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Candidate surname	Other names

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Advanced Level GCE

Centre Number | | | | | |

Candidate Number | | | | |

Monday 21 January 2019

Afternoon (Time: 1 hour 45 minutes) | Paper Reference **WBI05/01**

Biology

Advanced

Unit 5: Energy, Exercise and Coordination

You must have:
A copy of the scientific article (enclosed), calculator, HB pencil, ruler

Total Marks

Instructions

- Use **black** ink or ball-point pen.
- **Fill in the boxes** at the top of this page with your name, centre number and candidate number.
- Answer **all** questions.
- Answer the questions in the spaces provided
  – *there may be more space than you need.*

Information

- The total mark for this paper is 90.
- The marks for **each** question are shown in brackets
  – *use this as a guide as to how much time to spend on each question.*
- Questions labelled with an **asterisk** (*) are ones where the quality of your written communication will be assessed
  – *you should take particular care with your spelling, punctuation and grammar, as well as the clarity of expression, on these questions.*
- Candidates may use a calculator.

Advice

- Read each question carefully before you start to answer it.
- Keep an eye on the time.
- Try to answer every question.
- Check your answers if you have time at the end.

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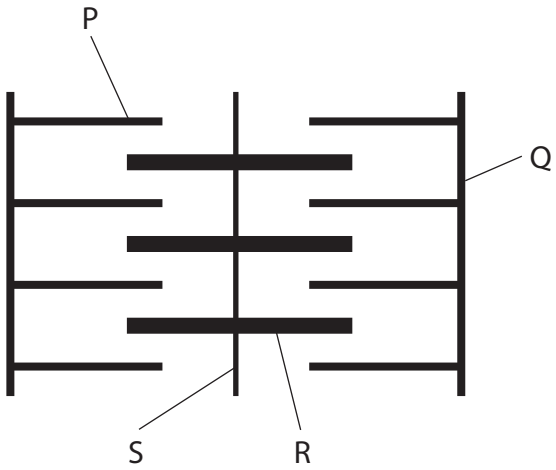
Answer ALL questions.

Some questions must be answered with a cross in a box ☒. If you change your mind about an answer, put a line through the box ☒ and then mark your new answer with a cross ☒.

1 Muscles, tendons and the skeleton all interact when a human arm moves.

(a) The diagram below shows a sarcomere of a muscle.



Put a cross ☒ in the box that completes each statement about the sarcomere.

(i) Structure R contains

(1)

☒ **A** actin only

☒ **B** actin and tropomyosin

☒ **C** myosin only

☒ **D** myosin and tropomyosin

(ii) The structures that move when a sarcomere contracts are

(1)

☒ **A** P and Q

☒ **B** P and R

☒ **C** R and Q

☒ **D** R and S

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(b) Describe the role of calcium ions in the sliding filament theory of muscle contraction.

(3)

(c) Explain the role of a tendon in the movement of an arm.

(2)

(Total for Question 1 = 7 marks)

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2 Breathing and heart rate are controlled and can respond to changes in the demand for oxygen.

(a) Put a cross ☒ in the box that completes each statement.

(i) The part of the brain involved in controlling the heart rate is the

(1)

☒ **A** cerebellum

☒ **B** cerebral hemisphere

☒ **C** hypothalamus

☒ **D** medulla oblongata

(ii) Changes in blood pH are detected by chemoreceptors in the

(1)

☒ **A** coronary arteries

☒ **B** medulla oblongata

☒ **C** skin

☒ **D** vena cava

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(b) The breathing of a person is affected by altitude, the height of the location above sea level.

The table below shows the responses of a group of 12 adults to changing altitude.

Altitude / m	Available oxygen concentration (%)	Mean breathing rate / breaths min^{-1}	Mean tidal volume / dm^3
0 (sea level)	21.0	16.0	0.50
2000	16.0	16.0	0.51
4000	12.5	16.2	0.54
6000	11.0	17.8	0.70

(i) Describe the effect of altitude on breathing.

(2)

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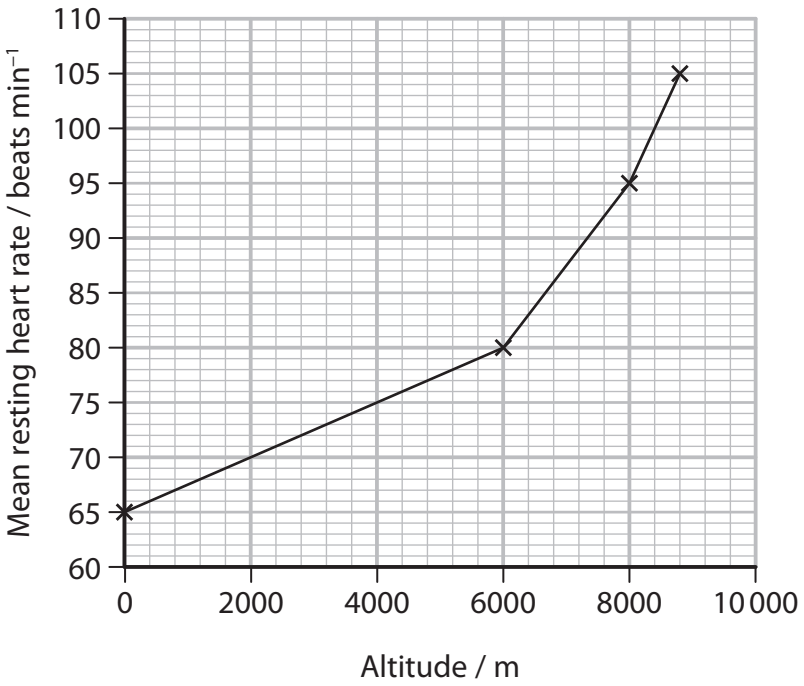
(ii) Explain how an increase in altitude from 4000 m to 6000 m will cause these changes in breathing.

(3)

(c) The graph below shows the effect of altitude on the mean resting heart rate for another group of adults.



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(i) Calculate the increase in heart rate per metre as the altitude increases from 6000 m to 8000 m.

Include appropriate units with your answer.

(2)

Answer .....

(ii) Explain why the resting heart rate changes as the altitude increases from 6000 m to 8000 m.

(3)

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(Total for Question 2 = 12 marks)

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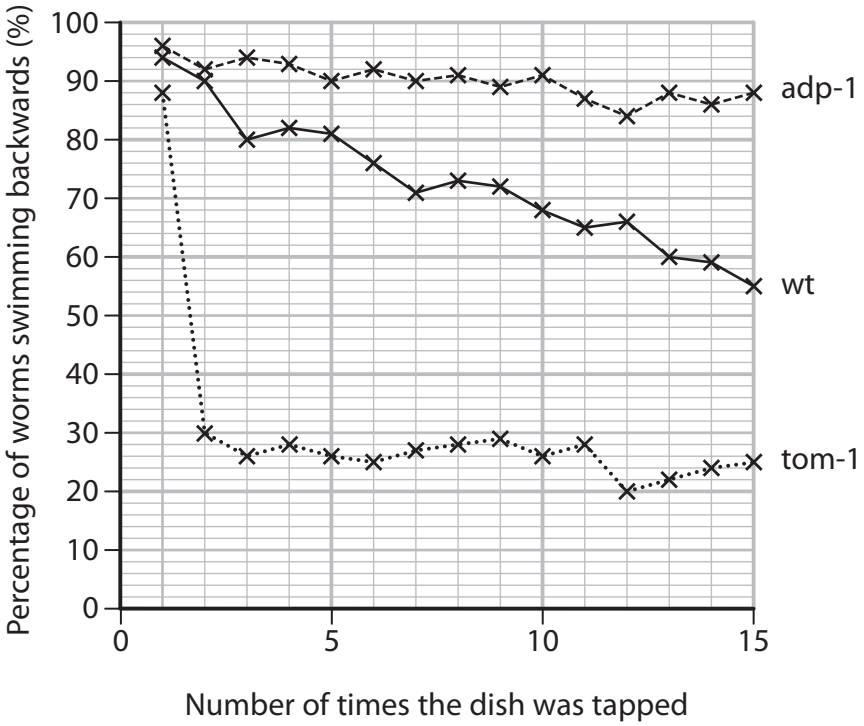
3 Habituation has been investigated in the nematode worm, *C. elegans*, kept in dishes.

When the dish is tapped, the worms swim backwards for a short period of time.

When the dish is tapped repeatedly, the *C. elegans* become habituated and some of the worms no longer swim backwards.

The habituation response of *C. elegans* (wt) was investigated. The response of two mutant strains of *C. elegans* (adp-1 and tom-1) was also investigated.

The graph below shows the results of these investigations.



(a) (i) Calculate the ratio of adp-1 to tom-1 mutants that respond when the dish is tapped 10 times.

(2)

Answer .....

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(ii) Using the information in the graph, compare the response of adp-1 and tom-1 mutants with the response of *C. elegans* (wt).

(3)

(b) The protein coded for by the tom-1 gene is involved in neurotransmitter release from a sensory neurone.

Suggest how a mutation in this gene could produce the results observed for the tom-1 mutant strain.

(4)

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(c) The role of the protein coded for by the adp-1 gene is not known.

Suggest how this mutation affects the transmission of nerve impulses at synapses.

(2)

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(Total for Question 3 = 11 marks)

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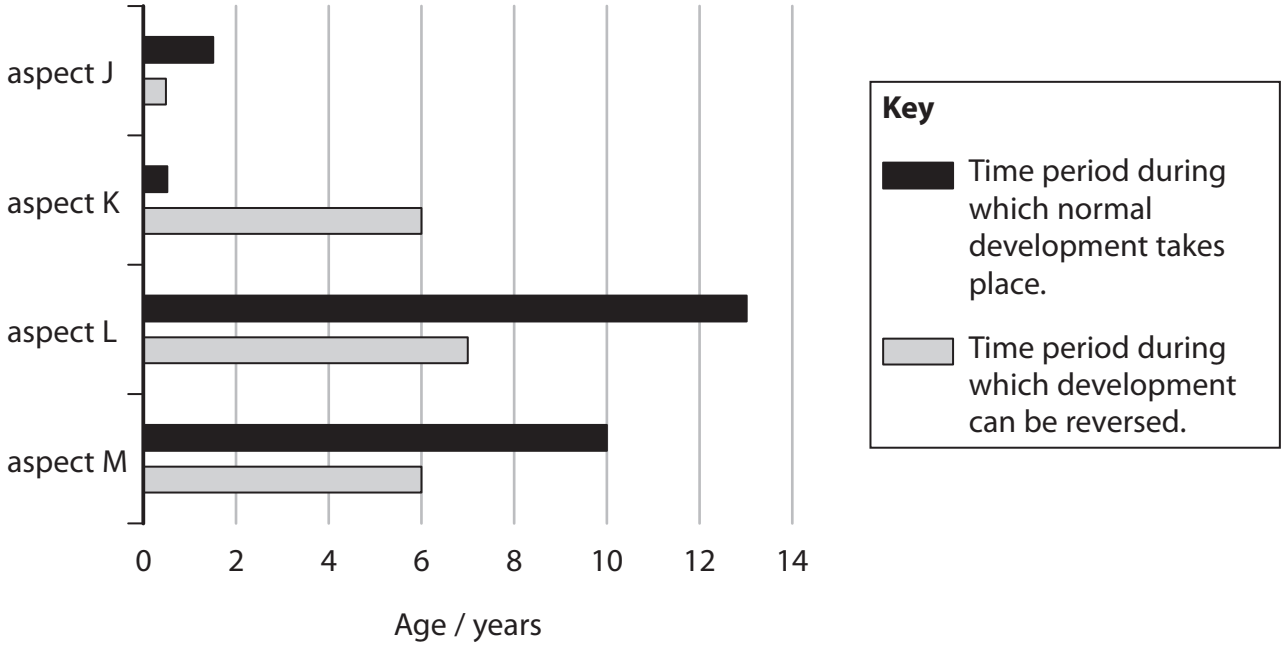
4 Development of the brain is affected by both genetic and environmental factors.

Critical windows have been identified during which the development of some aspects of the visual system take place.

The effect on visual development of the temporary loss of vision in children has been investigated.

Four aspects, J, K, L and M, were investigated.

The graph below shows the critical windows for these aspects.



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(a) Put a cross ☒ in the box that completes each statement about the development of the visual system.

(i) During the critical window for the development of the visual system, exposure to light stimulates

(1)

☒ **A** division of optic nerve cells

☒ **B** formation of rhodopsin in rod cells

☒ **C** formation of synaptic connections in the cortex

☒ **D** growth of rod cells in the retina

(ii) Temporary loss of vision at two years of age would damage the development of

(1)

☒ **A** aspect J only

☒ **B** aspect J and aspect K

☒ **C** aspect K only

☒ **D** aspect K and aspect L

(iii) After looking at the graph, a student made the following three statements.

- The critical window for normal development is always shorter than the critical window during which damage to development can take place.
- It is possible to reverse development of a visual process after normal development has been completed.
- The critical window during which normal development of aspect L takes place must be less than the critical window during which the response can be reversed.

The number of correct statements is

(1)

☒ **A** 0

☒ **B** 1

☒ **C** 2

☒ **D** 3

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(b) Describe the role of synapses in the development of the visual system during the critical window.

(3)

(c) A number of investigations have been carried out to study the effect of nature and nurture on human development.

Explain how twin studies could be used to compare the effects of nature and nurture on visual development in humans.

(3)

(Total for Question 4 = 9 marks)

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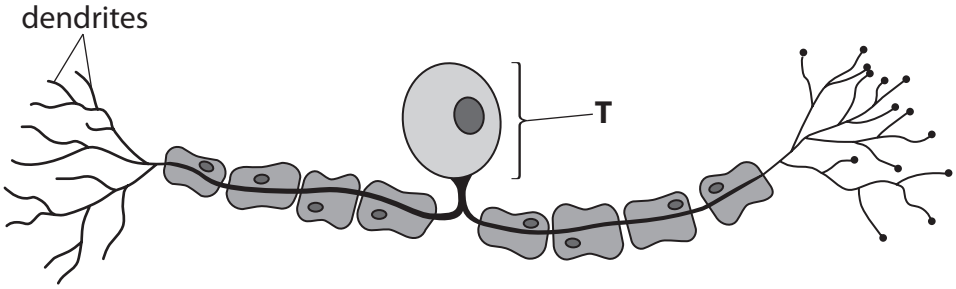
5 Neurones conduct nerve impulses.

(a) The diagram below shows a sensory neurone.



Put a cross ☒ in the box that completes each statement about the sensory neurone.

(i) The part labelled **T** is the

(1)

☒ **A** axon

☒ **B** cell body

☒ **C** nucleus

☒ **D** Schwann cell

(ii) Nerve impulses move in only one direction along the axon due to the

(1)

☒ **A** calcium channels

☒ **B** cell body

☒ **C** myelin sheath

☒ **D** restoration of the resting potential

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(b) Describe how a resting potential is maintained in an axon.

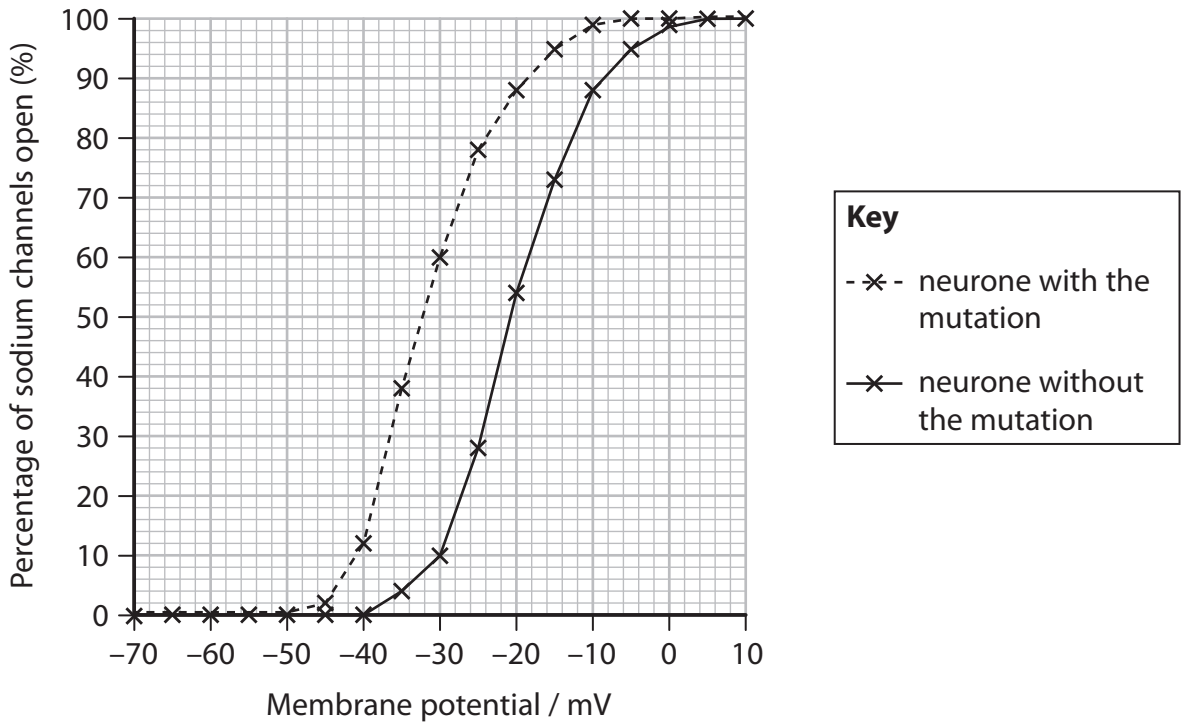
(3)

(c) Epilepsy is a condition in which an increase in electrical activity in the brain causes a seizure.

Some seizures involve strong and prolonged muscle contractions.

One type of epilepsy has been linked to a mutation in the gene coding for the sodium channel protein in neurones.

The graph below shows the membrane potential and the percentage of sodium channels that are open in neurones with the mutation and in neurones without the mutation.



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(i) Calculate the percentage difference in the membrane potential required to open 50% of the sodium channels in these two neurones.

(2)

..... %

(ii) Suggest how this change in the activity of the sodium channels can result in an increase in the electrical activity in the brain of a person with epilepsy.

(3)

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(Total for Question 5 = 10 marks)

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6 During exercise, ATP can be produced by both anaerobic and aerobic respiration.

*(a) Describe the process of anaerobic respiration.

(5)

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(b) Aerobic respiration involves the Krebs cycle.

One enzyme involved in the Krebs cycle is isocitrate dehydrogenase.

Two molecules that affect the activity of isocitrate dehydrogenase are ADP and reduced NAD.

The table below shows the effects of ADP and reduced NAD on the activity of isocitrate dehydrogenase.

ADP / mmol dm^{-3}	Reduced NAD / μmol dm^{-3}	Activity of isocitrate dehydrogenase / a.u.
0.0	0	0.40
0.1	0	1.00
0.5	0	2.40
0.5	10	1.40
0.5	50	0.24

(i) Describe the effects of ADP and reduced NAD on the activity of isocitrate dehydrogenase.

(2)

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(ii) Using the information in the table, suggest how exercise affects the activity of isocitrate dehydrogenase in muscles.

(4)

(Total for Question 6 = 11 marks)

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7 The scientific article you have studied is adapted from Education in Chemistry, Nobelprize.org and Science News.

Use the information from this article and your own knowledge to answer the following questions.

(a) Explain how mustard plants store energy during daylight hours (paragraph 4).

(2)

(b) Explain why an oscillator system gives an advantage over a photoreceptor (paragraphs 3 and 4).

(2)

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(c) Suggest how body clocks could regulate body temperature (paragraph 6).

(2)

(d) Suggest how a strain of fruit fly differs from a species of fruit flies (paragraph 13).

(2)

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(e) Describe how nonsense and missense mutations of the same gene can produce different phenotypes (Box 1).

(4)

(f) Suggest how TIM and PER control the circadian clock by affecting gene activity (paragraph 16).

(2)

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(g) Explain how the SCN can control the circadian rhythm in all cells (paragraphs 19 and 20).

(3)

(h) Explain how disruption of the circadian clock could result in depression by affecting the release of neurotransmitters (Box 4).

(3)

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*(i) 'Clock genes also exert a profound influence on metabolism' (Box 4).

Describe how the effect of the circadian rhythm on the rate of respiration of an organism could be investigated.

(6)

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(j) Describe how ATP acts as an energy source for cyanobacterial proteins (paragraph 22).

(2)

(k) The concentration of potassium ions in red blood cells increases during the day and decreases during the night (Box 5).

Explain how the higher concentration of potassium ions inside red blood cells is maintained.

(2)

(Total for Question 7 = 30 marks)

TOTAL FOR PAPER = 90 MARKS

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Paper Reference **WBI05/01**

Biology

Advanced

Unit 5: Energy, Exercise and Coordination

Scientific article for use with Question 7

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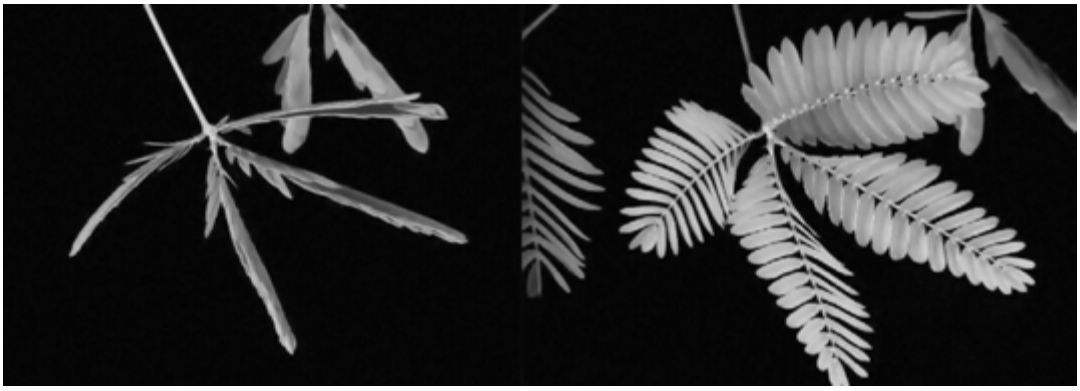
Scientific article for use with Question 7

The rhythm of life

Emma Davies explores how unravelling the complex mechanisms of the body clock has led to some fascinating discoveries and a 2017 Nobel prize.

1. Scientists knew that living organisms had internal clocks centuries before they began to understand them. In 1729, French astronomer Jean Jacques d'Ortous de Mairan placed a mimosa tree in the dark and noted that the leaves still opened and closed as if it were outside, suggesting an in-built rhythm. Then, in 1955, Max Renner from the Ludwig-Maximilian University of Munich, Germany, demonstrated an in-built system in bees. He trained Parisian bees by providing food at the same time each day. He then transported them to New York, keeping a light on them all the time. The bees stuck to their Parisian time despite jumping time zones.



In 1729, French astronomer Jean Jacques d'Ortours de Mairan placed a mimosa tree in the dark and noted that the leaves still opened and closed as if it were outside, suggesting an in-built rhythm.

2. The body's daily rhythm is described as 'circadian', from the Latin words circa (around) and diem (day). Circadian rhythms exist in all multi-cellular organisms, including fungi, plants, insects, and humans, as well as single-celled cyanobacteria. The systems consist of a 24-hour rhythm generator – otherwise known as an oscillator or clock.

3. The rhythm-generating oscillator system is infinitely better than a photoreceptor system because it can anticipate the rising and setting of the sun, rather than react to it, says Andrew Millar from the University of Edinburgh, UK. Photoreceptors are neurons in the retina that react when the sun appears to convert the light into signals that stimulate biological processes. But, a nocturnal rodent in its burrow needs to anticipate when darkness will fall – emerging too early could prove fatal.

4. The way that plants use an oscillator system was demonstrated by an experiment in which mustard plants used energy set aside in daylight during the hours of darkness; they used stored energy at a faster rate and grew more during short summer nights than long winter ones. 'It's a typical example of how an oscillator can be used to gain an advantage that a photoreceptor just responding to light or darkness could not achieve,' says Andrew.

5. Chemists may be surprised by the fact that the clock's pace doesn't change as the temperature increases in the warmer months – it stays at 24 hours. 'This is unusual as most oscillating chemical reactions speed up as the temperature increases,' he adds, such as the Belousov–Zhabotinsky reaction in which the ratio of concentrations of cerium(IV) and cerium(III) ions oscillate, causing the colour of the solution to oscillate between a yellow solution and a colourless solution.

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Health and the body clock

Jet lag can be debilitating because the master clock in the brain's hypothalamus, which can only change by 1–2 hours per day, has to adapt to a new time zone before the rest of the body can start to catch up.

6. Anyone who has had jet lag will know how strongly our body clocks govern us. Not only do the clocks help to regulate sleep patterns and feeding behaviour, they are also linked to hormone release, blood pressure, and body temperature.

7. Disrupting the body clock over long periods is associated with many diseases, such as type II diabetes, cancer and cardiovascular disease. Those with neurodegenerative disorders, such as Parkinson's and Alzheimer's, tend to see their circadian rhythms deteriorate, which can accelerate disease progression. 'All chronic ageing-related diseases seem to be more prevalent in individuals where there has been a circadian disruption,' says John O'Neill from the MRC Laboratory of Molecular Biology in Cambridge, UK. 'If you have consistently worked shifts, you are more than twice as likely – as a woman – to have breast cancer.'

8. Crucially, many medicines' efficacy depends on the time of day at which they are taken. Australian doctors noted that statins are only really effective if taken just before bedtime because the liver enzyme they inhibit, which helps to synthesise cholesterol, is mainly active at night. And, in his chronotherapy studies coordinating cancer medication with circadian rhythms, Francis Lévi at the University of Warwick, UK, noticed that the effectiveness and toxicity of chemotherapy varied depending on when it was administered.

9. However, synchronising medication to the circadian clock is easier said than done because individuals have different rhythms. This is made more complicated by the fact that patients suffering from lack of sleep, possibly through their illness, can have a disrupted biological clock.

10. So, there is a strong impetus to unravel the body clock's complex mechanisms.

Nobel prize for clock genes

11. Many trace circadian research progress to a now-famous US Cold Spring Harbor symposium in 1960, which was set up as a 'unifying influence on the entire field of study'. There, 150 leaders reported finding the same properties across all organisms. However, the mechanisms remained elusive. At the time, the idea of isolating single genes that could modulate the biological clock was 'considered a completely wacky hypothesis', says John. However, by the late 1960s, the chronobiology community was well established, and the idea of clock genes emerged.

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12. The story of the clock's deconstruction has many twists and turns and is not yet finished. Advances are such that Jeffrey Hall and Michael Rosbash of Brandeis University, US, and Michael Young of The Rockefeller University, US, were awarded the 2017 Nobel prize in physiology or medicine for their work in identifying clock genes and understanding the mechanisms.

13. The foundations for the Nobel discoveries were laid in 1971. Neuroscientist Seymour Benzer and his student Ronald Konopka from the California Institute of Technology, US, looked for fruit flies with circadian mutations, identifying three different strains with a short cycle of 19 hours, a long one of about 28 hours, or no rhythm at all. Mapping experiments using genetic markers showed that all three mutants came from the same region of the X chromosome. Further tests suggested that they were all linked to the same gene, later called 'period'.

Box 1

Benzer and Konopka isolated three different strains of mutant flies showing alterations in the normal 24 h cycle of pupal eclosion and locomotor activity. One mutant was arrhythmic, another had a shorter period of 19 h, and a third had a longer period of 28 h. Mapping experiments, using the genetic markers known at the time, roughly localized all three mutants to the same region of the X chromosome of the fruit fly.

Importantly, complementation tests suggested that the three mutations involved the same gene, later named period. Based on this, Benzer and Konopka presciently predicted that the arrhythmic mutant would carry a nonsense mutation that inactivated the gene, and that the mutants with longer and shorter periods would carry missense mutations that somehow altered the function of the gene product in opposite ways.

14. A decade later, Jeffrey, Michael and Michael cloned and sequenced the period gene. Yet there was still no mechanism. The key lay in a protein that the gene encodes called PER. Jeffrey and Michael Rosbash made a breakthrough with their discovery that PER levels in fly brain neurons peak at night. They suggested that a build-up of PER stopped cells making more.

Box 2

The Transcription-Translation Feedback Loop (TTFL)

In the years following the cloning of period, several models were proposed to explain how its protein product PER might function to produce circadian oscillations. A "membrane gradient" model was proposed in which PER was envisioned to function like a pump to build a gradient across the membrane which, upon reaching a threshold, gets dissipated through light-sensitive channels. In another model, the PER protein was proposed to be a proteoglycan that brings cells together, thereby facilitating the formation of inter-cellular connections through gap junctions. A series of breakthroughs were finally made possible with the availability of reliable PER antibodies. First was the discovery from the Hall and Rosbash laboratories of a 24 h cycle in the abundance of PER protein in neurons of the fly brain, with a peak during the night. The mRNA encoded by the period gene also showed circadian cycles of abundance in fly brain, showing that the cycling of PER protein resulted from the cycling of period mRNA. Intriguingly, the peak of period mRNA levels occurred early in the night, several hours before the peak in PER protein abundance.

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15. 'In broad terms, the function of the clock gene called period is to turn off its own expression,' explains Andrew. 'It works with several other components that the prize-winning labs were critical in identifying, and the process of turning itself off takes 24 hours.' He describes the process as an unusual negative feedback loop. 'The crucial point is that in the clocks, the negative feedback has a delay. The individual processes involved could all be pretty fast. Other genes turn themselves off within tens of minutes. In the clock, it takes tens of hours.'

16. Michael Young then discovered another gene influencing the circadian clock called 'timeless', which encodes a TIM protein. In a string of discoveries, Michael's laboratory found that TIM could bind directly to PER and move to the nucleus, effectively turning off the period gene until dawn.

Box 3

Current working models of the circadian molecular clockwork are highly complex and include many additional components which, collectively, contribute to its robustness and circadian periodicity. Importantly, as transcription and translation reactions are typically rapid, substantial delays must be imposed on the core TTFL mechanism to generate 24 h oscillations. This is achieved by a complex network of reactions involving regulated protein phosphorylation and degradation of TTFL components, protein complex assembly, nuclear translocation and other post-translational modifications. A key observation demonstrating the underlying mechanism for such a delay came from the discovery by Young of the doubletime gene, encoding a kinase DOUBLETIME (DBT) that phosphorylates PER and increases its degradation. Additional proteins integrate environmental inputs that can entrain the clock. For instance, light can activate the protein product of the cryptochrome cry gene (CRY) and promote its binding to TIM, leading to its degradation in the proteasome. When morning arrives, TIM is degraded, leaving PER vulnerable to phosphorylation by DBT and subsequent degradation.

17. The negative feedback loop is seen in plants and other organisms, but the identity of the clock genes differs. Clock genes are conserved across all animals, but are quite different in plants and different again in fungi, says Andrew. 'So that suggests that evolution solved the problem of anticipating the day/night cycle multiple times. And the solution in plants involved different proteins.'

18. In 2004, researchers at the Howard Hughes Medical Institute, US, found evidence of circadian rhythms of gene activity in isolated mouse cells. Then Steve Brown from the University of Geneva, Switzerland, measured circadian rhythms in isolated human skin cells kept either in constant darkness or light. The 24-hour activity cycles continued in all cells without any external cues, with genes being turned on or off and metabolic processes remaining active.

19. The idea of every cell having its own clock marked a huge leap and researchers scrambled to figure out how to fit all the pieces together. It was found that each clock centres on a control system in a part of the brain called the hypothalamus. Curt Richter at Johns Hopkins University, US, discovered that cutting out small sections from the hypothalamus disrupted circadian rhythms. The region, known as the suprachiasmatic nucleus (SCN), consists of around 20,000 neurons, is the same in all mammals, and coordinates circadian rhythms in the whole organism. Specialised cells in the retinas send day and night messages to the SCN, which is why those unfortunate enough to lose their sight can have rhythms that lose sync with the outside world.

20. For a long time, the SCN was considered to be the only clock in the body, but we now think of it as the master clock, says John. 'It communicates with each individual cell in the body, telling them what time of day it is, but your actual circadian rhythm and physiology depend on what the individual clocks in each cell are doing every day.'

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Box 4

Ablation of clock genes in animal models results in arrhythmic production of hormones, such as corticosterone and insulin. Clock genes also exert a profound influence on metabolism through the control of gluconeogenesis, insulin sensitivity and systemic oscillation of blood glucose. Sleep is vital for normal brain function and circadian dysfunction has been linked to sleep disorders, as well as depression, bipolar disorder, cognitive function, memory formation and some neurological diseases. In rare cases, sleep phase disorders are due to mutations in circadian clock genes resulting in advanced or delayed sleep-wake cycles. Studies have indicated that chronic misalignment between our lifestyle and the rhythm dictated by our endogenous circadian clock may be associated with increased risk for various diseases including cancer, neurodegenerative diseases, metabolic disorders and inflammation. Efforts are underway to develop approaches in chronobiology and pharmacology to modify the period, phase or amplitude of circadian clocks to improve human health.

21. This discovery explains why jet lag can be so debilitating. The master clock, which can only change by 1–2 hours each day, has to adapt to a new time zone first, before the rest of the body can catch up.

Different strokes

22. What is not celebrated by the Nobel prize is the fact there is an alternative way to build a 24-hour oscillator, says Andrew. Cyanobacteria have a clock that does not need genetic activity: Takao Kondo from Nagoya University in Japan showed that three cyanobacterial proteins – and the energy source adenosine triphosphate (ATP) – produced a 24-hour rhythm in a test tube. Unfortunately, the proteins don't exist in other organisms, but the 'work did challenge the paradigm,' says Andrew, and it led John, who did his PhD in Andrew's lab, to find similar results in marine algae.

23. Later, working with Akhilesh Reddy from the University of Cambridge, UK, John also found that human red blood cells, which have no nucleus and therefore no DNA, oxidise and reduce proteins in a 24-hour cycle.

Box 5

Red blood cells, similar to other cells in the body, have 24 hour biological clocks (circadian rhythms) that alter their activity between day and night. Unlike other cells, red blood cells do not have DNA and the 'clock genes' that control rhythms are not present. Until now it has been unknown how such cells are regulated.

Using a novel technique called dielectrophoresis, and new technology developed at the University of Surrey, researchers were able to study the electrochemical properties of human red blood cells, providing an in depth analysis on their workings. Researchers observed a significant variation in potassium content in the cells which corresponded with the circadian rhythm – increased levels during the day followed by a decrease at night.

By changing the amount of potassium the cell receives, the researchers were able to increase and decrease its levels in the cell and observe the effects on their circadian rhythms. The researchers found that higher levels of potassium negatively impacted the circadian rhythm of the cell, whilst lower levels were observed as extending the duration of the cell's perceived "day" by several hours.

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24. John thinks that evolution may have conserved an enzymatic timing mechanism. 'We see the same enzymes again and again even though the clock proteins are not conserved,' he says. His team is currently testing the enzymatic processes that are not only important to circadian timekeeping in mammalian cells but are also conserved through evolution. 'We hope that if we can work out a minimal set of components that you need in a human cell to be able to express circadian rhythms then, hopefully, we should be able to reconstitute that timekeeping mechanism in a test tube. Just as was done for cyanobacteria,' he says.

25. With many possible avenues to follow, John is determined to stay focused on the enzymes. But, as he points out, 'everything is interesting; there are so many questions.'

Emma Davies is a science writer based in Bishop's Stortford, UK

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