Evolutionary model of a population of DNA sequences through the interaction with an environment and its application to speciation analysis

Hitoshi Koyano\textsuperscript{1}\textsuperscript{*} and Kouji Yano\textsuperscript{2}

\begin{itemize}
\item \textsuperscript{1}Laboratory for Physical Biology, Quantitative Biology Center, Institute for Physical and Chemical Research (RIKEN), 2-2-3 Minatojima-Minamimachi, Chuo-ku, Kobe, Hyogo 650-0047, Japan
\item \textsuperscript{2}Department of Mathematics and Mathematical Analysis, Graduate School of Science, Kyoto University, Kitashirakawa-Oiwakecho, Sakyo-ku, Kyoto 606-8502, Japan
\end{itemize}

\textsuperscript{*}Corresponding author. E-mail: hitoshi.koyano@riken.jp

Abstract

In this study, we construct an evolutionary model of a population of DNA sequences interacting with the surrounding environment on the topological monoid $A^*$ of strings on the alphabet $A = \{a, c, g, t\}$. A partial differential equation governing the evolution of the DNA population is derived as a kind of diffusion equation on $A^*$. Analyzing the constructed model in a theoretical manner, we present conditions for sympatric speciation, the possibility of which continues to be discussed. It is shown that under other same conditions one condition determines whether sympatric speciation occurs or the DNA population continues to move around randomly in a subset of $A^*$. We next demonstrate that the population maintains a kind of equilibrium state under certain conditions. In this situation, the population remains nearly un-
changed and does not differentiate even if it can differentiate into others. Furthermore, we calculate the probability of sympatric speciation and the time expected to elapse before it.

**Keywords:** Topological monoid of strings, probability theory, population of DNA sequences, evolution, speciation.

1 Introduction

Evolution of a biological population is, at the most fundamental level, temporal change in a set of DNA sequences that the population has. Individuals, therefore DNA sequences that they have, living in an environment are under selection pressure from the environment and leave offspring the number of which is determined according to the pressure operating on them. Offspring’s DNA sequences can contain mutations that occur randomly. Consequently, a population of DNA sequences gradually changes as generations pass.

Let us attempt to formulate the sentences in the previous paragraph as a mathematical model as naturally and faithfully to them as possible. We denote the set of strings on an alphabet $A = \{a, c, g, t\}$ (i.e., finite sequences of elements of $A$) by $A^*$. Any DNA sequence is represented as an element of $A^*$. Let $A^*$ form a metric space, provided with the Levenshtein distance (denoted by $d_L$ hereafter), although various distance functions such as the extended Hamming distance, longest common subsequence distance, and Damerau–Levenshtein distance are defined on $A^*$, depending on the problem to be considered. The Levenshtein distance between two strings is the minimum number of three types of edit operation, insertion, deletion, and substitution, necessary to transform one into another and is frequently used to evaluate evolutionary change in DNAs and gene sequences. In this setting, temporal change in a set of DNA sequences that a biological population has can be captured as change in a subset of $A^*$ with time. Each DNA sequence in an environment is under selection pressure exerted by the environment and the pressure is determined according to the order of nucleotides that compose the sequence, in other words, its position in $A^*$. Therefore, the selection pressure is a nonnegative real-valued function on $A^*$ defined when an environment is given. The selection pressure can be considered a counterpart in evolutionary biology of a force
field in physics, although it is not a vector-valued function on a vector space. Furthermore, mutations randomly contained in offspring sequences are captured as a random transformation on $A^*$ that does not always return the same element of $A^*$ for each element of $A^*$. In the following sections, advancing this viewpoint, we develop an evolutionary model of a biological population as the dynamics of a subset of $A^*$ by combining functions and operators on $A^*$.

Various evolutionary models of biological populations have been proposed. See, for example, [5–9, 17, 19] for articles that put emphasis on the mechanisms of speciation. However, any model was constructed on the set $\mathbb{R}$ of real numbers or real vector space $\mathbb{R}^n$. No studies have been performed that formulated the evolution of a biological population as a mathematical model at the fundamental level of temporal change in a set of DNA sequences that the population has, theoretically analyzed the model, and performed numerical experiments based on the model. The reason for this would be that no tools have been prepared for model construction and analysis because $A^*$ has not been a space on which probability theory and statistics should be constructed, although the phenomenon that a population of DNA sequences evolves need to be treated in a probabilistic manner because it is necessary to incorporate mutations that occur randomly in a model.

In various dynamical systems in which lots of particles interact in a numerical vector space, particles that is analysis objects are represented as their coordinates, i.e., numerical vectors. By contrast, an evolutionary process can be seen as temporal change in a subset of $A^*$ because our objects, DNA sequences, are represented as elements of $A^*$. In this study, we model the phenomenon described in the first paragraph, adopting the course described in the second paragraph based on probability theory on $A^*$ developed in recent years [13–16]. We subsequently investigate the process of speciation (see, for example, [2, 4, 18] for a review) that is one of the most fundamental phenomena in biology based on the model. Here we construct an evolutionary model for asexual populations, but it is not difficult to extend the model into one for sexual populations.
2 Formulation of the model

2.1 Evolutionary model of a DNA population

In this subsection, we formulate a model of the evolution of a population of DNA sequences interacting with a surrounding environment on the topological monoid $A^*$. We denote a population of DNA sequences at time $t \in [0, \infty)$ by $S(t)$. If $s \in S(t)$, we have $s \in A^*$. Let $|X|$ represent the number of elements of $X$ if $X$ is a set and $|s|$ represent the length of $s$ (i.e., the number of elements of $A$ that composes $s$) if $s \in A^*$. We set $n(t) = |S(t)|$ and write $S(t) = \{s_1(t), \cdots, s_{n(t)}(t)\}$. Let $R(t)$ be a complete system of representatives of the quotient set $S(t)/=$ of $S(t)$ with respect to the equality relation $=$. We denote the number of elements of $S(t)$ that are equal to $s \in R(t)$ (i.e., the number of elements of the equivalent class of $s \in R(t)$) by $v(s, t)$ and set $q(s, t) = v(s, t)/n(t)$. We define $Q(t) = \{q(s, t) : s \in R(t)\}$ and refer to $Q(t)$ as the relative frequency distribution of $S(t)$. In the following, we suppose that the population size $n(t)$ is exogenously given.

Let $E$ represent the set of possible environments in geographical regions of the earth. We denote the selection pressure exerted by an environment $E \in E$ on a DNA sequence $s \in A^*$ in the case where $s$ exists in $E$ by $p(s, E)$. Therefore, the selection pressure is a function $p(\cdot, E) : A^* \to [0, \infty)$ defined when $E \in E$ is given. As formulated below, as $p(s, E)$ is larger, the fitness of $s$ to $E$ is lower, and consequently, the number of offspring of $s$ is smaller, and vice versa. We suppose that there exists a level of selection pressure under which any $s \in A^*$ cannot produce offspring in $E$ and denote its critical value by $p_E$. In Subsection 2.3, we introduce a model of $p(s, E)$.

We suppose that a ratio $\gamma$ of sequences in $S(t)$ produce offspring and die in a unit time $[t, t + \Delta t]$ for a constant $\gamma \in (0, 1]$. In this setting, the life span varies depending on the sequence if $\gamma < 1$, whereas the generation overlapping between a parent and children is not considered. We denote the set of sequences in $S(t)$ that produce offspring and die in $[t, t + \Delta t]$ by $\hat{S}(t)$ and suppose that $\hat{S}(t)$ is determined according to the following rule $C_1$: For a minimum integer $\hat{n}(t)$ satisfying $\hat{n}(t) \geq \gamma n(t)$, $\hat{S}(t)$ is a set of the first $\hat{n}(t)$ sequences when sequences in $S(t)$ are sorted in descending order with respect to the living time, where the order of sequences that are equal in living time is arbitrary. Let $g_t$ represent a mapping that returns $\hat{S}(t) \subset S(t)$ determined according to the rule $C_1$ given $S(t)$,
in other words \( \hat{S}(t) = g_t(S(t)) \).

Let \( \hat{R}(t) \) be a complete system of representatives of the quotient set \( \hat{S}(t)/ = \) of \( \hat{S}(t) \) with respect to the equality relation =. We denote the number of elements of \( \hat{S}(t) \) that are equal to \( s \in \hat{R}(t) \) by \( \hat{v}(s,t) \). We define the function \( f(\cdot,t,E) : \hat{R}(t) \to [0, 1] \) as

\[
f(s,t,E) = \begin{cases} 
\frac{p_E - p(s,E)}{\sum_{s' \in \hat{R}(t)} (p_E - p(s',E))} & \text{if } p(s,E) < p_E, \\
0 & \text{otherwise}.
\end{cases}
\]

We have \( 0 \leq f(s,t,E) \leq 1 \) for any \( s \in \hat{R}(t) \) and \( \sum_{s \in \hat{R}(t)} f(s,t,E) = 1 \).

We suppose that the total number \( o(s,t) \) of offspring of sequences in \( \hat{S}(t) \) that are equal to \( s \) for each \( s \in \hat{R}(t) \) is determined according to the following rule \( C_2 \): Letting \( [x] \) represent the integer part of \( x \in \mathbb{R} \), we set

\[
\hat{n}(t) = n(t + \Delta t) - n(t) + \hat{n}(t), \quad u(t) = \hat{n}(t) - \sum_{s \in \hat{R}(t)} \lfloor \hat{n}(t)f(s,t,E) \rfloor.
\]

\( \hat{n}(t) \) represents the number of offspring that \( \hat{S}(t) \) can produce. We sort sequences in \( \hat{R}(t) \) in descending order with respect to \( \hat{n}(t)f(s,t,E) \). The order of sequences that have an equal value of \( \hat{n}(t)f(s,t,E) \) is arbitrary. Then, \( o(s,t) = \lfloor \hat{n}(t)f(s,t,E) \rfloor + 1 \) for the first to \( u(t) \)th sequence \( s \) in \( \hat{R}(t) \) and \( o(s,t) = \lfloor \hat{n}(t)f(s,t,E) \rfloor \) for the \((u(t) + 1)\)th to last sequence \( s \) in \( \hat{R}(t) \). This is a rule of determining the number of offspring that satisfies \( \hat{n}(t) = \sum_{s \in \hat{R}(t)} o(s,t) \) and is as faithful as to \( p(s,E) \) possible. We set \( o(s,t) = 0 \) for \( s \notin \hat{R}(t) \). We denote the set of offspring sequences of \( \hat{S}(t) \) by \( \hat{S}(t) \). \( f(s,t,E)/\hat{v}(s,t) \) and \( o(s,t)/\hat{v}(s,t) \) can be regarded as the relative fitness and the fitness of one of sequences in \( \hat{S}(t) \) that are equal to \( s \in \hat{R}(t) \), respectively.

Let \( m \) be a random transformation on \( A^* \) that does not necessarily maps each element of \( A^* \) to the same element of \( A^* \). We denote the probability that \( m \) outputs \( s' \) given \( s \) as an input by \( \mu(s,s') \) for \( s, s' \in A^* \). We refer to \( m \) as a mutation operator if \( m \) satisfies the following three conditions for \( s, s', s'' \in A^* \): (i) \( d_L(s,s') < d_L(s,s'') \) implies \( \mu(s,s') > \mu(s,s'') \), (ii) \( d_L(s,s') = d_L(s,s'') \) implies \( \mu(s,s') = \mu(s,s'') \), and (iii) mutated sequences generated by \( m \) are independent. In Subsection 2.3, we construct \( m \) that satisfies these conditions for \( d_L \) in a concrete manner, using the operation of concatenation defined on \( A^* \), which makes \( A^* \) form a monoid. We define the mutation operator at
time \( t \) as a set \( m_t = (m_t^1, \ldots, m_t^{\tilde{n}(t)}) \) of \( \tilde{n}(t) \) mutation operators that operates a set \( \{s_1, \ldots, s_{\tilde{n}(t)}\} \) of \( \tilde{n}(t) \) strings in the following component-wise manner:

\[
m_t(s_1, \ldots, s_{\tilde{n}(t)}) = (m_t^1(s_1), \ldots, m_t^{\tilde{n}(t)}(s_{\tilde{n}(t)})).
\]

We denote the probability that an offspring sequence contains a mutation corresponding to Levenshtein distance one by \( \pi \in (0, 1) \).

For any \( n \in \mathbb{N} \) (\( \mathbb{N} \) represents the set of natural numbers including zero) and \( s \in A^* \), we set the symbol \( \bigcup^n \{s\} \) (\( \bigcup \) has only a superscript) as \( \bigcup^n \{s\} = \emptyset \) for \( n = 0 \) and \( \bigcup^n \{s\} = \{s\} \) for \( n \geq 1 \). We define the replication operator \( r_t = (r_t^1, \ldots, r_t^{\tilde{n}(t)}) : (A^*)^{\tilde{n}(t)} \to (A^*)^{\tilde{n}(t)} \) at time \( t \)

\[
r_t(s_1, \ldots, s_{\tilde{n}(t)}) = (r_t^1(s_1), \ldots, r_t^{\tilde{n}(t)}(s_{\tilde{n}(t)})) = \bigcup_{i=1}^{\tilde{n}(t)} \bigcup_{s_i} \{s_i\}.
\]

Lastly, we define the generating operator \( G_t \) at time \( t \) as \( G_t(S(t)) = S(t) \setminus g_t(S(t)) \cup m_t \circ r_t \circ g_t(S(t)) \) (\( \circ \) represents composition). A population \( S(t + \Delta t) \) is generated from a population \( S(t) \) in the following manner:

\[
m_t \circ r_t \circ g_t(S(t)) = m_t \circ r_t(S(t)) = m_t(r_t^1(s_1(t)), \ldots, r_t^{\tilde{n}(t)}(s_{\tilde{n}(t)}(t)))
\]

\[
= m_t \left( \bigcup_{i=1}^{\tilde{n}(t)} \bigcup_{s_i(t)} \{s_i(t)\} \right) = \left\{ m_t^1(s_1)', \ldots, m_t^{\tilde{n}(t)}(s_{\tilde{n}(t)}') \right\}
\]

\[
= \{ \tilde{s}_1(t), \ldots, \tilde{s}_{\tilde{n}(t)}(t) \} = \tilde{S}(t),
\]

\[
G_t(S(t)) = S(t) \setminus g_t(S(t)) \cup m_t \circ r_t \circ g_t(S(t)) = S(t) \setminus \tilde{S}(t) \cup \tilde{S}(t) = S(t + \Delta t),
\]

where \( \bigcup_{i=1}^{\tilde{n}(t)} \bigcup_{s_i(t)} \{s_i(t)\} = \{s_1', \ldots, s_{\tilde{n}(t)}'\} \) and \( m_t^{(i)}(s_i') = \tilde{s}_i(t) \) for each \( i = 1, \ldots, \tilde{n}(t) \).

### 2.2 Equation governing the dynamics of \( q(s, t) \)

In this subsection, we derive a partial differential equation that describes the time evolution of the relative frequency distribution \( q(s, t) \) of \( S(t) \) formulated above, letting \( \Delta t \to 0 \). We suppose that there exists an upper limit to the length of a sequence inserted between two nucleotides (two letters of \( A \)) in a DNA sequence by stochastic mutation and denote it by \( c \). We set \( \ell(s) = c(|s| + 1) + |s| \) for each \( s \in A^* \) and \( V(s, d) = \{s' \in A^* : d_L(s, s') = d\} \) for \( d \in \mathbb{N} \). We put \( W(s) = \{s' \in A^* : d_L(s', s) \leq \ell(s') \} \) for each
and \( W(s,d) = \{ s' \in W(s) : d_L(s',s) = d \} \). \( W(s) \) is the set of sequences that can produce offspring sequences that are equal to \( s \) by mutation, and we have \( W(s) = \bigcup_{0 \leq d < \infty} W(s,d) \). We set \( x(s,t) = |\{ s' \in S(t) : s' = s \}| \), \( \hat{x}(s,t) = |\{ s' \in \hat{S}(t) : s' = s \}| \), and \( y(s,t) = \hat{x}(s,t)/x(s,t) \) for \( t \in [0,\infty) \). \( n_C \) represents the number of combinations of \( n \) items taken \( r \) at a time.

**Proposition 1 (Evolutionary equation of a DNA population)** If there exists the limit \( b(s,t) \) of \( y(s,t), \Delta t \to 0 \) with the ratio \( y(s,t)/\Delta t \) constant, the time evolution of the relative frequency distribution \( q(s,t) \) of \( S(t) \) is described by the partial differential equation

\[
\frac{\partial q(s,t)}{\partial t} = o(s,t)b(s,t)q(s,t)(1 - \pi)^{\ell(s)} + \sum_{1 \leq d < \infty} \sum_{s' \in W(s,d)} o(s',t)b(s',t)q(s',t)\frac{\ell(s')C_d\pi^d(1 - \pi)^{\ell(s') - d}}{|V(s',d)|} - b(s,t)q(s,t)
\]

for any \( s \in A^* \) and \( t \in [0,\infty) \).

**Proof.** In the model of the time evolution of \( S(t) \) formulated above, the relative frequency \( q(s,t+\Delta t) \) of any \( s \in A^* \) at time \( t+\Delta t \) consist of the following three components. (i) the relative frequency of sequences equal to \( s \) and belonging to \( S(t) \setminus \hat{S}(t) \), (ii) the relative frequency of sequences equal to \( s \) and belonging to \( \hat{S}(t) \), and (iii) the relative frequency of sequences equal to \( s \) that are produced by sequences different from \( s \) and belonging to \( \hat{S}(t) \). An offspring sequence of any \( s \in S(t) \) is obtained by performing the edit operation corresponding to Levenshtein distance one on \( s \) at most \( \ell(s) \) times, and the probabilities that the edit operation is performed and that it is not performed are equal to \( \pi \) and \( 1 - \pi \), respectively (see the definitions of \( c \) and \( \ell(s) \) above and the definition of mutation probability \( \pi \) in the sixth paragraph of Section 2). In addition, there exist \( |V(s,d)| \) sequences to which the Levenshtein distance from \( s \) is equal to \( d \). Therefore, the probability that an offspring sequence of \( s \) is a sequence to which the Levenshtein distance from \( s \) is equal to \( d \) satisfying \( 0 \leq d \leq \ell(s) \) is equal to \( \ell(s)C_d\pi^d(1 - \pi)^{\ell(s) - d}/|V(s,d)| \). Furthermore, the relative frequency in \( S(t) \) of sequences that are equal to \( s \) and produce offspring and die in the unit time \([t,t+\Delta t]\) is \( y(s,t)q(s,t) \). Thus, using the strong law of large numbers, the above (iii) is represented as

\[
\sum_{1 \leq d < \infty} \sum_{s' \in W(s,d)} o(s',t)y(s',t)q(s',t)\frac{\ell(s')C_d\pi^d(1 - \pi)^{\ell(s') - d}}{|V(s',d)|}.
\]
We denote the truncated function of based on the model constructed in Subsection 2.1. To complete the model construction, which will be necessary in performing numerical experiments

\[
q(s, t + \Delta t) = \frac{x(s, t) - \dot{x}(s, t)}{x(s, t)} q(s, t) + o(s, t)y(s, t) q(s, t)(1 - \pi)^{\ell(s)} + \sum_{1 \leq d < \infty} \sum_{s' \in W(s, d)} o(s', t)y(s', t) q(s', t) \frac{\ell(s') C_d \pi'^d (1 - \pi)^{\ell(s') - d}}{|V(s', d)|}.
\]

\[\text{(2)}\]

Expanding the left hand side of Equation (2) as \(q(s, t + \Delta t) = q(s, t) + \Delta t \frac{\partial q(s, t)}{\partial t}\) in a Taylor series with respect to \(t\) and rearranging the equation provides

\[
\frac{\partial q(s, t)}{\partial t} = \frac{1}{\Delta t} o(s, t)y(s, t) q(s, t)(1 - \pi)^{\ell(s)} + \frac{1}{\Delta t} \sum_{1 \leq d < \infty} \sum_{s' \in W(s, d)} o(s', t)y(s', t) q(s', t) \frac{\ell(s') C_d \pi'^d (1 - \pi)^{\ell(s') - d}}{|V(s', d)|} - \frac{1}{\Delta t} y(s, t) q(s, t).
\]

Letting \(y(s, t), \Delta t \to 0\) and \(y(s', t), \Delta t \to 0\) with the ratios \(y(s, t)/\Delta t\) and \(y(s', t)/\Delta t\) constant, we obtain Equation (1) by the assumption of the proposition.

\(q(s', t)\) in the third term of the right hand side of Equation (2) cannot be expanded in a Taylor series with respect to \(s'\) because \(s\) is a discrete variable, and consequently, the resultant equation, Equation (1), does not include partial derivatives with respect to \(s'\) in the right hand side, unlike the diffusion equation.

2.3 Models of the selection pressure and mutation

In this subsection, we formulate models of the selection pressure \(p(s, E)\) and stochastic mutation \(m\) to complete the model construction, which will be necessary in performing numerical experiments based on the model constructed in Subsection 2.1.

We suppose that the critical value of selection pressure is \(p_E = 1\) for a given environment \(E \in \mathcal{E}\) without the loss of generality. Let \(D_j \subset A^*\) for each \(j = 1, \cdots, k\) and \(D_j \cap D_{j'} = \emptyset\) if \(j \neq j'\). For \(\lambda_j \in A^*\) and \(\rho_j \in (0, \infty)\), we define the function \(\phi(\cdot, \lambda_j, \rho_j) : A^* \to [0, 1]\) as

\[
\phi(s, \lambda_j, \rho_j) = \frac{1}{(\rho_j + 1)|V(\lambda_j, d_L(s, \lambda_j))|} \left(\frac{\rho_j}{\rho_j + 1}\right)^{d_L(s, \lambda_j)}.
\]

We denote the truncated function of \(\phi(s, \lambda_j, \rho_j)\) on \(D_j\) by \(\phi_{D_j}(s, \lambda_j, \rho_j)\), i.e., \(\phi_{D_j}(s, \lambda_j, \rho_j) = \phi(s, \lambda_j, \rho_j) / \sum_{s \in D_j} \phi(s, \lambda_j, \rho_j)\) if \(s \in D_j\) and \(\phi_{D_j}(s, \lambda_j, \rho_j) = 0\) if \(s \notin D_j\). We set \(\lambda = (\lambda_1, \cdots, \lambda_k), \rho = (\rho_1, \cdots, \rho_k),\)
\(D = (D_1, \cdots, D_k)\), and \(w = (w_1, \cdots, w_k)\) for \(w_1, \cdots, w_k \in (0, 1)\). \(\phi_D(s, \lambda, \rho, w)\) represents the mixture model of \(\phi_{D_1}(s, \lambda_1, \rho_1), \cdots, \phi_{D_k}(s, \lambda_k, \rho_k)\) with mixture coefficients \(w_1, \cdots, w_k\). We define the selection pressure \(p(s, E)\) exerted by the environment \(E\) on \(s \in A^*\) as

\[
p(s, E) = \begin{cases} 
1 - \phi_D(s, \lambda, \rho, w) & \text{if } s \in \bigcup_{j=1}^{k} D_j, \\
\text{arbitrary number } \geq 1 & \text{otherwise.}
\end{cases}
\]

In this setting, \(D_1, \cdots, D_k\) are reproductive sequence domains under \(E\) and the truncated function of \(\phi_D(s, \lambda, \rho, w)\) on \(\hat{S}(t)\) (or \(S(t)\)) provides the relative fitness of each sequence in \(\hat{S}(t)\) (or \(S(t)\)).

We next formulate the mutation operator \(m\). \(m\) cannot be written by an analytic expression. We construct an algorithm generating a new mutated sequence based on a given sequence that satisfies the conditions (i) to (iii) described in the fifth paragraph of Section 2. The algebraic structure of \(A^*\) as a monoid is required for constructing \(m\). We introduce the empty letter \(e\) and set \(e \in A^*\). We have \(|e| = 0\). We define the concatenation \(s \cdot s'\) as \(s \cdot s' = x_1 \cdots x_{|s|} x'_1 \cdots x'_{|s'|}\) for \(s = x_1 \cdots x_{|s|}, s' = x'_1 \cdots x'_{|s'|} \in A^*\). The concatenation \(\cdot\) is an interior operation in \(A^*\), and \(A^*\) forms a monoid with an identity \(e\). The metric topology of \(d_L\) on \(A^*\) is the discrete topology. Therefore, \(A^*\) forms a topological monoid. DNA replication is performed by DNA polymerase’s adding nucleotides to one end of the newly forming DNA strand based on the order of nucleotides in a template DNA sequence, and mutations are errors that occurred in this process. Therefore, we define the mutation operator \(m\) by combining the following algorithm and models of insertion, deletion, and substitution of nucleotides provided by Definitions 1 and 2. We set \(\bar{A} = A \cup \{e\}\).

**Definition 1** Model 1 (Insertion) Suppose that we are at the \(i_0\)th step of the \(i\)-loop of Algorithm 1. If (i) \(i_0 \geq 2\), (ii) the \((i_0 - 1)\)th letter of the input string \(s\) is equal to \(x \in A\), (iii) the letter \(x\) was deleted (i.e., \(y_2 = e\)) at the \((i_0 - 1)\)th step of the \(i\)-loop, and (iv) no letters except \(x\) was inserted (i.e., \(y_1 \notin A \setminus \{x\}\)) at all previous steps of the \(j\)-loop, generate \(y \in \bar{A}\) according to the probability function

\[
\psi_I(y; \pi) = \begin{cases} 
1 - \pi & \text{if } y = e, \\
\pi/3 & \text{if } y = A \setminus \{x\}, \\
0 & \text{if } y = x
\end{cases}
\]
Algorithm 1  Generate a mutated sequence

Require:  \( s \in A^*, c \in \mathbb{Z}^+, \pi \in (0, 1) \)

1: \( \ell \leftarrow |s|; s' \leftarrow e \)

2: for \( i = 1, \cdots, \ell \) do

3: \hspace{1em} for \( j = 1, \cdots, c \) do

4: \hspace{2em} Choose \( y_1 \in \bar{A} \) according to Model 1 \hspace{1em} \triangleright \text{Whether a substring is inserted or not before each letter is determined.}

5: \hspace{3em} if \( y_1 \neq e \) then

6: \hspace{4em} \( s' \leftarrow s' \cdot y_1 \) \hspace{1em} \triangleright \text{Insertion}

7: \hspace{3em} end if

8: \hspace{2em} end for

9: Choose \( y_2 \in \bar{A} \) according to Model 2 \hspace{1em} \triangleright \text{Whether each letter is substituted or deleted, or no edit is performed is determined.}

10: \hspace{2em} if \( y_2 \neq e \) then

11: \hspace{3em} \( s' \leftarrow s' \cdot y_2 \) \hspace{1em} \triangleright \text{Substitution}

12: \hspace{2em} else

13: \hspace{3em} \( s' \leftarrow s' \) \hspace{1em} \triangleright \text{Deletion}

14: \hspace{2em} end if

15: \hspace{2em} end for

16: for \( k = 1, \cdots, c \) do

17: \hspace{1em} Choose \( y_3 \in \bar{A} \) according to Model 1

18: \hspace{2em} if \( y_3 \neq e \) then

19: \hspace{3em} \( s' \leftarrow s' \cdot y_3 \) \hspace{1em} \triangleright \text{Insertion}

20: \hspace{3em} end if

21: \hspace{2em} end for

22: return \( s' \)
on $\bar{A}$, otherwise generate $y \in \bar{A}$ according to

$$\psi_I(y; \pi) = \begin{cases} 
1 - \pi & \text{if } y = e, \\
\pi/4 & \text{if } y \in A.
\end{cases}$$

In the $k$-loop after the $i$-loop, the above (ii) to (iv) are changed into the following (ii') to (iv'), respectively. (ii') The last letter of the input string $s$ is equal to $x \in A$. (iii') The letter $x$ was deleted (i.e., $y_2 = e$) at the last step of the $i$-loop. And (iv') no letters except $x$ was inserted (i.e., $y_3 \notin A \setminus \{x\}$) at all previous steps of the $k$-loop.

**Definition 2** Model 2 (Substitution and deletion) Suppose that we are at the $i_0$th step of the $i$-loop of Algorithm 1. If (i) the $i_0$th letter of the input string $s$ is equal to $x \in A$ and (ii) the last letter inserted during the $j$-loop is equal to $x$, generate $y \in \bar{A}$ according to the probability function

$$\psi_{DS}(y; \pi) = \begin{cases} 
1 - \pi & \text{if } y = x, \\
\pi/3 & \text{if } y \in A \setminus \{x\}, \\
0 & \text{if } y = e
\end{cases}$$

on $\bar{A}$, otherwise generate $y \in \bar{A}$ according to

$$\psi_{DS}(y; \pi) = \begin{cases} 
1 - \pi & \text{if } y = x, \\
\pi/4 & \text{if } y \in \bar{A} \setminus \{x\}.
\end{cases}$$

In actual replication of DNA, a complementary sequence including mutations is composed from a template sequence (in this case, a parent sequence). Therefore, to be exact, an input string $s$ of Algorithm 1 should be interpreted as a complementary sequence including no mutations of a parent sequence. However, no problems occur in numerical experiments even if $s$ is considered a parent sequence. It is verified that Algorithm 1 as a mapping from $A^*$ to $A^*$ satisfies conditions (i) to (iii) described in the fifth paragraph of Section 2. Therefore, we define the mutation operator $m$ as the operator that maps an element of $A^*$ to other element according to Algorithm 1.

### 3 Specification of the problem

In this section, we introduce several definitions and specify problems to be considered in the following sections. We begin by defining the differentiation of a population of DNA sequences. Any
subset of $A^*$ is open because the topology of $A^*$ with respect to $d_L$ is the discrete topology. Thus, $D \subset A^*$ is a domain in the mathematical sense if it cannot be represented as the union of two or more nonempty disjoint subsets of $A^*$.

**Definition 3 (Reproductive sequence domain)** We say that a domain $D \subset A^*$ is a reproductive sequence domain under an environment $E \in \mathcal{E}$ if $p_E - p(s;E) > 0$ holds for any $s \in D$.

A reproductive sequence domain is not a geographical region but a subset of $A^*$ of which DNA sequences that can produce offspring sequences in a given environment are composed.

For asexual populations such as microbial populations, we say that speciation occurred if DNAs of a new population are sufficiently far from those of an original population (homologies between any pair of DNAs or specific genes in the two populations are lower than a certain threshold).

On the other hand, for sexual populations, we say that speciation occurred if any pair of a male and female in a new and original populations cannot produce offspring that have reproductive capacities. It is frequently difficult to test whether a biological population differentiated in natural environments according to this definition for the latter populations. However, the reason why any pair of a male and female in the two populations cannot produce offspring that have reproductive capacities would be that DNA sets of the two populations are sufficiently different. Therefore, in this study, we formulate the differentiation of a population as follows:

**Definition 4 (DNA population differentiation)** We suppose that there exist two reproductive sequence domains $D_1, D_2 \subset A^*$ under the environment $E \in \mathcal{E}$. Let $S(t)$ be a population of DNA sequences at time $t$ from an ancestor sequence born in $D_1$. We say that $S(t)$ differentiated at time $t_0 \in [0, \infty)$ if (i) an offspring sequence $s' \in D_2$ was generated from a sequence $s \in S(t_0)$ at time $t_0$ by mutation and (ii) $S(t) \cap D_2 = \emptyset$ holds for any $t < t_0$.

Lastly, we define the equilibrium state of a DNA population $S(t)$. The extent to which two biological communities differ is called $\beta$ dissimilarity or $\beta$ diversity and have studied in ecology. Here, the difference includes that of a population between two time points and that between two different populations. The $\beta$ dissimilarity $d_\beta(S_1, S_2)$ between two populations $S_1$ and $S_2$ of DNA
sequences that two biological communities have was introduced and applied in [16] after investigating a method for estimating it. Using \( d_\beta \), the evolutionary rate of a DNA population \( S(t) \) at time \( t \) can be defined as

\[
\dot{S}(t) = \lim_{\Delta t \to 0} \frac{d_\beta(S(t + \Delta t), S(t))}{\Delta t}.
\]

(Lots of studies have been conducted with respect to evolutionary rate in evolutionary biology. See, for example, [20].) Therefore, according to the traditional manner, the equilibrium state of a population \( S(t) \) can be defined as follows: \( S(t) \) is in the equilibrium state during \( [t_0, t_1] \subset [0, \infty) \) if \( \dot{S}(t) = 0 \) holds for any \( t \in [t_0, t_1] \). However, this definition of equilibrium state is not useful for \( S(t) \) because there always exists a possibility that offspring sequences of sequences in \( S(t) \) include mutations that occur randomly. Therefore, in this study, we consider a sort of equilibrium state defined as follows:

**Definition 5 (near equilibrium state)** A population \( S(t) \) is in the near equilibrium state during \( [t_0, t_1] \subset [0, \infty) \) if \( S(t) \) satisfies the following conditions.

1. There exists \( M \subset D \) satisfying \( M \neq \emptyset \) such that if \( t \in [t_0, t_1] \), then \( S(t) \supseteq M \).
2. \( o(s, t) = 0 \) holds for any \( t \in [t_0, t_1] \) and \( s \in S(t) \cap M^c \).

In a state of near equilibrium, the population \( S(t) \) always includes sequences equal to \( s \) for any \( s \in M \), the relative frequency \( q(s, t) \) of them is updated at each time \( t \) according to Equation (1), and, even if sequences were born outside \( M \) by mutation, they cannot produce offspring. This is a minimum variation in \( S(t) \) under stochastic mutation and selection pressure from the environment.

In Section 4, we first consider the problem of under what conditions \( S(t) \) differentiates or not in the sympatric setting rather than in the allopatric setting, in other words, without supposing that \( S(t) \) is divided into two subpopulations that live in different environments \( E \) and \( E' \) and therefore are under selection pressures based on different selection pressure functions \( p(s, E) \) and \( p(s, E') \). We subsequently consider whether \( S(t) \) can reach and maintain a state of near equilibrium under some condition. Furthermore, we calculate the differentiation probability of \( S(t) \) and the time expected to elapse before \( S(t) \) differentiates.
4 Theoretical analysis

In this section, we address the problems specified in the previous section. We first consider in what situations a population of DNA sequences differentiates or not as time elapses. We set $U(s, d) = \{s' \in A^* : d_L(s, s') \leq d\}$ for $s \in A^*$ and $d \in \mathbb{N}$. We denote the almost sure convergence by $\overset{\text{a.s.}}{\rightarrow}$.

**Proposition 2 (Condition for differentiation)** We suppose that there exist two reproductive sequence domains $D_1, D_2 \subset A^*$ under an environment $E \in \mathcal{E}$. Let $S(t)$ be a population of DNA sequences at time $t$ from an ancestor sequence born in $D_1$. If the following conditions (1) to (3) are satisfied, the probability that $S(t)$ differentiates into $D_2$ approaches one as $t \to \infty$. Conversely, if the negation of the condition (1) holds, then $S(t)$ does not differentiate for any $t \in [0, \infty)$.

1. There exist $s_1 \in D_1$ and $s_2 \in D_2$ such that $d_L(s_1, s_2) \leq \ell(s_1)$ holds.
2. $p(s, E) = 1/|D_1|$ for any $s \in D_1$.
3. $n(t) \geq 1$ for any $t \in [0, \infty)$.

The former statement in the above proposition indicates that, wherever in a reproductive sequence domain $D_1$ an ancestor sequence was born, the population differentiates with high probability if there exists another reproductive sequence domain near to $D_1$ (condition (1)) and the selection pressure is close to the uniform distribution (condition (2)). The conditions of Proposition 2 do not include those of the split of one population into two geographically isolated populations for reproductive isolation. They are conditions for reproductive isolation to occur in a population living in one habitat. Therefore, if the differentiation described in the proposition is speciation, it is not allopatric but sympatric speciation (see, for example, [3, 10–12] for articles on theoretical studies on sympatric speciation and [1] for a review). Even if there exists another reproductive sequence domain nearby, $S(t)$ does not necessarily differentiate, as demonstrated in Corollary 2 below.

**Proof.** The set of sequences that can be produced by $s \in D_1$ is $U(s, \ell(s))$, and thus, the latter part of the proposition is trivial. Therefore, we demonstrate the former part.

(Step 1) We denote the numbers of sequences in the population $\{S(t') : 0 \leq t' \leq t\}$ that die by time $t$ and that are equal to $s$ and die by $t$ by $\kappa(t)$ and $\kappa(s, t)$, respectively, for $t \in [0, \infty)$ and $s \in D_1$. 

Noting that the number of strings that are equal to or less than \( \ell \) in length is equal to \( \sum_{\ell'=1}^{\ell} 4^{\ell'} + 1 \) for \( \ell \in \mathbb{N} \), we have \( |A^*| < \infty \) from the definition of a string (see the second paragraph of Section 1). Therefore,

\[
|D_1| < \infty
\]

(3)

holds from \( D_1 \subset A^* \). Using the conditions (3) of the proposition and \( C_1 \) described in the third paragraph of Section 2, we obtain

\[
\kappa(t) \rightarrow \infty
\]

(4)

as \( t \rightarrow \infty \). From Equations (3) and (4), there exists \( s \in D_1 \) such that \( \kappa(s, t) \rightarrow \infty \) as \( t \rightarrow \infty \). Choosing such a \( s \in D_1 \), we have \( o(s, t) \rightarrow \infty \) as \( t \rightarrow \infty \) from the conditions (2) and (3) and the definition of \( o(s, t) \) in the fifth paragraph of Section 2.

(Step 2) We arbitrarily choose \( s' \in U(s, \ell(s)) \) for \( s \in D_1 \) chosen in Step 1. We regard the production of an offspring sequence by a sequence in \( S(t) \) that is equal to \( s \) as a trial that is a success if the sequence produces an offspring sequence equal to \( s' \) by mutation and is a failure otherwise. Let \( p_i \) represent the success probability of the \( i \)th trial, counting from the first trial performed by a sequence in \( \{S(t) : t \geq 0\} \) that are equal to \( s \). By the definition of the mutation operator \( m \) in the sixth paragraph of Section 2, \( p_i \) is constant, not depending on \( i \) (hence, \( p_i \) is written as \( p \) hereafter), and the trials are independent. Therefore, this trial is a Bernoulli trial. We have

\[
p = \ell(s) C_{d_L(s, s')} \pi^{d_L(s, s')} (1 - \pi)^{\ell(s) - d_L(s, s')} > 0
\]

(5)

from \( d_L(s, s') \leq \ell(s) \) and \( \pi \in (0, 1) \). Let \( X_i \) be a Bernoulli variable that takes one if the \( i \)th trial is a success and zero otherwise. Using the result obtained in Step 1, the strong law of large numbers, and Equation (5), we obtain \( \sum_{i=1}^{n} X_i/n \overset{a.s.}{\longrightarrow} p \) and consequently \( \sum_{i=1}^{n} X_i \overset{a.s.}{\longrightarrow} \infty \) as \( n \rightarrow \infty \). This means that sequences in \( \{S(t) : t \geq 0\} \) that are equal to \( s \) produce offspring sequences equal to \( s' \) infinite times with probability one as \( t \rightarrow \infty \). The above discussion is independent of the choice of \( s' \in U(s, \ell(s)) \), and therefore, we have \( \kappa(s', t) \overset{a.s.}{\longrightarrow} \infty \) as \( t \rightarrow \infty \) for any \( s' \in U(s, \ell(s)) \). Thus, we have \( o(s', t) \overset{a.s.}{\longrightarrow} \infty \) as \( t \rightarrow \infty \) from the conditions (2) and (3) and the definition of \( o(s, t) \). Repeating the same discussion as above provides \( o(s'', t) \overset{a.s.}{\longrightarrow} \infty \) as \( t \rightarrow \infty \) for any \( s'' \in D_1 \) because \( D_1 \) is a domain in the mathematical sense.
(Step 3) From the result of 2, we have $o(s_1, t) \xrightarrow{a.s.} \infty$ as $t \to \infty$ for $s_1 \in D_1$ satisfying the condition (1). Therefore, conducting the same discussion as in Step 2, from the condition (1), we observe that sequences in $\hat{S}(t)$ that are equal to $s_1$ produce sequences in $D_2$ infinite times with probability one as $t \to \infty$. This completes the proof of the former part of the proposition.

$$\{ s \in S(t) : p(s, E) \geq p_E \}$$ is the set of sequences in a DNA population $S(t)$ that were produced outside all reproductive sequence domains by mutation and, therefore, cannot produce offspring.

If $\{ s \in S(t) : p(s, E) < p_E \} \subseteq M$ (proper subset) holds for $M \subset A^*$, we write $S(t) < M$. $\mathbb{Z}^+$ represents the set of positive integers. As the following proposition describes, under certain conditions, it is determined whether sympatric speciation occurs or a population continues to move around randomly in a subset of $A^*$, depending on the existence or nonexistence of other reproductive sequence domain nearby.

**Corollary 1** We suppose that there exist two reproductive sequence domains $D_1, D_2 \subset A^*$ under an environment $E \in \mathcal{E}$. Let $S(t)$ be a population of DNA sequences at time $t$ from an ancestor sequence born in $D_1$. If the following conditions (1) to (3) are satisfied, the probability that $S(t)$ differentiates into $D_2$ approaches one as $t \to \infty$. On the other hand, if the conditions (2) and (3) and the negation of the condition (1) are satisfied, then $S(t)$ continues to move around randomly in $D_1$ as $t \to \infty$.

1. There exist $s_1 \in D_1$ and $s_2 \in D_2$ such that $d_L(s_1, s_2) \leq \ell(s_1)$ holds.
2. $p(s, E) = 1/|D_1|$ for any $s \in D_1$.
3. There exist $t_0 \in [0, \infty)$ and $n^* \in \mathbb{Z}^+$ such that $1 \leq n(t) \leq n^*$ for any $t \geq t_0$ and $n^* < |D_1|$ hold.

**Proof.** The former part of the proposition is immediately obtained from the former part of Proposition 2. Therefore, we demonstrate the latter part. Using the conditions (2) and (3), we have $\kappa(s, t) \xrightarrow{a.s.} \infty$ as $t \to \infty$ for any $s \in D_1$ by the same discussion in Steps 1 and 2 in the proof of Proposition 2. However, from the negation of the condition (1) and Proposition 2, $S(t)$ does not differentiate into $D_2$ for any $t \in [0, \infty)$. Consequently, $S(t) < D_1$ holds from the condition (3). Therefore, we arbitrarily choose $s_0 \in D_1 \setminus S(t)$. Conducting the same discussion in Steps 1 and 2 in the proof of Proposition 2 from the conditions (2) and (3) again, we obtain $\kappa(s_0, t) \xrightarrow{a.s.} \infty$ as
Choosing a sequence from \( D_1 \setminus S(t) \) arbitrarily for each \( t \in [0, \infty) \) and repeating the above discussion, we see that \( S(t) \) continues to move around randomly in \( D_1 \) as \( t \to \infty \).

From the above proposition, we found that under the listed conditions a population of DNA sequences maintains a state of nonequilibrium. There exist species called living fossils whose phenotypes have been nearly unchanged for a long time. Therefore, we next consider whether it is possible that a DNA population have undergone little change for a long period. This problem is restated as whether a DNA population can maintain a state of near equilibrium under some condition. There exist examples (e.g., shark) in which phenotypes have been nearly unchanged, but DNA sequences have changed more than expected. Thus, depending on whether the above problem is positively solved or negatively solved, it is determined whether there exist two possible explanations or there exists only one explanation at the sequence level for the phenomena that phenotypes have been nearly unchanged for a long time.

To solve the above problem we introduce the following definition: \( \hat{n}(t) \) is consistent with \( p(s, E) \) if \( p(s, E) = p(s', E) \) implies \( o(s, t) = o(s', t) \) for any \( s, s' \in \hat{R}(t) \). In addition, we introduce the following condition \( C_3 \): For any \( t \in [0, \infty) \) and \( s \in S(t) \),

\[
o(s, t)b(s, t)q(s, t)(1 - \pi)^{\ell(s)} > o(s, t)b(s, t)q(s, t) \sum_{d=1}^{\ell(s)} C_d \pi^d (1 - \pi)^{\ell(s) - d}
\]

holds. \( C_3 \) means that the mutation probability \( \pi \) is sufficiently small, such that the number of offspring sequences without mutations that each sequence produces is less than that of offspring sequences with mutations. From here to the end of Corollary 2 below, we consider the case of \( \gamma = 1 \). Therefore, we have \( R(t) = \hat{R}(t) \). We set \( \langle R(t) \rangle = \{ s \in R(t) : o(s, t) \neq 0 \} \) for any \( t \in [0, \infty) \). As the following proposition shows, if the size of a population that an environment can accommodate decreases because of environmental change and so on, and subsequently the population size remains constant, a DNA population can maintain a state of near equilibrium in the case where the mutation probability is sufficiently low.

**Proposition 3 (Conditions for near equilibrium state)** Let \( D \subset \mathbb{A}^* \) be a reproductive sequence domain under an environment \( E \in \mathcal{E} \) and \( S(t) \) be a population of DNA sequences at time \( t \). We suppose that \( t_0, t_1, t_2 \in [0, \infty) \) are time points satisfying \( t_0 < t_1 < t_2 \). If the following conditions are
satisfied, $S(t)$ maintains a state of near equilibrium during $[t_1, t_2] \subset [0, \infty)$.

(1) $n(t)$ monotonically decreases with $t \in [t_0, t_1]$.

(2) There exists $n^* \in \mathbb{Z}^+$ such that $n(t) = n^*$ holds for any $t \in [t_1, t_2]$.

(3) $n^*$ is consistent with $p(s, E)$ (this condition makes sense from the condition (2) above and the assumption of $\gamma = 1$).

(4) Condition $C_3$ is satisfied.

(5) For any $s \in \langle R(t_1) \rangle$, there does not exist $s' \in (\bigcup_{t_0 \leq t \leq t_1} R(t))^c$ that satisfies

$$d_L(s, s') \leq l(s), \quad p(s', E) \leq \max\{p(s''', E) : s''' \in \langle R(t_1) \rangle\}.$$

**Proof.** First, we have

$$\langle R(t_1) \rangle \neq \emptyset$$

from the condition (2). Using the conditions (2) and (3) provides $o(s, t) \neq 0$ for any $s \in \langle R(t_1) \rangle$ and $t \in [t_1, t_2]$. Thus, $s \in R(t)$ holds from the condition (4), and therefore, we have

$$R(t) \supset \langle R(t_1) \rangle.$$  

From the condition (1), $\bigcup_{t_0 \leq t \leq t_1} \langle R(t) \rangle$ is a set obtained by adding sequences that can produce offspring when the population size is greater than $n^*$ to those that can produce offspring when it is equal to $n^*$. Hence, using the condition (2), we obtain

$$o(s'', t) = 0$$

for any $s'' \in \bigcup_{t_0 \leq t \leq t_1} \langle R(t) \rangle \setminus \langle R(t_1) \rangle$ and $t \in [t_1, t_2]$. Noting the condition (5), we observe that even if a sequence in $S(t)$ produces a sequence $s' \in (\bigcup_{t_0 \leq t \leq t_1} \langle R(t) \rangle)^c$ by mutation,

$$o(s', t) = 0$$

holds. From Equations (8) and (9) and $\langle R(t_1) \rangle \subset \bigcup_{t_0 \leq t \leq t_1} \langle R(t) \rangle$, we have

$$o(s, t) = 0$$

for any $s \in \langle R(t_1) \rangle$ and $t \in [t_1, t_2]$. Combining Equations (6), (7), and (10) completes the proof of the proposition.
Using Proposition 3, we see that it is possible that a DNA population maintains a state of near equilibrium and does not differentiate even if there exists other reproductive sequence domain nearby.

**Corollary 2** Let $D_1, D_2 \subset A^*$ be reproductive sequence domains and we consider the situation in which there exists $s \in D_1$ that can produce $s' \in D_2$ by mutation. $S(t)$ represents a population of DNA sequences at time $t$. We suppose that the conditions (1) to (5) of Proposition 3 with $t_2 = \infty$ are satisfied. If $S(t)$ does not differentiate into $D_2$ within $[0,t_1]$, then $S(t)$ no longer differentiate into $D_2$.

**Proof.** Trivial from Proposition 3. □

We next calculate the probability that a population $S(t)$ of DNA sequences at time $t$ from an ancestor sequence born in a reproductive sequence domain $D_1 \subset A^*$ differentiates into another reproductive sequence domain $D_2 \subset A^*$. Let $\hat{S}(t, D_2)$ be a set of $s \in \hat{S}(t)$ for which there exists $s' \in D_2$ such that $d_L(s, s') \leq \ell(s)$ holds. We denote a set of $s' \in D_2$ satisfying $d_L(s, s') \leq \ell(s)$ by $D_2(s \in \hat{S}(t))$ for each $s \in \hat{S}(t, D_2)$. We put $h(s) = \min\{d_L(s, s') : s' \in D_2\}$ for each $s \in \hat{S}(t, D_2)$. We set $z(s,d) = ||s' \in D_2(s \in \hat{S}(t)) : d_L(s, s') = d||$ for any $s \in \hat{S}(t, D_2)$ and $d \in \{h(s), \ldots, \ell(s)\}$.

**Lemma 1 (Probability of differentiation)** We suppose that there exist two reproductive sequence domains $D_1, D_2 \subset A^*$ under an environment $E \in \mathcal{E}$. Let $S(t)$ be a population of DNA sequences at time $t$ from an ancestor sequence born in $D_1$. If there exists the limit $b(s,t)$ of $y(s,t)$ letting $y(s,t), \Delta t \to 0$ with the ratio $y(s,t)/\Delta t$ constant for any $s \in A^*$ and $t \in [0,\infty)$, the probability that $S(t)$ differentiates into $D_2$ at time $t$ is provided by

$$\zeta(t) = \sum_{s \in \hat{S}(t, D_2)} o(s,t)b(s,t)q(s,t) \sum_{d=h(s)}^{\ell(s)} \frac{z(s,d)}{|V(s,d)|} C_d \pi^d (1-\pi)^{\ell(s)-d}. \quad (11)$$

**Proof.** Noting that only sequences in $\hat{S}(t)$ that belong to $\hat{S}(t, D_2)$ can produce sequences in $D_2$ by mutation, that we have $h(s) \leq d_L(s, s') \leq \ell(s)$ for any $s \in \hat{S}(t, D_2)$ and $s' \in D_2(s \in \hat{S}(t))$, and that the ratio of sequences that belong to $D_2$ of sequences $s' \in A^*$ satisfying $d_L(s, s') = d$ for $s \in \hat{S}(t, D_2)$ is $z(s,d)/|V(s,d)|$, we observe that the probability that $S(t)$ differentiates into $D_2$ at time $t$ is provided by Equation (11). □
Using Proposition 1, we derive a formula of the expected time for estimating how much time passes until population differentiation. We first consider the case where \( t \) is discrete and represents a generation number. The number of generations that elapse before population differentiation is the number of generations that elapse before the first success when the trial is repeated in which the probability that each sequence of each generation produces offspring in a reproductive sequence domain different from that where an ancestor sequence was born is a success probability. This trial is a Poisson trial because the success probability is \( \zeta(t) \) provided by Equation (11) and varies with each trial. Therefore, the distribution of probability that the first success is obtained by a sequence in the \( t \)th generation is the distribution of waiting time when the Poisson trial with a sequence \( \{\zeta(t) : t \in \mathbb{N}\} \) of success probabilities is repeated, and thus, its probability function is provided by \( f(t, \{\zeta(t') : t' \in \mathbb{N}\}) = \zeta(t) \prod_{t'=0}^{t-1} (1 - \zeta(t')) \). However, it is impossible to calculate the expected value of this probability function, i.e., the sum of the series \( \sum_{t=0}^{\infty} t \zeta(t) \prod_{t'=0}^{t-1} (1 - \zeta(t')) \). The expected value of the geometric distribution, which is the distribution of waiting time until the first success when the Bernoulli trial with a constant success probability \( p \) is repeated, is equal to \( 1/p \), i.e., the number \( n \) of trials satisfying \( np = 1 \). Following this idea, we referred to the minimum \( \tau \in \mathbb{N} \) satisfying \( \sum_{t=0}^{\tau} \zeta(t) \geq 1 \) as the pseudo expected number of trials repeated until the first success in the above Poisson trial is obtained and denote it by \( E^*(\tau) \). Note that there does not necessarily exist \( t \in \mathbb{N} \) satisfying \( \sum_{t=0}^{T} \zeta(t) = 1 \). Substituting \( E^*(\tau) \) for \( E(\tau) \), we can obtain the following result in the case where \( t \) is continuous.

**Proposition 4 (Expected time before differentiation)** We suppose that there exist two reproductive sequence domains \( D_1, D_2 \subset A^* \) under an environment \( E \in \mathcal{E} \). Let \( S(t) \) be a population of DNA sequences at time \( t \) from an ancestor sequence born in \( D_1 \). Then, the pseudo expected time \( E^*(\tau) \) until \( S(t) \) differentiates into \( D_2 \) is provided by minimum \( \tau \in [0, \infty) \) satisfying \( \int_{0}^{\tau} \zeta(t) dt \geq 1 \).

**Proof.** Obvious from Lemma 1 and the definition of \( E^*(\tau) \).
important to estimate the selection pressure $p(s,t,E)$, mutation probability $\pi$, population size $n(t)$, and location of a different reproductive sequence domain $D_2$. In some cases $\pi$ and $n(t)$ can be estimated and predicted, but it may be difficult for us human beings to estimate $D_2$. A method for estimating $p(s,t,E)$ was investigated in [13].

5 Conclusion

In this study, we constructed the evolutionary model of a population of DNA sequences on the noncommutative topological monoid $A^*$ formed by strings on the alphabet $A$ composed of four letters a, c, g, and t and analyzed the constructed model in a theoretical manner. No molecular-evolutionary models have been constructed on $A^*$, however $A^*$ is a natural stage for molecular-evolutionary modeling because DNA sequences are represented as elements of $A^*$. It is a task in the future to tackle problems in molecular evolution that are difficult to address theoretically, applying the model developed here in a numerical manner.

References

[1] D. I. Bolnick and B. M. Fitzpatrick. Sympatric speciation: models and empirical evidence. Annual Review of Ecology, Evolution, and Systematics, 38:459–487, 2007.

[2] J. A. Coyne and H. A. Orr. Speciation. Sinauer, Sunderland, MA, 2004.

[3] U. Dieckmann and M. Doebeli. On the origin of species by sympatric speciation. Nature, 400(6742):354–357, 1999.

[4] U. Dieckmann, M. Doebeli, J. A. J. Metz, and D. Tautz, editors. Adaptive Speciation. Cambridge University Press, Cambridge, UK, 2012.

[5] M. Doebeli and U. Dieckmann. Evolutionary branching and sympatric speciation caused by different types of ecological interactions. American Naturalist, 156(Supplement):S77–S101, 2000.
[6] B. Drossel and A. McKane. Competitive speciation in quantitative genetic models. *Journal of Theoretical Biology*, 204(3):467–478, 2000.

[7] S. A. H. Geritz, É. Kisdi, G. Mesze, and J. A. J. Metz. Evolutionarily singular strategies and the adaptive growth and branching of the evolutionary tree. *Evolutionary Ecology*, 12:35–57, 1998.

[8] S. A. H. Geritz, J. A. J. Metz, É. Kisdi, and G. Meszéna. Dynamics of adaptation and evolutionary branching. *Physical Review Letters*, 78(10):2024–2027, 1997.

[9] P. G. Higgs and B. Derrida. Stochastic models for species formation in evolving populations. *Journal of Physics A*, 24:L985–L991, 1991.

[10] P. A Johnson, F. C. Hoppensteadt, J. J. Smith, and G. L. Bush. Conditions for sympatric speciation: a diploid model incorporating habitat fidelity and non-habitat assortative mating. *Evolutionary Ecology*, 10(2):187–205, 1996.

[11] M. Kawata. Invasion of vacant niches and subsequent sympatric speciation. *Proceedings of the Royal Society of London B*, 269(1486):55–63, 2002.

[12] A. S. Kondrashov and F. A. Kondrashov. Interactions among quantitative traits in the course of sympatric speciation. *Nature*, 400(6742):351–354, 1999.

[13] H. Koyano, M. Hayashida, and T. Akutsu. Optimal string clustering based on a Laplace-like mixture and EM algorithm on a set of strings. arXiv:1411.6471[math.ST].

[14] H. Koyano, M. Hayashida, and T. Akutsu. Maximum margin classifier working in a set of strings. *Proceedings of the Royal Society A*, 2016.

[15] H. Koyano and H. Kishino. Quantifying biodiversity and asymptotics for a sequence of random strings. *Physical Review E*, 81(6):061912(1)–061912(8), 2010.

[16] H. Koyano, T. Tsubouchi, H. Kishino, and T. Akutsu. Archaeal β diversity patterns under the seafloor along geochemical gradients. *Journal of Geophysical Research G: Biogeosciences*, 119(9):1770–1788, 2014.
[17] F. Manzo and L. Peliti. Geographic speciation in the Derrida–Higgs model of species formation. *Journal of Physics A*, 27(21):7079, 1994.

[18] P. Nosil. *Ecological Speciation*. Oxford University Press, Oxford, UK, 2012.

[19] A. R. Templeton. The theory of speciation via the founder principle. *Genetics*, 94(4):1011–1038, 1980.

[20] J. L. Thorne and H. Kishino. Divergence time and evolutionary rate estimation with multilocus data. *Systematic Biology*, 51(5):689–702, 2002.