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下記の第1問と第2問をすべて解答しなさい。

第１問 以下の文章は、Yamashita らによる論文 (Development 2025 doi: 10.1242/dev.204403)のイントロダクションからの抜粋である。この文章をよく読み、以下の問 A~E に答えなさい。

The temporal dynamics of signalling pathways are crucial for appropriate cellular decision-making across various biological processes. Biological oscillations, such as circadian rhythms and somitogenesis, ensure precise timing through robust signalling networks, even in the face of environmental and genetic perturbations (Isomura and Kageyama, 2014; Pourquie, 2003). In contrast, pulsatile oscillations, such as those in calcium concentrations or kinase activation (e.g. ERK activity), are characterised by spontaneous firing or stochastic initiation triggered by external stimuli (Muta et al., 2018; Smedler and Uhlen, 2014). The features of these oscillatory dynamics – amplitude, frequency, duration, and phase – guide cellular decision-making in proliferation, differentiation, and migration. Modulating these parameters enables cells to adapt to environmental changes, as demonstrated by the frequency modulation of Crz1 in Saccharomyces cerevisiae and the regulation of sporulation timing in Bacillus subtilis (Cai et al., 2008; Hsu et al., 2019; Levine et al., 2012). These examples emphasise the importance of oscillation parameter modulation in enabling cells to decode environmental signals and make appropriate decisions.

Frequency modulation plays a significant role in the development of the social amoeba Dictyostelium discoideum, particularly during its transition from a unicellular to a multicellular stage triggered by starvation. This process is driven by synchronised oscillations of cAMP, which shift from random pulses to coordinated oscillations as aggregation progresses (Gregor et al., 2010; Siegert and Weijer, 1989; Tomchik and Devreotes, 1981). The oscillation frequency increases from approximately 5.6 min during early aggregation to 2.5 min in the loose *mound stage, enhancing aggregation and regulating long-range signalling through positive feedback between cellular excitability and cAMP oscillations (Ford et al., 2023; Hashimura et al., 2019). These oscillatory dynamics regulate key transcription factors, such as GtaC and the Hbx5-MybG complex, which shuttle between the nucleus and cytoplasm in response to cAMP oscillations and Erk2 phosphorylation (Cai et al., 2014; Hadwiger et al., 2022; Hao et al., 2024). A 2-min cAMP cycle suppresses GtaC translocation, potentially functioning as a 'low-pass filter' that activates GtaC during a 6-min cycle (Cai et al., 2014). This is further supported by the observed suppression of csaA transcription during high-frequency cAMP cycles (Corrigan and Chubb, 2014). However, this hypothesis has yet to be directly validated through experimental evidence. Conventional tools, such as periodic cAMP microinjection and caged cAMP, provide precise temporal control (Rietdorf et al., 1998; Westendorf et al., 2013), but they lack the capability to sustain long-term oscillations or achieve the spatial precision required for continuous cAMP oscillations.

（博士前期課程）

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*「マウンド期（mound stage）」は、細胞性粘菌の生活環における重要な発生段階の一つで、多数の単細胞アメーバが集まって形成されるドーム状の多細胞集合体（盛土状の塊）を指します。Dictyostelium discoideum：キイロタマホコリカビ---細胞性粘菌の 1 種

問 A シグナル伝達経路において「pulsatile oscillations」とは何を意味しますか？

a~c の中から最も適切なものを選び解答欄に記入しなさい。

a) 連続的な周期的サイクル

b) 自発的または刺激によって引き起こされる振動

c) シグナル分子の永久的な活性化

問 B　Dictyostelium discoideum で cAMP 振動に応答する 2 つの転写因子を挙げなさい。

問 C 強固な振動ネットワークの例として挙げられている生物学的プロセスはどれですか？

a~d の中から最も適切なものを選び解答欄に記入しなさい。

a) *Bacillus subtilis* の胞子形成

b) 概日リズム

c) カルシウムスパイクの開始

d) ERK 活性

問 D　GtaC 活性化における「low-pass filter」という概念は、周波数変調とどのように関連していますか？

問 E なぜ caged cAMP のような従来のツールでは、振動周波数と転写因子制御に関する仮説を完全に検証できないのですか？本文で述べられている理由を 1 つ挙げなさい。

解答欄

問 A	
問 B	
問 C	

問 D（100 字程度の日本語で記入してください）

問 E（100 字程度の日本語で記入してください）

採　点

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第２問 英文を読んで、下記の問に答えなさい。

When I was in my early 20s, I asked my parents for a Christmas present, (ア)Stephen J. Gould's book *Ontogeny and Phylogeny*. Gould, the great communicator of science and polymath, laid out a rich history of biological thought about the regulation of developmental stages as an important mode for evolutionary change. Although some of his claims were controversial at the time, he anticipated the field of Evolutionary Developmental Biology (EvoDevo). A key concept was (イ)heterochrony − changes in the relative timing of developmental events, particularly developmental stages. Heterochronic changes can serve as the raw material for (ウ) changes to body form and physiology. Some heterochronic changes involve later developmental events that occur at earlier stages, while others involve the extension or repetition of earlier events at later stages. For example, (エ)neoteny, first described in the 19th century, is a trait specific to axolotls, in which reproductive maturity occurs within a retained larval form. Gould recounted speculation among evolutionary biologists that heterochronic mechanisms might also explain aspects of human evolution.

In the late 1970s and early 1980s, Bob Horvitz and Martin Chalfie were leveraging the *Caenorhabditis elegans* lineage (the defined specific patterns of cell division), which Horvitz had recently described with visionary John Sulston. The idea was to identify mutations in genes that perturbed these patterns of cell division in interesting ways. In 1981, they described (オ)one mutation in a gene called *lin-4* (the 'lin' designation identifies an effect on the cell lineage). There was nothing particularly remarkable about the appearance of the animal − it was long and flaccid, and couldn't lay eggs. But when they looked closely at cell lineage patterns, they realized that cells were actually repeating first larval stage division patterns again and again at later stages. Moreover, the adult kept molting, as if the adult skin cells believed they were still larval cells. Therefore, the functional product of the *lin-4* gene must be important for regulating the temporal identity of the cells. With *lin-4*, the first (カ) mutation in *C. elegans* had been described. In the next few years, the Horvitz lab discovered mutations in another gene, *lin-14*, which would also prove to have heterochronic gene function.

引用（抜粋、一部改変）：Wightman B. It's about time: the heterochronic background for the 2024 Nobel Prize in Physiology or Medicine. Dis Model Mech. 2024 Nov 1;17(11):dmm052187. doi: 10.1242/dmm.052187. Epub 2024 Nov 27. PMID: 39601149; PMCID: PMC11625885.

2026年度 明治大学大学院 農学研究科Ⅱ期入学試験
（博士前期課程）

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問１．下線部(ア)の人物に関して、著者が記述している内容を日本語で記述しなさい。

問２．下線部(イ)の内容を日本語で記述しなさい。

問３．空欄(ウ)に入る最も適切な文中の単語を記しなさい。

問４．下線部(エ)が最初に記述された生物種が属するグループとして最も適切なものを選択肢から一つ選び、丸（○）で囲みなさい。

選択肢：　魚類　　両生類　　は虫類　　鳥類　　哺乳類

問５．下線部(オ)に関して、細胞系譜のパターンはどのようなものであったか、日本語で記述しなさい。

問６．空欄(カ)に入る最も適切な文中の単語を記しなさい。

採 点