2020年度
大学院理工学研究科【生命理学専攻】博士後期課程
一般選抜試験(第Ⅱ期)問題

英　　語

開始時刻　午前10時00分
終了時刻　午前11時00分

【注意事項】

1．解答用紙には受験番号、氏名を必ず記入してください。
2．配布された答案用紙は試験が終了したら、必ず提出してください（問題用紙は提出しなくてよい）。

1

以下の文章を読んで、各設問に答えなさい。
After reading the text below, answer the following questions.

Screening is used to detect breast cancer early in women who have no obvious signs of the disease. This image-analysis task is challenging because cancer is often hidden or masked in mammograms by overlapping 'dense' breast tissue. The problem has stimulated efforts to develop computer-based artificial-intelligence (AI) systems to improve diagnostic performance. McKinney *et al.* report the development of an AI system that outperforms expert radiologists in accurately interpreting mammograms from screening programs. The work is part of a wave of studies investigating the use of AI in a range of medical-imaging contexts.

Despite some limitations, McKinney and colleagues' study is impressive. Its strengths include the large scale of the data sets used for training and subsequently validating the AI algorithm. Mammograms for 25,856 women in the United Kingdom and 3,097 women in the United States were used to train the AI system. The system was then used to identify the presence of breast cancer in mammograms of women who were known to have had either biopsy-proven breast cancer or normal follow-up imaging results at least 365 days later. These outcomes are the widely accepted gold standard for confirming breast cancer status in people undergoing screening for the disease. (A)The authors report that the AI system outperformed both the historical decisions made by the radiologists who initially assessed the mammograms, and the decisions of 6 expert radiologists who interpreted 500 randomly selected cases in a controlled study.

(I) McKinney and colleagues' results suggest that AI might some day have a role in aiding the early detection of breast cancer, but the authors rightly note that clinical trials will be needed to further assess the utility of this tool in medical practice. The real world is more complicated and potentially more diverse than the type of controlled research environment reported in this study. For example, the study did not include all the different mammography technologies currently in use, and most images were obtained using a mammography system from a single manufacturer. The study included examples of two types of mammogram: tomosynthesis (also known as 3D mammography) and conventional digital (2D) mammography. It would be useful to know how the system performed individually for each technology.

(B) Another reason to temper excitement about this and similar AI studies is the lessons learnt from computer-aided detection (CAD) of breast cancer. CAD, an earlier computer system aimed at improving mammography interpretation in the clinic, showed great promise in experimental testing, but fell short in real-world settings. CAD marks mammograms to draw the interpreter's attention to areas that might be abnormal. However, analysis of a large sample of clinical mammography interpretations from the US Breast Cancer Surveillance Consortium registry demonstrated that there was no improvement in diagnostic accuracy with CAD. Moreover, that study revealed that the

addition of CAD worsened sensitivity (the performance of radiologists in determining that cancer was present), thus increasing the likelihood of a false negative test. CAD did not result in a significant change in specificity (the performance of radiologists in determining that cancer was not present) and the likelihood of a false positive test.

(II) Breast cancer screening is perhaps an ideal application for AI in medical imaging because large curated data sets suitable for algorithm training and testing are already available. Breast cancer screening programs routinely measure their diagnostic performance — whether cancer is correctly detected (a true positive) or missed (a false negative). Some areas found on mammograms might be identified as abnormal but turn out on further testing not to be cancerous (false positives). For most women, screening identifies no abnormalities, and when there is still no evidence of cancer one year later, this is classified as a true negative.

(III) Most other medical tasks have more complicated clinical outcomes, however, in which the clinician's decision is not a binary one (between the presence or absence of cancer), and thus further signs and symptoms must also be considered. In addition, most diseases lack readily accessible, validated data sets in which the 'truth' is defined relatively easily.

(modified from *Nature* 577, 35-36 (2020))

to annotate: 注釈をつける; anonymized: 匿名化; biopsy: 生検; to classify: 分類する;
to curate: キュレートする（必要な情報をたくさんの情報源から収集、整理、要約、公開（共有）すること）; to draw attention: 注意を引く; to fall short: 不足する; lack: 欠如;
likelihood: 可能性; mammogram: マンモグラム（乳房専用のレントゲン写真）; outperform: 優れる; oversight: 監視; performance: 性能; radiologist: 放射線科医;
sheer volume: 膨大な量; to temper: 和らげる; to train: 学習させる; utility: 効用

問１：本文章に適切な英語の演題をつけなさい。
Provide an appropriate title in English for this text.

問２：下線部(A)の文を２行以内で自分の言葉でまとめて英語または日本語で説明しなさい。
Summarize in your own words within two lines the text underlined (I) in English or Japanese.

問３：パラグラフ(I)，(II)，(III) を各々３行以内で自分の言葉で英語または日本語で要約しなさい。
Summarize in your own words within three lines each paragraph labeled (I), (II) and (III) in English or Japanese.

問４：パラグラフ(B)で CAD について議論している理由を McKinney らの研究と比較して英語または日本語で説明しなさい。
Explain in your own words, in English or Japanese, why the authors discuss CAD in relation to the work of McKinney et al. in paragraph (B).

問５：この文章の後に続く Discussion（考察）を英語で書きなさい。
Write a paragraph to follow this text as a Discussion in English.

2

次の文章を読んで問いに答えなさい。答えは、解答用紙に、問の番号と共に記入しなさい。

It has been said that Marie Antoinette's hair went completely white on the night before her beheading. This story might be apocryphal, but rapid greying of the hair is now widely referred to as Marie Antoinette syndrome. It is often assumed to be caused by stress — a phenomenon perhaps best exemplified by photographs of heads of state before and after they held office. However, the relative contributions of ageing, genetic factors and stress to greying are not known — in part owing to a lack of mechanistic understanding of the process.

The average human scalp has 100,000 hair follicles, and a wide range of hair colours can be found across the human population. Hair colour is determined by cells called melanocytes, which produce different combinations of light-absorbing melanin pigments. Melanocytes are derived from melanocyte stem cells (MeSCs), which are located in a part of the hair follicle called the bulge. The normal hair cycle is divided into three stages: hair-follicle regeneration (anagen), degeneration (catagen) and rest (telogen). Melanocyte production begins early in the anagen phase. [a]As people age, the pool of MeSCs is gradually depleted — and so pigmented hair becomes 'salt and pepper' coloured, and then turns to grey and finally to white after a complete loss of pigment in all hair follicles.

The researchers set out to test the role of stress in the greying process in mice. They exposed the animals to three different stressors — pain, restraint and a model of psychological stress — during different phases of hair growth. Each stressor caused depletion of MeSCs from the bulge region, eventually leading to the development of patches of white hair. Then they found that MeSCs express β2-adrenergic receptors, which respond to noradrenaline — a neurotransmitter molecule involved in the 'fight or flight' response to stress. Loss of this receptor specifically in MeSCs completely blocked stress-induced greying. They show that stressful stimuli activate the sympathetic nervous system, increasing noradrenaline release in hair follicles. Noradrenaline causes complete conversion of MeSCs into melanocytes, which migrate out of the niche in catagen and telogen. The hair follicle is depleted of MeSCs that would have differentiated to replace these melanocytes. Without any pigment cells to colour the hair in the next anagen phase, it begins to look grey or white.

[b]Are other pools of stem cells similarly susceptible to stem-cell depletion in response to stress, if they or the cells that make up their niche express β2-adrenergic receptors? In support of this idea, haematopoietic stem and progenitor cells (HSPCs), which give rise to blood and immune lineages, reside in a bone-marrow niche that contains stromal cells, and

stimulation of those cells by the sympathetic nervous system causes HSPCs to leave their niche. Perhaps, like MeSCs, stress depletes HSPCs — which could partially explain why immune function is impaired in response to chronic stress. Whether this type of relationship extends beyond MeSCs and HSPCs is an open question.

Connecting the dots between stress, fight or flight, stem-cell depletion and premature greying opens up several avenues for future research. Beyond developing anti-greying therapies, this work promises to usher in a better understanding of how stress influences other stem-cell pools and their niches.

pigment: 色素、haematopoietic stem cells: 造血幹細胞

問 2-1

[a]の下線を和訳しなさい。

問 2-2

どんな実験が行われて、何がわかったのか。日本語で、詳しく説明しなさい(回答用紙の 10 行以上)。

問 2-3

[b]の下線には何が書いてあるか。日本語で、要約しなさい(回答用紙の 5 行以内)。

問 2-4

この文章に題名を英文でつけなさい。

問 3

各自が博士課程で行う研究について、英文で述べなさい(回答用紙の 10 行以内)。