

Thursday 13 June 2019 – Morning

A Level Biology B (Advancing Biology)

H422/02 Scientific literacy in biology

Time allowed: 2 hours 15 minutes



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- the Insert (inserted)

You may use:

- a scientific or graphical calculator
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Candidate number

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First name(s)

Last name

INSTRUCTIONS

- The Insert will be found inside this document.
- Use black ink. You may use an HB pencil for graphs and diagrams.
- Answer **all** the questions.
- Where appropriate, your answers should be supported with working. Marks may be given for a correct method even if the answer is incorrect.
- Write your answer to each question in the space provided. If additional space is required, use the lined page(s) at the end of this booklet. The question number(s) must be clearly shown.

INFORMATION

- The total mark for this paper is **100**.
- The marks for each question are shown in brackets [].
- Quality of extended responses will be assessed in questions marked with an asterisk (*).
- This document consists of **28** pages.



Oxford Cambridge and RSA

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INSTRUCTIONS

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INFORMATION

- This Insert contains the Advance Notice.
- This document consists of **4** pages.

Learning from Iceland's model for genetic research

A few years ago, a group of scientists at the International Myeloma Foundation (IMF) identified a problem. Some people with monoclonal gammopathy of undetermined significance (MGUS), which is a benign condition, would later develop the malignant disease multiple myeloma. The risk was estimated to be as high as 40% over a lifetime.

Most doctors do not routinely screen for MGUS. As a result, most cases are never diagnosed unless patients develop multiple myeloma.

The chairman of IMF, Ian Durie, thought it might be possible to cure or prevent multiple myeloma. To do this, it would be necessary to intervene at an early stage and identify those patients with MGUS who later develop multiple myeloma. As only about 1% of people with MGUS go on to develop multiple myeloma each year, the IMF needed to have a clear way to identify the patients at risk.

In 2015, after discussions with other scientists working on myeloma, Durie proposed a potential solution and decided Iceland was a good place to test their ideas.

Iceland has a small population – only 320,000 people in 2013. About 20 new cases of multiple myeloma are reported in the country each year. It also has the most detailed genetic and medical databases of any country in the world. Iceland therefore offers a unique experimental setting. The IMF is able to detect and document all the people with MGUS. By studying MGUS patients, the scientists can work out which ones go on to develop myeloma. They will then have the opportunity to intervene, early on, and provide a cure.

The IMF launched a nationwide MGUS screening study in November 2016. The team of scientists has been encouraging all Icelanders older than 40 years of age to take part. More than 75,000 people had registered by April 2017, and the researchers had collected nearly 20,000 blood samples. This made the project the largest myeloma study ever conducted.

Celtic and Norwegian explorers settled in Iceland during the 9th century. The country's population has remained small ever since, owing to geographic isolation, its harsh environment, and several dramatic events. Two waves of plague hit Iceland during the 15th century, followed by a spate of smallpox in the early 1700s and a large volcanic eruption in 1783. As a result, the island has one of the most genetically homogeneous populations in Europe. This is important to the IMF's study because it is easier to pinpoint an unusual, disease-causing genetic variant in populations with little genetic diversity.

Iceland has a long tradition of recording family trees. In the 12th century, Icelandic priest Ari the Wise traced the country's history in a book called *Íslendingabók* – the book of Icelanders. Since then, church records and censuses have kept track of births, deaths and marriages, building a detailed picture of Icelandic ancestry.

This tradition was updated and modernised in 1996. Icelandic geneticist Kári Stefánsson founded the company deCODE Genetics and collected all available genealogical information in one online database, also called *Íslendingabók*.

The research power of this genealogical data has been boosted by integrating it with two more databases. One of them details genetic information collected from biological samples of more than 100,000 citizens; the other stores medical records of people participating in related research projects. Every single cancer that is diagnosed in Iceland is centrally registered, as are all medical procedures, clinical diagnoses and prescriptions.

Researchers at the IMF store thousands of blood samples from Icelanders. They test the samples with automated blood analysers which rely on flow cytometry. These expensive tests allow the identification of genetic variants that might be linked to the risk of developing multiple myeloma.

The results from these Icelandic studies will assist research into human genomic variation around the world. Although it might be difficult to replicate the IMF studies elsewhere, the information from Iceland can be extrapolated and applied globally.

Source: <http://www.the-scientist.com/?articles.view/articleNo/49439/title/Learning-from-Iceland-s-Model-for-Genetic-Research/>

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Answer **all** the questions.

1 This question is based on the Advance Notice article ‘**Learning from Iceland’s model for genetic research**’ in the **Insert**.

(a) The article explains how Iceland has one of the most genetically homogeneous populations in Europe.

(i) State what is meant by the following genetic terms.

1. Gene

.....

2. Allele

.....

[2]

(ii) Allele frequencies will remain constant in a stable population. However, population changes can alter allele frequencies.

For each of the following events, give the term used to describe the effect on allele frequencies.

1. Iceland was settled by a relatively small number of explorers in the 9th century.

.....

2. The Icelandic population decreased due to the two waves of plagues during the 15th century, smallpox in the early 1700s and a volcanic eruption in 1783.

.....

[2]

(iii) Explain how the events described in (ii) resulted in the low genetic diversity of the Icelandic population.

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[2]

- (b) The article describes the use of flow cytometry ('automated blood analysers') to identify genetic variants linked to the risk of developing multiple myeloma.

Explain how flow cytometry could be used to identify genetic variants linked to the risk of developing multiple myeloma.

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..... [4]

- (c) Some genetic diseases, such as sickle cell anaemia, are caused by single mutations.

Explain how a single gene mutation causes sickle cell anaemia.

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..... [3]

- (d) The goal of the researchers at the International Myeloma Foundation is to identify people who develop multiple myeloma after having monoclonal gammopathy of undetermined significance (MGUS).

Evaluate the advantages and disadvantages of this approach compared with pedigree analysis.

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..... [4]

- (e) In MGUS, B cells produce an abnormal polypeptide called M protein.

Production of M protein involves the processes of transcription and translation.

Complete the table by putting a tick (✓) in the appropriate box to indicate whether the feature is involved in transcription, translation, both or neither.

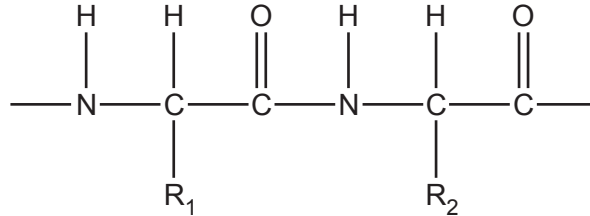
Feature	Transcription only	Translation only	Both	Neither
C pairs with G				
A pairs with T				
Phosphodiester bonds are made				
Peptide bonds are made				

[4]

- 2 Antimicrobial peptides (AMPs) are peptides found in animals and plants that destroy a wide range of pathogenic bacteria, fungi and viruses.

The α -defensins are a group of AMPs that contain 18–45 amino acids.

- (a) The diagram below shows part of the structure of an α -defensin molecule.



- (i) Draw a circle around the part of the structure that represents the peptide bond.

[The response to this question should be drawn on the diagram.]

[1]

- (ii) Name the chemical reaction that joins the amino acids together in a peptide.

..... [1]

- (b) A student used paper chromatography to investigate the amino acid composition of a sample of α -defensin.

- (i) Suggest the importance of the following steps in the paper chromatography procedure.

1. The sample of α -defensin was heated with hydrochloric acid.

.....

2. Care was taken not to touch the paper with fingers.

.....

[2]

(ii) Fig. 2 shows the results of one analysis.

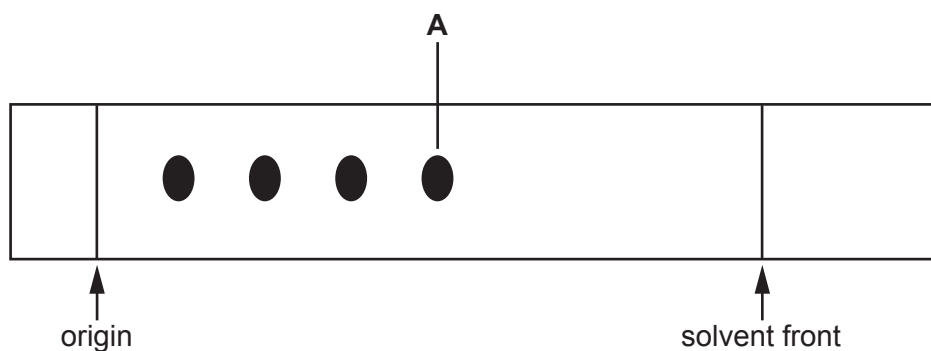


Fig. 2

Table 2 shows R_f values for six different amino acids.

Amino acid	R_f
Arginine	0.16
Cysteine	0.37
Glutamic acid	0.31
Isoleucine	0.53
Methionine	0.51
Tyrosine	0.55

Table 2

Using Fig. 2 and Table 2, calculate the R_f value for spot **A** and identify the amino acid.

R_f value for spot **A** =

amino acid =

[2]

(d) The β -defensins are another group of peptides found in the male reproductive tract.

One β -defensin is coded for by the *DEFB126* gene. Men who are homozygous for a mutation in *DEFB126* have a normal sperm count with normal motility, but the sperm have a reduced ability to penetrate hyaluronic acid (a model for female cervical mucus).

(i) Suggest why it is thought that the *DEFB126* mutation reduces the chance of successful fertilisation.

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..... [2]

(ii) It is estimated that 22% of all Europeans are homozygous for the recessive mutant form of *DEFB126*.

Calculate the allele frequency of the mutant form of *DEFB126* in all Europeans (men and women).

Use the Hardy-Weinberg equations:

$$p + q = 1 \qquad p^2 + 2pq + q^2 = 1$$

Give your answer to **2 significant figures**.

frequency = [2]

(iii) The fact that the *DEFB126* mutation reduces the chances of successful fertilisation means that, in theory, the allele frequency should have fallen.

Suggest why the allele frequency of the *DEFB126* mutation remains high.

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..... [1]

- 3 The extracellular matrix (ECM) can be thought of as the 'glue' that holds together the cells in a tissue. The ECM consists of water, proteins and polysaccharides.

Matrix metalloproteinases (MMPs) are a group of proteases that hydrolyse proteins in the ECM.

Each MMP consists of a single polypeptide chain.

- (a) For each of the following features of MMP structure, draw a line connecting the feature to the correct description.

Feature	Description
The active site of MMP contains a Zn^{2+} ion that is required for substrate binding.	Primary structure
The enzyme contains a β -pleated sheet and three α -helices.	Secondary structure
The amino acid histidine occurs in three places in the sequence making up the active site of all MMPs.	Tertiary structure
	Competitive inhibition
	Cofactor

[3]

(b) MMP activity has been linked to the development of cancer.

Women with tumours in their breasts will often have biopsies (tissue samples) taken and tested to see if the tumours are malignant (cancerous) or benign (non-cancerous).

In one study, the total MMP activity was measured in breast biopsies that were classed as either:

- benign
- malignant grade I (the least malignant)
- malignant grade II
- malignant grade III (the most malignant).

Table 3 shows the results of this study.

Tumour classification	MMP activity (units per μg protein)
Benign	6.58
Malignant grade I	1.34
Malignant grade II	6.80
Malignant grade III	32.29

Table 3

(i) The researchers carried out a statistical test to compare the MMP activity in grade III tumours with the mean activity in all other tumours (benign, grade I and grade II).

Suggest a null hypothesis that the researchers would have used.

.....
 [1]

(ii) The result of this test gave $p < 0.0001$.

Use the words 'probability' and 'chance' to describe the conclusion the researchers would make.

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 [1]

(iii) Use the data in Table 3 to evaluate the hypothesis that MMP activity increases the severity of breast cancer.

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..... [3]

(c) Marimastat is an MMP inhibitor that was used in clinical trials as a potential treatment for cancer.

Suggest how marimastat could inhibit MMPs to reduce the hydrolysis of proteins in the ECM.

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..... [2]

- 4 In the 1950s, Melvin Calvin studied the series of reactions that we now know as the Calvin Cycle.

Calvin's 'lollipop' experiment was so called because it used a lollipop-shaped glass flask containing single-celled photosynthetic algae growing in culture.

A diagram of the apparatus Calvin used is shown in Fig. 4.1.

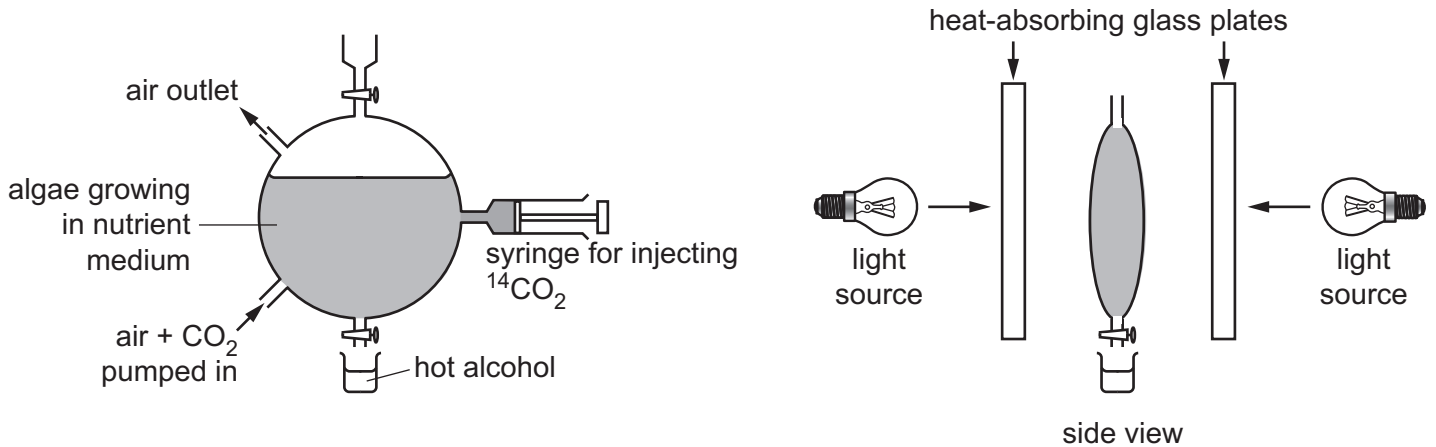


Fig. 4.1

The algae were illuminated for 30 minutes before the start of the experiment. Air and carbon dioxide were pumped into the suspension throughout.

At time zero, a small amount of radioactively-labelled carbon dioxide (¹⁴CO₂) was injected from the syringe.

At intervals after addition of the ¹⁴CO₂, samples of the suspension were run off into hot alcohol before being analysed.

(a) Suggest the reasons for the following steps in the experiment.

1. Illuminating the algae for 30 minutes before the start of the experiment.

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.....

2. Placing heat-absorbing glass between the light sources and the flask.

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3. Running each sample into hot alcohol before analysis.

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.....

[3]

- (b) Calvin measured the relative radioactivity in various compounds at 2 seconds, 10 seconds and 30 seconds after addition of the $^{14}\text{CO}_2$.

The results of the analysis are shown in Table 4. Presence of radioactivity is represented in the table as '+' and no radioactivity as '-'.

Organic compound	Relative radioactivity present at time after addition of $^{14}\text{CO}_2$		
	2 s	10 s	30 s
Amino acids	-	-	+
Glycerate-3-phosphate (GP)	+	+	+
Sucrose	-	-	+
Sugar phosphates	-	-	+
Triose phosphate (TP)	-	+	+

Table 4

- (i) Name the enzyme responsible for the initial incorporation of radioactive CO_2 into organic compounds.

..... [1]

- (ii) Use the results in Table 4 to explain the order in which the organic compounds are produced during photosynthesis.

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..... [3]

- (c) Calvin isolated the compounds formed at the earliest time points and found they contained three carbon atoms.

This led him to conclude that the first reaction in the cycle was between CO₂ and a 2-carbon compound.

Explain why Calvin's conclusion was **incorrect**.

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..... [2]

Question 4(d) begins on page 16

(d) Fig. 4.2 shows the relationship between the net rate of photosynthesis and light intensity in a plant growing at atmospheric CO₂ concentration (0.04%).

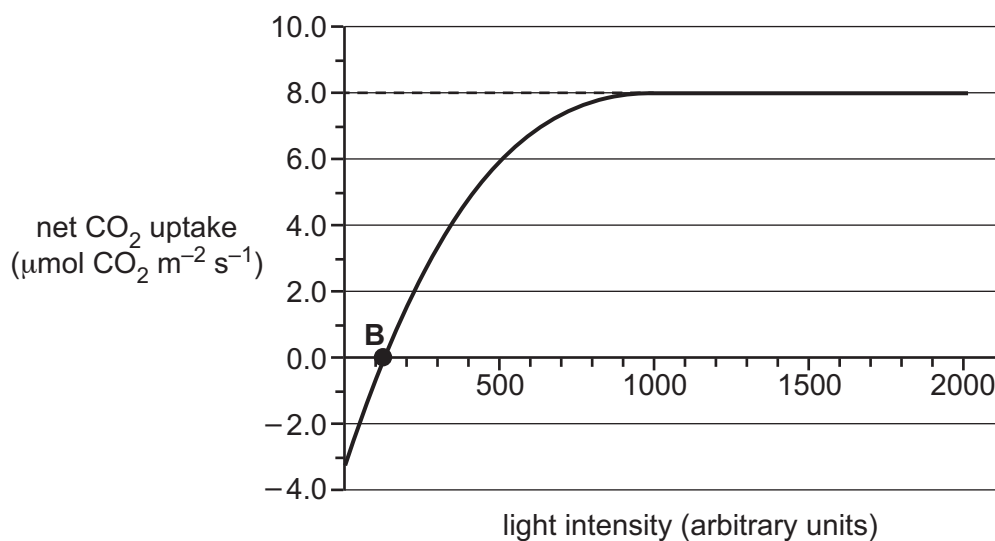


Fig. 4.2

(i) The plant had a leaf area of 0.97 m².

Calculate the maximum amount of CO₂ that the plant can take up in 1 minute.

maximum amount of CO₂ taken up in 1 minute = μmol [2]

(ii) Explain the significance of the point labelled **B** on Fig. 4.2.

.....

 [1]

- (e) Winter wheat seeds are usually sown in the autumn and flower the following summer. Seeds sown in the spring will usually not flower.

The Russian geneticist Lysenko discovered that winter wheat seeds can be treated with cold and moisture.

Explain why winter wheat seeds treated in this way and sown in spring are able to flower.

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..... [2]

- (f) Chrysanthemums normally flower only in autumn.

Commercial growers obtain flowers earlier in the year by growing the chrysanthemums in greenhouses where they can use screens or curtains to provide at least 12 hours of darkness.

Explain how this method stimulates early flowering and why it will not work if the plants are exposed to a brief period of light during the 12 hours of darkness.

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..... [3]

5 Fig. 5 shows a vertical section through the human eye.

The regions labelled **C**, **D** and **E** are affected by degenerative diseases of the eye associated with ageing.

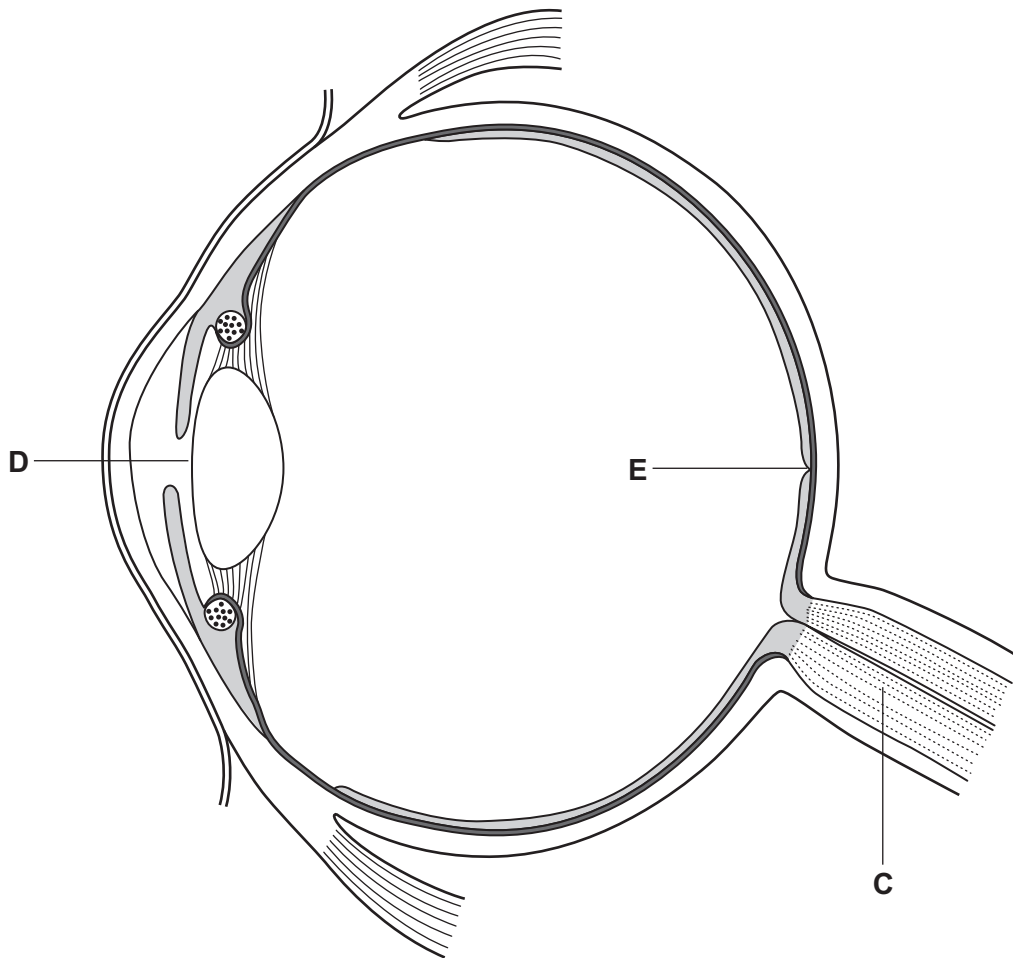


Fig. 5

- (a) (i) For regions **C** and **D** in Fig. 5, name the degenerative disease **and** explain why vision would be affected.

Region **C**

name of disease

explanation

.....

.....

.....

Region **D**

name of disease

explanation

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.....

.....

[4]

- (ii) Ranibizumab is a monoclonal antibody-based drug that inhibits the growth of new blood vessels.

Suggest how ranibizumab would be effective in treating a degenerative disease that affects the region labelled **E** in Fig. 5.

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..... [2]

(b) The retina contains light-sensitive photoreceptor cells.

(i) Explain why photoreceptor cells in the retina are described as transducers.

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..... [1]

(ii) Rod cells undergo various changes when they are stimulated by light.

Complete the following table by writing 'Rest' or 'Light' in the space provided to indicate whether the description refers to a rod cell at rest or when stimulated by light.

The first row has been completed for you.

Process in rod cell	Rest or Light
Rhodopsin is broken down to form opsin and <i>trans</i> -retinal	Light
Rod cell membrane is hyperpolarised	
Neurotransmitter is released by exocytosis from the rod cell into the synaptic cleft	
Sodium ion channels open	

[2]

(c) Red-green colour blindness is a sex-linked inherited disorder that affects mostly males.

Suggest why red-green colour blindness affects mostly males.

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.....
..... [2]

6 (a) Meiosis is the nuclear division that forms gametes.

(i) Explain why meiosis is referred to as a **reduction** division.

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..... [1]

(ii) Errors in meiosis can lead to chromosome mutations.

State the name of an event in meiosis that leads to chromosome mutations.

..... [1]

(iii) State the name of one syndrome caused by a chromosome mutation.

..... [1]

(iv) Some cancers that develop later in life are caused by chromosome mutation.

Suggest why these cancers are unlikely to be the result of errors in meiosis.

.....
..... [1]

7 (a) Fig. 7 is a diagram of a maize plant showing the male and female flowers.

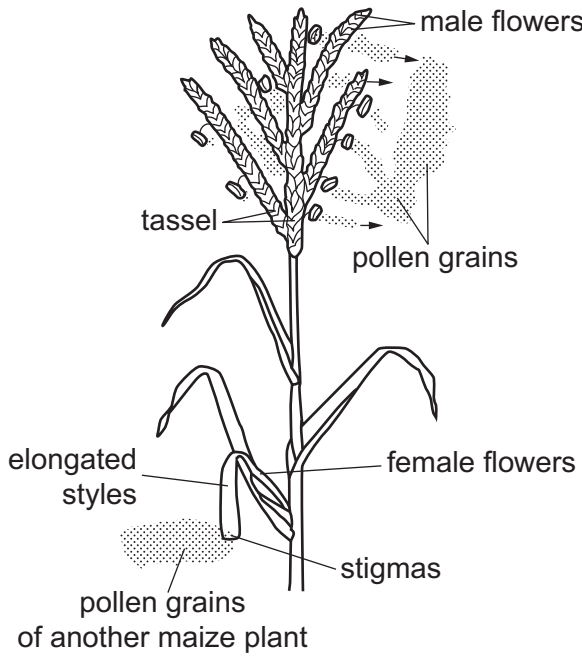


Fig. 7

Using the information in Fig. 7, identify **one** way in which maize is adapted for wind pollination.

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..... [1]

(b) When maize pollen grains land on the stigma of a maize plant, a pollen tube grows towards the ovule.

Describe the events that lead to the formation of the embryo **and** the endosperm.

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..... [3]

- (c) As well as being a popular food (corn on the cob), maize is a useful model for studying patterns of inheritance.

Each maize cob contains hundreds of seeds known as kernels.

In maize, one gene determines the colour of the kernels, which is either yellow or colourless.

Another gene determines the amount of endosperm in each kernel. Kernels filled with endosperm are smooth whereas kernels with shrunken endosperm appear wrinkled.

- (i) Two pure breeding strains of maize were crossed. One strain had smooth yellow kernels. The other strain had wrinkled colourless kernels.

All the kernels of the offspring (F_1) were smooth and yellow.

The plants in the F_1 generation were then crossed with plants that had pure-bred wrinkled colourless kernels.

State the parental genotypes and gametes of this cross.

Use the following to represent the alleles:

- **A** and **a** for colour (yellow or colourless)
- **B** and **b** for appearance (smooth or wrinkled).

parental genotypes: ×

gametes:

[2]

- (ii) Using a genetic diagram and your answer to (c)(i), predict the phenotypic ratio that you would expect from the second cross.

phenotypic ratio: [2]

(iii) The actual results of the second cross are shown in Table 7.1.

Phenotype	Number of kernels
Smooth yellow	275
Wrinkled yellow	277
Smooth colourless	235
Wrinkled colourless	213

Table 7.1

Calculate χ^2 for these data.

Use the formula: $\chi^2 = \sum \frac{(f_o - f_e)^2}{f_e}$

You may use the table below for working out.

$\chi^2 = \dots\dots\dots$ [3]

(iv) Table 7.2 shows a χ^2 probability table.

Degrees of freedom	Probability (p)				
	0.50	0.10	0.05	0.01	0.001
1	0.46	2.71	3.84	6.64	10.83
2	1.39	4.61	5.99	9.21	13.82
3	2.37	6.25	7.82	11.35	16.27
4	3.36	7.78	9.49	13.28	18.47

Table 7.2

What can you conclude about the results shown in Table 7.1 based on the χ^2 value you calculated in (c)(iii)?

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..... [1]

(v) Suggest an explanation for your conclusion in part (iv).

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..... [2]

END OF QUESTION PAPER

ADDITIONAL ANSWER SPACE

If additional space is required, you should use the following lined page(s). The question number(s) must be clearly shown in the margin(s).

A large area of lined paper for writing. It consists of a vertical solid line on the left side, creating a margin. To the right of this line, there are numerous horizontal dotted lines spaced evenly down the page, providing a guide for writing.

A large area of the page is reserved for writing, featuring a vertical solid line on the left side and horizontal dotted lines extending across the page.



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