D3.2 Inheritance

Continuity and change—Organisms

Standard level and higher level: 5 hours

Additional higher level: 3 hours

Guiding questions

• What patterns of inheritance exist in plants and animals?

• What is the molecular basis of inheritance patterns?

SL and HL

D3.2.1—Production of haploid gametes in parents and their fusion to form a diploid zygote as the means of inheritance
Students should understand that this pattern of inheritance is common to all eukaryotes with a sexual life cycle. They should also understand that a diploid cell has two copies of each autosomal gene.
In eukaryotes with a **sexual** life cycle, the means of inheritance involves the production of **haploid** gametes in each parent and their fusion to form a **diploid** zygote. • The diploid zygote contains 46 chromosomes in total; 22 paternal and 22 maternal autosomal chromosomes, and 1 paternal and 1 maternal sex chromosomes. • Haploid gametes contain 22 autosomal chromosomes (whether they are maternal or paternal is random due to meiosis) and 1 sex chromosome.

D3.2.3—Genotype as the combination of alleles inherited by an organism
Students should use and understand the terms “homozygous” and “heterozygous”, and appreciate the distinction between genes and alleles.
Genes are the basic units of heredity in all organisms, which are composed of DNA nucleotides that carry instructions for cell functioning. **Alleles** are different versions of a gene (i.e. eye color) which arise due to mutations. Most cell functions are controlled by two (identical or different) alleles, one from each parent. The **genotype** is the combination of alleles inherited by an organism, represented as case-sensitive letters (i.e. AA, Aa, aa, etc.) and named according to the alleles that constitute it: • **Homozygous genotypes** contain the SAME alleles (i.e. AA, bb, aa, BB) • **Heterozygous genotypes** contain DIFFERENT alleles (i.e. Aa, Bb)

D3.2.4—Phenotype as the observable traits of an organism resulting from genotype and environmental factors
Students should be able to suggest examples of traits in humans due to genotype only and due to environment only, and also traits due to interaction between genotype and environment.
The **phenotype** is the observable traits of an organism resulting from genotype and/or environmental factors. For example: 1. **Genotype only**: eye color, blood type 2. **Environment only**: scars from injuries, tattoos 3. **Genotype and environment**: height, diabetes

D3.2.5—Effects of dominant and recessive alleles on phenotype

Students should understand the reasons that both a homozygous-dominant genotype and a heterozygous genotype for a particular trait will produce the same phenotype.

Alleles can interact with each other, influencing the trait/phenotype the gene is responsible for, via **complete dominance**:

1. **Dominant alleles** mask the effects of the recessive allele in both homozygous- and heterozygous-dominant genotypes. By convention, they are represented by a capital letter.
2. **Recessive alleles** only influence the gene's phenotype if the genotype is homozygous recessive. By convention, they are represented by a small-case letter.

D3.2.6—Phenotypic plasticity as the capacity to develop traits suited to the environment experienced by an organism, by varying patterns of gene expression

Phenotypic plasticity is not due to changes in genotype, and the changes in traits may be reversible during the lifetime of an individual.

Phenotypic plasticity is the extent to which an organism can change its physiology, morphology, behavior, or development in response to environmental cues; its capacity to develop different phenotypes suited to its environment by varying patterns of genetic expression (NOT due to changes in genotype).

These changes may or may not be reversible, depending on the trait (i.e. tanning is reversible).

D3.2.2—Methods for conducting genetic crosses in flowering plants

Use the terms "P generation", "F1 generation", "F2 generation" and "Punnett grid". Students should understand that pollen contains male gametes and that female gametes are located in the ovary, so pollination is needed to carry out a cross. They should also understand that plants such as peas produce both male and female gametes on the same plant, allowing self-pollination and therefore self-fertilization. Mention that genetic crosses are widely used to breed new varieties of crop or ornamental plants.

- **P generation** = parental generation
- **F1 generation** = **first filial** (Latin for son and daughter) generation; offspring of P generation
- **F2 generation** = second filial generation; offspring of F1 generation
- A **Punnett grid** is a square diagram that depicts all the possible genotypes from a cross.

Early genetic studies by Mendel involved using plants to study patterns of inheritance, as they can either be **monoecious** (produce both male and female gametes, like peas) or **diecious** (produce 1 gamete only).

- Monoecious plants can undergo self-pollination and therefore self-fertilization
- Diecious plants cross with other ones, ensuring genetic diversity

Genetic crosses are widely used to breed new varieties of crops (i.e. crossing high yield crops) and ornamental plants.

D3.2.8—Single-nucleotide polymorphisms and multiple alleles in gene pools

Students should understand that any number of alleles of a gene can exist in the gene pool but an individual only inherits two.

A **gene pool** consists of all the genes and their different alleles present in a population *or* species; changes in the gene pool over time is evolution. Multiple alleles can exist in the gene pool but an individual only inherits two.

Alleles can differ by hundreds of base pairs or by a single point/base substitution, which are called **single-nucleotide polymorphisms (SNPs)**.

D3.2.7—Phenylketonuria as an example of a human disease due to a recessive allele

Phenylketonuria (PKU) is a recessive genetic condition caused by mutation in an autosomal gene that codes for the enzyme needed to convert phenylalanine to tyrosine.

Phenylketonuria (PKU) is a **recessive** genetic disorder caused by mutations in the autosomal gene that codes for the enzyme **phenylalanine hydroxylase (PAH)**. PAH catalyzes the conversion of the amino acid phenylalanine (found in all proteins) to tyrosine, but individuals with PKU are deficient in PAH, leading to the accumulation of phenylalanine levels in the body. High levels of phenylalanine can cause intellectual and developmental disabilities if not treated properly.

D3.2.10—Incomplete dominance and codominance

Students should understand the differences between these patterns of inheritance at the phenotypic level. In codominance, heterozygotes have a dual phenotype. Include the AB blood type (I^AI^B) as an example. In incomplete dominance, heterozygotes have an intermediate phenotype. Include four o'clock flower or marvel of Peru (*Mirabilis jalapa*) as an example.
Note: When students are referring to organisms in an examination, either the common name or the scientific name is acceptable.

Alleles can interact with each other in ways *other* than complete dominance, including:

1. **Incomplete dominance**: the 2 different alleles are neither dominant or recessive with respect to each other, so the overall phenotype is a blend / intermediate / mix of the two.
    - For example, if a *Mirabllis jalapa* plant with red flowers is crossed with a white-flowered one, the offspring will all have pink flowers. This is because the red genotype (C_RC_R) leads to the production of a lot of red pigment, whereas the white one (C_WC_W) does not produce any, so a heterozygous genotype (C_RC_W) will produce intermediate levels of red pigment, appearing pink.
2. **Codominance**: the 2 different alleles are both expressed (not blended) in the phenotype.
    - For example, a person with the I^AI^B genotype expresses both A and B antigens on their RBCs.

Both of these types of interactions are considered non-Mendelian.

D3.2.9—ABO blood groups as an example of multiple alleles

Use I^A, I^B and i to denote the alleles.

Three alleles, I^A (antigen A), I^B (antigen B) and i (no antigen modifications; group O) determine the ABO blood group of an individual by interacting differently:

- I^A and i interact via complete dominance
- I^B and i interact via complete dominance
- I^A and I^B interact via codominance

Genotype	I^AI^A	I^AI^B	I^BI^B	I^Ai	I^Bi	ii
Phenotype	Antigen A	Antigens A + B	Antigen B	Antigen A	Antigen B	Blood group O

D3.2.11—Sex determination in humans and inheritance of genes on sex chromosomes

Students should understand that the sex chromosome in sperm determines whether a zygote develops certain male-typical or female-typical physical characteristics and that far more genes are carried by the X chromosome than the Y chromosome.

In humans, males are the **heterogametic sex** (2 different chromosomes, XY, are needed to result in a male) and females are the **homogametic sex** (2 chromosomes of the same type (but not identical), XX, are needed to result in a female).

The X chromosome (containing ~900 protein-coding genes) is 3 times as large as the Y chromosome (contains only ~100 protein-coding genes, the fewest of any chromosome).

The Y chromosome contains the **SRY gene** (also known as the **testes-determining factor TDF**), which codes for a protein that activates other genes that cause the embryo to develop testes and other male sexual characteristics.

If the Y chromosome is not present, the X chromosomes will cause the development of the gonads into ovaries, which produce the hormones necessary for the development of female sexual characteristics.

Genes present on either the X or Y chromosomes are said to be **sex-linked**. Since the X chromosome contains more genes than the Y chromosomes, most sex-linked genes are **X-linked** (present only in the X chromosome). X-linkage (non-Mendelian pattern of inheritance) changes the patterns of inheritance:

X-linked dominant traits will be more common in women

- Sons only inherit the trait from their mother
- Daughters can inherit the trait from both parents

X-linked recessive traits will be more common in men

- Sons only inherit the trait from their mother
- Daughters must inherit the trait from both parents to possess the trait

D3.2.12—Haemophilia as an example of a sex-linked genetic disorder

Show alleles carried on X chromosomes as superscript letters on an uppercase X.

Haemophilia is an **X-linked recessive** genetic disorder caused by deficiency in one of the factors (Factor VIII or IX) within the blood clotting cascade in humans, leading to prolonged bleeding. The recessive allele is usually represented as X^h and the dominant one as X^H. Since males cannot carry 2 copies of the gene, they are **hemizygous**.

D3.2.13—Pedigree charts to deduce patterns of inheritance of genetic disorders

Students should understand the genetic basis for the prohibition of marriage between close relatives in many societies.

Pedigree charts are diagrams of genetic history of a family over several generations. To solve for the pattern of inheritance in a specific pedigree chart, inferential reasoning must be employed by examining how different patterns of inheritance (X-linked, recessive, dominant) lead to different probabilities of possible genotypes, and comparing them to the observed genotypes in the chart.

Inbreeding is the mating of close relatives, with self-fertilization being the most extreme form. The frequency of heterozygous genotypes decreases, and as a result homozygous recessive genotypes increase in frequency within the gene pool. This decreases genetic diversity and raises the probability of the offspring inheriting genetic disorders (since many disorders are recessive), so many species evolve **inbreeding avoidance** mechanisms. This is also why prohibition of marriage between close relatives exists in many societies.

D3.2.14—Continuous variation due to polygenic inheritance and/or environmental factors

Use skin colour in humans as an example.
Application of skills: Students should understand the distinction between continuous variables such as skin colour and discrete variables such as ABO blood group. They should also be able to apply measures of central tendency such as mean, median and mode.

Genetic variation can be:

1. **Discrete** (countable), like the human ABO blood group
2. **Continuous** (exists in a range/spectrum, uncountable), like human skin color (many genes control melanin production and the environment also affects it)

Continuous variation (a type of non-Mendelian inheritance) is caused by:

1. **Polygenic inheritance**: multiple genes affect the phenotype
2. **Environmental factors**: influence gene expression on a wide range

Continuous variation can be represented using histograms, normal distributions, line graphs, and box plots.

D3.2.15—Box-and-whisker plots to represent data for a continuous variable such as student height

Application of skills: Students should use a box-and-whisker plot to display six aspects of data: outliers, minimum, first quartile, median, third quartile and maximum. A data point is categorized as an outlier if it is more than 1.5 × IQR (interquartile range) above the third quartile or below the first quartile.

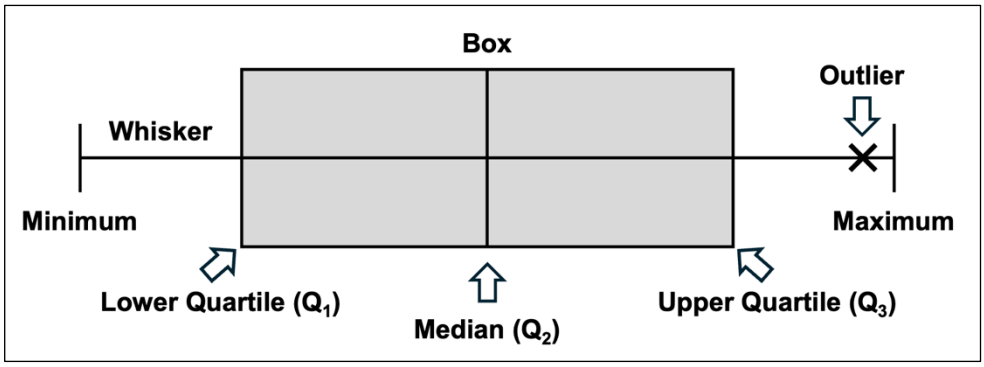

Figure 1: Box-and-whisker plot.

- **Median** is the middle value of a data set when the data is sorted in order from least to greatest. It is NOT the same as the mean or mode; all three terms refer to different measures of **central tendency**:
    - The mean is most appropriate when the data is symmetrical and there are no outliers.
    - The median is most appropriate when the data is asymmetrical with outliers.
    - The mode is most appropriate when the data is nominal / categorial.
- **Quartiles** are special percentiles. The first quartile, Q1, is the same as the 25th percentile, and the third quartile, Q3, is the same as the 75th percentile. The median, M, is called both the second quartile and the 50th percentile.
- **Minimum**: the smallest numerical value in the data set.
- **Maximum**: the largest numerical value in the data set.
- **Interquartile range (IQR)**: the difference between Q3 and Q1.
- **Outlier**: 1.5 × IQR more than Q3 or less than Q1.

NOS: Scientists draw general conclusions by inductive reasoning when they base a theory on observations of some but not all cases. A pattern of inheritance may be deduced from parts of a pedigree chart and this theory may then allow genotypes of specific individuals in the pedigree to be deduced. Students should be able to distinguish between inductive and deductive reasoning.

Deductive reasoning involves using concrete, empirical lines of evidence to support a theory. For example, the theory of evolution has been verified by a lot of empirical evidence.

Inductive reasoning involves using probabilistic evidence to support a theory, often leading to generalizations. For example, inferring patterns of inheritance in pedigree charts is done inductively.

Additional higher level

D3.2.16—Segregation and independent assortment of unlinked genes in meiosis

Students should understand the link between the movements of chromosomes in meiosis and the outcome of dihybrid crosses involving pairs of unlinked genes.

Independent assortment is the inheritance of alleles of two (or more) different genes independently of one another (i.e. genes do not influence patterns of inheritance of other genes far away on the same chromosome or on different chromosomes).

Segregation is the inheritance of only one allele per gamete. Whether this is from paternal or maternal origin is random due to **random orientation** of chromosomes at the equatorial plate in metaphase I, and whether it is one allele or the other is also random due to fertilization (i.e. any sperm can penetrate the ovum in humans).

D3.2.17—Punnett grids for predicting genotypic and phenotypic ratios in dihybrid crosses involving pairs of unlinked autosomal genes

Students should understand how the 9:3:3:1 and 1:1:1:1 ratios are derived.

Monohybrid crosses investigate the inheritance of 1 gene. **Dihybrid crosses** investigate the inheritance of 2 distinct genes. When 2 individuals heterozygous (AaBb) for unliked autosomal genes are crossed, the results are:

- **9**/16 of the offspring will be dominant for both traits
- **3**/16 of the offspring will be dominant for trait 1 and recessive for trait 2
- **3**/16 of the offspring will be dominant for trait 2 and recessive for trait 1
- **1**/16 of the offspring will be recessive for both traits

This leads to the characteristic **9:3:3:1 phenotypic ratio**.

When a heterozygous (AaBb) individual is crossed with a homozygous recessive (aabb) individual, the results are:

- **1**/4 of the offspring will be dominant for both traits
- **1**/4 of the offspring will be dominant for trait 1 and recessive for trait 2
- **1**/4 of the offspring will be dominant for trait 2 and recessive for trait 1
- **1**/4 of the offspring will be recessive for both traits

This leads to the characteristic **1:1:1:1 phenotypic ratio**. A cross between any individual and a homozygous recessive individual is also called a **test cross**. This is because with individuals exhibiting a dominant trait for 2 unlinked genes, it is difficult to determine whether they are homozygous dominant or heterozygous, so they are crossed with a homozygous individual. If the 1:1:1:1 phenotypic ratio is observed, we can then confirm the heterozygosity of that individual.

Pure breeding individuals are those that are homozygous (dominant or recessive) for all traits under investigation.

NOS: 9:3:3:1 and 1:1:1:1 ratios for dihybrid crosses are based on what has been called Mendel's second law. This law only applies if genes are on different chromosomes or are far apart enough on one chromosome for recombination rates to reach 50%. Students should recognize that there are exceptions to all biological "laws" under certain conditions.

Mendel's Second Law, also called the **law of independent assortment**, only applies if genes are on different chromosomes or far apart enough on one chromosome for recombination to reach 50% or more. Most biological "laws" operate under a few assumptions/conditions, so there are exceptions to all of them once these assumptions/conditions are not met.

D3.2.18—Loci of human genes and their polypeptide products

Application of skills: Students should explore genes and their polypeptide products in databases. They should find pairs of genes with loci on different chromosomes and also in close proximity on the same chromosome.

A **locus** (plural loci) is the position of a specific gene on a chromosome. The polypeptide product of a locus depends on the allele that occupies it. Since there are 2 copies of an autosomal gene, one on each parental chromosome, loci on different chromosomes can have the same or different alleles.

The **NCBI Gene Database** and **Ensembl** are databases that include information about genes in many organisms, including humans, like gene position on the chromosome, its polypeptide product, number of transcripts that can be produced by alternative splicing, and location of the gene promoter and enhancer sequences.

D3.2.19—Autosomal gene linkage

In crosses involving linkage, the symbols used to denote alleles should be shown alongside vertical lines representing homologous chromosomes. Students should understand the reason that alleles of linked genes can fail to assort independently.

Gene linkage refers to the tendency of genes located in close proximity to each other on the **same** chromosome to be inherited together. The probability of crossing over in linked genes decreases because recombination frequencies decrease below 50%. Since the genes are physically located on the same chromosome, they fail to assort independently during metaphase I, so they are inherited together.

This means that, for dihybrid crosses, if the traits under investigation are close to each other on the same chromosome, the genotypes with the highest frequencies will be those that are identical to the parents' genotypes, whereas the recombinant genotypes will have the lowest frequencies. Thus, the typical phenotypic ratios for unlinked genes will NOT be observed.

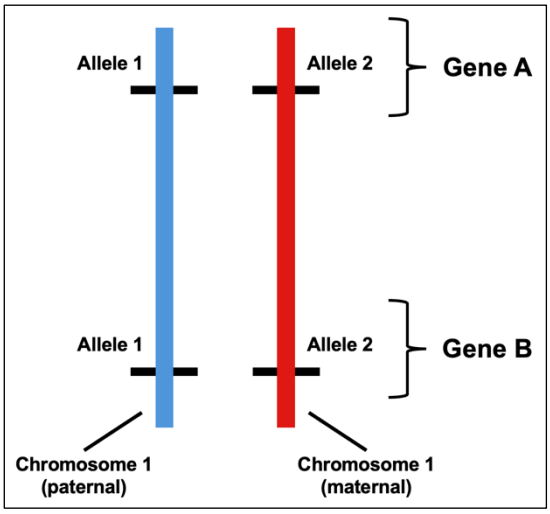

Figure 2: lines are used to represent homologous chromosomes and dashes are used to represent alleles. Sometimes, the dashes are omitted and the letter of that specific allele is instead used to represent it.

D3.2.20—Recombinants in crosses involving two linked or unlinked genes

Students should understand how to determine the outcomes of crosses between an individual heterozygous for both genes and an individual homozygous recessive for both genes. Identify recombinants in gametes, in genotypes of offspring and in phenotypes of offspring.

Dihybrid crosses of two genes:

1. Determine the genotypes of the gametes
2. Create a 4 x 4 Punnett square and determine the genotypes of the offspring

Recombinants are allele pairs that are not found in the parents which arise due to crossing over in meiosis I. For example, in a dihybrid cross between two heterozygotes (AaBb), the recombinants are homozygous allele pairs, i.e. AA, aa, BB, bb.

D3.2.21—Use of a chi-squared test on data from dihybrid crosses

Students should understand the concept of statistical significance, the p = 0.05 level, null/alternative hypothesis and the idea of observed versus expected results.

In dihybrid crosses in which gene linkage is unknown, the **chi-squared test** needs to be used in order to determine whether or not the observed genotype frequencies differ significantly from Mendelian inheritance (thus suggesting gene linkage).

Statistical significance is the claim that the experimental results or data are attributable to a specific cause rather than random chance. Two hypotheses can be predicted based on this:

- **Null hypothesis (H_0)**: there is **no** statistically significant difference between the expected and observed phenotype frequencies. Any difference is due to **random chance**, and Mendelian inheritance applies.
- **Alternative hypothesis (H_1)**: there is a statistically significant difference between the expected and observed phenotype frequencies. The differences cannot be explained by random chance alone, suggesting non-Mendelian inheritance (i.e. gene linkage).

Statistical significance of results is determined by the **p-value (probability value)**:

- If **p > 0.05**, the null hypothesis is accepted (we fail to reject it). It indicates that most of the variation can be explained by random chance alone.
- If **p ≤ 0.05**, the null hypothesis is rejected and the alternative hypothesis is accepted. It indicates that less than 5% of the variation can be explained by random chance, aka over 95% of the variation is attributable to a specific cause (i.e. gene linkage).

To carry out the chi-squared test for the F_2 generation of a dihybrid cross:

1. Determine the phenotypic ratios through carrying out a Punnett square with the assumption that the genes are unlinked
2. Multiply the total number of individuals by the frequency of each phenotype to determine the expected phenotypic frequencies (E)
3. Record the number of individuals in the actual across as observed frequencies (O), which will usually be given in the question
4. Calculate the chi-squared (χ^2) value,

$$\chi^2 = \sum \frac{(O - E)^2}{E}$$

5. Determine the **degree of freedom (df)** and identify the corresponding **critical value**,

$$df = (\text{number of distinct phenotypes produced by the Punnett square in step 1}) - 1$$

6. Compare the chi-squared value to the critical value,
   a. If χ^2 > critical value, the null hypothesis is rejected and the inheritance pattern is non-Mendelian (i.e. the two traits are genetically linked)
   b. If χ^2 < critical value, the null hypothesis is accepted and the inheritance pattern is Mendelian (i.e. the two traits are not genetically linked)

NOS: Students should recognize that statistical testing often involves using a sample to represent a population. In this case the sample is the F2 generation. In many experiments the sample is the replicated or repeated measurements.

In statistical testing, a **population** is the entire group of organisms or objects that we want to draw conclusions about, and a **sample** is a subset of that population that is actually involved in scientific testing. This is because, often, populations are too large to feasibly conduct experiments on, so a representative group of that population is used for practical purposes. This is the case when conducting chi-squared on dihybrid crosses, as the F2 generation is usually used as a sample instead of the entire population (parents, F1, and F2 combined) because the F2 generation is a larger sample than both the parents and F1 combined.

Linking questions

• What are the principles of effective sampling in biological research?

• What biological processes involve doubling and halving?

Review questions

SL and HL

- Define inbreeding. [1]
- Define phenotypic plasticity. [1]
- State **two** causes of continuous genetic variation. [1]
- Distinguish between single-nucleotide polymorphisms and heterozygosity. [1]
- Outline the pattern of inheritance in sexually reproducing eukaryotes. [2]
- The extent to which a gene can exhibit plasticity is a trait that can be selected for. Outline the advantages of this. [2]
- Distinguish between phenotypic plasticity and evolutionary adaptation. [2]
- Outline the genetic basis of inbreeding avoidance in close relatives. [2]
- Compare and contrast patterns of inheritance in plants and humans. [3]
- Explain how plants of the same species can adapt to various environmental gradients. [3]
- Compare and contrast self-fertilization and asexual reproduction. [3]
- Explain how identical twins can exhibit different phenotypes. [3]
- Compare and contrast evolution and phenotypic plasticity. [3]
- Outline how transect studies can help distinguish between speciation and plasticity. [4]
- Distinguish between deductive and inductive reasoning, using **two** examples from biology. [4]
- Explain how sex-linked genes lead to different patterns of inheritance in humans. [4]
- Explain the different ways alleles interact to determine the ABO blood group of an individual. [4]
- Describe how sex is determined in humans. [5]
- Explain how genetic disorders can lead to disease. [5]
- Describe the different ways alleles interact with each other, using examples for each. [8]
- Describe the different patterns of inheritance that violate Mendelian laws. [7]

Additional Higher Level

- Define gene linkage. [1]
- Explain why the F2 generation is often used to conduct chi-squared tests. [3]
- Explain how rates of recombination influence patterns of inheritance in dihybrid crosses. [3]
- Explain why gene linkage occurs. [3]
- Explain the outcomes of gene-linkage in dihybrid crosses. [3]
- Explain why a polymorphic gene may have no heterozygous individuals but multiple alleles. [3]
- Describe how a chi-squared test is used to determine whether 2 genes are linked or not. [8]
- Describe the different patterns of inheritance that violate Mendelian laws. [8]

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