c^s and c^a (and **W**), but also by a recently discovered dominant gene **Oa**, whose only consequences on color are blue eyes and white tail tip. This gene is distinctive of one breed, the Ojos Azules. It has been recently discovered that the Ojos Azules gene can have dangerous effects on the cat's health, and the breeding projects have been abandoned.

Problem. *What are the colors (and their probabilities) of the kittens of a brown tabby carrying siamese **Aa $t^b t^b$ Bb o- Cc^s** and a seal mink tortie **aa Tt^bBB Oo c^{b}c^s**?*

Genetics of coat structure: longhair, rex, wirehair and hairless. The somatic traits controlled by principal Mendelian genes are not limited to coat color. Here we consider coat structure. First of all, let us deal with coat length, controlled by a principal gene **L**, which gives rise to short hair, and the recessive allele **l**, which produces long hair. The effect of **l** is strenghtened or attenuated by a group of modifier genes, so that coat can have many levels of length (long, semi-long, and so on). For example, let us consider breeding a persian **ll** to an exotic shorthair heterozygotic for **L** (that is, carrying longhair).

	l	*l*
L	Ll	Ll
l	ll	ll

Statistically half of the kittens are persian and the other half exotic shorthairs carrying longhair. Please note that the longhair kittens are genetically persians, because they have two longhair alleles and the part of the genotype controlling morphology is the same for exotics and persians. This conflicts with the registration rules of a large cat fancy association, CFA.

There are other genes that control coat texture. Of particular interest is a group of genes producing curly hair. It is called the Rex family, and consists of the Cornish Rex gene **r**, the Devon Rex gene **re** and the Selkirk Rex gene **Rs**. Consistently with our use of small and capital letters, **r** and **re** are recessive, but **Rs** is dominant.
The Cornish gene produces a coat without guard hairs, consisting only of short, dense, soft undercoat arranged in smooth parallel waves. The Devon gene allows both undercoat and guard hairs, but both types of hair are wavy and weak; the coat is sparser than in Cornish Rex. The waves of individual hairs do not repeat consistently, so that the coat does not follow a wavy pattern: the arrangement has no particular order. Finally, the Selkirk Rex' coat consists of semi-long curly hairs, whose shape resembles a cork-screw.

The genetics of rex genes is straightforward. Let us see some examples. Half of the kittens of a Cornish Rex stud and a dam with normal coat carrying Cornish Rex have Cornish Rex coat, and the other half has normal coat (but these kittens carry **r**):

	R	*r*
r	R r	r r

Similarly, a Devon Rex bred to a cat with normal hair but carrying **re** produce 50% kittens with Devon Rex coat, and 50% with normal coat (carrying **re**):

	Re	*re*
re	Re re	re re

In our last example, we cross a Selkirk Rex heterozygotic for **rs** with a cat with normal coat (hence homozygotic for **rs**). Statistically half of the kittens have Selkirk Rex coat; the other half has normal coat. Obviously, the latter do *not* carry Selkirk Rex, since **Rs** is dominant!

	Rs	*rs*
rs	Rs rs	rs rs

The three Rex genes are at different loci, hence they interact as independent genes. For instance, here is what happens when crossing a Cornish Rex not carrying Devon (**rr ReRe**) with a Devon Rex not carrying Cornish (**RR re re**): all kittens have normal coat, but they carry both Cornish and Devon.

	r Re
R re	R r Re re

In second generation, we cross the cats obtained in the previous example, and get the following.

	R Re	*R re*	*r Re*	*r re*
R Re	RR Re Re	RR Re re	R r Re Re	R r Re re
R re	RR Re re	RR re re	R r Re re	R r re re
r Re	R r Re Re	R r Re re	r r Re Re	r r Re re
r re	R r Re re	R r re re	r r Re re	r r re re

The first row and the first column yield kittens with normal coat. So do the third cell of the second row and the second cell of the third row. The second and fourth cells of the second column yield kittens with Devon coat, and the last two cells of the third column correspond to kittens with Cornish coat. Finally, the last cell of the second row yields Devon coat structure, the last cell of the third row yields Cornish coat, and the cell in the lower right corner corresponds to kittens whose coat has at the same time the characteristics of Cornish and Devon. It may be difficult to spot these kittens. They should have an intermediate texture, with only a partial wave pattern and irregular curls in other body areas, sparse guard hairs and weak hair structure.

Another gene that controls hair structure is the Wirehair (**Wh**), a dominant gene which produces rigid curly hairs, twisted at the tip. This hair structure is the distinguishing feature of the American Wirehair, which has some similarity with a wire-hair version of the American Shorthair. The next table shows the outcome of the mating of a heterozygotic American Wirehair (**Wh wh**) and an American Shorthair (**wh wh**): 50% of the kittens are heterozygotic American Wirehairs, the other half American Shorthairs.

	Wh	*wh*
wh	Wh wh	wh wh

Still another breed with curly hair is the Laperm: its gene is dominant, and produces loose bouncing ringlets. This gene is probably not the same as **Sr** and/or **Wh**, since the coat structures are different.

Finally, we mention the recessive Hairless gene **hr**, which stops hair growth almost completely. The cat is naked or with only a fine down everywhere except on the back of the ears, nose bridge, tail and feet, where the coat may be a fine down but is usually just a bit longer. The dominant allele **FullHair** produces normal coat. Lack of hair is the distinctive feature of Sphynx, a breed homozygotic for **hr**. If a Sphynx is mated to a normally coated cat (say, homozygotic for normal hair, **FullHair FullHair**), all kittens have normal hair and carry **hr**. Crossing together the cats obtained this way, in second generation 25% of the kittens are hairless, 50% have normal coat but carry **hr** and 25% have homozygotic normal coat (that is, they do not carry **hr**). We can

double check this statistical distribution by looking at the corresponding table:

	FullHair	*hr*
FullHair	FullHair FullHair	FullHair hr
hr	FullHair hr	hr hr

the Devon Rex and the Hairless genes are variants at the same locus, called KRT71 because it is responsible for coding for cheratine, an essential constituent of the hair. The "normal hair" alleles **Fullhair** and **Re** coincide, and the order of dominance at the Hairless-Devon locus is: **Fullhair**, **re**, **hr**. That is, Devon Rex curliness is dominant over hairlessness. Another gene at the same locus KRT71, **Hr**, is fully dominant on these and produces complete lack of hair: it is the gene of the Don Sphynx, or Donskoy Sphynx.

There is another gene which produces lack of hair, the Peterbald gene **Pd**. It is a dominant gene, at a different locus than KTR71, hence with an independent action. Therefore a cat may be naked because of either one *or both* the genes **hr** and **Pd**: to avoid phenotypes with dubious genotypes, outcrosses of Sphynx to Peterbald (or Donskoi Sphynx) are not allowed in championship. There are modifiers (or maybe other alleles at the same locus) that give rise to non-naked cats with various types of relatively sparse curled coat type in the Peterbald (*chamois, flock* or *brush coat*).

Boning and ear-shape genetics: polydactylism, manx, fold, curl, bobtail, munchkin.
Somatic traits related to boning and cartilage are controlled by several principal Mendelian genes. These genes may possibly be dangerous, because they may cause anomalies or deviations from normality in somatic traits which are important for survival. Here we restrict our attention to six of them, all dominant. Genetic transmission of dominant genes should be obvious by now, hence we shall skip offspring tables in this chapter.

The first gene to be studied is the polydactyly gene **P**, that produce a higher than normal number of toes: more than five in the front feet and/or more than four in the back feet. The recessive allele **p** yields the correct number of toes. Some cats have less toes than normal. Here we ignore this phenomenon, because it is not clear if it is the consequence of a principal gene, and if this hypothetical gene is at the locus **P**. Polydactyl cats or cats with abnormal numbers of toes are accepted in championship only in a few specific breeds. They are accepted in the household pet class, because household pets are not inbred, hence no genetic fixation occurs (anyway, they should be neutered when they become adults).

We consider next the Manx gene **M**, which produces tailless cats; its recessive allele **m** allows the tail to be normal. Unfortunately, this gene is not only potentially dangerous: it is specifically dangerous, since it may yield severe anomalies of the hip boning and weak back leg bones. It is usually lethal if homozygotic. Homozygotic Manx kittens usually die before birth (often so early that the fetus is reabsorbed). Therefore all Manx cats (or Cymric, the longhair Manx) are heterozygotic Mm. In order to avoid frequent and dangerous prenatal deaths, matings of two Manx are severely discouraged. Breeding programs are based on outbreedes to breeds whose type is close to the Manx, but with normal tail (like British Shorthair or American Shorthair, or even better, the cats born in Manx breeding lines but not tailless, that is homozygotic **mm**). The action of M is somewhat gradual: there are completely tailless Manx, and others whose tail is a stump or even longer. Any visible length of tail is penalized in TICA championship.

Another gene that acts on tail shape (but does not produce dangerous side-effects) is the

Japanese Bobtail gene, a recessive which produces the curly pon-pon tail of the Japanese Bobtail. In some associations, the curly tail phenotype due to the Bobtail gene is accepted in other breeds too (for instance, the American Bobtail in TICA: however, the gene is different, it is dominant). These genes in all likelihood are not alleles of the Manx gene (that is, they are at different loci). The fact that the **jb** and **Mm** genes are not at the same locus would be easy to determine by breeding Japanese Bobtails to Manx, but -as it is easy to understand- the breeders are not interested in this outcross. The Bobtail gene has not been given a symbol. We could denote it by **jb**. Other variants of the kinked tail genes appear in various other breeds of bobtailed cats: sometimes the differences are probably due to a group of polygenes, as in the case of American Bobtails and Kurilean Bobtails.

We consider next two genes which modify the ear cartilage. They are the Fold gene **Fd** and the Curl gene **Ac**. The recessive alleles **fd** and **ac** produce normal ears. The effect of **Fd** is to fold the ears forward, in a cap-like fashion, close to the skull. This is the distinctive feature of the Scottish Fold breed. The gene **Ac** makes the ears curl backward, the typical feature of the American Curls breeds (longhair and shorthair). The Fold gene is particularly dangerous because it may induce skull deformations (the two lobes may not merge), and boning problems in the hips, back legs and tail (the vertebrae may thicken and glue rigidly, the cat may be unable to walk normally and die because of boning degeneration). In homozygotic form this gene is usually lethal: the kittens die before birth. To avoid this risk, Scottish Folds are not bred to Scottish Folds: they are usually bred to British Shorthairs or American Shorthairs, or better to *Scottish Fold straight,* that is, cats from Scottish Fold breeding lines (hence with the Scottish Fold type) which are homozygotic **fd fd** (hence with straight ears). On the opposite end, the American Curl gene does not seem to have any dangerous side-effects.

The fold and Curl genes are at different loci, so they interact as independent genes. For practice, the reader may fill up the table of the breeding of a Scottish Fold to an American Curl shorthair, in the two cases of homozygotic Curl **Ac Ac** or heterozygotic Curl **Ac ac**. Of course, the Fold must be heterozygotic **Fd fd** (homozygotic **Fd** is lethal!). In the first case, the genotypes of the two parents are: American Curl **fd fd Ac Ac** and Scottish Fold **Fd fd ac ac**; in the second case, they are respectively **fd fd Ac ac** and **Fd fd ac ac**. Here we list the outcome of the second case, that is more complicate. It is immediately seen that 25% of the kittens have straight ears, 25% folded, 25% curled and 25% percent in between these two extremes. It is difficult to imagine what is the look of the intermediate phenotypes between Fold and Curl... and, luckily enough, we should have no experimental evidence, because this type of breeding is probably not going to be tried by anybody (except maybe somebody fond of genetic anomalies). The straightforward task of adapting these results to the case of a homozygotic American Curl parent is left to the reader.

Finally, the Munchkin gene (or should we say dachshund?) is a dominant gene recently found and fixed. The Munchkin breed is not accepted in championship, but can be seen at TICA shows as a New Breed, and is been bred by an enlarging group of TICA breeders. Its name is taken by a kind of dwarfs from the novel*The Wonderful Wizard of Oz.* The phenotype has some similarity to the dog breed Dachshund. The gene produces very short legs, so the body is very low on the legs, and the Munchkins walk snakily. This gene does not produce dwarfism, because only the legs are short: the body size is normal. Undoubtedly the Munchkin gene changes considerably the usual bone structure, but Munchkin breeders seem to have gathered enough evidence to infer that the gene is not dangerous. That is, it does not produce dangerous bone deformities or serious constraints on movements (for instance, the Munchkins are able to jump without problems). We'll need to wait and obtain conclusive evidence, but to some extent, the fact that the Munchkin breed may at first glance appear not acceptable could be explained by its unusual, somewhat queer look. Perhaps the same diffidence might have existed for dachshunds

at the beginning. The Munchkin gene has not been assigned a symbol yet.

We complete this chapter by observing that another somatic trait related to boning, and probably due to a principal gene, is frequently seen in purebred cats: the tail kink. It is an anomalous form of tail boning. It is formed when two consecutive tail vertebrae coalesce at an angle. It is a disqualification in all pure breeds, but it is accepted in household pets, for the same reasons explained above for polydactilism.

Determining possible colors of kittens without using tables. So far we have analyzed the results of breedings between complex genotypes by means of large comprehensive tables containing a cell for each possible combination of all involved genes. This procedure is too slow: we often need to derive the results quickly and without writing.

This is trivial when the genotypes are simple and involve only one or two genes. For instance, recall what happens in the breeding of a black carrying chocolate to a homozygotic chocolate (as usual, the homozygotic gametes appear once, not twice in the table):

	B	*b*
b	Bb	bb

Half of the kittens are blacks carrying chocolate, the other half are homozygotic chocolates.

Now let us increase the complexity, one step up: we introduce a second gene. let u consider a black carrying chocolate*and maltese dilution,* **Bb Dd**, mated to a chocolate *carrying maltese dilution,* **bb Dd**. For this, we made use of the following table.

	BD	*Bd*	*bD*	*bd*
bD	BbDD	BbDd	bbDD	bbDd
bd	BbDd	Bbdd	bbDd	bbdd

Statistically, out of eight kittens, one should be black carrying chocolate, two should be blacks carrying chocolate and dilution, one blue carrying chocolate (that is to say, carrying lilac!), one chocolate, two chocolates carrying dilution, one homozygotic lilac. there is an intrinsic symmetry in these results, which reflects into symmetry between the left and right halves of the table. This suggests the possibility of splitting the full 2 by 4 table into two separate tables. This possibility is actually reality. Here are the two "component partial tables".

	B	*b*
b	Bb	bb

	D	*d*
D	DD	Dd
d	Dd	dd

The full table is recovered by "multiplying" each cell of one of the partial tables by all the cells of the other, a straightforward operation called "tensor product' in mathematics.

The partial tables show that:
-        the probability that a kitten is black heterozygotic to chocolate or homozygotic chocolate is the same, 50% in each case;

-        the probability that a kitten is: pure undiluted (that is, homozygotic for full color) is 25%; full color carrying dilution, 50%; diluted (homozygotic for maltese dilution), 25%.

By combining these data (that is, multiplying the corresponding probabilities), one obtains the full probability distribution: the genotypes **BbDD**, **bbDD**, **Bbdd**, **bbdd** have probability 12.5% each, and both **BbDd** and **bbDd** have probability 25%. Exactly what we obtained by looking at the full table!

Now let us investigate the results of breeding a black stud carrying chocolate and maltese dilution, **BbDdo**, to a chocolate *tortie* dam carrying dilution, **bbDdOo**. We only need to throw in an additional component table, the partial table which describes the transmission of the orange gene:

	o	-
O	O o	O -
o	O o	o -

Then we immediately see that a quarter of the genotypes are those obtained in the last example, and another quarter is obtained by replacing black with red, (or blue with cream): these are now the genotypes of that half of the kittens that are males). The other half (for the females) is obtained by replacing these with the corresponding tortie colors. In short, one has:

-        males: eumelanistic solid colors (black, blue, chocolate or lilac) **BbDDo**, **bbDDo**, **Bbddo**, **bbddo** with probability 3.125% each, and **BbDdo**, **bbDdo** with probability 6.25% each; pheomelanistic solid colors (red or cream) **BbDDO**, **bbDDO**, **BbddO**, **bbddO** with probability 3.125% each, and **BbDdO**, **bbDdO** with probability 6.25% each;

-        females: tortie colors **BbDDOo**, **bbDDOo**, **BbddOo**, **bbddOo** with probability 6.25% each, and **BbDdOo**, **bbDdOo** with probability 12.5% each.

Let us step up to more genes. Let us mate a black *silver tabby* stud carrying chocolate and dilution, **Aa Tt^b Bb o Dd Ii Sv Sv** (here, for the sake of simplicity, we adopt the two-gene theory discussed in the chapter on silvers, in order to avoid computations involving polygenes as the wide-band modifiers), to a chocolate tortie *smoke* dam carrying dilution, **aa t^{b}t^b bb Oo Dd Ii Sv sv**. Note that (except for dilution) this problem is almost the same as the one given at the end of the chapter on silvers. To find the solution quickly, just throw in four additional tables: agouti, tabby pattern, eraser gene **I** and silver (=bleaching) gene **Sv**.

	A	*a*
a	Aa	aa

	T	*t^b*
t^b	Tt^b	t^{b}t^b

	I	*i*
I	II	Ii
i	Ii	ii

	Sv
Sv	Sv Sv
sv	Sv sv

Step by step, one can recover the probability of each genotype resulting from this breeding, by multiplying the probabilities in the tables of the individual factors (for instance, multiplying by ¼ if we are looking for dilute kittens coming from two undiluted carriers, or for non-agouti kittens coming from two agouti parents, but by 1/2 in case of pointed kittens of solid carrier and a pointed). It only takes a little patience, and much less time and frustration than the compilation of the full table. Often we only look for the possible genotypes, not for their probabilities: by this method, the answer is very fast and safe.

Problem. *A black smoke longhair is bred to a blue tabby point shorthair. Two of their kittens are silver tabby shorthairs. These kittens are bred together. What is the probability that their offspring is blue point longhair (not silver, not agouti)?*
(Hint: we are looking for kittens recessive for several genes. Which genes? Anyway, kittens of heterozygotic parents which are homozygous for a recessive gene have probability ¼, so the result should be some power of ¼).

Solution. Both parents carry the following recessive genes: non-agouti, non-silver, maltese dilution, colorpoint and longhair. Among their kittens, we are looking for those who are homozygotic for the recessive genes: blue point longhair, non-agouti and non-silver.
At each of these five loci the probability of the homozygotic recessive combination is ¼. Therefore the required probability is ¼ x ¼ x ¼ x ¼ x ¼ = (¼)^5 =1/1024. We should expect only one such kitten in 1024…
Here are the five Punnet diagrams (combination tables) at each locus:

	A	a
A	AA	Aa
a	Aa	aa

	C	cs
C	CC	Ccs
cs	Ccs	cscs

	D	d
D	DD	Dd
d	Dd	dd

	L	l
L	LL	Ll

l	Ll	ll

	I	i
I	II	Ii
i	Ii	ii

Observe that each locus restricts the total probability to ¼=25%. The tabby locus does not give any restriction, since we do not restrict attention a spacific tabby pattern, we accept all patterns in these kittens (as usual with pointed kittens: in most breed the pattern is not discernible because it does not show on the body). But if we want to ask for some specific pattern in the kittens we must specify the pattern of the parents. For instance, suppose that the parents both have the mackerel pattern in heterozygotic form, carrying the classic allele (of course it is difficult to know what recessive pattern they carry, since their black smoke parent is non-agouti and its pattern cannot be seen, except maybe at birth: this information should be determined by the pedigree). Then, if we ask what is the probability of kittens with classic pattern, we are again selecting the homozygotic recessive pattern, and that restricts further the probability to ¼, so the answer would now be one kitten out of 4096. Instead, if we ask what is the probability of mackerel kittens, we are looking for the homozygotic dominant and heterozygotic combinations, and this restricts the probability by a factor ¾ : in this case the answer becomes one kitten out of 4096-1024=3072.

Problem. *Consider the same problem in the case where the two original cats are particolor. More precisely, assume the following:*
- *male: black smoke and white longhair*
- *female: blue tabby point and white shorthair*

and their kittens are
- *A: silver tabby and white shorthair*
- *B: silver tabby shorthair*

These kittens are bred together. What is the probability that their offspring is blue point longhair (not silver, not agouti, not particolor)?

Solution: we are only considering one additional locus, the piebald spotting. Clearly the parents must be heterozygotic at this locus, because one kitten is not particolor. Therefore, kitten B is certainly homozygotic for no piebald spotting (**ss**), but kitten A can be either homozygotic for piebald spotting or heterozygotic. We must consider the two cases separately and combine the results. The following table gives us the probability that A be heterozygotic **Ss** or homozygotic **SS**. The table has for entries, but we know that one of them does not apply to the present case, because A, being particolor, cannot have the genotype **ss**. So, in the table we see that only three entries are allowed, each with the same probability of the others. In two cases A turns out to heterozygotic **Ss** (probability 2/3, or 66.66…%), in one case homozygotic **SS** (probability 1/3, that is 33.33…%). So we must now solve the problem in case A is heterozygotic and multiply the resulting probability by 2/3, then solve the problem again under the assumption that A is homozygotic and multiply the resulting probability by 1/3, and then add the two results.

	S	s
S	SS	Ss
s	Ss	ss

Let us consider the homozygotic case first. So A has genotype **SS** at the piebald spot locus and B has **ss**. The following table shows that all kittens of A and B are heterozygotic **Ss**, that is particolors. So the probability of kittens that are not particolors in thi case is zero.

	S	S
s	Ss	Ss
s	Ss	Ss

Now let us consider the case of A heterozygotic **Ss**. Then the probability that the kittens of A and B are particolors (heterozygotic **Ss**) is **½,** and the probability that they have no white is also ½, as seen in the following table.

	S	s
s	Ss	ss
s	Ss	ss

Now we can add the contributions of the two cases. If A is homozygotic **SS** the probability of the desired kittens is 0: this probability should then be multiplied by 1/3, but of course the result remains 0.

Instead, consider the case of A heterozygotic **Ss**. This event has probability 2/3, as we saw above; furthermore, in this case the probability of kittens with no white is ½. Therefore the probability that A be heterozygotic and the nkittens be without white is ½ multiplied by 2/3 that is 1/6.

Let us use again our multiplicativity principle. The result from all loci except the piebald spot locus was that only one blue point longhair kitten (non-agouti, non-silver) would arise in 4096. Now, if we include the piebald spot locus, this result must further be multiplied by 1/6, so we should expect only one such kitten (non-agouti, non-silver, non-particolor) out of 4096 x 6 = 24576. Not very likely… this means many more kittens that A and B can produce in a lifetime…

Problem. *Solve the same problem if both A and B are **both** particolors. Warning: the argument is similar but now we cannot assume any longer that neither parent is homozygotic **SS**; both A and B can have the two different genotypes **SS** and **Ss**. If either A or B has genotype **SS** then the probability of their kittens being non-particolor is zero. Compute the remaining case.*