

ESAT

Biology

Gene technologies, variation and evolution

Free lesson notes

Covers	B6.1, B6.2, B6.3, B7.1 and B7.2
Format	Lesson, worked examples, self-check
Price	Free

About this lesson

This lesson joins two big ideas. First, **we can now change genes on purpose**: cutting a gene out of one organism and putting it into another (genetic engineering, B6.1), growing stem cells that can become many cell types (B6.2), and the older method of breeding plants and animals for features we want (selective breeding, B6.3). Second, **living things also change without our help**: individuals of a species differ (variation, B7.2), and when the environment favours some of them, the species changes over generations by natural selection, which also explains why bacteria evolve resistance to antibiotics (B7.1).

The same logic runs through everything: *variation* comes first, then something *selects*, then the selected features are *inherited*. Cover each worked example and try it first. Finish with the self-check, then the practice set.

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1 Genetic engineering: the idea (B6.1)

Genetic engineering (also called genetic modification, GM) means **transferring a gene from one organism into another** so that the second organism makes a new protein and shows a new characteristic. The organism that receives the gene is called **transgenic** or genetically modified.

Why does this work at all? Because *every organism uses the same genetic code*: a triplet of bases codes for the same amino acid in a bacterium, a plant and a human. A bacterium given the human gene for insulin reads it with its own ribosomes and builds human insulin, exactly as the gene instructs. (Compare the DNA lesson: gene → mRNA → amino acids → protein.)

Genes are carried between organisms using a **vector**. In bacteria the usual vector is a **plasmid**: a small ring of DNA, separate from the main chromosome, which bacteria can take up and copy. Plasmids are easy to cut open and to put back into cells, which is why they are so useful.

To do the job you need two tools, both of which are **enzymes** (proteins from the previous lessons, with shapes that fit a particular substrate):

- **Restriction enzymes** are “molecular scissors”: they **cut DNA at a specific base sequence**.
- **DNA ligase** is “molecular glue”: it **joins pieces of DNA together**.

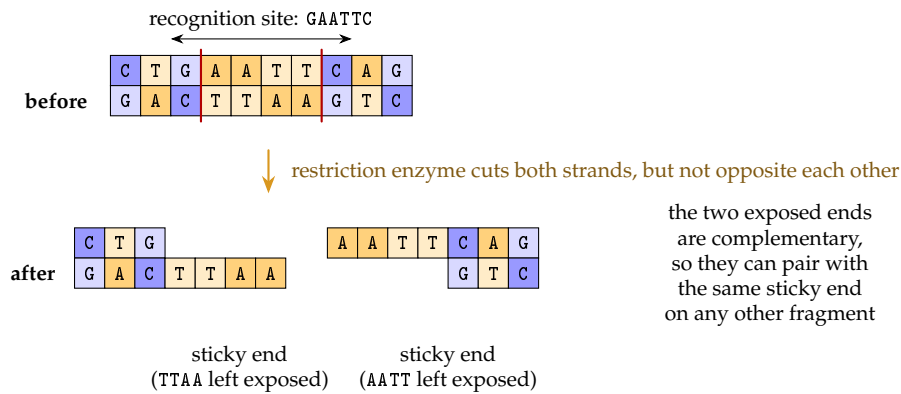
Common mistakes

- Saying genetic engineering moves *proteins* or *cells*. It moves a *gene*, a section of DNA.
- Thinking the gene only works in the same species. The genetic code is universal, so a human gene can work in a bacterium.
- Mixing up the two enzymes: restriction enzymes **cut**, ligase **joins**.

2 Restriction enzymes and sticky ends (B6.1)

Each restriction enzyme has an active site that fits one particular short sequence of bases, its **recognition site**, and cuts the DNA only there (the same lock-and-key idea as for any enzyme). A well-known example, EcoRI, recognises the six bases GAATTC. Look at the opposite strand: pairing A–T and C–G gives CTTAAG. Reading each strand in its own direction, the site looks the same on both strands.

The enzyme does not cut straight across. It cuts the two strands at *different* places, so that each end of the cut has a short stretch of unpaired bases. These are **sticky ends**.



Sticky ends are important because the unpaired bases can form base pairs with *any other* sticky end that is complementary. If the *same* restriction enzyme cuts both the human DNA and the plasmid, **all the fragments have matching sticky ends**, so the human gene can pair with the opened plasmid. The pairing alone is weak, so **DNA ligase** then joins the sugar-phosphate backbones to make a permanent join. The result is a **recombinant plasmid**: plasmid DNA with the new gene inside.

How often does an enzyme cut? A recognition site of n bases can be in 4^n different sequences (four choices of base at each place). In random DNA, a particular site therefore turns up about once in every 4^n bases. The longer the site, the more rarely it occurs, so the fewer the cuts.

Worked example: how many cuts?

A circular plasmid of 2048 base pairs contains random DNA. A restriction enzyme recognises a four-base site. On average, how many cuts does it make, and into how many fragments does it break the plasmid?

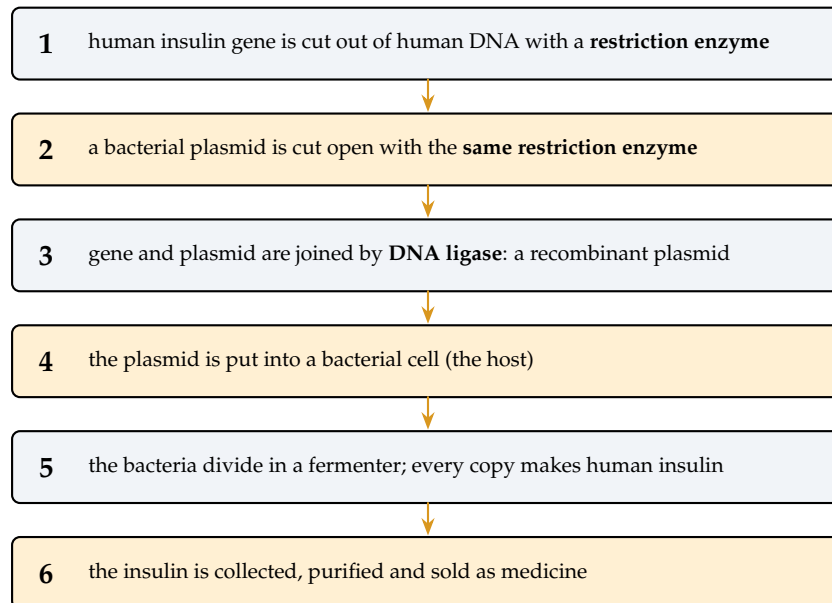
A four-base site occurs about once in $4^4 = 256$ bases, so in 2048 bases about $2048 \div 256 = 8$ times. Each cut opens the ring; for a *ring*, 8 cuts give 8 fragments (for a straight piece, 8 cuts would give 9).

Common mistakes

- Saying ligase cuts DNA. Ligase *joins*; restriction enzymes *cut*.
- Using different restriction enzymes on the gene and the plasmid. They would leave different sticky ends that do not match, so the pieces would not join easily.
- Thinking a restriction enzyme cuts anywhere. It cuts only at its own recognition sequence.
- Forgetting that the cut leaves *unpaired* bases on each strand (sticky ends); this is what lets fragments find each other.

3 Making human insulin, and GM crops (B6.1)

People with type 1 diabetes cannot make insulin and must inject it. It used to be extracted from the pancreases of pigs and cattle; now it is made by genetically engineered bacteria. The steps are:



Step 5 is the key advantage: bacteria divide quickly (as often as every 20 minutes in good conditions), and each new cell carries a copy of the plasmid, so one engineered bacterium becomes billions that all make the protein. The product is *human insulin*, which the body accepts, and it can be made in large amounts, cheaply, without using animals.

Genetically modified crops. Genes can be put into plants, too. Examples: a gene from the bacterium *Bacillus thuringiensis* (Bt) that makes a protein poisonous to certain insect pests; genes that make a crop tolerant to a weedkiller; and “golden rice”, given genes that make beta-carotene, which the body turns into vitamin A, to help prevent deficiency in places where rice is the main food.

Benefits and risks. You should be able to give a balanced view.

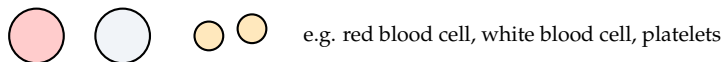
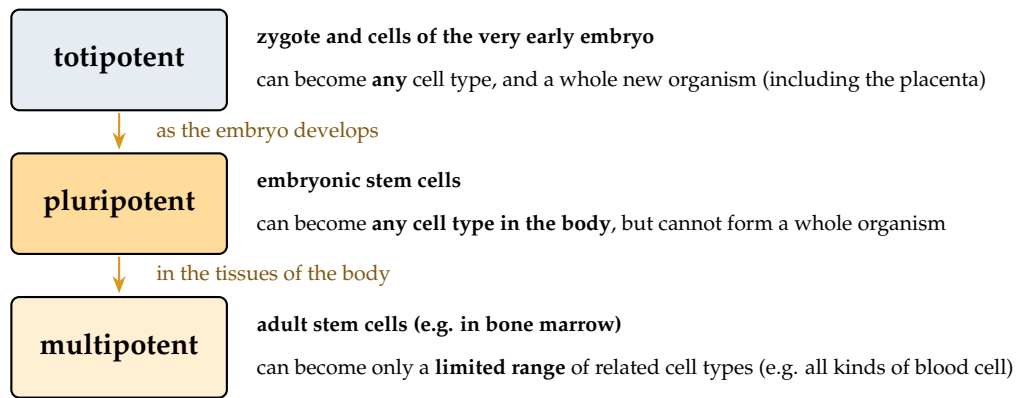
Possible benefits	Possible risks or concerns
Higher yields; less loss to pests and weeds, so more food	Genes may spread to wild plants (for example herbicide tolerance to weeds)
Less insecticide needed, so less pollution and cost	Effects on other organisms, such as harmless insects and food webs, may be unknown
Crops with extra nutrients (golden rice)	Worries that the food could cause allergies or harm health, which must be tested
Medicines such as insulin made cheaply and in quantity	Cost: seeds can be expensive and controlled by companies; ethical objections to moving genes between species

Common mistakes

- Saying the bacteria “produce” the insulin gene. The gene is put in by scientists; the bacteria make the *protein*.
- Using the same cell for each step. The human gene is cut out of human DNA; the *plasmid* is cut from a bacterium; they are joined outside the cell.
- Claiming GM food is definitely harmful or definitely harmless. The risks and benefits are weighed, and the evidence must be tested case by case.

4 Stem cells (B6.2)

Your body has about 200 different cell types, all from one fertilised egg. A **stem cell** is an **undifferentiated cell that can divide (by mitosis) and can become specialised**. The spec asks you to know three levels of ability, called **potency**:



- **Totipotent:** can become *any* cell type, including the cells needed to form a whole new organism (and the placenta). In humans these are the zygote and cells of the very early embryo.
- **Pluripotent:** can become *any cell of the body*, but cannot form a whole organism. Embryonic stem cells (from a slightly older embryo) are pluripotent.
- **Multipotent:** can become only a *limited range of related cell types*. Adult stem cells, such as those in bone marrow, can make all the types of blood cell but not nerve cells.

As development proceeds, cells lose potency as different genes are switched on and off. A specialised cell has the same genes as a stem cell; it simply uses a different set of them.

Uses. Stem cells may be used to replace damaged or diseased cells, for example bone-marrow transplants to replace the blood cells of patients with leukaemia, or research towards treating conditions such as spinal injuries and some forms of blindness, and for testing new drugs on human tissue. **Concerns** include ethical objections to using embryos (human embryos are destroyed to obtain embryonic stem cells), the risk that transplanted cells could grow out of control as tumours, the risk of rejection (if the cells are not genetically matched to the patient), and the risk of passing on viral infection.

Common mistakes

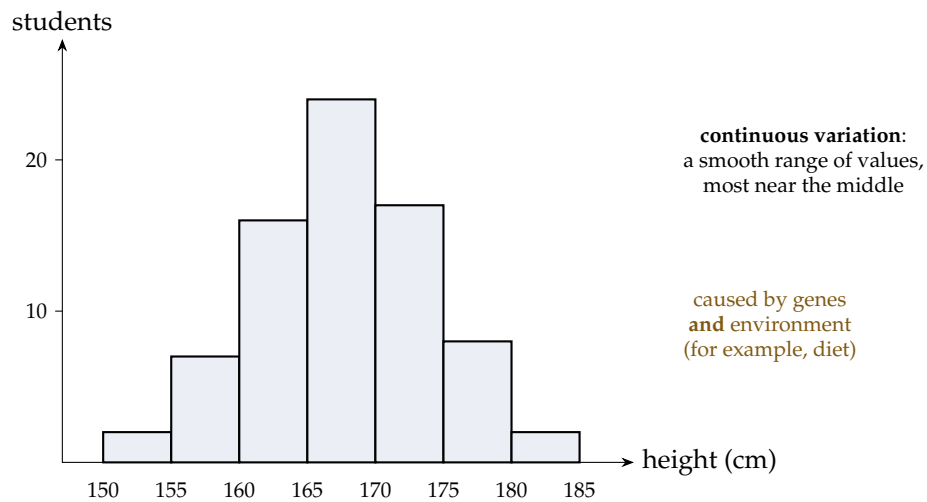
- Saying stem cells are specialised. They are *unspecialised*; that is the point.
- Mixing up pluripotent (any body cell) with totipotent (can make a whole organism too).
- Saying adult stem cells can become any cell. They are multipotent: a limited range.
- Saying a specialised cell has lost genes. It has all of them, but most are switched off.

5 Variation (B7.2)

Variation means differences between individuals of the same species. Variation has two causes, and many features depend on both.

- **Genetic variation:** differences in the alleles inherited from parents. It arises from **mutation** (the only source of completely new alleles), and in sexual reproduction from **meiosis** (random assortment of chromosomes and crossing over), **random fertilisation** (which sperm fertilises which egg) and the mixing of two parents' genes. Examples: blood group, eye colour.
- **Environmental variation:** differences caused by surroundings and way of life, for example diet, climate, sunlight, accident or injury (such as a scar, or a tree bent by the wind). Environmental effects are *not* inherited.
- **Both:** height (genes set the possible range; diet and health affect where in the range you end up), body mass, skin colour in sunshine.

Continuous or discontinuous. Some features take only a few separate values (blood group A, B, AB or O): **discontinuous variation**, usually controlled by one or two genes with little environmental effect. Others can take any value in a range (height, mass): **continuous variation**, usually controlled by many genes together with the environment. Plotted as a histogram, a continuous feature typically gives a smooth, bell-shaped curve with most individuals near the middle.



Twins are a natural experiment. Identical twins have identical genes, so differences between them are caused by the environment. Non-identical twins share about half their varying alleles, like ordinary siblings. If identical twins brought up apart are much more alike than non-identical twins brought up together, genes must matter greatly for that feature.

Worked example: reading a histogram

In the histogram the bars (to the nearest student) for the height classes 150, 155, 160, 165, 170, 175 and 180 cm show 2, 7, 16, 24, 17, 8 and 2 students. How many students were measured, and what fraction were in the tallest-but-one three classes (165, 170 and 175)?

Total = $2 + 7 + 16 + 24 + 17 + 8 + 2 = 76$. The three classes contain $24 + 17 + 8 = 49$ students, so the fraction is $49/76$. The shape (most in the middle, few at the ends) shows continuous variation.

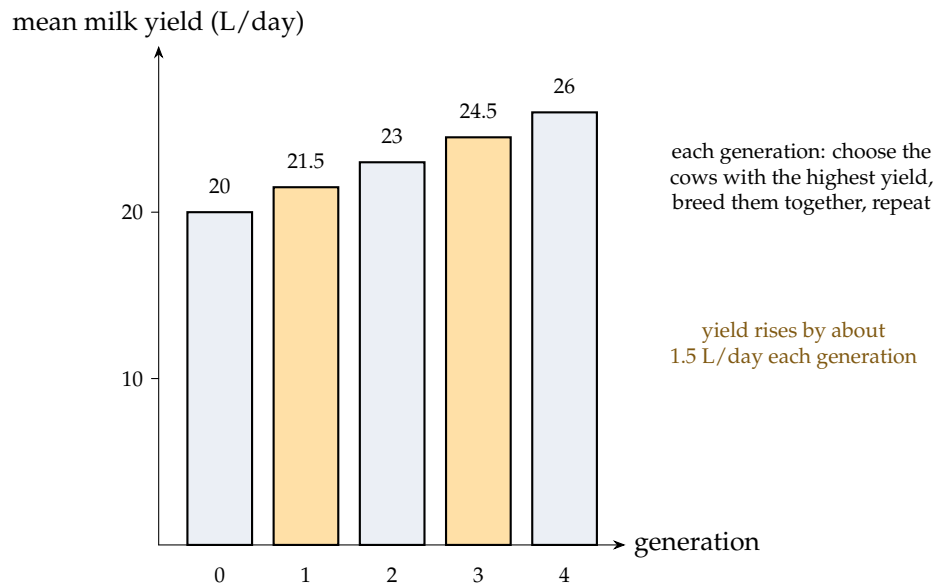
Common mistakes

- Saying all variation is caused by genes, or all by the environment. Many features (like height) are both.
- Saying a scar or a trained muscle can be inherited. Only changes in the DNA of gametes are inherited.
- Saying mutation is the cause of variation in all sexual reproduction. Mutation makes *new* alleles, but shuffling existing alleles (meiosis and fertilisation) causes most of the differences between siblings.
- Describing height as discontinuous. Height can take any value in a range, so it is continuous.

6 Selective breeding and natural selection (B6.3, B7.1)

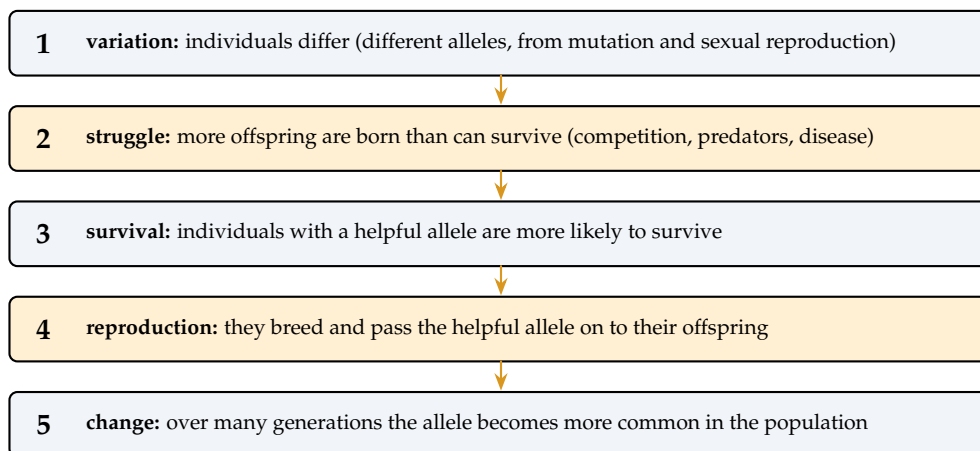
Selective breeding (artificial selection) is when **humans choose** which individuals breed, to produce offspring with features we want: milk yield in cows, large fruit, disease resistance in wheat, gentle temperament in dogs. The method is the same every time:

1. Decide the feature wanted. Choose the individuals that show it most strongly.
2. Breed them together.
3. From the offspring, again choose those with the best form of the feature, and breed them.
4. Repeat over many generations.

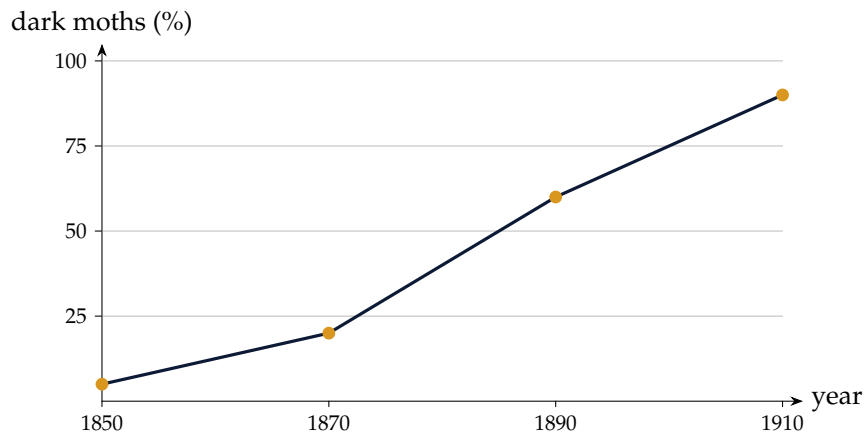


It works because the feature varies and the variation is inherited: each generation of parents is better than the average of the last, so their offspring are too. The **disadvantages** are that the population loses genetic variation (because only a few individuals breed), and that **inbreeding** (breeding closely related individuals) makes harmful recessive alleles more likely to meet in the offspring, giving inherited diseases. A population of near-identical individuals is also at greater risk: one new disease may kill them all.

Natural selection (Darwin and Wallace) is the same logic with *nature* doing the choosing.



Over many generations, natural selection changes the characteristics of a species (**evolution**), and when groups of a species become so different that they can no longer interbreed to produce fertile offspring, new species form. The **peppered moth** is a classic example. Before the Industrial Revolution most were pale, camouflaged against lichen-covered bark; as soot killed the lichen and blackened the trees, dark moths were better camouflaged, escaped being eaten by birds more often, and became common. When pollution laws later cleaned the air, pale moths again became commoner.



	Selective breeding	Natural selection
who chooses	humans	the environment
selected for	features useful to humans	features that help survival and reproduction
speed	fast, with planned breeding	slow, over many generations
variation needed	yes	yes

Worked example: progress under selective breeding

A farmer's herd has a mean milk yield of 20 litres per day. Choosing the best cows for breeding raises the mean by 1.5 litres per day each generation. What is the mean after 4 generations?
 $20 + 4 \times 1.5 = 26$ litres per day.

Worked example: selection in numbers

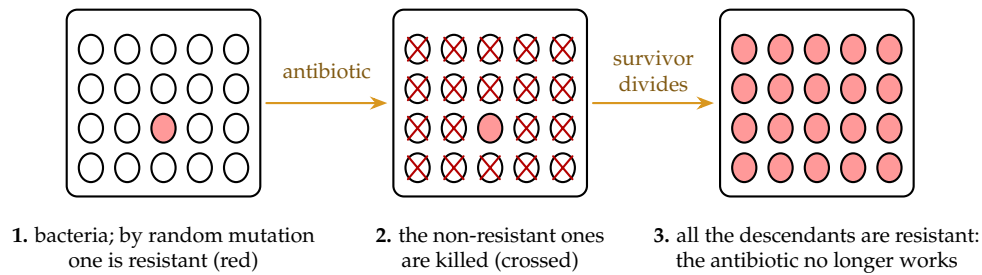
A population has 1000 moths of which 10% are dark. Birds eat so many that 60% of dark moths survive but only 10% of pale ones. What percentage of the survivors are dark?
 Dark: 100, pale: 900. Survivors: dark $0.6 \times 100 = 60$, pale $0.1 \times 900 = 90$. Dark moths are $60/150 = 40\%$ of the survivors, up from 10%. If the dark moths pass the allele to offspring, the allele becomes more common.

Common mistakes

- Saying individuals *change* to suit the environment ("the moth turned dark"). Individuals do not change; those with the helpful feature survive and breed, so the *population* changes.
- Saying "survival of the fittest" means the strongest. "Fittest" means best suited to the environment, measured by how many offspring survive.
- Forgetting that the helpful feature must be *inherited*. A feature gained during life (for example big muscles from training) is not passed on.
- Saying mutations happen *because* the organism needs them. Mutations are random; the environment only selects among the variation that exists.

7 Antibiotic resistance (B7.1)

Antibiotics (such as penicillin) are medicines that kill bacteria or stop them growing. They do not work on viruses. Bacteria evolve resistance to them by natural selection, and you should be able to tell the story step by step.



1. In a large population of bacteria, **variation** exists. By chance, through a **random mutation**, a few bacteria have an allele that makes them resistant.
2. The antibiotic kills the non-resistant bacteria. The resistant ones **survive**.
3. They **reproduce** (bacteria divide quickly) with less competition, and pass on the resistance allele; bacteria can even pass resistance genes on plasmids to other bacteria.
4. The **population** now consists mainly of resistant bacteria and the antibiotic no longer works. A well-known example is MRSA, a “superbug” resistant to many antibiotics.

The mutation arose *before* the antibiotic was used; the antibiotic does not cause it, it only selects it. Resistant bacteria spread when antibiotics are overused or misused (for example, prescribed for viral infections, or not finished), so doctors should prescribe antibiotics only when needed, and patients should complete the course so that the weakest survivors are not left to multiply. Because bacteria evolve faster than new antibiotics are developed, antibiotic resistance is a serious threat to medicine.

Worked example: how fast do resistant bacteria multiply?

A patient has 1000 bacteria, only one of which is resistant to an antibiotic. The antibiotic kills all the others. The resistant bacterium divides once every 30 minutes. How many resistant bacteria are there 3 hours later (assuming no deaths)?

3 hours is 6 divisions of 30 minutes, and each division doubles the number: $2^6 = 64$ bacteria.

Common mistakes

- Saying the bacteria “become used to” the antibiotic or “learn” resistance. Resistance comes from random mutation in some bacteria, which are then selected.
- Saying the *person* becomes resistant to the antibiotic. It is the *bacteria*.
- Saying antibiotics cause the mutation. The mutation was already there, by chance.
- Saying antibiotics are useful against viral infections such as colds and influenza. They are not.

Exam tip

For any “how did it evolve” question, write the chain: **variation** (random mutation) → **selection** (the environment or antibiotic kills some) → **survivors reproduce** → **allele becomes more common** in the *next generation*. Every mark scheme follows this order, and the commonest lost mark is skipping the first or last step.

8 Worked problems and exam technique

Here are two problems that combine several ideas.

Worked example: evaluating a genetic-engineering process

Scientists cut a gene for a pest-killing protein from a bacterium with a restriction enzyme and join it into a plant’s DNA. The plant makes the protein. (a) Why can a bacterial gene work in a plant? (b) What is the role of ligase? (c) Give one benefit and one risk.

- (a) The genetic code is universal: the plant’s ribosomes read the same triplets as the amino acids they code for. (b) DNA ligase joins the gene to the plant’s DNA (or vector) by forming bonds between the sugar–phosphate backbones. (c) Benefit: fewer crops lost, less insecticide. Risk: the gene could spread to wild relatives, or harm non-target insects.

Worked example: explaining a graph

The moth graph shows the percentage of dark moths in a wood: 5% in 1850, 20% in 1870, 60% in 1890 and 90% in 1910. By how many percentage points did the dark form rise between 1870 and 1910, and how would you explain the trend?

$90 - 20 = 70$ percentage points. Explanation: soot darkened the trees; pale moths were easier for birds to see, so fewer survived to breed; dark moths survived and passed on the dark allele; so the allele became more common over generations.

Exam technique.

1. Name the tool: *cut* = restriction enzyme, *join* = ligase, *carry* = plasmid vector.
2. Match potency to the words “whole organism” (totipotent), “any body cell” (pluripotent), “limited range” (multipotent).
3. For variation, ask: is it inherited (genetic) or acquired during life (environmental)? If both, say so.
4. In every evolution question, write the full chain: variation, selection, survival, reproduction, inheritance. State that it is the *population* that changes.
5. For ratio and percentage questions, work with real numbers (like 1000 moths), not just percentages.
6. For data questions, use numbers from the graph in your answer.

Spec coverage (B6.1 to B6.3, B7.1, B7.2). Genetic engineering (restriction enzymes, ligase, risks and benefits); stem cells (totipotent, pluripotent, multipotent); selective breeding compared with natural selection; natural selection, evolution and antibiotic resistance; genetic and environmental variation.

Check yourself

Try these without looking back, then compare with the answers on the next page.

1. Which enzyme cuts DNA at a specific base sequence, and which enzyme joins DNA fragments?
2. Why does a human gene work when it is put into a bacterium?
3. Name the type of stem cell that can form any cell of the body but not a whole organism.
4. Give one environmental cause and one genetic cause of variation.
5. Give one advantage and one disadvantage of selective breeding.
6. A cow herd starts with a mean yield of 18 litres per day and rises by 2 litres per day each generation. What is the mean after 5 generations?
7. A recognition site has 5 bases. About how often does it occur in random DNA?
8. Explain how antibiotic resistance spreads through a population of bacteria.

Answers to the self-check

1. Restriction enzyme cuts; DNA ligase joins.
2. The genetic code is universal, so the bacterium reads the triplets as the same amino acids.
3. Pluripotent.
4. Environmental, for example diet or a scar from injury. Genetic, for example a mutation (or random fertilisation, meiosis).
5. Advantage: produces useful features such as high yield, quickly. Disadvantage: reduces genetic variation, so inbreeding and a risk from new diseases.
6. $18 + 5 \times 2 = 28$ litres per day.
7. $4^5 = 1024$: about once every 1024 bases.
8. A random mutation gives resistance to a few bacteria; the antibiotic kills the others; the survivors reproduce and pass on the allele; the population becomes resistant.

Next step

Heurisco's *ESAT Biology: Gene Technologies, Variation and Evolution Practice Set* has twenty original exam-style questions on this lesson, with diagrams and data, in order of difficulty, with a full worked solution and a note on the trap in each.