Automata for DNA Splicing Languages with Two Restriction Enzymes

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DNA splicing system is modelled by the process of recombinant DNA that generates a language which is known as a splicing language. In DNA splicing system, molecules are cut and recombined with the existence of restriction enzymes and a ligase to produce new molecules. The molecules resulting from the splicing system depict the splicing language using formal language theory. In nature, the sequences of restriction enzyme can be recognised as palindromic or non-palindromic, where palindrome is a sequence of string which reads the same forwards and backwards. Research on splicing languages from DNA splicing systems has been done based on palindromic and non-palindromic restriction enzymes. In this research, the relation between DNA splicing language and concepts in automata theory is discussed. The splicing languages from the splicing system with one cutting site each of two palindromic or two non-palindromic restriction enzymes are deduced from the grammars. Then, the graphical representations of the languages generated by the grammars depicting the splicing languages are visualised as automata diagrams.

Keywords: Automata; DNA; Splicing language; Splicing system

I. INTRODUCTION

In 1987, (Head, 1987) introduced a study relating between formal language theory and informational macromolecules which is called a Deoxyribonucleic acid (DNA) splicing system. The splicing system is simulated by the process of recombinant DNA where restriction enzymes and a ligase cut and recombine DNA molecules to produce further molecules. The molecules resulting from the splicing system generate a language using formal language theory which is named as DNA splicing language (Head, 1987). In formal language, a set of strings consists of symbols derived from an alphabet. Some notations of regular expression in formal languages are applied in this research such as empty string λ, empty set ∅, union +, star-closure * and parentheses {} or () (Linz, 2006). A grammar G is a set of production rules for strings in formal language (Linz, 2006). The grammar generates strings by arranging the production rules in sequential order, known as a language, generated by the grammar.

The splicing system is made up of three sets via formal language theory. The first set consists of double stranded DNA (dsDNA) symbols formed by nitrogenous base pairings: adenine (A) pairs with thymine (T), while cytosine (C) pairs with guanine (G) (Paun et al., 1998). Next, the second set is the set containing initial DNA molecules or strings which is obtained from some fragments of protein or nucleotide sequences (Brejová et al., 2000). The third set involves the cleavage of restriction enzymes which acts as rules in the form of a triple (Head, 1998).

From splicing systems, the resulting splicing languages can be generalised based on the sequences of restriction enzymes. Palindrome refers to the sequence of
restriction enzyme that reads the same forwards and backwards (Tomohiro, 2013). Previously, research on the generalised splicing languages resulting from DNA splicing systems involving palindromic and non-palindromic restriction enzymes has been done (Ismail et al., 2019, Fong, 2019). The name, sequence and cleavage for all restriction enzymes used in this research are obtained from the New England Biolabs (NEB) catalogue (New England Biolabs Inc., 2017).

This research focuses on the relation between DNA splicing systems and the concepts of automata. An automaton is constructed with a set of states where the current state can either accept or reject the input when moving to the next state through the transition functions (Linz, 2006). The inputs accepted from every transition depict the language generated by the automaton.

In this research, the graphical representations for DNA splicing systems with two palindromic or two non-palindromic rules for restriction enzymes with the same and different crossings are illustrated as deterministic finite automata using grammars.

II. PRELIMINARIES

In this research, the modelling of DNA splicing systems with palindromic and non-palindromic rules is done using Head’s splicing model. The definitions of Head’s splicing model and splicing language are stated in the following.

Definition 1 (Head, 1987) Splicing System and Splicing Language
A splicing system \( S = (A, I, B, C) \) consists of a finite alphabet \( A \), a finite set \( I \) of initial strings in \( A^* \), and finite sets \( B \) and \( C \) of triples \((c, x, d)\) with \( c, x \) and \( d \) in \( A^* \). Each such triple in \( B \) or \( C \) is called a pattern. For each such triple the string \( cxd \) is called a site and the string \( x \) is called a crossing. Patterns in \( B \) are called left patterns and patterns in \( C \) are called right patterns. The language \( L = L(S) \) generated by \( S \) consists of the strings in \( I \) and all strings that can be obtained by adjoining to \( ucxfq \) and \( pexdv \) whenever \( ucxdv \) and \( pexfq \) are in \( L \) and \((c, x, d) \) and \((e, x, f) \) are patterns of the same hand. A language, \( L \) is a splicing language if there exists a splicing system \( S \) for which \( L = L(S) \).

Next, the definition of a palindromic string is presented.

Definition 2 (Yusof, 2012) Palindromic String
A string \( I \) of a dsDNA is said to be palindromic if the sequence from the left to the right side of the upper single strand is equal to the sequence from the right to the left side of the lower single strand.

The definition of a deterministic finite automaton is presented next.

Definition 3 (Linz, 2006) Deterministic Finite Automaton
A deterministic finite automaton \( M \) is a 5-tuple, \((Q, \Sigma, \delta, q_0, F)\) consisting of a finite set of states \( Q \), a finite set of input symbols called the alphabet \( \Sigma \), a transition function \((\delta : Q \times \Sigma \rightarrow Q)\), an initial state \( q_0 \in Q \) and a set of final states \( F \subseteq Q \).

Lastly, the definition of a grammar is shown below.

Definition 4 (Linz, 2006) Grammar
A grammar \( G \) is defined as a quadruple \( G = (V, T, S, P) \), where \( V \) a is finite set of objects called variables, \( T \) is a finite set of objects called terminal symbols, \( S \in V \) is a special symbol called the start variable and \( P \) is a finite set of productions.

The set \( L(G) = \{w \in T^* : S \Rightarrow w\} \) is the language generated by \( G \), where \( \Rightarrow \) denotes zero or more steps of sequence of productions.

Figure 1 shows an example of a deterministic finite automaton that accepts the language \( L((a+b) \cdot c^*) \) generated by the grammar with \( P \) consisting of the productions

\[
\begin{align*}
S_0 & \rightarrow aS_1 \mid bS_1, \\
S_1 & \rightarrow cS_1 \mid \lambda,
\end{align*}
\]

where \( Q = \{S_0, S_1\} \), \( \Sigma = \{a, b, c\} \), \( S_0 \) is the initial state, \( F = \{S_1\} \) and \( \delta \) is given by

\[
\delta(S_0, a) = S_1,
\]
\[
\delta(S_n, b) = S_n,
\delta(S_n, c) = S_n.
\]

Figure 1. A deterministic finite automaton

The automaton makes a move from the current state to another state based on the transition function and accepts the input symbols. In the automaton, single circle, double circle, arrows and arrow labels denote as the state, final state, transitions, and input symbols respectively.

### III. RESEARCH METHODOLOGY

The graphical representations for DNA splicing systems with one cutting site each of two palindromic or two non-palindromic rules for the same and different crossings are visualised as automata diagrams using the generalised splicing languages obtained from the respective DNA splicing systems.

Table 1 shows the generalised splicing languages from DNA splicing systems with two palindromic rules where Theorem 1 involves the same crossing and Theorem 2 involves different crossings of palindromic rules. While Table 2 shows the generalised splicing languages from DNA splicing systems with two non-palindromic rules where Theorem 3 involves the same crossing and Theorem 4 involves different crossings of non-palindromic rules.

| Theorem | Theorem 1 (Ismail et al., 2019) | Theorem 2 (Ismail et al., 2019) |
|---------|---------------------------------|---------------------------------|
| Initial String | \(N_1N_1 \ldots N_1N_2 \ldots N_2\) | \(N_1N_1 \ldots N_1N_2 \ldots N_2\) |
| First Restriction Enzyme | \(X_1YX_2\) | \(X_1YX_2\) |
| Second Restriction Enzyme | \(W_1YW_2\) | \(W_1YW_2\) |
| Splicing Language | \(\{N_1N_1 \ldots N_1N_2 \ldots N_2\}\) | \(\{N_1N_1 \ldots N_1N_2 \ldots N_2\}\) + \(\{N_1N_1 \ldots N_1N_2 \ldots N_2\}\) |
| | \(\{X_1YX_2\}\) | \(\{X_1YX_2\}\) |
| | \(\{W_1YW_2\}\) | \(\{W_1YW_2\}\) |

| Table 2. Generalised Splicing Languages from DNA Splicing Systems with Two Non-Palindromic Rules |
|---|---|
| Theorem | Theorem 3 (Fong et al., 2019) |
| Initial String | \(N_1N_1 \ldots N_1N_2 \ldots N_2\) |
| First Restriction Enzyme | \(X_1YX_2\) |
| Second Restriction Enzyme | \(W_1YW_2\) |
| | \(X_1YX_2\) |
| | \(W_1YW_2\) |
| Theorem 4 (Fong et al., 2019) | |
| Initial String | \(N_1N_1 \ldots N_1N_2 \ldots N_2\) |
| First Restriction Enzyme | \(X_1YX_2\) |
| Second Restriction Enzyme | \(W_1YW_2\) |
| | \(X_1YX_2\) |
| | \(W_1YW_2\) |
The symbols $N_1 X_1 Y X_2 M W_1 Z W_2 N_2$ and $N_2 Z'$ denote arbitrary dsDNA symbol(s), where $N_1, X_1, Y', X_2', M', W_1', Z', W_2'$ and $N_2'$ are complements for $N_1, X_1, Y, X_2, M, W_1, Z, W_2$, and $N_2$ respectively, and $Y'$ and $Z'$ are the crossings.

**IV. RESULTS AND DISCUSSIONS**

In this research, the automata diagrams for DNA splicing systems with one cutting site each of two palindromic or two non-palindromic rules for the same and different crossings are constructed using grammars where the splicing languages from the splicing system are deduced from the grammars.

The automaton for DNA splicing system with one cutting site each of two palindromic restriction enzymes with the same crossing is presented as Theorem 5.

**Theorem 5**

Given

$$S = \left\{ N_1 N_1 ... N_1 X_1 Y X_2 M M' M ... M W_1' Y W_2' W_2 N_2 ... N_2 \right\}$$

is a splicing system involving one cutting site each of two palindromic rules $X_1 Y X_2$ and $W_1 Y W_2$, with the same crossing $Y$, where $N_1, X_1, Y, X_2, M, W_1, W_2$, and $N_2$ are variables used to denote any arbitrary dsDNA and $N_1', X_1'$, $Y', X_2'$, $M', W_1'$, $W_2'$ and $N_2'$ are complements for $N_1, X_1, Y, X_2, M, W_1, W_2$, and $N_2$ respectively, $M_1 = (Q, \Sigma, \delta, q_0, F)$ is a deterministic finite automaton for the DNA splicing system that accepts the language $L(S)$, in which $Q = \{q_0, q_1, q_2, q_3\}$ is the set of states where $q_0$ is the initial state and $F = \{q_3\}$ is the set of final states, $\Sigma = \{N_1 N_1 ... N_1 X_1 N_2 N_2', N_2 W_1 M M' M ... M W_1 W_2, N_1 N_1', N_2 N_2', N_2 N_2, \}$ is the set of input and $\delta$ are given by illustrating the automata diagram in Figure 2.

**Proof**

The splicing language $L(S)$ from the splicing system can be written as a language generated by a grammar $G$, where

$$G = (\{S_0 \ S_1 \ S_2 \ S_3 \}, \\{N_1 N_1 \ N_1 X_1 Y X_2 M W_1' \ W_2' \ W_2 N_2 ... N_2 \}, M W_1' W_2' N_2 \ M), S_0, P_1)$$

with $P_1$ consisting of the productions,

$$S_0 \rightarrow X_1 Y X_2 M M' M ... M W_1' Y W_2' W_2 N_2 ... N_2$$

$N_1 N_1, N_1 X_1 Y X_2 M W_1' Z W_2' N_2 N_2$.

$S_1 \rightarrow Y \ S_3$,

$S_2 \rightarrow Y \ S_3$ and

$S_3 \rightarrow X_1 Y X_2 M M' M ... M W_1' Y W_2' W_2 N_2 ... N_2$.

Figure 2. An automaton diagram for $M_1$.
Then, a sequence for the language generated by the grammar $G_s$, $L(G_s)$ is

\[
S_0 \rightarrow N_1N_1 \cdots N_1X_1 \quad N_1N_1' \cdots N_1X_1', S_1 + N_2N_2 \cdots N_2W_1 S_2 \\
N_1N_1 \cdots N_1X_1 \quad N_1N_1' \cdots N_1X_1', Y \quad S_3 \\
N_2N_2 \cdots N_2W_1 \quad N_2N_2' \cdots N_2W_1', Y \quad S_5 \\
N_1N_1' \cdots N_1X_1' \quad N_1N_1' \cdots N_1X_1', Y \quad S_6 \\
\{ Y \left( X_2M'M \cdots M W_1 + W_2M'M \cdots M X_1 \right) \}^* \\
\{ Y \left( X_2M'M \cdots M W_1 + W_2M'M \cdots M X_1 \right) \}^* \\
\{ Y \left( X_2M'M \cdots M W_1 + W_2M'M \cdots M X_1 \right) \}^*
\]

which depicts the splicing language $L(S)$ from Theorem 1 in Table 1.

Based on $G_s$, the automaton for the splicing system is constructed using productions in $G_s$. The relation between productions in $G_s$ and transition functions, $\delta$ for $M_s$ from Figure 2 is given in Table 3.

Table 3. Productions in $G_s$ and transition functions for $M_s$.

| Production in $G_s$ | Transition Function, $\delta$ |
|---------------------|-----------------------------|
| $S_0 \rightarrow N_1N_1 \cdots N_1X_1 \quad N_1N_1' \cdots N_1X_1', S_1 + N_2N_2 \cdots N_2W_1 S_2$ | $\delta(q_0, N_1N_1 \cdots N_1X_1') = q_1$ |
| $S_0 \rightarrow N_2N_2' \cdots N_2W_1' S_4$ | $\delta(q_0, N_2N_2' \cdots N_2W_1') = q_2$ |
| $S_1 \rightarrow Y S_3$ | $\delta(q_1, Y) = q_3$ |
| $S_2 \rightarrow Y S_3$ | $\delta(q_2, Y) = q_3$ |
| $S_3 \rightarrow X_2M'M \cdots M W_3 S_1$ | $\delta(q_3, X_2M'M \cdots M W_3) = q_1$ |
| $S_3 \rightarrow W_2M'M \cdots M X_1 S_1$ | $\delta(q_3, W_2M'M \cdots M X_1) = q_1$ |
| $S_3 \rightarrow X_2M'M \cdots M W_3 S_1$ | $\delta(q_3, X_2M'M \cdots M W_3) = q_1$ |
| $S_3 \rightarrow W_2M'M \cdots M X_1 S_1$ | $\delta(q_3, W_2M'M \cdots M X_1) = q_1$ |
| $S_3 \rightarrow \{ X_2N_1N_1 \cdots N_1 \}$ | $\delta(q_3, X_2N_1N_1 \cdots N_1) = q_5$ |

Thus, Theorem 5 is proved.

Automaton for DNA splicing system with one cutting site each of two palindromic restriction enzymes with different crossings is presented as Theorem 6.

**Theorem 6**

Given $S = \{ A, C, G, T \}^*$, $N_1N_1 \cdots N_1X_1 Y X_2 M \cdots MW_1 Z W_2 N_2 N_2' \cdots N_2'$ is a splicing system involving one cutting site each of two palindromic rules $X_1 Y X_2$ and $W_1 Z W_2$ with different crossings $Y$ and $Z$, where $N_1, N_2, X_1', Y, X_2', W_1', Z$ and $W_2'$ are variables used to denote any arbitrary dsDNA and $N_1, N_2, X_1', Y, X_2', W_1', Z$ and $W_2'$ are complementaries for $N_1, X_1, Y, X_2, M, W_1, Z$ and $W_2$, respectively, $M_2 = (Q, \Sigma, \delta, q_0, F)$ is a deterministic finite automaton for the DNA splicing system that accepts the language $L(S)$, in which $Q = \{ q_0, q_1, q_2, q_3, q_4 \}$ is the set of states where $q_0$ is the initial state and $F = \{ q_3, q_4 \}$ is the set of final states, $\Sigma = \{ N_1N_1 \cdots N_1X_1 Y X_2 N_2 N_2' \cdots N_2' W_1 Z W_2 N_2 N_2' \cdots N_2' \}$ is the set of inputs and $\delta$ are given by showing the automata diagram in Figure 3.

![Figure 3. An automaton diagram for $M_2$](image-url)
Theorem 7
Given 
\[ S = (A, C, G, T) \rightarrow N_1, N_2 \ldots N_{x_1} Y X_{2} M, M \ldots W_{i} Y, W_{2} N_{2} N_{2} \ldots N_{2} \rightarrow X_{1}, Y X_{2} \rightarrow (W_{1}, Y, W_{2}) \rightarrow \emptyset \]
is a splicing system involving one cutting site of two non-palindromic rules \( X_{1} Y X_{2} \) and \( W_{1} Y W_{2} \) with the same cutting site \( Y \), where \( N_{i}, N_{j} \) are variables used to denote any arbitrary dsDNA and \( N_{i} \).

Theorem 8
Given 
\[ S = (A, C, G, T) \rightarrow N_1, N_1 \ldots N_{x_1} Y X_2 M, M \ldots W_{i} Y, W_{2} N_{2} N_{2} \ldots N_{2} \rightarrow X_{1}, Y X_{2} \rightarrow (W_{1}, Z, W_{2}) \rightarrow \emptyset \]
is a splicing system involving one cutting site of two palindromic rules \( X_{1} Y X_{2} \) and \( W_{1} Z W_{2} \) with different crossings \( Y \) and \( Z \), where \( N_{i}, N_{j} \) are variables used to denote any arbitrary dsDNA and \( N_{i} \).

V. CONCLUSION
In this research, the relation of DNA splicing systems and automata theory is discussed. The automata diagrams for the DNA splicing systems with one cutting site each of two palindromic or two non-palindromic rules for the same
and different crossings of the restriction enzymes are modelled using deterministic finite automata. The languages resulting from the automata depict the languages generated by the grammars.

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