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On the Mathematical Modeling of Splicing Systems in DNA Computing: A Review

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Abstract. A splicing system involves the process of cutting and pasting on DNA molecules with the presence of restriction enzymes and ligase, respectively. A mathematical model of the splicing system has been developed by using the concept of formal language theory, which is a branch of theoretical computer science and applied discrete mathematics, and informational macromolecules. The splicing system consists of a set of alphabets, a set of rules and a set of initial strings. Over the years, the model of splicing system has grown intensively. In this research, there are two issues that are of interest of the researchers - either a model based on the generation of language, or a model based on the preservation of biological traits of the splicing process. In this paper, basic concepts on different types of splicing systems are presented. The current trend and results on the splicing system with other related fields such as computer science and molecular biology are given and discussed.

Keywords: mathematical modeling, splicing systems, DNA computing.

INTRODUCTION

Biomolecular computing, also known as DNA computing, has replaced traditional silicon-based computer technologies by using DNA, biochemistry and molecular biology hardware. DNA computing has implemented two fundamental features of DNA which are Watson-Crick complementarity and the massive parallelism of DNA strands. The potential of handling the massive and complex computations made the DNA computing promising tool and devices of computing. Adleman [1] has initiated the study on DNA computing to solve the seven point Hamiltonian path problems. Splicing system and sticker system have been recognised as languages generating devices in formal language theory for DNA-based computing devices. They are modeled mathematically to generate some strings over the four-symbol alphabets similar to the deoxyribonucleotide pairs [1].

In addition, formal language theory, which is originally developed from applied discrete mathematics and theoretical computer science, is an abstraction of the general characteristics of programming languages. A formal language is a set of strings over a finite alphabet which follows some rules in order for those strings to form a language. The study of families of formal languages leads to the formal language theory [1]. Surprisingly, the cutting and pasting phenomenon on DNA molecules can be represented into some terms of the formal language that inspired the study on the mathematical modelling of the splicing system. Head, who is the pioneer on this study, had established the interdisciplinary study between formal language theory and the study of informational macromolecules in 1987 [2]. As years passed by, this study has developed tremendously. The focus of the researchers has been split into two directions: on the generation of languages or the preservation of biological traits in the splicing process [3].

In this paper, the fundamental knowledge of formal language theory and some related molecular biological terms are presented. A mutual relation that exists in these fields is then explained. Besides that, the historical review on the different models and some types of splicing systems, various types of splicing languages and more are discussed.

PRELIMINARIES

A mathematical model of the splicing system which has been initiated by Head [2] comprises of four different set of elements such as a set of alphabets, a set of initial strings, and two sets of rules which are presented in triple forms. Therefore, some fundamental terms regarding formal language theory are given.

In the following, some definitions related to formal language theory which will be used throughout this paper, namely alphabet, string and language, are listed below.

Definition 1. [1] *An alphabet, A, is a finite, nonempty set of symbols.*

Definition 2. [1] *A string is a finite sequence of symbols from the alphabet.*

Definition 3. [1] *A set of strings all of which are chosen from some A^*, where A is a particular alphabet, is called a language and A^* denotes the set of all strings over an alphabet A, which is obtained by concatenating zero or more symbols from A.*

The operations involved between the splicing languages are called concatenations. The concatenation between two languages, L_1 and L_2 has been given in [4] where $L_1L_2 = \{xy \mid x \in L_1, y \in L_2\}$. The operation between the languages are written in the following general form:

$$
\begin{aligned}
&L^0 = \varnothing, \\
&L^{i+1} = LL^i,\ i \geq 0, \\
&L^* = \bigcup_{i=0}^{\infty} L^i \left(\text{the } * \text{ - Kleene closure}\right), \\
&L^+ = \bigcup_{i=1}^{\infty} L^i \left(\text{the } + \text{ - Kleene closure}\right).
\end{aligned}
$$

Next, some molecular biological terms are introduced and the relations with formal language theory are then emphasized.

The presence of DNA in each living organism has offered variety in them such as their physical looks. It is important to study the structure of DNA as knowing the structure leads to the discovery of its important functions and also its significant role in the hereditary processes [5]. This unique molecule plays two important roles which are coding for the production of proteins and also self-replication that transfers information from the parent cells to the offspring cells [4]. This is to ensure some similar traits are inherited to the offsprings from the parent. Basically, a DNA molecule is composed of nucleotides. A complete nucleotide is made up of three distinct components which are a phosphate group, a sugar group (deoxyribose) and a nitrogenous base. There are four types of nitrogenous bases which can be grouped as pyrimidine: Cytosine (C) and Thymine (T) and purine: Adenine (A) and Guanine (G) [6]. By Watson-Crick complementarity, the only possible pairings allowed between the nucleotides are A with T, C with G and vice versa. In 1940s, Erwin Chargaff had performed the base compositions of DNA from various species and concluded the amount of A and T was approximately equal and likewise for C and G [5] which reason the pairings. In reality, the representation of a double-stranded DNA (dsDNA) molecule as two linear strands bound together by Watson-Crick complimentarity is already a simplification since in a DNA molecule, the two strands wind around each other to form the famous double helix [4].

Besides that, restriction enzymes are enzymes isolated from the bacteria which have a significant role on DNA molecules [6]. The restriction enzyme cuts the DNA molecules within a particular nucleotide sequence called restriction sites [5]. DNA molecules also consist of hundreds of thousands of nucleotides. Besides cutting the DNA molecules, restriction enzymes also help recognise specified region of the entire DNA molecules and locate the restriction site. When the restriction enzyme acts on the DNA molecule that has a cutting site, two fragments with complementary sticky ends or blunt ends will exist [2]. The pasting process then takes place with the presence of ligase when two conditions are met: the two fragments end with complementary bases, and the two fragments are from the same overhang. Then, either a new hybrid DNA or the same DNA molecule is formed. After a cutting process has taken place, there will be three types of cuts namely $5'$- overhang, blunt end or $3'$- overhang. They can be categorised in left ($5'$- overhang and blunt end) or right ($3'$- overhang) pattern [2].

Mathematically, the complementary bases which are known as *a*, *c*, *g* and *t* are presented as a set of alphabets, *A*. Besides, the dsDNA molecules are represented as a set of initial strings, *I* and restriction enzymes which act upon dsDNA molecules are represented as a set of rules: set *B* represents $5'$- overhang and blunt end cut while set *C* represents $3'$- overhang cut. Meanwhile, dsDNA molecules obtained from the splicing process are represented as a language. In the next section, the definitions of the splicing system by Head, Paun, Pixton, Goode-Pixton and Yusof-Goode (Y-G) are presented. The differences among the models are then discussed.

DEVELOPMENT OF SPLICING SYSTEMS

In this section, the pioneer model proposed by Head is first given. Besides, the differences with the other models are discussed. In addition, two examples are proposed where the first is inspired by molecular biology. The second example establishes the relation between molecular biology and formal language theory.

The inspiration of the mathematical modelling of splicing system is triggered by the presentation of DNA molecules as a series of alphabets adenine (A), cytosine (C), guanine (G) and thymine (T). Hence, by considering the actual process of DNA splicing, Head carefully designed the following mathematical model of the splicing system.

Definition 4. [2] *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 the words ucxfq and pexdv to L 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).*

As years passed by, researchers made intensive works on the concept of splicing system introduced by Head. Several model were developed namely Paun [7], Pixton [8], Goode-Pixton [9] and Y-G [10] splicing systems. Initially, Head splicing system was bounded to finite case only. Paun had introduced a new formalism where it is found to be a powerful approach at some cases due to its rule that is set to consider also the infinite cases. Comparison between Paun's and Head's model is then made in [11]. It has been shown that Paun's model works terrific in theory but not biologically. This difference will be further discussed in the next section. The definition of Paun's splicing system is presented as follows.

Definition 5. [7] *A Paun splicing scheme is defined as a pair* $\sigma(A,R)$ *where A is an alphabet and* $R \subseteq A^* \# A^* \$ A^* \# A^*$ *is a set of splicing rules, for #, $ two special symbols not in A. Two initial strings x and y in* A^* *can be spliced via rule r in R to produce the following language:*

$$\sigma(x,y) = \{uu_1u_4v' \mid x = uu_1u_2v,\ y = u'u_3u_4v' \text{ for some } u,u',v,v' \in A^* \text{ and } u_1 \#u_2 \$v_1 \#v_2\}.$$

Pixton splicing system [8] had been introduced in the same year as Paun's, a substitution approach is used where an intervening factor called β is applied in between the left part of the first string and the right part of the second string. The following is the definition of Pixton splicing system.

Definition 6. [8] *A Pixton splicing system is defined as a pair* $\zeta = (R, L_0)$ *where R is a splicing scheme (A, r) and* L_0 *is a set of strings, called initial language generated from* A^**. The rule r in R is presented in triple of* $(\alpha, \alpha'; \beta)$*. Given two strings* $\varpi = \xi a \eta$ *and* $\varpi' = \xi' a' \eta'$*, then by applying the rule r to these strings, the string* $\xi \beta \eta'$ *is produced.*

Bonizzoni *et al*. [11] later claimed that Pixton's concept was a mere substitution operation regarding splicing since it is against the earliest concept proposed by Head and Paun. To overcome the misunderstanding of the previous concept, Goode and Pixton came out with Goode-Pixton splicing system. The following is the definition of Goode-Pixton splicing system.

Definition 7. [9] *Let A denote a finite alphabet. A splicing rule, also called a rule for simplicity, is a quadruple* $(u,v:u',v')$ *where u, v,* u' *and* v' *come from* A^*. *Given a rule r =* $(u,v:u',v')$ *and two strings w = xuvy and* $w' = x'u'v'y'$ *in* A^*, *w and* w' *can be spliced via r, generating the splicing product xuv'y'. This is denoted by the following shorthand:*

$$\{xuvy, x'u'v'y'\} \xrightarrow{(u,v;u',v')} xuv'y'.$$

A concern has arisen since it is ambiguous to determine whether the rule lies in the left or right pattern. Therefore, a new notation for writing rules in a splicing system, and a new extension of splicing system rooted from Head's and Goode-Pixton's version of splicing system which is called the Yusof-Goode (Y-G) splicing system is introduced. The following is the definition of Y-G splicing system.

Definition 8. [10] *A splicing system* $S = (A, I, R)$ *consists of a set of alphabets A, a set of initial strings I in* A^* *and a set of rules,* $r \in R$ *where r = (u, x, v: y, x, z). For* $s_1 = \alpha uxv\beta$ *and* $s_2 = \gamma yxz\delta$ *elements of I, splicing* s_1 and s_2 *using r produces the initial string I together with* $\alpha uxz\delta$ and $\gamma yxv\beta$, *presented in either order where* $\alpha, \beta, \gamma, \delta, u, x, v, y$ and $z \in A^*$ *are the free monoids generated by A with the concatenation operation and 1 as the identity element.*

Here, *R* represents a set of rules in either left pattern (*u*; *x*, *v*: *y*; *x*, *z*), right pattern (*u*, *x*; *v*: *y*, *x*; *z*) or both (*u*, *x*, *v*: *y*, *x*, *z*). This version of splicing system presents the transparent behaviour of the DNA biological process. It is claimed so because the splicing model itself is inspired by the characteristics of the restriction enzymes contained in the model.

Next, to portray the relation of splicing system and molecular biology, a molecular based example that takes place on dsDNA molecules with the presence of restriction enzyme, ligase and other appropriate substances is given.

Example 1. Let the dsDNA molecules be presented as:

$$\begin{array}{l} 5'-\text{MMMM}CCGC\text{MMMM}-3' \\ 3'-\text{WWWW}GGCG\text{WWWW}-5 \end{array}$$

where the symbol M denotes any arbitrary symbols from a set of alphabets that fulfilled the Watson-Crick complementarity. When a restriction enzyme namely *Aci*I is added to the solution containing the molecule, the dsDNA molecule is spliced as follows:

$$\begin{array}{l} 5'-\text{MMMM}C \quad CGC\text{MMMM}-3' \\ 3'-\text{WWWW}GGC \quad G\text{WWWW}-5 \end{array}.$$

Therefore, the following two new molecules are formed with the presence of a ligase despite the initial dsDNA molecule:

$$\begin{array}{l} 5'-\text{MMMM}CCGG\text{WWWW}-3' \\ 3'-\text{WWWW}GGCC\text{MMMM}-5 \end{array} \text{ and } \begin{array}{l} 5'-\text{WWWW}CCGG\text{MMMM}-3' \\ 3'-\text{MMMM}GGCC\text{WWWW}-5 \end{array}.$$

The molecular example above can be expressed in term of Head splicing system as shown in Example 2.

Example 2.
Let $S = (A, I, B, C)$ be a splicing system where $A = \{a, c, g, t\}$, $I = \{mmmmccgcmmmm\}$, $B = \{(c, cg, c)\}$ and $C = \phi$. When splicing occurs, the following strings are formed:

$$\{mmmmccgcmmmm\} \xrightarrow{B,C} I \cup \{mmmmccggwwww, wwwwgcgcmmmm\}.$$

The splicing language, $L(S)$ generated from this splicing language is given by

$$L(S) = I \cup \{mmmmccggwwww, wwwwgcgcmmmm\}.$$

Besides, some interesting findings were discovered by Head such as persistent, null-context, uniform splicing system and also strictly locally testable (SLT) language. These types of splicing systems have contributed to the exploring of new properties to the existing splicing systems. As an example, an in-depth study on the characterization of persistent splicing system has shown a relation with strictly locally testable language [2]. Gatterdam [12] has extended the study on persistent splicing system by introducing permanent splicing system that has quite similar meaning but with different approach. These two related definitions have been used by Yusof [13] in the study of the characterization of a non semi-simple splicing system. Karimi *et al*. [14] has explored these two systems in detail where some sufficient conditions were provided and some new definitions that is closely related to the original definitions such as self-closed, crossing-preserved and extended crossing-preserved were introduced. Recently, Mudabber *et al*. [15] has conducted a study on two stages splicing system in which its properties are explored in terms of persistency and permanency of the splicing system.

Since then, few types of splicing system were introduced. For instance, Mateescu *et al*. [16] has introduced a definition on simple splicing system which was then further studied by Laun based on the continuity aspect. An extension version of a simple and null-context splicing system has been introduced namely a semi-simple and semi-null splicing system [17] respectively. Then, it is proven that S_kH system is a simple splicing system if k = 1 which proves that the union of S_kH families is a family of SLT languages. Furthermore, a solid code is applied to the S_kH system to reduce it to the simple splicing system [18]. By the presence of various types of splicing system, some relations are established where simple splicing system $\subset$ semi-simple splicing system $\subset$ semi-null splicing system, and simple splicing system $\subset$ uniform splicing system $\subset$ S_k splicing system $\subset$ null-context splicing system [19]. Fong has conducted an intensive study to explore more properties and also some sufficient conditions of strictly locally testable language [18]. Some examples with different number of restriction enzymes were illustrated to show languages that are not strictly locally testable.

The varieties of the splicing system have been used to explore some properties on two different directions: either on the generation of languages or the preservation of biological traits in the splicing process. In the next section, recent advances on both the approaches in the splicing systems are presented.

RECENT ADVANCEMENT OF SPLICING SYSTEMS

A splicing language is produced by a splicing system. Head splicing system and its improved version, Y-G splicing system are normally chosen in studying the behavior of restriction enzyme on the dsDNA molecules. Based on the experiment, when the restriction enzymes react with a collection of DNA molecules, the splicing language is produced [2]. There are few types of splicing languages such as adult or inert, transient, and limit language [9]. In order to verify the results obtained from the splicing system such as to verify the model used, the existence of a specific language and its characteristics, a mathematical modelling of the splicing system is developed. As years passed by, several laboratory experiments have been conducted. For instance, Laun and Reddy in 1999 [20] has pioneered the first experiment on validating the accuracy of the Head model, which predicts the behavior of the corresponding biological process by using two restriction enzymes namely *Bgl*I and *Dra*III. Several other experimental works have also been performed such as Fong *et al*. in 2008 [21] to verify the mathematical model and to show the difference between adult and limit language by also using two restriction enzymes, namely *Aci*I and *Hpa*II. In 2013, Karimi [3] conducted an experiment to biologically validate the behavior of persistent splicing systems by using *CviQ*I and *Acc*65I. In early 2015, Ahmad *et al*. [22] conducted a laboratory experiment to verify the mathematical model and the existence of second order limit language [23] by using a restriction enzyme namely *Dpn*II. The model is validated if the generated DNA molecules through the experiment are same with the prediction in the model of the splicing language.

In the study of the splicing system that focuses on the generation of language, Paun and Pixton splicing system are used. Infinite cases which can be represented by the rules in Paun's or Pixton's model made it suitable to study the characterizations of the languages. In addition, splicing system that involves a set of finite axioms and rules produces only regular languages. Some restrictions are implemented to the splicing system to increase the computational power of the language from regular to the recursive enumerable language [7]. Karimi in [3] used fuzzy threshold languages approach to the persistent splicing system of Paun splicing system perspective to increase the computational power of splicing systems and to produce some non-regular languages. Besides that, Gan *et al*. [24] used weights where its properties are explored from some properties of group in term of automata to achieve higher computational power of the splicing system. Selvarajoo *et al*. [25] used probability instead to increase the computational power of the splicing system where probability is imposed to the splicing system.

CONCLUSION

As a conclusion, a relation between the formal language theory and the study of informational macromolecules is presented where some fundamental terms of formal language theory and some motivational background of DNA and its related subjects are given. Besides, five different models of the splicing system namely Head, Paun, Pixton, Goode-Pixton and Y-G splicing systems have been discussed and their differences shown. Some types of the splicing system and the relations that exist among them are presented. The current trends of the research which cover two directions of the research are provided to show the development of the splicing system throughout the years.

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REFERENCES

1. P. Linz, *An Introduction to Formal Languages and Automata* , Jones and Barlett Publisher, USA, 2006), pp. 1–25.
2. T. Head, B. Math, Biol. **49**, 737–759 (1987).
3. F. Karimi, "Mathematical Modelling of Splicing Persistent Splicing Systems in DNA Computing," Ph. D. thesis, Universiti Teknologi Malaysia, 2013.
4. G. Paun, G. Rozenberg and A. Salomaa, *DNA Computing New Paradigms* (Springer-Verlag, Germany, 1998), pp. 1–80.
5. I. E. Alcamo, *DNA Technology Awesome Skill*, 2nd Edition (Academic Press, USA, 2001), pp. 1–93.
6. R. H. Tamarin, *Principles of Genetics* (The Mac-Graw Hill Companies, USA, 2001), pp. 359–382.
7. Gh. Paun, *Discrete Appl. Math*. **70**, 57–79 (1996).
8. D. Pixton, *Discrete Appl. Math*. **69**, 101–124 (1996).
9. E. Goode and D. Pixton, "Splicing to the Limit," in *Aspects of Molecular Computing*, edited by N. Janoska, Gh. Paun and G. Rozenberg, (Springer Berlin, Heidelberg, New York, 2004), pp. 189–201.
10. Y. Yusof, N. H. Sarmin, T. E. Goode, M. Mahmud and W. H. Fong, "An Extension of DNA Splicing System," in *6th International Conference on Bio-Inspired Computing: Theories and Application (BIC-TA 2011)*, IEEE Conference Proceedings, edited by R. Abdullah *et al*. (IEEE, Piscataway, NJ, 2011), pp. 246–248.
11. P. Bonizzoni, C. Ferretti, G. Mauri and R. Zizza, Inform. Process Lett. **79**, 255–259 (2001).
12. R. W. Gatterdam, SIAM J. Comput. **21**, 507–520 (1992).
13. Y. Yusof, "DNA Splicing System Inspired by Bio-Molecular Operations," Ph. D. thesis, Universiti Teknologi Malaysia, 2011.
14. F. Karimi, N. H. Sarmin and W. H. Fong, Aust. J. Basic Appl. Sci. **5**, 20–24 (2011)
15. M. H. Mudaber, Y. Yusof and M. S. Mohamad, "Some Sufficient Conditions for Persistency and Permanency of Two Stages DNA Splicing Languages via Yusof-Goode Approach," in *Proceedings of the 21st National Symposium on Mathematical Sciences (SKSM21)*, AIP Conference Proceedings 1605, edited by M. T. Ismail, S. Ahmad and R. A. Rahman, (American Institute of Physics, Melville, NY, 2014), pp. 591–595.
16. A. Mateescu, Gh. Paun, G. Rozenberg and A. Salomaa, Discrete Appl. Math. **84**, 145–163 (1998).
17. T. E. G. Laun, "Constants and Splicing Systems," Ph.D. thesis, State University of New York, 1999.
18. W. H. Fong, "Modelling of Splicing Systems using Formal Language Theory," Ph. D. thesis, Universiti Teknologi Malaysia, 2008.
19. Y. Yusof, N. H. Sarmin, T. E. Goode, M. Mahmud and W. H. Fong, "Hierarchy of Certain Types of DNA Splicing Systems," in *International Conference Mathematical and Computational Biology 2011*, International Journal of Modern Physics: Conference Series 9, edited by K. A. M. Atan *et al*. (World Scientific, Hackensack, NJ, 2012), pp. 271–277.
20. E. Goode and D. Pixton, "Wet Splicing System," in *DIMAC Series in Discrete Mathematics and Theoretical Computer Science*, edited by H. Rubin and D. H. Wood (American Mathematical Society, Rhode Island, USA, 1999), pp. 73–83.

21. W. H. Fong and N. H. Sarmin, "Mathematical Modelling of Splicing Systems," in *Proceedings of the 1st International Conference on Natural Resources Engineering & Technology*, (2006), pp. 524–527.
22. M. A. Ahmad, N. H. Sarmin, M. F. A. Wahab, Y. Yusof and W. H. Fong, *J. Theor. Biol.* (submitted).
23. M. A. Ahmad, N. H. Sarmin, W. H. Fong and Y. Yusof, "An Extension of First Order Limit Language," in *Proceedings of the 3rd International Conference on Mathematical Sciences*, AIP Conference Proceedings 1602, edited by W. Z. W. Zain *et al*. (American Institute of Physics, Melville, NY, 2014), pp. 627–631.
24. S. Turaev, Y. S. Gan, M. Othman, N. H. Sarmin and W. H. Fong, "Weighted Splicing System," in *Advanced Methods for Computational Collective Intelligence*, edited by Z. Li *et al*. (Springer Berlin, Heidelberg, New York, 2012), pp. 416–424.
25. S. Turaev, M. Selvarajoo, M. S. Selamat, N. H. Sarmin and W. H. Fong, "Probabilistic Splicing System," in *Computational Intelligence and Intelligent Systems*, edited by N. T. Nguyen *et al*. (Springer Berlin, Heidelberg, New York, 2013), pp. 259–268.