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Surname	Other names

Pearson Edexcel Level 3 GCE

Centre Number	Candidate Number

Biology A (Salters-Nuffield)

Advanced

Paper 3: General and Practical Applications in Biology

Additional Specimen Material for first teaching September 2016

Time: 2 hours

Paper Reference

9BN0/03

You must have:
Calculator, HB pencil, ruler and a copy of the scientific article adapted from Discover Magazine (enclosed).

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.
- Show your working in any calculation questions and include units in your answer where appropriate.
- Answer the questions in the spaces provided
  – *there may be more space than you need.*
- You may use a scientific calculator.
- In questions marked with an **asterisk (*)**, marks will be awarded for your ability to structure your answer logically showing how the points that you make are related or follow on from each other where appropriate.

Information

- The total mark for this paper is 100.
- The marks for **each** question are shown in brackets
  – *use this as a guide as to how much time to spend on each question.*

Advice

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

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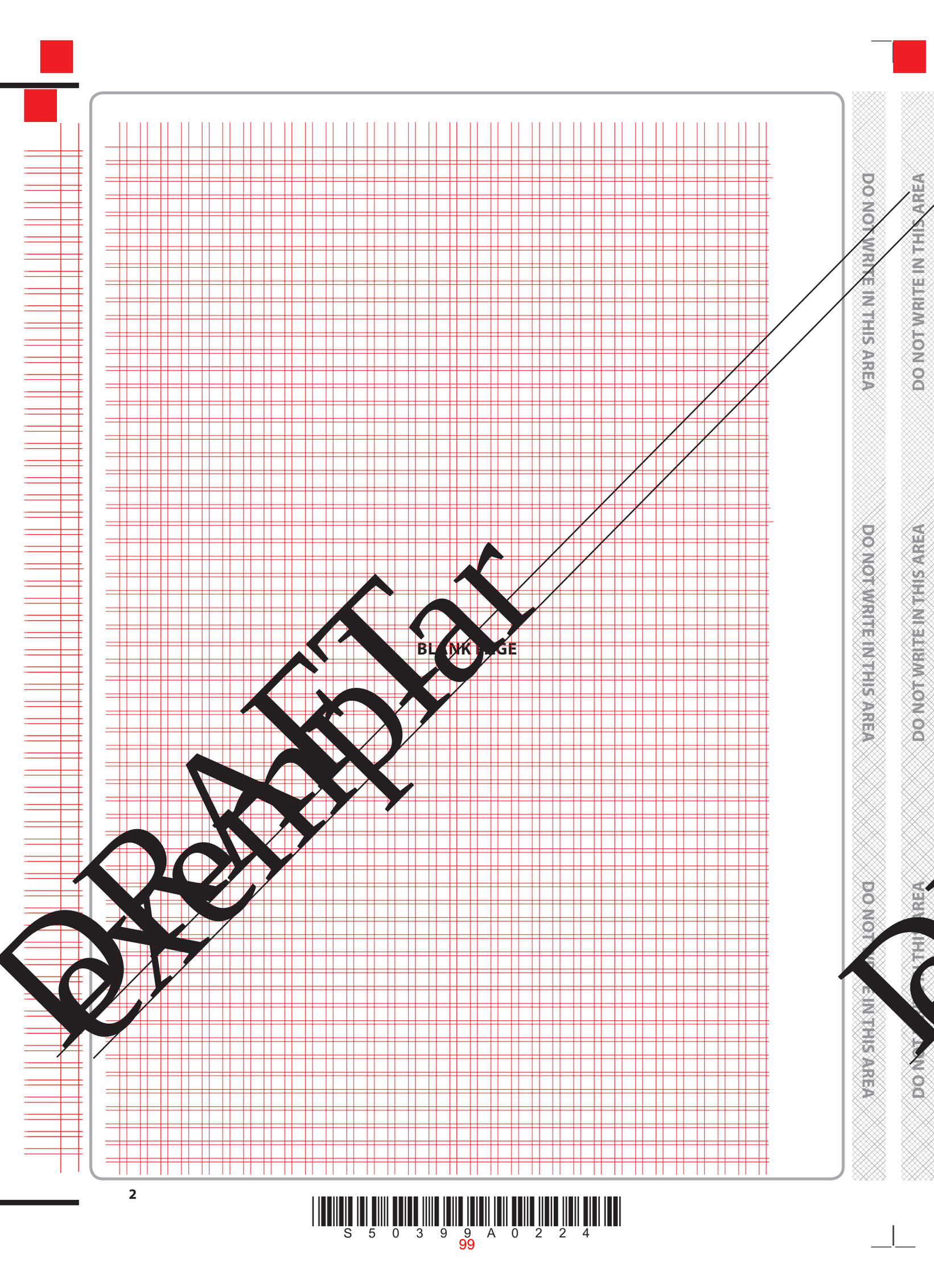
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Answer ALL questions.

Write your answers in the spaces provided.

1 Cinnamon is a spice that contains a substance called cinnamaldehyde. It is thought that cinnamaldehyde has antimicrobial properties.

A student investigated the antimicrobial properties of a cinnamon extract on bacteria.

The lid of a sterile Petri dish was raised and a sample of one species of bacterium was spread on the surface of sterile agar. The lid was then replaced.

(a) Explain why the agar and the Petri dish had to be sterilised before the bacteria were added.

(2)

The Petri dish lid was raised and a sterile paper disc soaked in full-strength cinnamon extract was placed on the agar. A second disc, soaked in half-strength extract, was placed on the agar and a third disc, soaked in distilled water and then placed on the agar.

The Petri dish was replaced and sealed with sticky tape.

(b) Explain why the seal was designed to allow air to enter the Petri dish.

(2)

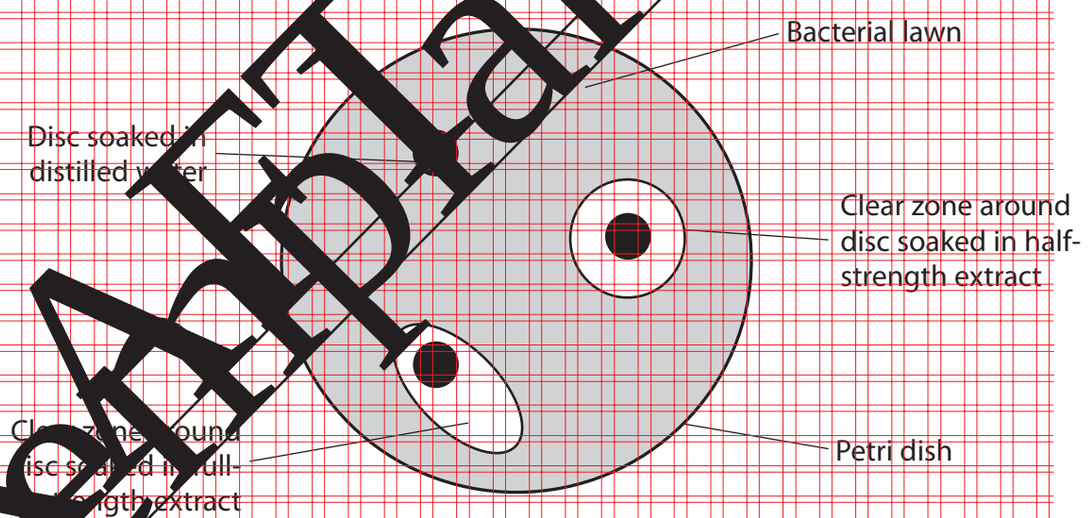
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(c) The student then placed the Petri dish in an incubator set at 25 °C for two days.

Give reasons why the incubator was set at this temperature rather than at 40 °C.

(2)

(d) After two days in the incubator, the Petri dish was observed and a copy of the results is shown.



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(i) Explain the presence of the clear zone around the disc soaked in half-strength extract.

(2)

(ii) The student concluded that the full-strength extract and half-strength extract showed the same level of antimicrobial properties for this species of bacterium.

Explain how the results observed could be used to support this conclusion.

(2)

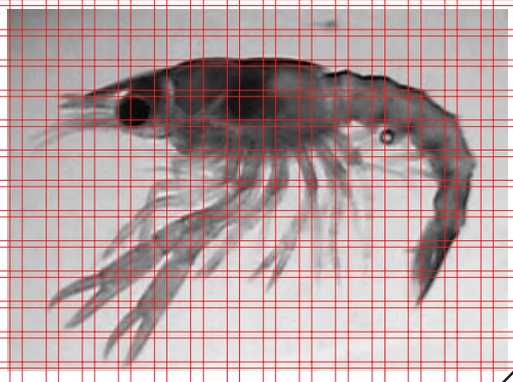
(Total for Question 1 = 10 marks)

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2 Some scientists have predicted that the atmospheric level of carbon dioxide may reach 0.09% by the year 2100.

(a) An investigation was carried out to study the effect of increased carbon dioxide in seawater on the development of the European lobster.

The photograph shows the larva of a European lobster.



Fertilised eggs from three different European lobsters were allowed to hatch. The newly hatched larvae were divided into two groups. One group was placed in a container of fresh seawater with an increased level of carbon dioxide, the other group acted as a control.

(i) Explain why temperature would have to be a controlled variable.

(2)

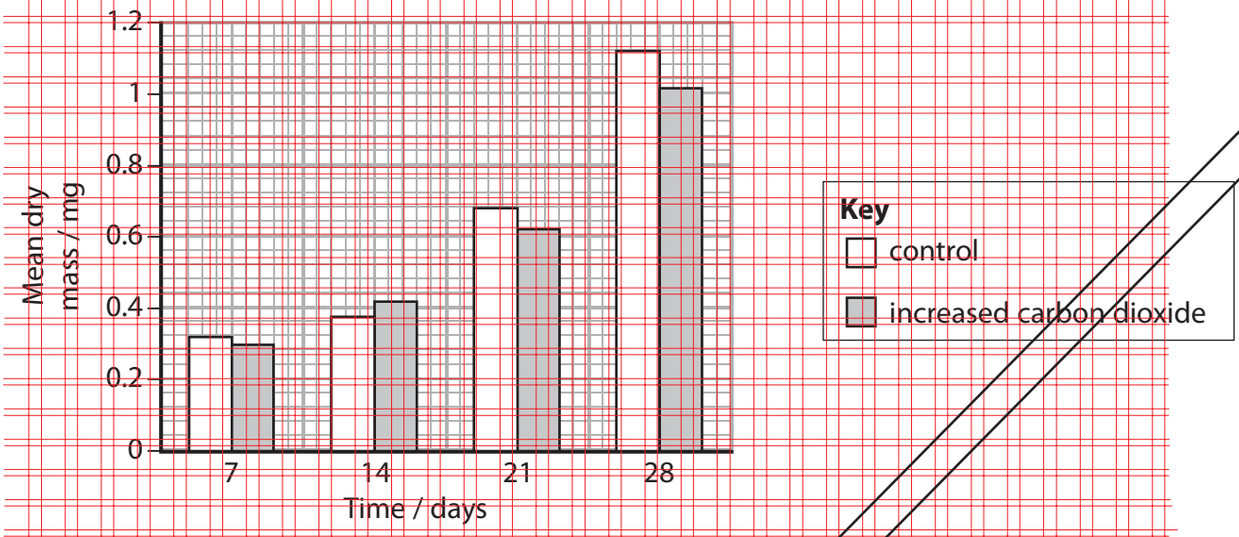
(ii) Explain why fertilised eggs were obtained from more than one lobster.

(2)

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(iii) At regular time intervals samples of larvae were removed. The dry mass of each larva was measured and the mean dry mass was calculated.

The results are shown in the graph.



Deduce the effect of increased carbon dioxide on the growth of lobster larvae.

(3)

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Exemplar

(b) It has been suggested that a change in the level of atmospheric carbon dioxide may affect the temperature of the oceans.

Explain how an increase in the level of atmospheric carbon dioxide may lead to an increase in seawater temperature.

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(c) Devise an investigation to determine the effect of seawater temperature on the hatching rate of fertilised lobster eggs.

(4)

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Exemplar

(Total for Question 2 = 14 marks)

3 Fruit drinks are a good source of vitamin C.

(a) A student investigated the concentration of vitamin C in three different fruit drinks.

The table shows the results for these fruit drinks.

Fruit drink	Concentration of vitamin C / mg 100 g^{-1}
A	85.85
B	67.59
C	119.77

(i) Explain how the student may have determined the concentrations of vitamin C in these fruit drinks.

(4)

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(ii) The concentration of vitamin C given on the packaging of fruit drink **C** was 67% greater than the concentration found by the student.

Calculate the concentration that was shown on the packaging.

(2)

Answer .... mg 100 g^{-1}

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Exemplar

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(iii) Explain how the student could determine whether the difference between the concentrations of vitamin C in the three fruit drinks was significant.

(3)

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(b) A study showed that an increase in the concentration of vitamin C in blood plasma increased the production of lymphocytes.

Describe how this may help the body fight infection.

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(Total for Question 3 = 11 marks)

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Exemplar

4 It has been estimated that, on average, each person in the UK eats 100 bananas every year.

An unripe banana contains starch. As bananas ripen the starch is broken down by enzymes.

(a) A student investigated ripening in bananas.

The student placed five unripe bananas, of the same age, in a fridge set at 3 °C. One day later, one banana was taken out of the fridge and put in an incubator set at 23 °C for five days.

A second banana was removed from the fridge after two days and placed in the same incubator for four days.

This was repeated for the three remaining bananas as shown in the table.

Banana	Time in fridge / days	Time in incubator / days
1	1	5
2	2	4
3	3	3
4	4	2
5	5	1

(i) The Q_{10} for the banana ripening process was found to be 2.

Explain how much faster the ripening process is in the incubator than in the fridge.

(2)

(ii) The student predicted that the rate of ripening would be higher the longer a banana has been in the incubator.

State a null hypothesis.

(1)

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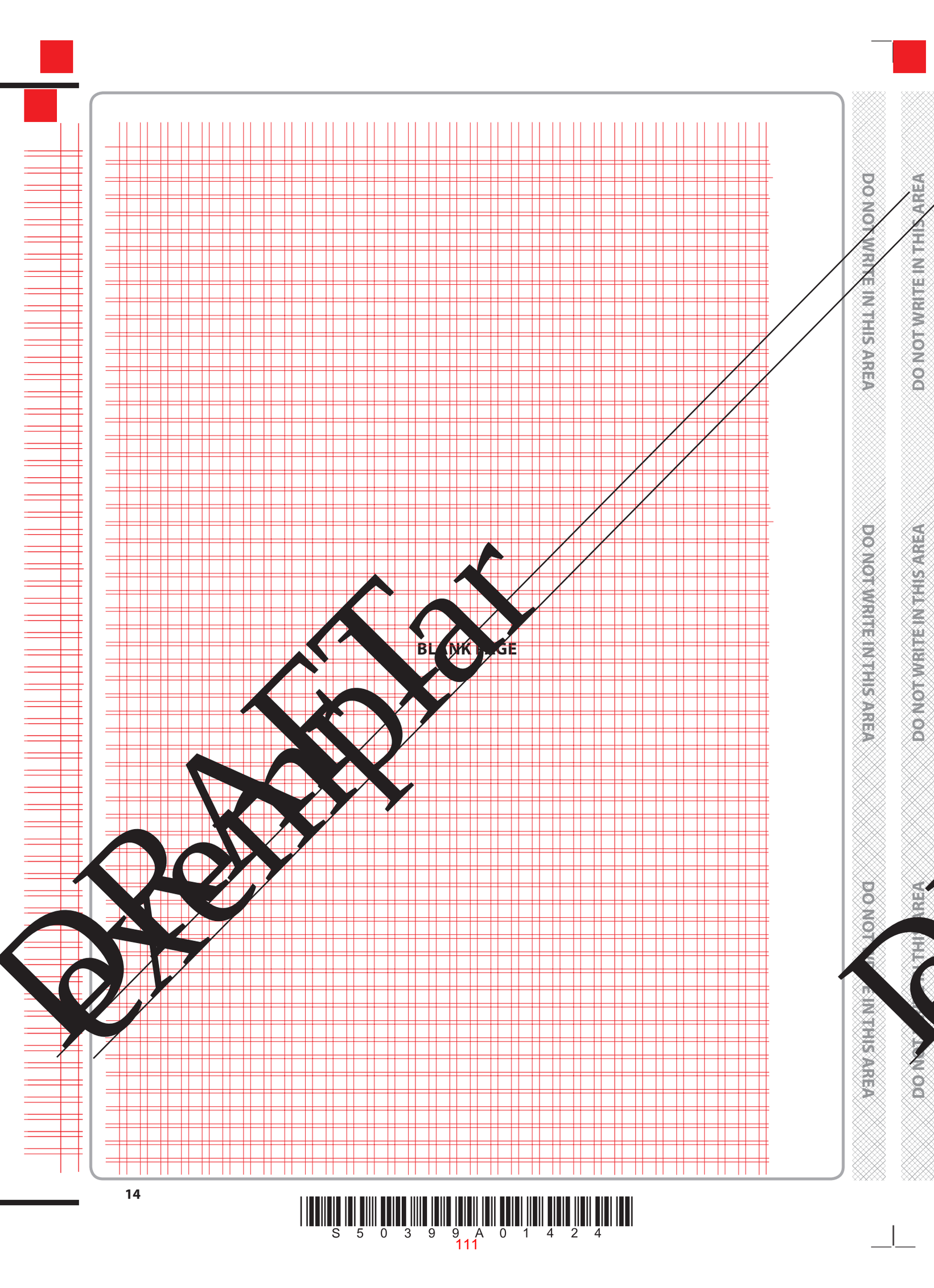
(b) As bananas ripen they produce catalase enzyme. Catalase breaks down hydrogen peroxide to water and oxygen.

Devise a procedure to test the hypothesis that "increased temperature increases the initial rate of reaction of catalase in bananas".

(5)

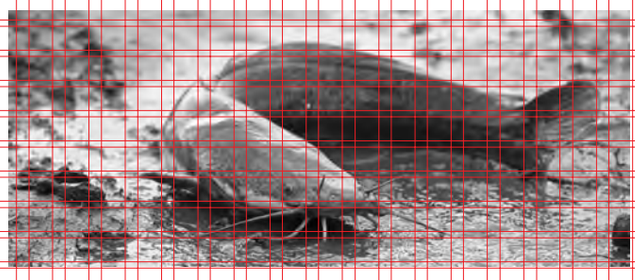
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(Total for Question 4 = 8 marks)


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5 The walking catfish, *Clarias batrachus*, shown in the photograph, is a freshwater fish found in Thailand.



The genetic diversity of this species of catfish has been investigated.

(a) The number of different alleles per gene locus was found for two populations of these catfish from two different regions of Thailand.

The results are shown in the table.

Region of Thailand	Mean number of different alleles per gene locus	Range
East	1.46	± 0.10
South	1.32	± 0.09

(i) State what is meant by the term **gene locus**.

(1)

(ii) Comment on the genetic diversity of the walking catfish in East Thailand compared with those in South Thailand.

(4)

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(b) Walking catfish have a gene for the enzyme glucose-6-phosphate isomerase (GPI).

An investigation studied the frequency of three different alleles for this gene.

The table shows the results for three different populations of walking catfish in Thailand.

Population	Frequency of allele at the GPI locus		
	Allele 1	Allele 2	Allele 3
X	1.000	0.000	0.000
Y	0.980	0.020	0.000
Z	0.950	0.038	0.012

(i) State and justify the genotype of population **X** for the GPI locus.

(2)

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(ii) Population **Y** was made up of 50 individuals.

Use the Hardy-Weinberg equation $p^2 + 2pq + q^2 = 1$, to calculate the maximum number of individuals in this population that are likely to be heterozygous at the GPI locus.

(2)

Answer .....

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(iii) Give reasons why allele 3 was only found in population **Z**.

(3)

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6 Lysosomes are a type of vesicle that may be made by the Golgi apparatus.

(a) Draw a labelled diagram of a Golgi apparatus.

(3)

(b) Explain how the presence of a lysosome in a cell would indicate that the cell is from an organism belonging to the Eukaryota domain.

(2)

Exemplar

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*(c) The contents of secretory vesicles are released from cells by the process of exocytosis. It has been claimed that complex organisms such as animals could not function without the process of exocytosis.

Discuss the evidence that supports this statement.

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(Total for Question 6 = 14 marks)

7 The scientific article you have studied is taken from Discover Magazine.

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

(a) Explain how 'epigenetic changes could be passed on from parent to child, one generation after the next' (paragraph 12).

(3)

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(b) Explain why the genome is 'known as the blueprint of life' (paragraph 16).

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Exemplar

(c) Explain how 'evolution selects the variance that is most successful' (paragraph 18).

(4)

(d) Explain how the evidence from paragraphs 19 and 21 supports the idea that nurture affects the development of behaviour.

(3)

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(e) Once RNA has been produced by transcription it is involved in building 'whatever proteins the cell needs' (paragraph 26).

Describe the roles of mRNA and tRNA in the building of proteins needed by cells.

(4)

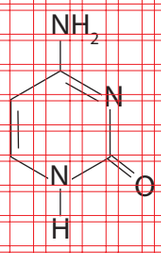
(f) Explain how trichostatin A allows methylated DNA to be transcribed to produce mRNA (paragraphs 27 to 35).

(4)

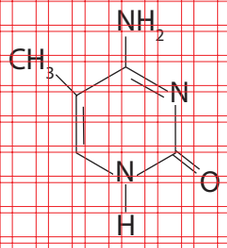
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(g) The diagram shows the methylation process that occurs on cytosine.

Cytosine



5-Methylcytosine



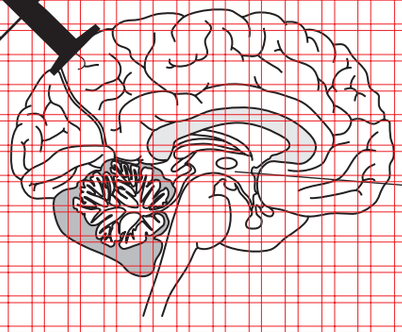
In a section of a double helix of DNA that comprises 68 nucleotides, this methylation process occurs on all eight of the cytosine bases that are present.

Calculate the percentage of adenine bases in this section of a DNA double helix.

(3)

Answer = ... %

(h) The diagram shows the site of the hippocampus (paragraph 42).



State the position of the hippocampus relative to the hypothalamus.

(1)

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(i) Deduce how the observations described in paragraphs 52 to 54 appear to provide evidence that epigenetic changes are not passed on by male parents.

(3)

(j) Explain how pharmaceutical companies may carry out double blind trials to test the effectiveness of epigenetic medication in treating the conditions described in paragraph 59.

(4)

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(Total for Question 7 = 31 marks)

TOTAL FOR PAPER = 100 MARKS

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Grandma's Experiences Leave a Mark on Your Genes

1 Darwin and Freud walk into a bar. Two alcoholic mice — a mother and her son — sit on two bar stools, lapping gin from two thimbles.

2 The mother mouse looks up and says, "Hey, geniuses, tell me how my son got into this sorry state."

3 "Bad inheritance," says Darwin.

4 "Bad mothering," says Freud.

5 For over a hundred years, those two views — nature or nurture, biology or psychology — offered opposing explanations for how behaviors develop and persist, not only within a single individual but across generations.

6 And then, in 1992, two young scientists following in Freud's and Darwin's footsteps actually did walk into a bar. And by the time they walked out, a few beers later, they had begun to forge a revolutionary new synthesis of how life experiences could directly affect your genes — and not only your own life experiences, but those of your mother's, grandmother's and beyond.

7 The bar was in Madrid, where the Cajal Institute, Spain's oldest academic center for the study of neurobiology, was holding an international meeting. Moshe Szyf, a molecular biologist and geneticist at McGill University in Montreal, had never studied psychology or neurology, but he had been talked into attending by a colleague who thought his work might have some application. Likewise, Michael Meaney, a McGill neurobiologist, had been talked into attending by the same colleague, who thought Meaney's research into animal models of maternal neglect might benefit from Szyf's perspective.

8 "I can still visualize the place — it was a corner bar that specialized in pizza," Meaney says. "Moshe, being kosher, was interested in kosher calories. Beer is kosher. Moshe can drink beer anywhere. And I'm Irish. So it was perfect."

9 The two engaged in animated conversation about a hot new line of research in genetics. Since the 1970s, researchers had known that the tightly wound spools of DNA inside each cell's nucleus require something extra to tell them exactly which genes to transcribe, whether for a heart cell, a liver cell or a brain cell.

10 One such extra element is the methyl group, a common structural component of organic molecules. The methyl group works like a placeholder in a cookbook, attaching to the DNA within each cell to select only those recipes — er, genes — necessary for that particular cell's proteins. Because methyl groups are attached to the genes, residing beside but separate from the double-helix DNA code, the field was dubbed epigenetics, from the prefix *epi* (Greek for over, outer, above).

11 Originally these epigenetic changes were believed to occur only during fetal development. But pioneering studies showed that molecular bric-a-brac could be added to DNA in adulthood, setting off a cascade of cellular changes resulting in cancer. Sometimes methyl groups attached to DNA thanks to changes in diet; other times, exposure to certain chemicals appeared to be the cause. Szyf showed that correcting epigenetic changes with drugs could cure certain cancers in animals.

12 Geneticists were especially surprised to find that epigenetic change could be passed down from parent to child, one generation after the next. A study from Randy Jirtle of Duke University showed that when female mice are fed a diet rich in methyl groups, the fur pigment of subsequent offspring is permanently altered. Without any change to DNA at all, methyl groups could be added or subtracted, and the changes were inherited much like a mutation in a gene.

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13 Now, at the bar in Madrid, Szyf and Meaney considered a hypothesis as improbable as it was profound: If diet and chemicals can cause epigenetic changes, could certain experiences — child neglect, drug abuse or other severe stresses — also set off epigenetic changes to the DNA inside the neurons of a person's brain? That question turned out to be the basis of a new field, behavioral epigenetics, now so vibrant it has spawned dozens of studies and suggested profound new treatments to heal the brain.

14 According to the new insights of behavioral epigenetics, traumatic experiences in our past, or in our recent ancestors' past, leave molecular scars adhering to our DNA. Jews whose great-grandparents were chased from their Russian shtetls; Chinese whose grandparents lived through the ravages of the Cultural Revolution; young immigrants from Africa whose parents survived massacres; adults of every ethnicity who grew up with alcoholic or abusive parents — all carry with them more than just memories.

15 Like silt deposited on the cogs of a finely tuned machine after the seawater of a tsunami recedes, our experiences, and those of our forebears, are never gone, even if they have been forgotten. They become a part of us, a molecular residue holding fast to our genetic scaffolding. The DNA remains the same, but psychological and behavioral tendencies are inherited. You might have inherited not just your grandmother's knobby knees, but also her predisposition toward depression caused by the neglect she suffered as a newborn.

16 Or not. If your grandmother was adopted by nurturing parents, you might be enjoying the boost she received thanks to their love and support. The mechanisms of behavioral epigenetics underlie not only deficits and weaknesses but strengths and resiliencies, too. And for those unlucky enough to descend from miserable or withholding grandparents, emerging drug treatments could reset not just mood, but the epigenetic changes themselves. Like grandmother's vintage dress, you could wear it or have it altered. The genome has long been known as the blueprint of life, but the epigenome is life's Etch A Sketch. Shake it hard enough, and you can wipe clean the family curse.

Voodoo Genetics

17 Twenty years after having to set off a revolution, Meaney sits behind a wide walnut table that serves as his desk. Janu[illegible]ion has deposited half a foot of snow outside the picture windows lining his four[illegible]r corner office at the Douglas Institute, a mental health affiliate of McGill. He has the rugged good looks and tousled salt-and-pepper hair of someone found on a ski slope — precisely wh[illegible]e plans to go this weekend. On the floor lies an arrangement of helium balloons in various stages of deflation. "Happy 60th!" one announces.

18 "I've always been interested in what makes people different from each other," he says. "The way we, the w[illegible]w, behave — some people are optimistic, some are pessimistic. What produces that variation? Evolution selects the variance that is most successful, but what produces the grist for the mi[illegible]

Meaney pursued the question of individual differences by studying how the rearing habits of mother rats caused lifelong changes in their offspring. Research dating back to the 1950s had shown that rats handled by humans for as little as five to 15 minutes per day during their first three weeks of life grew up to be calmer and less reactive to stressful environments compared with their non-handled littermates. Seeking to tease out the mechanism behind such an enduring effect, Meaney and others established that the benefit was not actually conveyed by the human handling. Rather, the handling simply provoked the rats' mothers to lick and groom their pups more, and to engage more often in a behavior called arched-back nursing, in which the mother gives the pups extra room to suckle against her underside.

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20 "It's all about the tactile stimulation," Meaney says.

21 In a landmark 1997 paper in *Science*, he showed that natural variations in the amount of licking and grooming received during infancy had a direct effect on how stress hormones, including corticosterone, were expressed in adulthood. The more licking as babies, the lower the stress hormones as grown-ups. It was almost as if the mother rats were licking away at a genetic dimmer switch. What the paper didn't explain was how such a thing could be possible.

22 "What we had done up to that point in time was to identify maternal care and its influence on specific genes," Meaney says. "But epigenetics wasn't a topic I knew very much about."

23 And then he met Szyf.

Postnatal Inheritance

24 "I was going to be a dentist," Szyf says with a laugh. Slight, pale and balding, he sits in a small office at the back of his bustling laboratory — a room so Spartan, it contains just a single picture, a photograph of two embryos in a womb.

25 Needing to write a thesis in the late 1970s for his doctorate in dentistry at Hebrew University of Jerusalem, Szyf approached a young biochemistry professor named Aharon Razin, who had recently made a splash by publishing his first few studies in some of the world's top scientific journals. The studies were the first to show that the action of genes could be modulated by structures called methyl groups, a subject about which Szyf knew precisely nothing. But he needed a thesis adviser, and Razin was there. Szyf found himself swept up to the forefront of the hot new field of epigenetics and never looked back.

26 Until researchers like Razin came along, the basic story line on how genes get transcribed in a cell was neat and simple. DNA is the master code, residing inside the nucleus of every cell; RNA transcribes the code to build whatever proteins the cell needs. Then some of Razin's colleagues showed that methyl groups could attach to cytosine, one of the chemical bases in DNA and RNA.

27 It was Razin, working with fellow biochemist Howard Cedar, who showed these attachments weren't just brief, meaningless affairs. The methyl groups could become married permanently to the DNA, getting duplicated right along with it through a hundred generations. As in any good marriage, however, the attachment of the methyl groups significantly altered the behavior of whichever gene they were inhibiting its transcription, much like a jealous spouse. It did so, Razin and Cedar showed, by tightening the thread of DNA as it wrapped around a molecular spool, called a histone, inside the nucleus. The tighter it is wrapped, the harder to produce proteins from the gene.

28 Consider what that means: Without a mutation to the DNA code itself, the attached methyl groups caused long-term, heritable change in gene function. Other molecules, called acetyl groups, were found to play the opposite role, unwinding DNA around the histone spool, and so making it easier for RNA to transcribe a given gene.

29 By the time Szyf arrived at McGill in the late 1980s, he had become an expert in the mechanics of epigenetic change. But until meeting Meaney, he had never heard anyone suggest that such changes could occur in the brain, simply due to maternal care.

DRAFT

30 "It sounded like voodoo at first," Szyf admits. "For a molecular biologist, anything that didn't have a clear molecular pathway was not serious science. But the longer we talked, the more I realized that maternal care just might be capable of causing changes in DNA methylation, as crazy as that sounded. So Michael and I decided we'd have to do the experiment to find out."

31 Actually, they ended up doing a series of elaborate experiments. With the assistance of postdoctoral researchers, they began by selecting mother rats who were either highly attentive or highly inattentive. Once a pup had grown up into adulthood, the team examined its hippocampus, a brain region essential for regulating the stress response. In the pups of inattentive mothers, they found that genes regulating the production of glucocorticoid receptors, which regulate sensitivity to stress hormones, were highly methylated; in the pups of conscientious moms, the genes for the glucocorticoid receptors were rarely methylated.

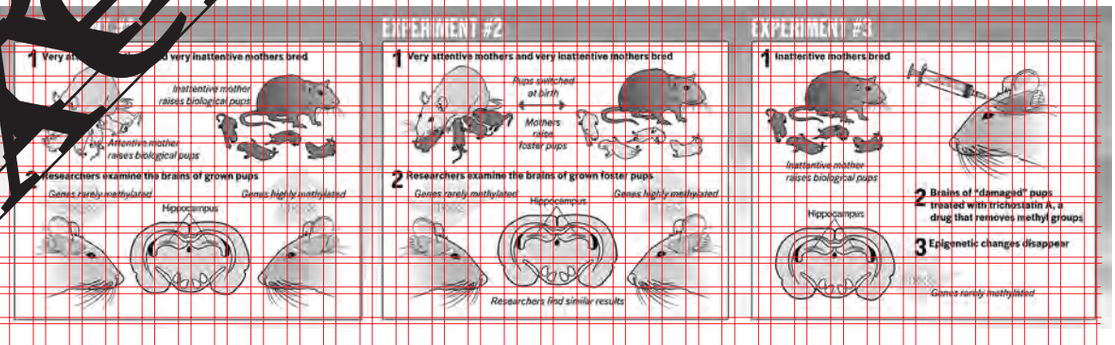
32 Methylation just gums up the works. So the less the better when it comes to transcribing the affected gene. In this case, methylation associated with miserable mothering prevented the normal number of glucocorticoid receptors from being transcribed in the baby's hippocampus. And so for want of sufficient glucocorticoid receptors, the rats grew up to be nervous wrecks.

33 To demonstrate that the effects were purely due to the mother's behavior and not her genes, Meaney and colleagues performed a second experiment. They took rat pups born to inattentive mothers and gave them to attentive ones, and vice versa. As they predicted, the rats born to attentive mothers but raised by inattentive ones grew up to have low levels of glucocorticoid receptors in their hippocampus and behaved skittishly. Likewise, those born to bad mothers but raised by good ones grew up to be calm and brave and had high levels of glucocorticoid receptors.

34 Before publishing their findings, Meaney and Szyf conducted a third crucial experiment, hoping to overwhelm the inevitable skeptics who would rise up to question their results. After all, it could be argued, what if the epigenetic changes observed in the rats' brains were not directly causing the behavioral changes in the adults, but were merely co-occurring? Freud certainly knew the enduring power of bad mothers to screw up people's lives. Maybe the emotional effects were unrelated to the epigenetic change.

35 To test that possibility, Meaney and Szyf took yet another litter of rats raised by rotten mothers. This time, after the usual damage had been done, they infused their brains with trichostatin A, a drug that can remove methyl groups. In these animals showed none of the behavioral deficits usually seen in such offspring, and their brains showed none of the epigenetic changes.

36 "It was crazy to think that injecting it straight into the brain would work," says Szyf. "But it did. It was like resetting the computer."



37 Despite such seemingly overwhelming evidence, when the pair wrote it all up in a paper, one of the reviewers at a top science journal refused to believe it, stating he had never before seen evidence that a mother's behavior could cause epigenetic change.

Excerpt

38 "Of course he hadn't," Szyf says. "We wouldn't have bothered to report the study if it had already been proved."

39 In the end, their landmark paper, "Epigenetic programming by maternal behavior," was published in June 2004 in the journal *Nature Neuroscience*.

40 Meaney and Szyf had proved something incredible. Call it postnatal inheritance: With no changes to their genetic code, the baby rats nonetheless gained genetic attachments due solely to their upbringing — *epi*genetic additions of methyl groups sticking like umbrellas out the elevator doors of their histones, gumming up the works and altering the function of the brain.

The Beat Goes On

41 Together, Meaney and Szyf have gone on to publish some two-dozen papers, finding evidence along the way of epigenetic changes to many other genes active in the brain. Perhaps most significantly, in a study led by Frances Champagne — then a graduate student in Meaney's lab, now an associate professor with her own lab at Columbia University in New York — they found that inattentive mothering in rodents causes methylation of the genes for estrogen receptors in the brain. When those babies grow up, the resulting decrease of estrogen receptors makes them less attentive to *their* babies. And so the beat goes on.

42 As animal experiments continue apace, Szyf and Meaney have entered into the next great step in the study of behavioral epigenetics: human studies. In a 2008 paper, they compared the brains of people who had committed suicide with the brains of people who had died suddenly of factors other than suicide. They found excess methylation of genes in the suicide brains' hippocampus, a region critical to memory acquisition and stress response. If the suicide victims had been abused as children, they found, their brains were more methylated.

43 Why can't your friend "just get over" her upbringing by an angry, distant mother? Why can't she "just snap out of it"? The reason may well be due to methyl groups that were added in childhood to genes in her brain, handcuffing her mood to feelings of fear and despair.

44 Of course, it is generally impossible to sample the brains of living people. But examining blood samples from humans is routine, and Szyf has gone searching there for markers of epigenetic methylation. Su[illegible], in 2011 he reported on a genome-wide analysis of blood samples taken from 40 men who participated in a British study of people born in England in 1958.

45 All were men living at a socioeconomic extreme, either very rich or very poor, at some point in their lives ranging from early childhood to mid-adulthood. In all, Szyf analyzed the methylation state of about 20,000 genes. Of these, 6,176 genes varied significantly based on poverty or wealth. More striking, however, was the finding that genes were more than twice as likely to show methylation changes based on family income during early childhood versus economic status as adults.

46 Timing, in other words, matters. Your parents winning the lottery or going bankrupt when you're 2 years old will likely affect the epigenome of your brain, and your resulting emotional tendencies, far more strongly than whatever fortune finds you in middle age.

47 Last year, Szyf and researchers from Yale University published another study of human blood samples, comparing 14 children raised in Russian orphanages with 14 other Russian children raised by their biological parents. They found far more methylation in the orphans' genes, including many that play an important role in neural communication and brain development and function.

DRAFT

48 "Our study shows that the early stress of separation from a biological parent impacts long-term programming of genome function; this might explain why adopted children may be particularly vulnerable to harsh parenting in terms of their physical and mental health," said Szyf's co-author, psychologist Elena Grigorenko of the Child Study Center at Yale. "Parenting adopted children might require much more nurturing care to reverse these changes in genome regulation."

49 A case study in the epigenetic effects of upbringing in humans can be seen in the life of Szyf's and Meaney's onetime collaborator, Frances Champagne. "My mom studied prolactin, a hormone involved in maternal behavior. She was a driving force in encouraging me to go into science," she recalls. Now a leading figure in the study of maternal influence, Champagne just had her first child, a daughter. And epigenetic research has taught her something not found in the *What to Expect* books or even her mother's former lab.

50 "The thing I've gained from the work I do is that stress is a big suppressor of maternal behavior," she says. "We see it in the animal studies, and it's true in humans. So the best thing you can do is not to worry all the time about whether you're doing the right thing. Keeping the stress level down is the most important thing. And tactile interaction — that's certainly what the good mother rats are doing with their babies. That sensory input, the touching, is so important for the developing brain."

The Mark Of Cain

51 The message that a mother's love can make all the difference in a child's life is nothing new. But the ability of epigenetic change to persist across generations remains the subject of debate. Is methylation transmitted directly through the fertilized egg, or is each infant born pure, a methylated virgin, with the attachments of methyl groups slathered on solely by parents after birth?

52 Neuroscientist Eric Nestler of the Mount Sinai School of Medicine at Mount Sinai in New York has been seeking an answer for years. In one study, he exposed male mice to 10 days of bullying by larger, more aggressive mice. At the end of the experiment, the bullied mice were socially withdrawn.

53 To test whether such effects could be transmitted to the next generation, Nestler took another group of bullied mice and bred them with females, but kept them from ever meeting their offspring.

54 Despite having no contact with their depressed fathers, the offspring grew up to be hypersensitive to stress. It was a subtle effect; the offspring were dramatically more susceptible to developing signs of depression, he says.

55 In further testing, Nestler took sperm from defeated males and impregnated females through in vitro fertilization. The offspring did not show most of the behavioral abnormalities, suggesting that epigenetic transmission may not be at the root. Instead, Nestler proposes, "the female might know she had sex with a loser. She knows it's a tainted male she had sex with, so she cares for her pups differently," accounting for the results.

56 Despite his findings, no consensus has yet emerged. The latest evidence, published in the Jan. 25 issue of the journal *Science*, suggests that epigenetic changes in mice are usually erased, but not always. The erasure is imperfect, and sometimes the affected genes may make it through to the next generation, setting the stage for transmission of the altered traits in descendants as well.

Draft

What's Next?

57 The studies keep piling on. One line of research traces memory loss in old age to epigenetic alterations in brain neurons. Another connects post-traumatic stress disorder to methylation of the gene coding for neurotrophic factor, a protein that regulates the growth of neurons in the brain.

58 If it is true that epigenetic changes to genes active in certain regions of the brain underlie our emotional and intellectual intelligence — our tendency to be calm or fearful, our ability to learn or to forget — then the question arises: Why can't we just take a drug to rinse away the unwanted methyl groups like a bar of epigenetic Irish Spring?

59 The hunt is on. Giant pharmaceutical and smaller biotech firms are searching for epigenetic compounds to boost learning and memory. It has been lost on no one that epigenetic medications might succeed in treating depression, anxiety and post-traumatic stress disorder where today's psychiatric drugs have failed.

60 But it is going to be a leap. How could we be sure that epigenetic drugs would scrub clean only the dangerous marks, leaving beneficial — perhaps essential — methyl groups intact? And what if we could create a pill potent enough to wipe clean the epigenetic slate of all that history wrote? If such a pill could free the genes within your brain of the epigenetic detritus left by all the wars, the rapes, the abandonments and cheated childhoods of your ancestors, would you take it?

Grandma's Experiences Leave a Mark on Your Genes, Discover Magazine, By Dan Hurley Thursday, June 25, 2015

http://discovermagazine.com/2013/may/13-grandmas-experiences-leave-epigenetic-mark-on-your-genes

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