First chapter: Formal and Mendelian Genetics

This discipline is named after the Austrian priest Gregor Mendel, who lived between 1822 and 1884. Over several years, he carried out hybridizations of pea plants, which allowed him, for the first time, to derive statistical laws that could be applied to the transmission of hereditary traits from one generation to the next.

Mendelian or qualitative genetics studies genes that have a significant effect. The first generation, or initial generation, also called the parental generation, is designated by convention as P. Subsequent generations, or filial generations, are designated as F1, F2, F3… in chronological order of appearance. The term pure lines applies to homozygous populations that always produce offspring identical to themselves for the trait in question. By cultivating the different varieties he had chosen for two years, Mendel succeeded in selecting seven pairs of pure lines. Each pair differed from the others by only one trait:

- Seed color: yellow or green,
- Seed shape: smooth or wrinkled,
- Stem length: long or short,
- Flower position: axial or terminal,
- Flower color: violet or white,
- Immature pod color: green or yellow,
- Pod shape: inflated or constricted.

He could then begin his hybridizations by crossing pure lines differing in one trait (monohybridism), and then pure lines differing in two traits (dihybridism).

I. MONOHYBRIDISM

As shown in the following table, by crossing two pure lines differing in only one trait (for example, peas with yellow seeds and peas with green seeds), one of the two traits disappears in the next generation (first filial generation or F1).

From this, we can deduce that the trait present in F1 is dominant, while the absent trait is recessive. This is Mendel's First Law, or the Law of Uniformity: all first-generation hybrids resulting from the cross of two pure lines resemble each other and exhibit the trait of one parent, and that parent alone.

Thus, if homozygous yellow-seeded peas (pure line) are crossed with homozygous green-seeded peas (another pure line), in F1 all peas will have yellow seeds. The "yellow seed" trait is therefore dominant, and the "green seed" trait is recessive. In terms of genotype and phenotype, this can be stated as follows, using the allele Y for dominant yellow and the allele g for recessive green:

Genotype (Y/Y) x (g/g) → Genotype Y/g

Phenotype Yellow x Green → Phenotype Yellow

Each parent being homozygous (Y/Y or g/g), they can only form one type of gamete: one carrying the Y allele, the other carrying the g allele. Fertilization will therefore necessarily bring together the two alleles Y and g, but since Y is dominant, it will be the only one expressed.

Consequently, all first-generation hybrids will have the "yellow seed" phenotype. Then, by crossing the first-generation hybrids (F1) among themselves, the following results are obtained:

This time, both parental traits reappear, but in a 3:1 ratio: 75% of the second-generation hybrids exhibit the dominant trait and 25% exhibit the recessive trait. This is Mendel's Second Law, or the Law of Segregation (also called the Law of Purity of Gametes):

All second-generation hybrids resulting from the cross of two heterozygotes for the same pair of alleles do not resemble each other and exhibit one or the other of the traits from the parental generation.

A crossbreeding grid, or Punnett square, can explain this result. It consists of creating a double-entry table where the different types of gametes produced by the parents are represented on a horizontal line and a vertical column. It is then sufficient to combine the male and female gametes in each square to obtain the product of fertilization, or, equivalently, the different genotypes resulting from the cross and their relative distribution.

Returning to the case where two F1 yellow-seed hybrids (Y/g) are crossed together, we obtain 1/4 Y/Y, 1/2 Y/g, and 1/4 g/g, resulting in 3/4 of individuals with the "yellow seed" phenotype and 1/4 with the "green seed" phenotype.

II. DIHYBRIDISM

The phenomena described so far only concerned pure parental lines distinguished by a single trait. Now let us see what happens when they differ by two distinct traits, and let's revisit Mendel's experiments conducted with yellow/wrinkled seed peas and green/smooth seed peas.

As before, these are of course homozygous lines, so that crossing yellow/wrinkled seed peas among themselves only produces yellow/wrinkled seed peas, and the same applies to green/smooth seed peas. However, if one crosses the two varieties with each other, all F1 peas exhibit the same phenotype (yellow and smooth seeds), and no green/wrinkled seed peas appear.

We can therefore conclude once again that the traits "yellow seed" and "smooth seed" are dominant, while the traits "green seed" and "wrinkled seed" are recessive. In terms of genotype and phenotype, this can be stated as follows, using the allele Y for dominant yellow, the allele S for dominant smooth, the allele g for recessive green, and the allele w for recessive wrinkled:

Genotype (Y/Y ; w/w) x (g/g ; S/S) → Genotype Y/g ; S/w

Phenotype (Yellow ; Wrinkled) x (Green ; Smooth) → Phenotype Yellow ; Smooth

Mendel then crossed the hybrids obtained in F1 with each other and observed that the four parental traits reappear in F2, but in a 9:3:3:1 ratio. 9/16 of the peas have yellow and smooth seeds (Y ; S), 3/16 have yellow and wrinkled seeds (Y ; w), 3/16 have green and smooth seeds (g ; S), and 1/16 have green and wrinkled seeds (g ; w), as confirmed by the following Punnett square.

3rd Law: Independent Assortment of Traits: The two laws of uniformity and segregation are thus verified again: all first-generation hybrids resemble each other, but not those of the

second generation. And any combination of traits would lead to identical proportions: 3/4-1/4 in the case of monohybridism, 9/16-3/16-3/16-1/16 in the case of dihybridism.

Thus, the number of traits studied can be multiplied (polyhybridism), but their observation quickly becomes tedious.

A trihybrid, for example, will produce eight types of gametes (2^3), the Punnett square will have 64 squares (8 x 8), and it will be possible to obtain 27 different genotypes in F2 (3^3).

A tetrahybrid: 16 types of gametes (2^4) and 81 genotypes in F2 (3^4)… of which one actually has only a 1 in 256 chance of appearing in the offspring.

Here is the translation of the provided text into English:

III. Use of the Chi-Square Test

Since chance sometimes seems to govern the appearance of a given phenotype in offspring, it is sometimes useful to be able to check whether this distribution conforms to expectations. This involves using a statistical test to verify whether the proportions of the different observed phenotypes agree with those that should have been found by applying the rules of Mendelian genetics.

Thus, if the test reveals that there is no significant difference between the observed distribution and the theoretical distribution that can be calculated from crossbreeding grids, the initial hypothesis is retained. Conversely, if the statistical test shows that the two values are too far apart, the hypothesis must be rejected.

Table. 1. Chi-Square critical value

Number of the studied characters	Chi-Square critical value
2	3.841
3	5.991
4	7.815
5	9.488
6	11.070
7	12.592
8	14.067

The statistical chi-square (χ^2) test is then used, in which (O) represents the observed value, (A) the expected value, and (i) the number of traits studied.

Let us take the example of the cross-carried out by Mendel between a pure line of peas with smooth seeds and a pure line of peas with wrinkled seeds. In F1, all the hybrids obtained have the "smooth seed" phenotype.

It can therefore be concluded that the "smooth seed" trait is dominant and the "wrinkled seed" trait is recessive. Consequently, the F2 hybrids should show the reappearance of the parental traits in a 3:1 ratio: 75% of peas with smooth seeds and 25% with wrinkled seeds.

However, out of a total of 7,324 seeds, 5,474 are smooth (O = smooth) and 1,850 wrinkled (O=wrinkled), whereas the expected prediction is 5,493 (7,324 x 75%) smooth seeds (A smooth) and 1,831 (7,324 x 25%) wrinkled seeds (A wrinkled).

The calculation is as follows:

$$\chi^2 = \Sigma [(Oi - Ai)^2 / Ai]$$

$$\chi^2 = (5474 - 5493)^2 / 5493 + (1850 - 1831)^2 / 1831$$

$$\chi^2 = (-19)^2 / 5493 + (19)^2 / 1831$$

$$\chi^2 = 361 / 5493 + 361 / 1831$$

$$\chi^2 \approx 0.0657 + 0.1972$$

$$\chi^2 \approx 0.2629$$

Since this result is well below 3.841 (the critical value for 1 degree of freedom at the 5% significance level), the hypothesis tested is correct: the second-generation hybrids are distributed according to Mendel's laws in a 3:1 ratio. If this had not been the case, another hypothesis would have been necessary.

IV. Autosomal Heredity

The transmission from one generation to the next of a particular trait, expressed or not, encoded in a gene located on a chromosome (autosome) that is not involved in sex determination.

During fertilization, the fusion of the spermatozoon and the oocyte allows the union of the father's genetic material (23 paternal chromosomes) with that of the mother (23 maternal chromosomes) to form a diploid zygote, i.e., containing 23 pairs of chromosomes. The child will resemble its parents because it will have inherited the traits that each parent transmitted via their chromosomes.

This transmission of characteristics or traits from one generation to the next constitutes heredity. This allows us to acquire various characteristics from our parents and to transmit some of our own to our children. This principle of trait transmission also applies when a mutated gene, responsible for a genetic disease, is transmitted to offspring.

The study of heredity thus makes it possible to predict a couple's offspring, as well as the risk of transmitting a serious pathology.

The nucleus of the zygote, and by extension that of all human somatic nucleated cells, therefore contains 23 pairs of chromosomes, or 46. They are said to be diploid (2n = 46). Each pair comprises one chromosome from the mother and one from the father.

The two chromosomes of the same pair therefore contain genes that govern the same traits. These two chromosomes are called “homologous”. For example, the paternal chromosome 11 contains the gene coding for hemoglobin, as does the maternal homologue 11.

4.1. Gene Interactions

- Interactions between allelic genes;

- Interactions between non-allelic genes.

4.1.1. Interactions between Genes Located at the Same Locus (Allelic Genes)

When the two alleles of a locus are identical, they manifest in the same way at the phenotype level. When they are different, several modes of gene action can explain the genotype-phenotype relationships.

A. Dominance

A.1. Definition

The manifestations of one allele can completely mask the manifestations of the other. The first is termed dominant, the second recessive. For a recessive allele to be expressed in the phenotype, it must be in the homozygous state.

For a locus with two alleles A and a, we obtain:

3 possible genotypes: A/A, A/a, a/a

2 phenotypes: [A] and [a].

By convention, it is convenient to write the phenotype in brackets [ ].

Dominance is observed in heterozygotes, whose phenotype corresponds to the expression of the dominant gene.

Dominance can be:

- Complete, when the phenotypes of the heterozygote and the dominant homozygote are identical.

- Partial or incomplete, when the recessive allele manifests itself more or less discreetly in heterozygotes.

For example, in cattle, the "solid coat" gene incompletely dominates the "piebald coat" gene because some white patches remain in crossbred heterozygous animals.

Examples of traits governed by dominant or recessive genes of zootechnical interest:

In cattle, a pair of alleles governs the presence of horns: “P” (polled = absence of horns), “p” (presence of horns). Three genotypes (PP, Pp, pp) can be encountered, but only two phenotypes [P] and [p] due to the dominance of P over p. Some breeds are genetically hornless.

B- Codominance or Intermediate Dominance

Codominance corresponds to the joint expression of two alleles. The phenotype of the heterozygote is composed of the juxtaposition of the phenotypes of the two homozygotes.

For a locus with 2 alleles A and a, we obtain:

3 possible genotypes: AA, Aa, aa

3 phenotypes: [A], [Aa], [a]

Example of traits governed by dominant, recessive, or codominant genes of zootechnical interest:

In dairy cattle, at the Kappa-casein locus located on chromosome pair 4, there are two alleles, A and B. At this locus, a cow can be:

- "Homozygous AA": its milk contains Kappa-casein A; its phenotype is written [A].

- "Homozygous BB": its milk contains Kappa-casein B; its phenotype is [B].

- "Heterozygous AB": its milk contains both Kappa-casein A and Kappa-casein B; its phenotype is [AB].

Note: Kappa-casein B is favorable for cheese-making yield and curd firmness.

C- Penetrance

In some cases, a dominant allele has an irregular action, meaning that the dominant trait does not manifest in all heterozygotes.

4.1.2. Interactions between Genes Located at Different Loci (Non-Allelic Genes)

The action of a gene can be modified by non-allelic genes, called, depending on their mode of action, "modifier genes" and "epistatic genes".

These include: Epistatic genes, Complementary genes, Pleiotropy, Multiple alleles, Linkage between genes located on the same chromosome.

4.1.2.1. Epistatic Genes

Epistasis is the interaction between two different loci that act on the same trait. An epistatic gene masks the expression of a non-allelic gene. Epistasis occurs when at least two non-allelic genes combine to produce an effect that is not the cumulative result of the action of these genes.

Epistasis involves at least two loci. Example: Maize (yellow seeds x yellow seeds) F1 100% purple (presence of a pigment/anthocyanin). F2 ratio 9/16 purple and yellow, controlled by two or more genes. Consequently, knowledge of dihybrid ratios is important for the study of epistasis, as it allows one to decide whether epistasis exists or not, and if so, what type of epistasis is involved.

Evidence of epistasis occurs when dihybrid frequencies are produced such that two or more phenotypic classes are combined. Genes controlling pigment deposition in plumage or hair are subject to the epistatic effect of non-allelic inhibitor genes.

4.1.2.2. Complementary Genes

These are non-allelic genes that, through their combined action, give rise to a phenotype different from those they induce separately; they complement each other to produce a new effect.

4.1.2.3. Pleiotropy

Pleiotropy occurs when a single gene controls several traits that are apparently not functionally related. The gene is said to have a pleiotropic effect.

The most cited example in animal breeding is that of hornlessness (polled) and intersexuality in goats. Thus, homozygous (PP) animals carry severe malformations of the genital tract.

- Females PP exhibit more or less pronounced masculinization and are all sterile. Consequently, there are no adult breeding does of genotype PP. Fertile does are either Pp (if polled) or pp (if horned).

- Males: All three genotypes PP, Pp, and pp are present, but 50 to 80% of PP males are sterile.

4.1.2.4. Multiple Alleles

Multiple alleles are referred to when more than 2 alleles can exist for a given locus. Multiple alleles constitute an **allelic series**.

Example: Multiple alleles – ABO system in humans.

4.1.3. Sex-Linked Genetics

The somatic cells of animals possess a constant number of chromosomes equal to 2n, which in vertebrates can be broken down into (2n-2) autosomes + 2 sex chromosomes, also called heterochromosomes or gonosomes.

In mammals, the female possesses two identical heterosomes: XX, while they are dissimilar in the male: XY.

The female sex is termed homogametic because it produces only one type of gamete, with the chromosomal formula (n-1) autosomes + X. The male is termed heterogametic because it produces two types of gametes: those carrying (n-1) autosomes + X and those carrying (n-1) autosomes + Y.

In birds, it is the female sex that is heterogametic (ZW), whereas the male is ZZ.

These sex chromosomes have a particular constitution. Indeed, genes located on the X chromosome often do not have corresponding alleles on the Y chromosome.

Consequently, if the genes governing certain traits are carried by the sex chromosomes, the results in F1 and F2 differ from those obtained in the case of autosomal heredity.

The Y sex chromosome carries almost exclusively sex determinants, i.e., genes whose expression enables sex determination. The X chromosome, on the other hand, carries, in

addition to sex determinants, a large number of other genes. Thus, sex-linked heredity is essentially X-linked heredity.

Practically speaking, a trait is recognized as sex-linked by performing a reciprocal cross between the individuals under study. For example:

1st cross: (Male XY, "white") x (Female XX, "black")

2nd cross: (Female XX, "white") x (Male XY, "black")

Suppose the black trait is dominant and the crossed individuals belong to pure lines. Two possibilities can occur:

The gene responsible for color is carried by an autosome.

In this case, the offspring of both crosses will all be black, regardless of sex. The gene responsible for color is carried by a sex chromosome (X).

In this case, the first cross will give homogeneous offspring composed of black individuals (males and females).

4.1.4. Dominant Sex-Linked Heredity

An affected male mated with a normal female transmits the abnormality to all his daughters, but not to his sons. Unless the abnormality is very common, an affected female mated with a normal male transmits the abnormality on average to half her sons and half her daughters.

Any affected descendant has at least one affected parent, except in the case of a new mutant.

4.1.4.1. Recessive Sex-Linked Heredity

The incidence of the abnormality is lower in females than in males. Affected males are born from the mating of a heterozygous mother (normal but carrier) with a normal father. The abnormality can skip generations.

4.1.4.2. Lethal Genes and Undesirable Genes

An anomaly is a deviation, more or less pronounced, from the normal type. Anomalies of genetic origin are more often harmful; they then result in the more or less early death of the animal (lethal gene). However, some rare anomalies present both favorable and unfavorable effects; they may therefore be sought after under certain conditions.

The existence of anomalies of genetic origin is explained by mutations that spontaneously and abruptly transform a gene. The responsible genes are generally autosomal and recessive.

A.1. Genetic Anomalies Sometimes Sought

Their frequency of appearance varies according to breed. They present both advantages and disadvantages. In this case, any selection decision for or against such an anomaly must be preceded by an economic study.

1. The "double-muscled" trait in cattle:

The double-muscled trait (or muscular hypertrophy) has long been observed in numerous cattle breeds where it appears at very variable frequencies.

Double-muscled cattle have a much higher slaughter value than their contemporaries with a normal phenotype, but they pose breeding problems.

The gene involved, symbolized by mh, has the following characteristics:

It is autosomal, since it is located on bovine chromosome pair 2; the + sign designates the normal allele.

It behaves as a recessive gene, as it is not visually distinguishable among normal cattle between heterozygous carriers (mh/+) and non-carriers (+/+).

The breeds in which the mh gene exists are numerous, particularly beef breeds (Charolais, etc.).

Genetic improvement for qualitative traits uses the following steps:

- Understand the hereditary mechanism involved, which consists of determining the number of genes and the mode of expression of each gene pair (dominant, recessive).
- Inventory possible linkages between the desired trait and other traits.
- Increase the frequency of the desired genotypes.

What is the Belgian Blue cattle breed?

The Belgian Blue breed is raised exclusively for meat production. The animals are easily recognizable by their very impressive musculature, particularly on the rear part of the body. This morphological characteristic is due to muscular hypertrophy obtained through genetic selection aimed at increasing the profitability of these animals. Males easily reach over 700 kg at two years of age.

This breed has exceptional slaughter value. It has the highest carcass yield of all cattle breeds. It is used in pure breeding or in crossbreeding with dairy breeds to produce higher weight beef calves.

How was the morphology of the Belgian Blue breed created?

The myostatin protein regulates the proliferation of muscle cells during development. The inactivation of this protein is the cause of muscular hypertrophy in so-called double-muscled cattle. This inactivation is enabled by the "double-muscling gene." This results in a proliferation of muscle fibers and thus muscle hypertrophy. Genetic selection allowed the preservation of this gene and the development of the Belgian Blue breed.

While all representatives of this breed possess the double-muscling gene, this gene can also be present in some individuals of other breeds (e.g., Blonde d'Aquitaine, Charolais, etc.).

2. Horned/Polled Condition in Goats

- Undesirable Genes: The PIS Mutation (Polled Intersex Syndrome)

Today, thanks to molecular genetics, it is known that sex reversal in hornless goats (Polled Intersex Syndrome) results from a mutation at the locus called "P," which affects gonadal differentiation. The mode of inheritance is dominant for the hornless trait and recessive for the presence of horns. The mutation corresponds to a large deletion of 11.7 kb, which induces the deletion of at least two genes, PISRT1 (PIS regulated transcript 1) and FOXL2, which act in synergy to promote ovarian differentiation.

These two genes share the same transcriptional regulatory region, PIS. The extinction of their expression leads to the formation of testes in PIS (-/-) XX individuals, previously indicated as PP, following the blockage of the female pathway.

References

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