H2

ANDERSON SERANGOON JUNIOR COLLEGE
HIGHER 2
ANSWERS

2024 JC2 PRELIMINARY EXAMINATION

CANDIDATE NAME	
CLASS	
INDEX NUMBER	

BIOLOGY 9744/03

PAPER 3
LONG STRUCTURED AND FREE RESPONSE QUESTIONS

10 SEPTEMBER 2024
TUESDAY

Candidates answer on the Question Paper.
No Additional Materials are required.

2 HOURS

READ THESE INSTRUCTIONS FIRST

Write your name and class on all the work you hand in.
Write in dark blue or black pen.
You may use an HB pencil for any diagrams or graph
Do not use paper clips, highlighters, glue or correction fluid.

Section A
Answer **all** questions in the spaces provided on the Question Paper.

Section B
Answer **any one** question in the spaces provided on the Question Paper.

The use of an approved scientific calculator is expected, where appropriate.
You may lose marks if you do not show your working or if you do not use appropriate units.

For Examiner's Use	
1	/ 30
2	/ 10
3	/ 10
4 / 5	/ 25
Total	/ **75**

At the end of the examination, fasten all your work securely together.
The number of marks is given in brackets [ ] at the end of each question or part question.

This document consists of **13** printed pages and **1** blank page

Section A

Answer **all** the questions in this section.

1 Malaria is a disease caused by the *Plasmodium* parasite. There are four species of the *Plasmodium* parasite, of which *Plasmodium falciparum* is responsible for most of the deaths from this disease.

Fig. 1.1 shows part of the life cycle of *P. falciparum*, which requires two hosts.

A female mosquito carrying *P. falciparum* injects the parasite, in a form known as a sporozoite, into the bloodstream of an uninfected person. The *P. falciparum* parasite multiplies in a liver cell before emerging as a different form, known as a merozoite, wrapped in the liver cell surface membrane. It enters a red blood cell and multiplies before causing the rupture of the red blood cell, releasing more parasites.

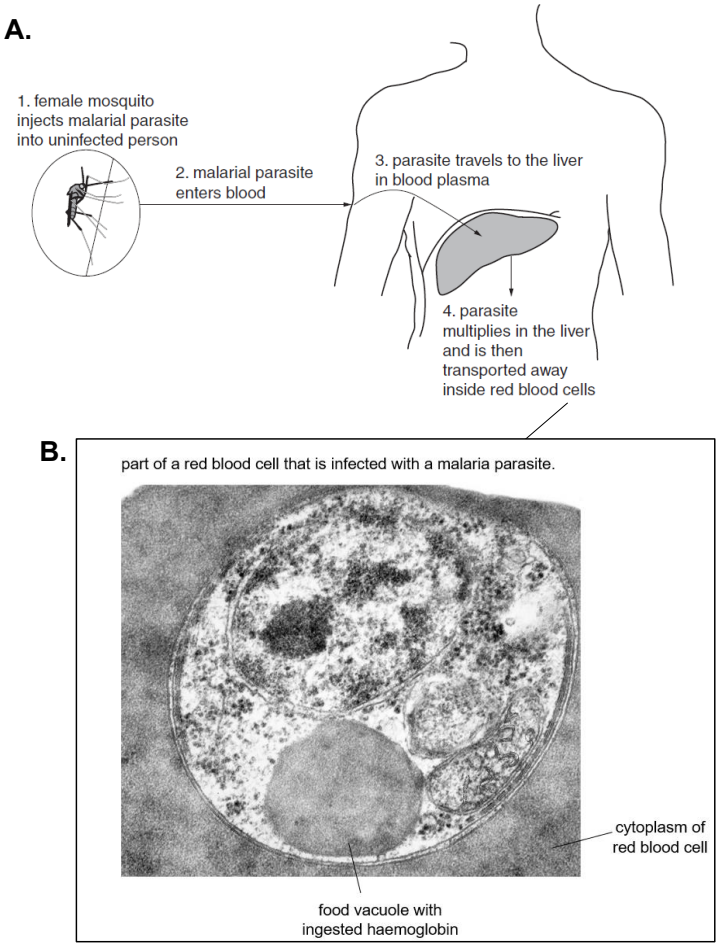

Fig. 1.1

(a) State **two** features, visible in Fig. 1.1B, that indicate that *P. falciparum* is eukaryotic.

1. Presence of **membrane bound organelle / compartmentalisation via membranes**

Named example

2. Presence of **nucleus / nuclear envelope**
3. Presence of (membrane bound) **food vacuole**
4. Presence of a **mitochondrion**

[2]

(b) To control the spread of malaria, research has been directed towards the development of a malarial vaccine. Much of this research relies on the fact that *P. falciparum* has different forms in its life cycle.

During a trial, researchers were able to extract both the sporozoite form (the form injected by mosquitoes) and the merozoite form (the form that leaves the liver, before entering red blood cells) of *P. falciparum*.

With reference to Fig. 1.1, suggest why researchers chose to use the sporozoite form of *P. falciparum* instead of the merozoite form in the malarial vaccine.

1. idea of sporozoite of parasite not **wrapped in liver surface membrane** / merozite form is wrapped in liver cell surface membrane / in red blood cell

AND

2. idea of **antigens** in the sporozoite form can be more easily **exposed** OR **antigens** in merozoites cannot be exposed to **immune system** to stimulate immune system (during vaccination) / for killing by immune cells during actual an actual infection

OR

3. sporozoite form has not **multiplied** compared to merozoite form which would have **multiplied in numbers** (in the liver) / prevent sporozoite from multiplying

AND

4. immune cells has less parasites to **destroy/ limit spread** within the body

3. vaccination against form leaving liver would, not protect against **liver invasion** / still cause **liver damage** (since sporozoite form is not quickly removed by the immune cells during actual infection) /

[2]

(c) In another trial, a naturally occurring mutant form of *P. falciparum* parasite discovered in Africa was tested for use as a vaccine against malaria. The mutant parasite develops normally in mosquitos. In humans, however, the mutant *P. falciparum* infects liver cells but does not multiply and cannot enter red blood cells.

An investigation was conducted to test this vaccine using mice. Four test groups of 10 mice each were injected (inoculated) with mutant *P. falciparum* cells, followed by booster doses every six months after the first inoculation.

The effectiveness of the vaccine was then tested by injecting non-mutant (wild type) *P. falciparum* cells into all the mice.

Table 1.1 shows the results of investigation.

Table 1.1

	number of mutant *P. falciparum* cells given to mice			percentage of mice not infected by non-mutant (wild type) *P. falciparum*
test group	first inoculation	first booster inoculation	second booster inoculation	
1	0	0	0	0 Means 100% infected
2	50 000	25 000	25 000	100 Means 0% infected
3	10 000	10 000	10 000	100 Means 0% infected
4	10 000	10 000	0	70 Means 30% infected

(i) Evaluate whether the results of this investigation is sufficient for researchers to recommend an effective vaccination plan against malaria.

Sufficient because results show

1. **Gp 1** (not inoculated) **0% not infected/ 100% infected vs Gp 2 /3/4** (inoculated) : **100% not infected / 0% infected**

2. Inoculating with **higher** amount of mutant cells (quote either 50000, 25000) gives the same just 3 time of 10 000 mutant plasmodium cells (test group 3) provided **same** immunity/ same effectiveness as giving 50 000, 25 000 , 25000 mutant cells (test group 2) : quote values- both resulted in 100% of mice not infected by wild type parasite
3. 2nd Booster inoculation is needed for vaccine to remain effective as shown in test group 4 where **only** (accept only) 70% of mice were not infected without a second booster compared to test group 3 of 100%

[4]

Limitations of the investigation (any 2)

1. Vaccine was made using *P. falciparum*, may not be effective against **other** (3) **species of plasmodium** that cause malaria/
2. Vaccine was made using made using *P. falciparum* from Africa, may not be effective against people in **other countries** due to different genetic makeup in different people
3. No information about **side effects** of vaccine
4. Done in **mice**, do **not know effects** in humans / need for human trial

   Reject merely saying mice versus humans / accept not tested for use in humans
5. No information on mice, same age/ species which may have different immune systems (must relate to immune system)
6. **Small sample size of 10 mice**

(ii) Volunteers who were injected with killed mutant *P. falciparum* cells produced antibodies, which provided some protection against malaria.

Outline the events that occur following injection of the killed mutant *P. falciparum*, which lead to the eventual production of antibodies.

At least 1 from antigen presentation, activation of T lmyphocytes , B lymphocytes

Activation of T lymphocytes (at least 1)

1. **antigen presenting cells/ macrophages/ dendritic cells** engulf/ take in parasites via **phagocytosis** (accept engulf to form phagosome/ phagocytic vacuole) → **antigen presentation**

   Antigen presentation MP 2,3,4(at least 1) Can be marked under description of B cells / T cells

2. The **hydrolytic enzymes**(reject lysozyme) in the **lysosome/ phagolysosome digest/ breakdown** the **pathogen / antigen**

3. Phagosome / phagocytic vacuole/ vesicle (accept endocytic vesicle **fuses with lysosome** → (phagolysosomes fuses with **vesicles containing MHCs**

4. (parasite is digested to) **antigen/ peptides (**peptides which) presented on the(cell) **surface** (membrane of)**APC** via **MHC molecules**

5. (Clonal selection **) (Naïve) T cells** with **receptors complementary to** (the shape of) **epitope** of the antigen peptide binds

6. This activate T cells to **divide/ undergoes mitosis** / **clonal expansion** and **differentiate** to form **T helper cells** (cytotoxic T cells , memory T cells)

[5]

Activation of B lymphocytes (at least 1, max 3)

7. (Naïve) B cell with **complementary receptor** binds to **epitope** of antigen on parasite *(only mark once for complementary shape binding in MP 4 or 6)*

8. BCR and antigen taken in by **receptor mediated endocytosis** -→ **antigen** presented (via MHC molecules on cell surface of) **B cells**

9. (receptors on) Activated T helper cells binds/ recognise to **same specific** (epitope on) **antigen / peptid**e (MHC complex) B lymphocytes **helper T cells secrete cytokines** to activate B lymphocytes

10. This activate B cells to **divide/ undergoes mitosis** / **clonal expansion** and **differentiate** to form **plasma cells** which secrete **antibodies** *(only mark once for mitosis and differentiation in MP 4 or 7)*

(d) While vaccination provides protection against malaria, the severity of a person's malarial infection can be influenced by the type of red blood cells (RBCs) present in their blood.

Haemoglobin (Hb) is the protein found in RBCs that is responsible for delivery of oxygen to tissues. HbS is a mutant form of the normal HbA protein and is responsible for causing sickle cell anaemia. Individuals who carry one copy of the HbS allele are protected against severe malaria.

From your knowledge of Hb structure, explain how having HbS protein protects such individuals against severe malarial infection.

At least 1 compulsory point from MP1 – 3 and/or address Hb structure

1. at low oxygen concentration / where Hb is at the deoxygenated conformation, **insoluble fibres** are formed
2. because **hydrophobic** areas on **different** HbS molecules will **stick together/ polymerise (accept crystallise)**
3. results in **sickle shaped red blood cell**

At least 1, Max 3

4. parasites unable to digest break down (accept take in) the insoluble fibre (for nutrients for growth)
5. these sickle shaped red blood cells are fragile/ shorter life span and they are destroyed together with the parasites (in the spleen)
   accept less rbc available for malarial parasites to reproduce/ oxygen uptake
6. less efficient / oxygen level lower inside these RBC, cannot support parasite growth/ respiration

[4]

(e) The human ABO blood typing system is based on the presence or absence of A and B antigens on the surface of RBCs. A and B antigens are glycoproteins.

The ABO blood type is controlled by a single gene with three alleles: O, A and B.

- Individuals with RBC genotype AO and AA have type A blood with A antigens on the surface of their RBCs.
- Individuals with RBC genotype BO and BB have type B blood with B antigens on the surface of their RBCs.
- Individuals with RBC genotype AB have type AB blood with A and B antigens on the surface of their RBCs.
- Individuals with RBC genotype OO have type O blood. They do not have either A or B antigens on the surface of their RBCs.

Recent research has shown that type O blood may provide protection against severe malaria as blood type O is found to be more common in regions with high cases of malaria. This protection could be related to the formation of rosettes during malarial infection. Rosettes are clusters of cells formed when RBCs infected with *P. falciparum* bind spontaneously to uninfected RBCs.

Fig. 1.2 shows RBCs containing *P. falciparum* (arrow) surrounded by uninfected RBCs in a rosette formation. Rosettes are thought to shield infected RBCs from the host immune system as infected RBCs express parasite-specific proteins on their cell surface. The formation of rosettes is associated with severe malaria because the clustering of red blood cells can lead to blood vessel obstruction, causing impaired blood flow to organs.

Commented [RBGM1]: Sry maybe I'm confused. Type O blood is protected by formation of Rosettes --> but rosettes still lead to severe malaria. ?

Commented [RBGM2R1]: After reading (i), I understand it should be type O will not form rosettes.

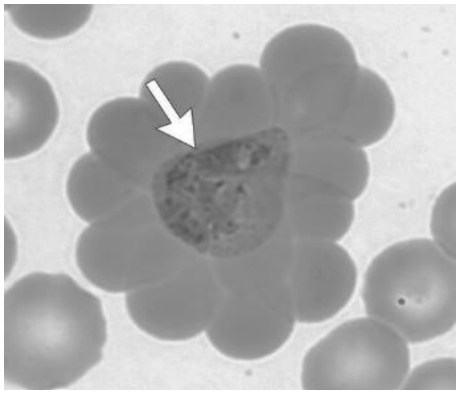

Fig. 1.2

(i) Suggest why individuals with type O blood type are less likely to form rosettes compared to individuals with type A, B or AB blood type when infected with malaria.

1. Rosettes form through the binding of **parasite-specific proteins/ antigens** on the surface of infected RBCs on parsite) to the **(A and/or B) antigens/ glycoproteins** on surface of uninfected RBCs [2]

Commented [RBGM3]: I understand the concept but am just wondering why the parasite-specific proteins binds to the A/B antigens (since these are blood group antigens). But if it's supported by literature, then ok!

2. RBCs with non-O genotypes have the (A and/or B) antigens/ glycoproteins while RBCs with OO genotypes do not have these antigens/ glycoproteins

(ii) Scientists hypothesised that when infected with malaria, individuals with blood type O are less likely to form large rosettes compared to individuals with blood type A , B or AB.

An investigation was carried out to test the scientists' hypothesis.

RBCs of different genotypes isolated from donors were incubated with *P. falciparum* allowing infection to take place. Rosette size and frequency of large rosettes (more than 4 uninfected RBCs per rosettes) formed were measured.

Fig. 1.3 and Fig 1.4 shows the results of the investigation. Horizontal bars represent the mean rosette size and mean frequency of large rosettes for each genotype.

t-tests were conducted to compare the mean rosette size and the mean frequency of large rosettes for each genotype against those of the OO genotype.

The p-value calculated for each comparison is shown in bracket ( ).

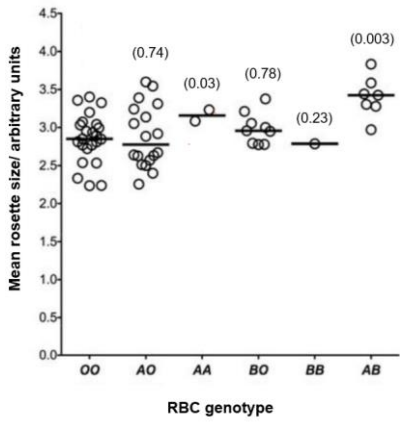

Fig. 1.3

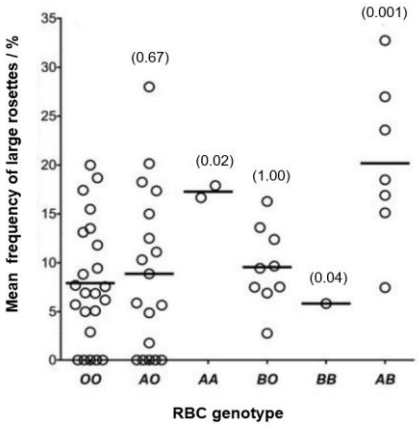

Fig. 1.4

Complete Table 1.2 to show whether the result of each genotype support the scientists' hypothesis.

Write **yes** if the result supports the hypothesis
Write **no** if the result does not support the hypothesis

Table 1.2

Genotype	Do the results support the scientists' hypothesis?	
	Fig. 1.3	Fig. 1.4
AO	**no**	**no**
AA	yes	yes
BO	**no**	**no**
BB	**no**	**no**
AB	**yes**	**yes**

[2]

(f) Drug therapy is the main method of treating malaria.

Chloroquine was one of the first drugs used to treat malaria. However, chloroquine-resistant (CQR) *P. falciparum* soon emerged and are now widespread.

The resistance is caused by mutations of a gene called *pfcrt*. *pfcrt* encodes for a membrane transporter found in the haemoglobin-containing food vacuole in *P. falciparum*. In parasites that are still susceptible to chloroquine (non-CQR), chloroquine accumulates in the food vacuole of *P. falciparum* and interferes with the acquisition of nutrients, resulting in parasite death.

(i) Explain why CQR *P. falciparum* are now widespread.

Many did not realise question is askng about natural selection
Some say climate change: But this will widespread both CQ and CQR parasite

1. Use of **chloroquine** acts as **selection pressure** on the *P. falciparum* population
2. Chloroquine-**resistant** *P. falciparum* at **selective advantage** because they can **acquire more nutrients**]
3. and are likely to survive to **reproduce** and **pass down/ on** their **CQR allele/ mutated *pfcrt* allele** to their **offspring/ next generation**
4. **allele frequency** for **CQR allele/ mutated *pfcrt* increases** over **many generations/ time** (within the *P. falciparum* population/ in the gene pool)

[3]

(ii) Analysis of the alleles of *pfcrt* gene in CQR *P. falciparum* from different parts of the world shows differences in one section of the gene only. The amino acid sequences coded for by this section are shown in Table 1.3, together with the amino acid sequence coded for by the allele found in non-CQR *P. falciparum*.

The amino acid sequence coded for by the rest of the gene is the same in all cases.

Table 1.3

allele of *pfcrt* gene	amino acid sequence coded for by allele of *pfcrt* gene
non-CQR	—Cys—Met—Asn—Lys—His—Ala—Glu—Asn—Ile —Met—
CQR from Africa	—Cys—Ile —Glu—Thr—His—Ser—Glu—Ser—Ile —Ile —
CQR from Asia	—Cys—Ile —Glu—Thr—His—Ser—Glu—Ser—Thr—Ile —
CQR from Peru and Brazil	—Ser—Met—Asn—Thr—His—Ser—Gln—Asp—Leu—Arg—
CQR from Colombia	—Cys—Met—Glu—Thr—Gln—Ser—Gln—Asn—Ile —Thr—

With reference to Table 1.3, calculate the mean number of amino acid changes coded for by the four CQR alleles in comparison with the non-CQR allele.

Show your working

$$\frac{6 + 7 + 7 + 6}{4}$$

= **6.5**

[1]

(iii) Suggest why the CQR alleles from Africa and Asia code for such similar sequences.

1. **similar environment/ selection pressure** where the mutation/ allele gives selective advantage **/ allow the same mutation / allele to be passed down/ same adapatation**
2. Parasites (not people!) **share/ diverge/ evolve** from a (more) **recent common ancestor**

[1]

(iv) It was found that the mutation that changes the amino acid from lysine (Lys) to threonine (Thr) occurs at the binding site of the chloroquine-resistance transporter.

Explain how this mutation of *pfcrt* gene results in chloroquine resistance in *P. falciparum*.

1. **(Base-pair) substitution** (at the 1st or 2nd nucleotide) of the triplet in the *pfcrt* gene of CQR *P. falciparum* → **change in (mRNA)/ codon** that codes for threonine instead of lysine / **missense mutation**

2. Lysine has **different R-group property** from threonine which results in change in **R groups interactions** between amino acids in the polypeptide chain

3. changes polypeptide chain *(reject protein)* **folding** → change in **tertiary structure / (3D) shape/ conformation** of transporter

4. alters the **shape of the binding site** of pfcrt protein to become **complementary to chloroquine /** change the **charge of the binding site** in pfcrt protein to allow **binding to chloroquine**

5. chloroquine is **transported out** of the digestive vacuole [4]

[Total: 30]

2 In Asian cultivated rice crop *Oryza sativa*, the growth of red rice variety alongside the Loto variety has become a serious problem in rice cultivation. In the cultivation of Loto variety, red rice plants are considered weeds because they compete strongly for light and nutrients and have a negative effect on growth and grain yield of the Loto variety.

In order to develop suitable techniques against the expansion of weedy red rice, the complete sets of chromosomes (karyotypes) of red rice variety and Loto variety are compared to detect differences at the chromosomal level so as to obtain information on their genetic diversity.

The chromosomal analysis of both varieties was done by means of a chromosomal imaging method, as shown in Fig. 2.1. Intensity of the shaded regions represent level of chromatin condensation at the particular region of the chromosome.

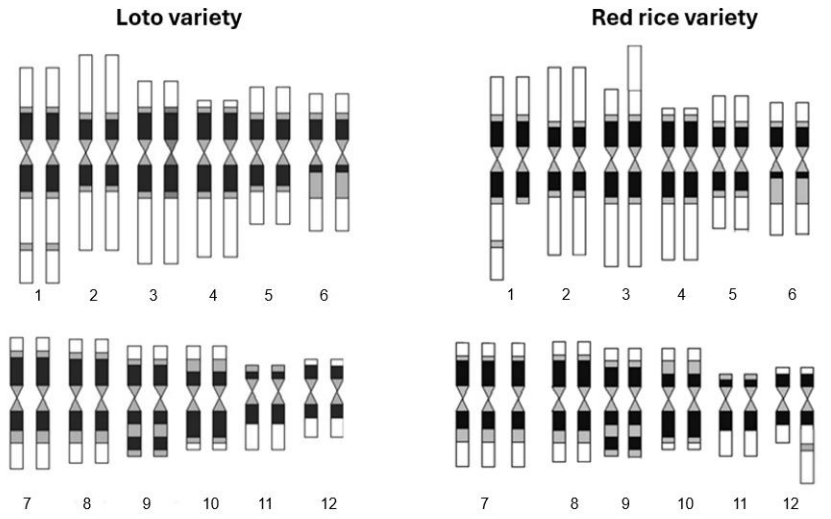

Fig. 2.1

(a) With reference to Fig. 2.1, describe the changes that occurred in the karyotype of red rice variety.

1. (Change in structure) Translocation of segment of chromosome 1 to chromosomes 3 and 12 (A: deletion of segment of chromosome 1 + addition of chromosome segment to chr 3 and 12)
2. (change in number) Aneuploidy/one more copy of chromosome 7 or total 25 chromosomes instead of 24

[2]

(b) Explain how the changes mentioned in **(a)** may have arisen.

Translocation/deletion and addition

1. Unequal crossing over of chromosome segments of non-sister chromatids of chromosome 1, that result in addition of these segments to chromosome 3 and 12.
2. presence of chemical or physical mutagens (name any causative factors) /errors in DNA replication that results in breakage of chromosome at chromosome 1 and then addition to chr 3 and 12.

Aneuploidy

3. Non-disjunction/unequal separation of chromosomes 7 during formation of gametes
4. Due to errors in the attachment of the mitotic spindle to the kinetochores of chromosome 7 (R: related to centrioles)
5. Results in the fusion of a **normal n gamete** with a **n+1 gamete**

[2]

In West Africa, *Oryza sativa* (Asian cultivated rice) and *Oryza glaberrima* (African cultivated rice) are two important cultivated rice species that co-exist within the region.

- *O. sativa* has 24 chromosomes (2n = 24).
- *O. glaberrima* also has 24 chromosomes (2n = 24).
- Both species can be found growing in similar lowland tropical regions.
- *O. sativa* and *O. glaberrima* can be cross bred but the resulting offspring are usually sterile.
- Occasionally, cross breeding between these species can result in fertile offspring with 48 chromosomes.

(c) **(i)** Explain why the resulting offspring of *O. sativa* and *O. glaberrima* are usually sterile.

a) **chromosomes** of the two species may **differ in structure / chromosomes are not homologous**

b) hence chromosomes **cannot pair up** during prophase I of meiosis and so do not produce gametes

c) **chromosomes** of the two species may contain **genes that interact negatively** when combined

d) that does not lead to gamete formation / leads to death of gametic cells [2]

(ii) Suggest how a new fertile rice species may have evolved from *O. sativa* and *O. glaberrima*.

1. **sympatric speciation** occurs
2. through the formation of **allopolyploids**
3. as spontaneous chromosome doubling (24 to 48 chromosomes / two extra sets of chromosomes) occurs in the hybrid
4. due to nondisjunction that occur during meiosis or mitosis
5. doubling restores fertility as chromosomes are now able to pair up during meiosis and form viable gametes
6. new species are able to interbreed to produce fertile and viable offspring [4]

7. new species are reproductively isolated from both parental species (or other species) / unable to interbreed with either parental species due to differences in chromosome numbers

[Total: 10]

3 The production and consumption of animal proteins and plant proteins have different greenhouse gas emissions. Table 3.1 shows the mass of greenhouse gas released in the production of one serving of a variety of sources of protein.

Table 3.1

source of protein	mass of greenhouse gas released in the production of one serving of the protein / kg
beef	7.0
mutton	5.0
chicken	2.5
tofu (from soy beans)	1.0
nuts	0.5

(a) With reference to Table 3.1, explain why a diet based on animal proteins and plant proteins have different greenhouse gas emissions.

- *(quote data)* a diet based on **plant protein** such as **tofu (from soya beans) and nuts** has **lower** greenhouse gas emissions. **emit 1.0 kg and less of carbon dioxide per serving** while a diet based on **animal protein (chicken, mutton and beef)** emit **2.5 kg and more of carbon dioxide per serving**/ accept description of largest gap of 14 times and smallest gap of 2.5 times
- *(state processes)* Plants able to **photosynthesis** and **respiration** while animal **only respire**
- *(ref to carbon dioxide)* plants **remove carbon dioxide** from atmosphere (to produce organic compound/ biomass) while animals have more output of **carbon dioxide / lower nett CO_2**
- Beef from cows emit the most **greenhouse gases 7.0kg per serving,** because it also produces **methane (**on top of CO_2 emisson)
- through **enteric fermentation** and their **manure/** Cow then expels this methane mostly through **belching (eructation)** and **flatulence**

[3]

A research team is investigating a gene that has many different types of mutations, but only one specific mutation that generate a specific allele which is linked to reduced greenhouse gas emission.

This mutation, associated with reduced greenhouse gas emissions, involves a large segment of bases being deleted from the normal allele, which is 650bp long.

Scientists identified the allele by analyzing the DNA of different cattle using molecular techniques in the following order: Polymerase Chain Reaction (PCR), gel electrophoresis, and southern blotting.

(b) Explain the basis of the molecular techniques used to identify this allele.

PCR .....

- **amplify/** Production of **many** copies of gene/sequence of interest for analysis, from **initial small amounts**;
- using (specific) **primers** (forward and backward primers) that have complementary sequence/ binds/ anneal via complementary base pairing to sequences on the **DNA which flank the allele** linked to reduced (greenhouse gas) methane emissions

gel electrophoresis .....

- gel electrophoresis **separate DNA fragments** (reject DNA strands) by **size/ length**
- under the influence of **direct electric current**
- **Negatively charged** DNA will move towards the **positive electrode** / **anode**;
- *(using context)* larger fragment of the normal allele move slower thus found closer to the well/ cathode or further from anode or smaller fragment of mutant allele move faster, found further away from the well/ cathode, closer to the anode

[3]

Scientists are exploring whether specific cattle possess this allele. They collect DNA samples from four different cattle populations (cattle **A**, cattle **B**, cattle **C**, and cattle **D**). Table 3.2 shows the data collected for the different cattle after gel electrophoresis and southern blotting.

Table 3.2

cattle	size of DNA band / bp	presence of probe (identified by southern blotting)
A	400	no
B	450	yes
C	650	yes
D	850	yes

(c) Based on the data in the Table 3.2, state the cattle (s) that is (are) likely to have the allele linked to reduced greenhouse gas emissions.

Justify your answer.

- *(correct cattle)* Cattle **B** (reject other wrong combination like A and B or A, B and D or B and D)
- *(correct data)* It has both smaller a 450 bp fragment as a result of deletion mutation)
- show the presence of the probe → ss probe was complementary to specific sequence of mutant allele.

[3]

(d) Suggest how the data collected by the scientists could be used in a cattle breeding program aimed at reducing greenhouse gas emissions.
select cattle that carry the allele linked to reduced methane emissions **to breed → increase the frequency of the favorable allele** in the population, potentially reducing overall methane emissions from the herd. [1]

[Total: 10]

Section B

Answer **one** question in this section.

Write your answers on the lined paper provided at the end of this Question Paper.

Your answers should be illustrated by large, clearly labelled diagrams, where appropriate.

Your answers must be in continuous prose, where appropriate

Your answers must be set out in sections **(a)**, **(b)**, as indicated in the question.

4 The control of cellular activities has important implications.

(a) Outline how gene expression is controlled in cells. [15]

(b) Pharmacogenetics is the study of how genes control an individual's response to medicinal drugs, such as genes encoding drug-metabolising enzymes and proteins that drugs act upon. Drug response within a population can appear as either continuous or discontinuous variation.

Distinguish between continuous and discontinuous variation **and** suggest why it is more difficult to design drugs for responses showing continuous variation within a population. [10]

[Total:25]

5 Cycles involve a series of biochemical reactions that are tightly regulated and interconnected.

(a) Outline the different cycles occurring in eukaryotic cells. [15]

(b) Phagotherapy is the therapeutic use of bacteriophages, which exploit their reproductive cycles, to treat pathogenic bacterial infections.

Distinguish the lysogenic and lytic cycles of bacteriophages **and** suggest the disadvantages of using phagotherapy to treat bacterial infections. [10]

[Total:25]

4 **(a)** Outline how gene expression is controlled in cells. [15]

A. Gene expression in EUKARYOTIC cells

Chromatin Control

1. In eukaryotes, **gene expression** is upregulated / turned on via **histone acetylation** / **histone demethylation** / **DNA demethylation** (any 2)

Details of chromatin control (max 2)

2. when **lysines** on **histone tails** are **acetylated/ added with acetyl groups,**
3. **their** positive charges **are** neutralised → causes decreased **interaction** of **histone tails** with (the negatively charged (phosphate groups of) **DNA** that is being wrapped around the histones
4. addition of **methyl groups/ methylation** of **lysine and/or arginine** R-groups in **histone tails** (histone methylation) OR to **DNA** (DNA methylation)
5. **attract proteins** to bind to the **histones** (histone methylation) / attract **histone deacetylase** (DNA methylation) → **condensed chromatin**

Accept converse

6. **When chromatin** is **decondensed**, it allows **RNA polymerase** and **general transcription factors** to **bind** to **promoter**
7. to form **transcriptional initiation complex**, allowing transcription to take place

Accept converse for MP2 – MP7

(transcriptional control)

8. **Activators** binds to **enhancer → increased rate** of transcription due to
9. **accelerate** and **stabilise the formation of transcriptional initiation complex** on the **promoter**
10. Modifying chromatin structure by recruiting **histone modification enzymes**/ **chromatin remodeling complexes** / **histone chaperone proteins** to decondense chromatin

11. **Repressors** binds to **silencer → inhibit / decreased rate of** transcription

through these mechanisms (max 2)

12. Activator and repressor proteins **compete** to **bind** to the **same sequence** of **DNA** → prevent activator form binding to enhancer
13. **repressor** also binds to **activator** to prevent a**ctivator** from **binding** and stablising TIC
14. repressor binds with some **general transcription factors** to blocks the assembly of the TIC
15. Once bound, repressors may recruit / **chromatin remodeling complexes** / **histone deacetylases** / **histone methyltransferase** to **condense chromatin**

(post-transcriptional control)

Pre- mRNA processing occurs in the following sequence:

16. Pre-mRNA must undergo **RNA processing** before they can **leave the nucleus for translation**

17. mRNA processing involves: **Splicing , Poly-A tailing and 5' capping**

18. **Alternative RNA splicing** : **excising/cleaving different introns** / **different number of introns** from the same **type of** pre-mRNA
19. to generate **different mature mRNA** with **different combinations of exons**
20. **different proteins**

(translational control)

21. The longer the **poly (A) tail** of **mRNA** , the **longer time taken** for mRNA to be completely **degraded**
22. hence **longer duration** for **translation** to occur, **more proteins** synthesized
    Accept converse for MP 20 and 21
23. **poly-A tails** of *specific* mRNAs are **lengthened** by specific enzymes in the cytoplasm**.**
24. Translation can be **initiated** or **inhibited** by the activation and inactivation of **translation initiation factors** respectively.
25. Initiation of translation of ***specific*** mRNA can be blocked by **translational repressor proteins** that bind to the mRNA at the **5'UTR (Untranslated region)**.
26. The binding of the repressor prevents the ribosomal subunits from binding to the ribosome binding site at the 5' end of mRNA.

(Post-translational control)

27. For proteins to be fully functional, they need to undergo cleavage : **cutting** of polypeptides into **smaller, active** final products.
28. and chemical modifications : addition of carbohydrate chains (glycosylation), addition of lipids, methylation, acetylation, phosphorylation and dephosphorylation. *(give at least 2 examples)*
29. **Protein degradation:** Proteins that are no longer required are **ubiquitinated** and degraded **by proteasomes.**

<u>Gene expression in PROKARYOTOC cells</u>

(types of operons)

1. **Operons** (accept if lac / trp operon example is mentioned) **: a group of structural** genes
2. These genes involved in **same metabolic pathway** / lactose metabolism/ tryptophan synthesis are under control of a **single promoter** and **operator**
3. **repressible** operon (using trp as example) transcription of genes in the operon is **<u>usually</u> on/ expressed** as the amino acid tryptophan is *absent* from the environment.
4. the presence of tryptophan as the **end-product** of the pathway then **represses/ switches off** the transcription of genes in the operon.

5. **inducible** operon (using lac as example) the transcription of genes in the operon is **usually off** as lactose is absent in the environment most of the time.
6. the presence of lactose as the **substrate** of the pathway then **activates / switches on** the transcription of genes in the operon.

(Mechanism)

7. Presence of lactose in the environment **inactivates lac repressor**
8. Presence of tryptophan in the environment **activates trp respressor**

Accept converse for absence

9. Lac **repressor** does not bind **operator** , **RNA polymerase** binds **promoter** *(accept trp / lac example as long as interaction between molecules are correct. Do not double award for trp and lac operon)*

(Positive gene contro)l

10. Absence of **glucose** results in high **cAMP**.
11. **cAMP** activates **catabolite activator protein (CAP)** → bind to **CAP binding site**
12. bends the DNA/ which makes it **easier** for / **facilitates** *(reject allow binding)* RNA polymerase to bind at the promoter.--> **high rate of transcription**

Accept converse for presence of glucose

QWC: Proper paragraphing, writes in continuous prose, at least 2 markpoints from A: eukaryotic cells - 2 markpoints must be form different levels , at least 1 markpoint from B: prokaryotic cells

(b) Distinguish between continuous and discontinuous variation and suggest why it is more difficult to design drugs for responses showing continuous variation within a population. [10]

A.Distinguish between continuous and discontinuous variation

Feature	Continuous variation	Discontinuous variation
Types of phenotypes	**Characteristics/ traits/ phenotypes/ variation** fall within a range **/ intermediate** values (between 2 extremes)	**Characteristics** fall into **distinct classes** with **no intermediates**.
Number of genes involved	It (characteristic/ trait/ phenotype) is controlled (reject coded for) by a **number of genes/ polygenes**.	It is controlled by **1 or 2 major** genes/ **few** genes
Effects of individual genes	Each gene has a small effect on the phenotype/ have **little overall effect**.	Each gene exerts a large effect on the phenotype.
Additive effect of genes	The **phenotypic effects** of these genes are additive / Hence phenotypic expression is the result of **combined effect of these** genes .	Effects of the genes are **absolute/ no additive effec**t.
Effect of environment on phenotype	It is **largely affected** by the environment.	It is **largely unaffected** by the environment.
Investigation of type of inheritance	Mechanisms of inheritance investigated using statistical methods	Mechanisms of inheritance investigated by counting and determining phenotypic ratios of offspring.
Example in the context of the question	Slow metaboliser (3 hours) vs fast metaboliser (8 hours)	Drug can be metabolized in any range of time between 3 to 8 hours

Why it is more difficult to design drugs for responses showing continuous variation within a population (max 8)

1. Lack of clear categories to **group/ classify individuals** based on drug response

Before administration of drug,

2. It is difficult to **tailor/ customise drugs** to the specific individuals or groups of individuals

3. difficult a specific/ exact **optimal/ exact dose** of drug

After administration of drug,

4. it is difficult to determine if drug is effective or not effective / what is considered effective vs not effective since there is **no clear cut response to decide**

Because (idea of)

5. polygenic nature complicates the **identification** of **specific genes** that can guide drug design/ **specific proteins/genes** that the drug can **target**
6. difficult to have a drug that can **target all the genes/ proteins** involved
7. we do not know the **interactions between** the genes/ proteins involved in the drug response
8. responses with continuous variation are often influenced by environmental and lifestyle factors + leading to **less predictable/ inconsistent outcome** *(consequence to drug design is often not elaborated)*
9. AVP

QWC 1mark : Proper paragraphing, writes in continuous prose, at least 1 mark from each section

5 (a) Outline the different cycles occurring in eukaryotic cells. [15]

1. The cell cycle, Krebs cycle, and Calvin cycle are called "cycles" because they involve **a series of biochemical reactions** that **return to their starting point/** allowing the process to continue repeatedly

2. The Cell Cycle:

a) *(what/ definition of cell cycle)* The cell cycle is a series of phases that a **cell** undergoes to **divide** and produce **two genetically identical daughter cells.**

b) has **specific order of sequential events** controlled by a **cyclically operating set of** signalling and regulatory proteins in the cell's cytoplasm that triggers and coordinates/ regulate/ control key events in the cell cycle/ accept at different checkpoints of cell cycle

c) *(overall function)* The cell cycle ensures **accurate cell division** and **genetic continuity**/ thus **genetic stability** (across all cells in the same multicellular organism)

d) Three main stages: **interphase, nuclear division, cytokinesis/** accept G1, S, G2, M and cytokinesis

e) Growth and Development (of cells): During interphase - Cell **grow in size** and **synthesize organelles, ATP, microtubules and proteins** *(name two)* necessary for DNA replication and mitosis respectively;

f) DNA Replication: Cell **replicates its DNA** (during **S phase of interphase**) to prepare for nuclear division (via semi-conservative replication);

g) ensuring that each daughter cell *(meaning of genetically identical)* Nuclei of the 2 daughter cells receive **same number** and **type of chromosomes** as the original parent nucleus.

h) **Cell Division:** Mitosis ensures **accurate segregation** of chromosomes, while cytokinesis divides the cytoplasm, resulting in two genetically identical daughter cells + **meiosis** – for formation of **gametes**;

3. The Calvin Cycle:

a) *(what/ definition of Calvin cycle)* It is a cycle because the **same starting** molecule, **ribulose-1,5-bisphosphate (RuBP),** is **regenerated** at the end of the cycle, enabling the continuous fixation of CO2. *(different from pt 1 because RuBP is mentioned)/* Carbon dioxide combines with RuBP / **carbon fixation**, followed by the **reduction** of **glycerate-3-phosphate** to **glyceraldehyde-3-phosphate** and then **regeneration of RuBP**;
b) *(overall function)* enables the conversion of CO2 into organic molecules necessary for energy and growth in plants

c) **Carbon Fixation:** The enzyme **Rubisco** fixes/capture atmospheric CO2 into an organic molecule, 3-phosphoglycerate. Product is an unstable 6C intermediate that will immediately split to form 2 molecules of **glycerate phosphate** (for every one molecule of CO_2);

d) To allow for **continual** formation of **glucose** / formation of **large amounts** of glucose and other carbohydrates,
e) which serve as energy sources and structural components for the plant / which is used for **synthesis of ATP** via **respiration** / for building of cellular components such as **cellulose cell wall**;

f) Carbon fixation - This step involves **carbon dioxide** combining with **RuBP** (ribulose bisphosphate, a 5C sugar);
g) PGA reduction - **GP is reduced (gains electrons)** to form a 3C compound, **glyceraldehyde-3-phosphate (G3P)**;
h) This reaction requires the reducing power of **NADPH** and energy of **ATP** (products of non-cyclic light-dependent reaction);
i) RuBP regeneration - G3P has to be used to regenerate **RuBP;**
j) **5** molecules of **G3P** (a 3C molecule; total 15C) used to regenerate **3 RuBP** 5C molecule; total 15C);

k) **3 ATP** from the light-dependent reaction is used;

4. The Krebs Cycle:

l) *(what/ definition of Krebs cycle)* It is a cycle because the **same starting** molecule, oxaloacetate, is regenerated to combine with another acetyl-CoA molecule, allowing the cycle to repeat/ **Acetyl-coA** combines with **OAA** to produce **citrate/6C compound**, followed by **regeneration of OAA**
m) *(overall function)* This cyclic nature efficiently supports continuous energy release and production of metabolic intermediates for various cellular processes
n) **Pyruvate** from glycolysis is converted to **acetyl-CoA** via **oxidative decarboxylation**;
o) Krebs cycle involves 3 main stages:
p) Acetyl CoA (2C) joins the cycle by combining with **oxaloacetate** (4C) to form **citrate** (6C);
q) Citrate is **decarboxylated** and **oxidised by dehydrogenation** to form **α-ketoglutarate** (5C) and **NADH;** This process is also an **oxidative decarboxylation** reaction;
r) **Oxaloacetate** (4C) is regenerated;
s) Krebs cycle involves multiple reactions, including 1 substrate-level phosphorylation, 1 decarboxylation, and 3 dehydrogenation reactions;

t) As a result 1 ATP, 1 CO_2, 2 NADH, and 1 $FADH_2$ are produced per molecule of α-ketoglutarate;

u) For **each** molecule of glucose, glycolysis yields **2 molecules of pyruvate**, and hence **2 molecules of acetyl CoA**. As such, **two rounds of Krebs cycle** are needed to **completely oxidise one molecule of glucose**;

v) All 6 carbon atoms in glucose are lost as 6 CO_2;

w) To result in the **continual production of** high-energy electron carriers **NADH** and **$FADH_2$** via a series of redox reactions;(subsequently transferred to the electron transport chain, leading to the production of ATP through oxidative phosphorylation)

x) **Production of Metabolic Intermediates:** The cycle produces intermediates such as alpha-ketoglutarate and oxaloacetate, which are used in various anabolic pathways for synthesizing amino acids and other important biomolecules.

5. Cyclic photophosphorylation

y) Photo-excited **electrons** from **PS I** are transferred to the **ETC** before returning to PS I; / accept details The photo-excited **electron from P700** is captured by the **PS I primary electron acceptor** and then passed on to the middle part of the **first electron transport chain (ETC);**

z) Allows for the **synthesis of ATP** only via **chemiosmosis** for **Calvin cycle** to **continue**;

aa) **No NADPH** is produced / **No O_2** is produced as there is **no photolysis of water;**

6. Electron transport

bb) **Cyclical reduction** of **NAD, FAD** / **electron carriers of ETC**, and **oxidation** of **NADH, $FADH_2$** and **reduced electron carriers of ETC**; (must have)

cc) To allow for **continual oxidation** of respiratory substrate **glucose**, for the **synthesis of ATP**; (fn)

OR

dd) **Cyclical reduction** of **$NADP^+$** and **oxidation** of **NADPH**; (must have)

ee) To allow for **light-dependent reaction / Calvin cycle** to **continue** to produce **glucose**; (fn)

AVP (max 3)

Sustained Operation: Cycles allow for the continuous operation of essential biological processes. For example, the Krebs cycle continually produces energy as long as there are inputs (acetyl-CoA), and the Calvin cycle continually fixes carbon dioxide to produce sugars during photosynthesis/ **Energy Efficiency**: The recycling of intermediates and continuous regeneration of substrates allow cells to operate these cycles with minimal energy wastage, making the overall process highly efficient.

Resource Recycling: Key intermediates, like oxaloacetate in the Krebs cycle and RuBP in the Calvin cycle, are regenerated within the cycle. This means the cell doesn't need to constantly produce new intermediates, conserving energy and resources/ **Metabolic Flexibility**: In the Krebs cycle, intermediate products can be used for various biosynthetic pathways, allowing the cell to respond to different

metabolic needs. This flexibility is crucial for adapting to changing environmental conditions/

Feedback Mechanisms: Cycles often include feedback loops that regulate their pace. For example, the cell cycle has checkpoints to ensure that cells only proceed to the next phase when conditions are favorable, preventing errors like DNA damage from being passed on during cell division.

QWC: Proper paragraphing, writes in continuous prose, at least 1 mark from each of the big cycles (Cell cycle, Calvin cycle, Krebs cycle)

(b) Distinguish the lysogenic and lytic cycles of bacteriophages **and** suggest the disadvantages of using phagotherapy to treat bacterial infections. [10]

Max ?

Feature of comparison	**Lytic cycles** *T4 bacteriophage*	**Lysogenic cycles** *Lambda bacteriophage*
Degradation of bacterial DNA	Bacterial host DNA is degraded by endonucleases encoded by phage dsDNA.	Bacterial DNA is not degraded.
Integration of phage DNA	Phage DNA does not integrate into host bacterium chromosome.	Phage DNA integrates into a specific site in host bacterium chromosome, as a prophage.
Replication of phage DNA	Phage DNA **replicated along** with host bacterium DNA or phage DNA replication is **independent** of its host cell division.	Phage DNA is replicated along with the bacterial DNA (as prophage) or Phage DNA is replicated each time **host cell divides** by binary fission.
Repressor	**No synthesis of repressor proteins** that prevent other phage genes from being expressed.	Synthesis of **(lambda) repressor protein** encoded by phage gene, **prevents other phage genes from being expressed**.
Spontaneous induction	No spontaneous induction takes place.	Spontaneous induction results in **phage DNA** being **excised from bacteria DNA** and phage enters into **lytic cycle**.
Osmotic lysis of host cells	**Osmotic lysis of host cells** occur upon **release of new viral particles/phages.**	**Osmotic lysis of host cells** does not occur.

Disadvantages (related points to H2 Bio syllabus) max 6 m

- **Narrow Host Range:** Phages are often specific to particular strains of bacteria, which can limit their effectiveness against diverse or unknown bacterial infections.
- **Development of Phage Resistance**: Bacteria can develop resistance to phages, similar to antibiotic resistance, potentially reducing the long-term efficacy of phage therapy.
- **Potential Immune Responses**: The human immune system can recognize phages as foreign agents and mount an immune response, potentially neutralizing the phages before they can target the bacteria.
- **Potential for Horizontal Gene Transfer**: Phages can sometimes facilitate the transfer of genetic material between bacteria, potentially spreading virulence factors or antibiotic resistance genes between different bacterial populations/ communities, unintentionally increase antibiotic resistance of bacterial pathogens.

Possible AVP:

- Regulatory and **Safety** Concerns: Phage therapy is not as well-regulated as antibiotic treatments in many regions, raising concerns about safety, quality control, and standardization.
- **Regulatory Hurdles**: Gaining regulatory approval for phage therapy can be challenging due to the need for extensive testing and validation to ensure safety and efficacy.
- Lack of Comprehensive **Clinical Trials**: There is a relative scarcity of **large-scale**, randomized clinical trials to fully validate the safety and efficacy of phage therapy compared to conventional antibiotics.
- **Complicated Production** Process: Producing, purifying, and characterizing phages for therapeutic use can be complex and time-consuming, making it difficult to scale up production.
- Limited Understanding of **Phage-Host Dynamics**: The **interactions between phages and their bacterial hosts**, as well as the impact of these interactions on the human microbiome, are not fully understood.
- **Public and Medical Skepticism**: There may be skepticism and lack of acceptance among healthcare providers and patients, given the novelty and limited mainstream use of phage therapy.

*QWC: Proper paragraphing, writes in continuous prose, **at least 1 mark** from each section (comparison and disadvantages)*