

DNA INTUITIONISTIC FUZZY TURING MACHINE

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ABSTRACT. The restriction enzymes of bacteria are used to cut and insert the two strands of double-stranded DNA at different positions that cause overhangs of single stranded DNA. We developed an encoding transition table of an intuitionistic fuzzy Turing machine that processes series of restriction(cut) and ligation of DNA fragments or oligonucleotides that can be used to find the Body Mass Index of human being.

Keywords:DNA implementation of Turing Machine, Splicing operation, Restriction enzyme, Molecular Turing machine, DNA computation, DNA Oligonucleotide, DNA Wet lab implementation, Ligation of DNA fragments.

AMS Subject Classification: 68Q45, 03D110

1. INTRODUCTION

James Watson was a young American geneticist who found the building plan of the DNA molecule in 1953. It is hereditary material of cells and organisms. He showed how the DNA pass the information to their off spring and also he established that the evolution is possible by mutations of DNA.

In 1973 Charles Bemet[4] compared the operation of RNA polymerase to a Turing machine and he used imaginary enzymes in Turing Machine which are capable of recognizing and changing single base of DNA in 1982[5].

In 1986 Atanassov[3] introduced the concept of an intuitionistic fuzzy set which is characterized by two functions expressing degree of belongingness and the degree of non-belongingness, respectively.

The construction of chemical neural net works may be used to make general computers like Turing machines was described by Hjelmfelt et al[6].

A series of operation on "DNA test tubes" that simulate a memory model of computation is presented by Adlema[2].

The Hamiltonian path problem was solved by Leonard Adleman[1] by using the chemistry of DNA.

Computational problems are autonomously solved by a programmable finite automaton

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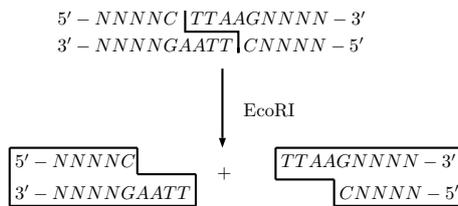
comprising of fuzzy DNA and DNA-manipulating enzymes. Such finite automata operated by information encoded biopolymers produces some design study for molecular DNA computing.

We begin the paper with important definitions such as splicing system, restriction enzyme with example, ligase with example, DNA structure, fuzzy Turing machine(**FTM**) and intuitionistic fuzzy Turing machine(**IFTM**). In section 3 we see the operations on class II restriction enzymes and class IIS restriction endonucleases. In section 4 we see the process of Busy Beaver Machine and in section 5 we find body mass index using intuitionistic fuzzy DNA.

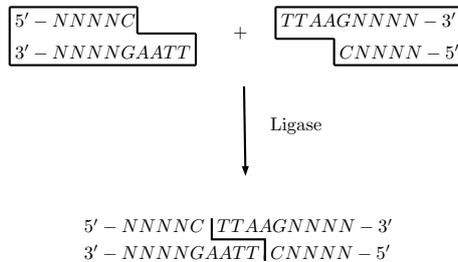
2. PRELIMINARIES

Definition 2.1. [7] *A splicing system is a mathematical model of generative capacity of linear DNA molecules using restriction enzymes and ligase.*

Definition 2.2. [7] *Restriction enzyme is a specific endonuclease that recognizes specific short sequences of DNA and cleaves the DNA at or near the recognition site.*



Definition 2.3. [7] *Ligase is one of the enzyme that ligates the ends of DNA sequences cut by restriction enzyme.*



Definition 2.4. [9] *A single strand of DNA can be likened to a storage tape that can support a four symbol alphabet, $\Sigma = \{A, G, C, T\}$ denoting the nucleotides adenine, guanine, cytosine and thymine. Taken as pairs the nucleotides A and T and the nucleotides C and G are said to be complementary base pair(an A-T pair or a C-G pair).*

Definition 2.5. [10] *A single tape fuzzy Turing machine(Fuzzy-NTM) is a nine-tuple $F = (S, T, I, \Delta, b, q_0, q_f, \mu, *)$, where*

- S is the finite set of states,*
- T is the finite set of tape symbol,*
- I is the set of input symbols,*
- Δ is a subset of $S \times T \times S \times T \times \{-1, 0, 1\}$,*
- b is the blank,*
- q_0 is the initial state,*
- q_f is the final, or accepting state,*

$\mu : \Delta \rightarrow [0, 1]$ is a function that to each move δ assigns the truth degree $\mu(\delta)$ of its membership in Δ ,
 $*$ is a t – norm.

Definition 2.6. [8] A nondeterministic intuitionistic fuzzy Turing machine (NIFTM) is defined by $(Q, \Sigma, \Gamma, \Delta, q_0, \square, F, *, *', \mu, \gamma)$ where

- Q is a finite set of states,
- Σ is the input alphabets,
- Γ is a finite set of symbols called the tape alphabets,
- Δ is an intuitionistic fuzzy subsets of $Q \times \Gamma \times 2^{Q \times \Gamma \times \{L,R,S\}}$ and
- $\mu, \gamma : Q \times \Gamma \times 2^{Q \times \Gamma \times \{L,R,S\}} \rightarrow [0, 1]$ are fuzzy functions where $0 < \mu(\delta) + \gamma(\delta) \leq 1 \forall \delta \in \Delta$,
- $q_0 \in Q$ is the initial state,
- $\square \in \Gamma$ is a special symbol called the blank,
- $F \subseteq Q$ is the set of accepting states,
- $*$ is a computable t – norm and $*'$ is its computable t – conorm.

3. RESTRICTION ENZYME OPERATIONS ON DNA

There are some operations on DNA that are used to correspond with the primitive operations of a Turing machine. The subgroup of the class IIS restriction endonucleases are found to have some operation which is used to design Turing machine.

3.1. Operations of class II restriction enzymes. The restriction enzymes of bacteria are employed to cut double-stranded DNA at restriction sites. Some times the viruses of foreign DNA enters the bacterium. These restriction enzymes are used to chop up the foreign DNA. The reaction of DNA with a restriction enzyme is called a restriction digest. This restriction digest resulting from one restriction enzyme is called single digest, if two or three enzymes are used, these are called double or triple digest.

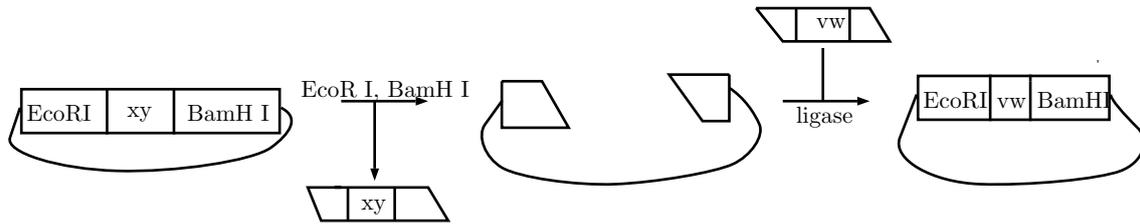
Deletion of a fragment from a plasmid



Fig;3.1.1: Deletion of a fragment

In figure 3.1.1, a fragment can be removed if it is flanked by two restriction sites for the same enzyme.

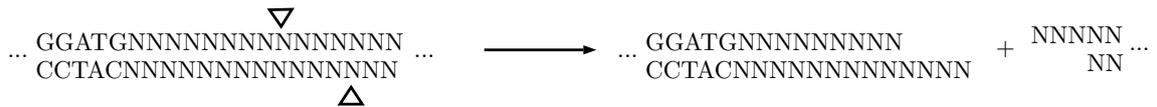
Replacement of a fragment in a plasmid with orientation control



Fig;3.1.2: Replacement of a fragment with orientation control

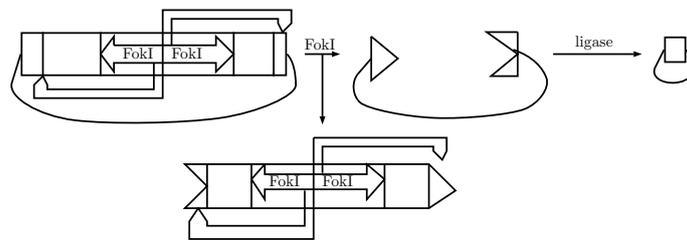
In figure 3.1.2, the second restriction site BamH I an oligonucleotide XY with two different sticky ends using EcoR I and then ligate a fragment vw that has two different ends with same orientation.

3.2. Operations of IIS restriction endonucleases. A subgroup of class II restriction enzymes is called the Class IIS restriction enzymes. This IIS restriction enzyme does not recognize palindromic recognition sites and they cut far away from their restriction sites.



where $N \in \{A, C, G, T\}$. These restriction endonucleases are also known as non palindromic or asymmetric restriction enzymes.

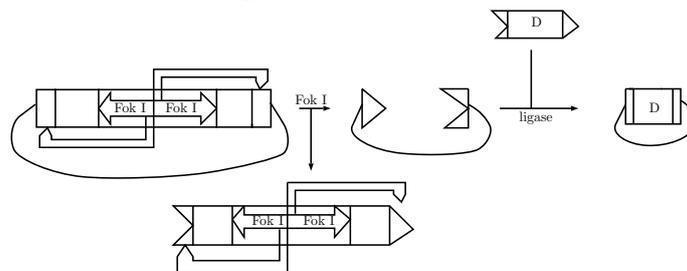
Deletion of a fragment with auto-excision of restriction sites



Fig;3.2.1 Replacement of an oriented fragment

In figure 3.2.1. Class IIS restriction enzymes can cut back to back themselves out of a plasmid and the plasmid can be rejoined without the regeneration of a restriction site.

Replacement of an oriented fragment with the excision of restriction sites



Fig;3.2.2. Replacement of an orientation with excision of restriction sites

In figure 3.2.2. two back to back restriction sites are used to prepare overhangs created from various cleavage site sequences.

4. BUSY BEAVER MACHINE BB-3

Busy Beaver Machine is one of the Turing machines which has 3-states, two alphabet $A=\{b, w\}$ and three states $Q = \{q_0, q_1, q_2\}$. The symbols b and w are denoted by black and white boxes. A movement to the left is given by a left arrow and a movement to the right by a right arrow. The next move for the BB-3 machine, if it is in q_0 and the head points to a w is (b, q_1, R) that is $(q_1, w) \vdash (b, q_1, R)$. The machine halts when, if ever, it is in state q_2 and the head points to a b . On a blank tape of white symbols it takes 13 steps to print 6 black symbols and halt.

4.1. A DNA Schematic for the BB-3 Turing machine. Encoding an instantaneous description We encode an ID of the BB-3 TM .Suppose the string holds the string wbw , the head points at the symbol b and the machine is in state q_1 . The representation of symbols, head position and the machine state, as well as the reason we allow two versions of any particular ID, are explained below.

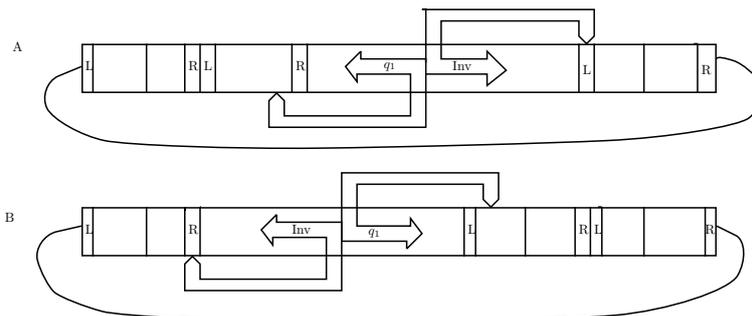
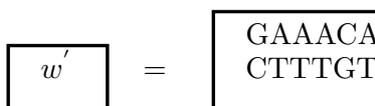


Fig: 4.1.1: schematic representation of BB 3 TM

Symbols Two different DNA sequences are used to denote the symbols w and b . Each is subdivided into a left and right half. The b and w symbols of sequences are called the left and right invariant sequences.

The head The two back to back asymmetric restriction sites labeled Inv and q_1 in figure 4.1.1 represent the head of the TM. The restriction site labeled with current symbol and Inv always points to an adjacent invariant sequence. In fig 4.1.1.A positions the head sequence to the right of the current symbol and the other figure 4.1.1.B positions the head sequences to the left. Finally if the head is to the left of the current symbol then the last move of the machine was to the right.

The state spacing between the restriction site labeled q_1 and the current symbol that encode the state of this TM. Consider the 6 base pair oligonucleotide w' the first half of the symbol w , shown below:



The 4 base pair cutting region of FokI may be used to cut sequence w' in any one of the three different cutting frames by varying the number of intervening bases between the

FokI recognition site and the symbol sequence (figure 4.1.2).

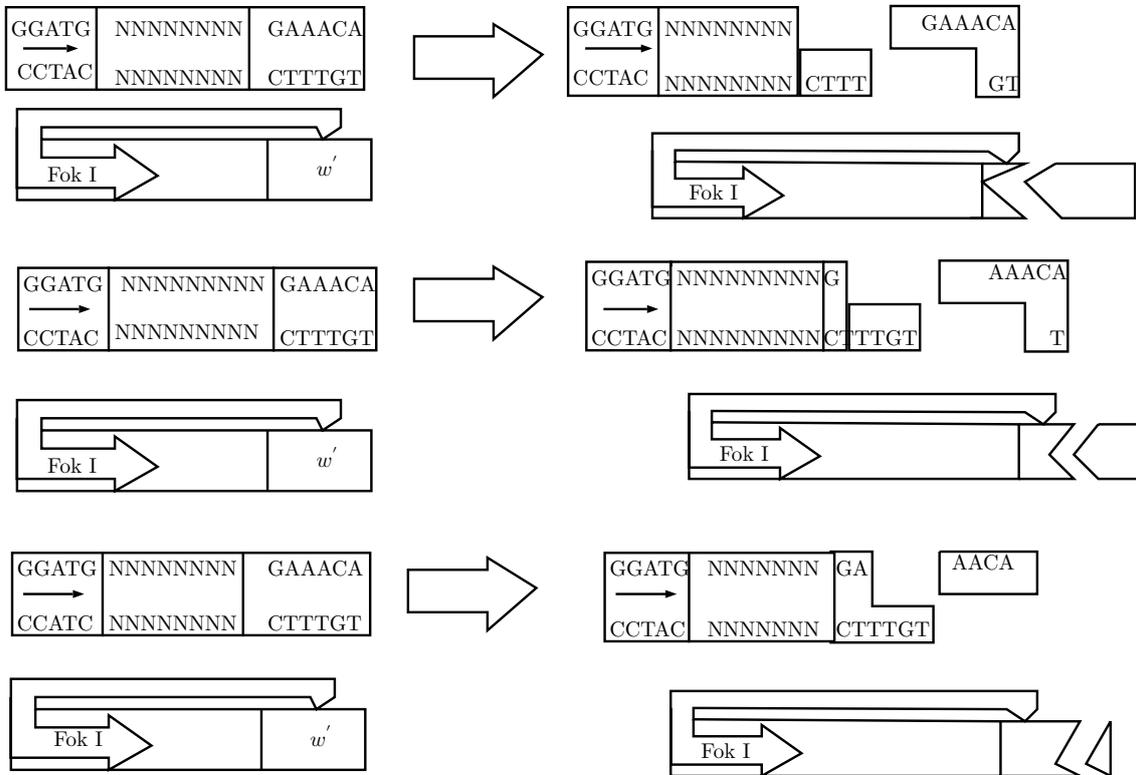


Fig:4.1.2: schematic representations of FokI cutting a six base pair sequence.

Encoding the transition table The unique sticky ends which can be generated by cutting a symbol with **state** cutter allow us to ligate, into our DNA tape, a **transition oligonucleotide** which encodes the new state, symbol, and direction of the TM.

sta is a restriction site for the **state** restriction enzyme. It cuts the current symbol according to the state of the machine.

Em is the restriction site for the **end-maker** restriction enzyme.

Res for 'result' is a sequence encoding the new symbol.

L and **R** are two distinct 'invariant' DNA sequences that separate symbol pairs in the DNA sequence.

X and **Inv** are class IIS restriction sites whose enzymes cleave **L** or **R** to give the same size and orientation overhang. These sites are used to cleave **L** or **R** sequences at various stages of the computation. **Inv** by the invariant enzyme, and **X** by the **symbol-excision** enzyme.

5. INTUITIONISTIC FUZZY DNA(DEOXYRIBONUCLEIC ACID)

For intuitionistic fuzzification of DNA sequences are used for wet lab DNA computing. Let us consider five bases long DNA sequence which indicates a particular membership degree and non-membership degree. These DNA sequences are joined to each other to represent a primary intuitionistic fuzzy set of a specific domain. The membership degrees

Table 1:Range of height

range of height(domain I)	Linguistic value
$4.0' \leq H < 4.5'$	very short
$4.5' \leq H < 5.0'$	short
$5.0' \leq H < 5.5'$	medium
$5.5' \leq H < 6.0'$	tall
$6.0' \leq H < 6.5'$	very tall

Table 2: Range of weight

range of weight(domain II)	Linguistic value
$36 \leq W < 45$	very light
$45 \leq W < 54$	light
$54 \leq W < 63$	medium
$63 \leq W < 72$	heavy
$72 \leq W < 81$	very heavy

Table 3: Range of body mass index

range of body mass index(domain III)	DNA oligonucleotide 5' – 3'	Linguistic value
$bmi < 18.5$	CTAAGTACGT	under weight
$18.5 \leq bmi < 25$	AGGAACCTCG	normal weight
$25 \leq bmi < 30$	TAGCTATGTC	over weight
$30 \leq bmi < 35$	GCGCGAATTC	obesity(class I)
$35 \leq bmi < 40$	GTAACTACGC	obesity(class II)
$40 \leq bmi$	AAATACCGCT	morbid obesity

Table 4: Representation of height and weight

domain	DNA oligonucleotide sequence (5' – 3')
height	TACT
weight	A

of domain are assigned in increasing order($t - norm *$) and the non-membership degrees of domain are assigned in decreasing order($t - comorm *$). That is the distribution of the membership and non-membership degrees($0 < \mu + \gamma \leq 1$) indicates the nature of a specific domain.

Example: Let us encode intuitionistic fuzzy set '*medium*' of '*height*' domain I(Table 1). This particular intuitionistic fuzzy set '*medium*' represents the range $5.0' \leq H < 5.5'$ of domain I(Table 1), an intuitionistic fuzzy degrees are mention in table 5 and the DNA sequences are mention in Table 7 and also encode an intuitionistic fuzzy set '*light*' of '*weight*' domain II(Table 2). This particular intuitionistic fuzzy set '*light*' represents the range $45 \leq W < 54$ of domain II(Table 2), an intuitionistic fuzzy degrees are mention in table 6 and the DNA sequences are mention in Table 7.

5.1. Applicable form of DNA Turing Machine. We first consider the dynamic range of three domains Height(H), Weight(W) and Body Mass Index(BMI) and corresponding quantized ranges are also represented in the following table.

Problem: Let us consider the height= $5.4'$ and weight = 45kg and find out the body mass index using the intuitionistic fuzzy Turing machine.

Table 5: Represent the intuitionistic fuzzy(IF) set of I domain with IF degree

height(H)	very short	short	medium	tall	very tall
very short	(0.9,0.1)	(0.7,0.2)	(0.5,0.3)	(0.3,0.5)	(0.1,0.7)
short	(0.7,0.2)	(0.9,0.1)	(0.7,0.2)	(0.5,0.3)	(0.31,0.5)
medium	(0.5,0.3)	(0.7,0.2)	(0.9,0.1)	(0.7,0.2)	(0.5,0.3)
tall	(0.3,0.5)	(0.5,0.3)	(0.7,0.2)	(0.9,0.1)	(0.7,0.2)
very tall	(0.1,0.7)	(0.3,0.5)	(0.5,0.3)	(0.7,0.2)	(0.9,0.1)

Table 6: Represent the IF set of II domain with IF degree

weight(W)	very light	light	medium	heavy	very heavy
very light	(0.9,0.1)	(0.7,0.2)	(0.5,0.3)	(0.3,0.5)	(0.1,0.7)
light	(0.7,0.2)	(0.9,0.1)	(0.7,0.2)	(0.5,0.3)	(0.31,0.5)
medium	(0.5,0.3)	(0.7,0.2)	(0.9,0.1)	(0.7,0.2)	(0.5,0.3)
heavy	(0.3,0.5)	(0.5,0.3)	(0.7,0.2)	(0.9,0.1)	(0.7,0.2)
very heavy	(0.1,0.7)	(0.3,0.5)	(0.5,0.3)	(0.7,0.2)	(0.9,0.1)

Table 7: Representation of IF degree by DNA sequence

intuitionistic fuzzy degree	DNA sequence(5' - 3')
(0.1, 0.7)	ATACG
(0.2, 0.7)	CTGGT
(0.3, 0.5)	GTGTC
(0.4, 0.4)	TCAAT
(0.5, 0.3)	TGCCA
(0.6, 0.3)	AGGCT
(0.7, 0.2)	CCTTA
(0.8, 0.1)	GTATC
(0.9, 0.1)	AGCTA
(1.0, 0.0)	TAACC

5.2. **Wet lab implementation of Intuitionistic Fuzzy Turing Machine.** The rules are coded in terms of double stranded DNA sequences.

Example

Encoding 'medium' in terms of DNA sequence

(0.5,0.3) (0.7,0.2) (0.9,0.1) (0.7,0.2) (0.5,0.3)

5' TGCCACCTTAAGCTACCTTATGCCA 3'
 3' ACGGTGGAATTTCGATGGAATACGGT 5'

Encoding 'Light' in terms of DNA sequence

(0.7,0.2) (0.9,0.1) (0.7,0.2) (0.5,0.3) (0.3,0.5)

5' CCTTAAGCTACCTTATGCCAGTGTC 3'
 3' GGAATTTCGATGGAATACGGTCACAG 5'

Encoding the rule: If height=medium and weight=light then body mass index is normal weight

antecedent
consequence

5' TGCCACCTTAAGCTACCTTATGCCACCTTAAGCTACCTTATGCCAGTGTCAGGAACCTCG 3'
 3' ACGGTGGAATTTCGATGGAATACGGTGGGAATTTCGATGGAATACGGTCACAGTCCCTGGAGC 5'

The initiator is added at the beginning of every rule so that the restriction enzyme can start the work. The initiator contains

Table 8: Represents the production rules

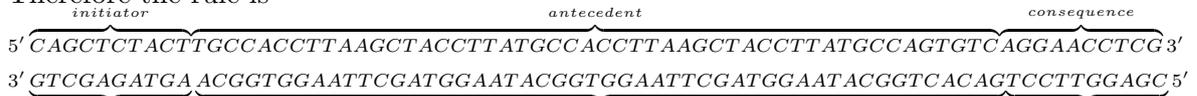
height	weight	consequent body mass index
very short	very light	normal weight
very short	light	over weight
very short	medium	obesity (class II)
very short	heavy	morbid obesity
very short	very heavy	morbid obesity
short	very light	normal weight
short	light	normal weight
short	medium	over weight
short	heavy	obesity class(I)
short	very heavy	obesity class(II)
medium	very light	under weight
medium	light	normal weight
medium	medium	normal weight
medium	heavy	over weight
medium	very heavy	obesity class(I)
height	weight	consequent body mass index
tall	very light	under weight
tall	light	under weight
tall	medium	normal weight
tall	heavy	normal weight
tall	very heavy	over weight
very tall	very light	under weight
very tall	light	under weight
very tall	medium	under weight
very tall	heavy	normal weight
very tall	very heavy	normal weight

- (i) The restriction site of the enzyme Ace III and
(ii) spacer which represents a specific domain.

The initiator is



Therefore the rule is



Transition molecules:

Domain I



$T_4 : 5' CAGCTCTACT 3'$
 $3' GTCGAGATGAGATG 5'$
 $T_5 : 5' CAGCTCTACT 3'$
 $3' GTCGAGATGAGGAA 5'$
 $T_6 : 5' CAGCTCTACT 3'$
 $3' GTCGAGATGAATAC 5'$

Domain II:

$T_7 : 5' \overbrace{CAGCTC}^{\text{recognition site}} \overbrace{T}^{\text{spacer}} 3'$
 $3' \overbrace{GTCGAG}^{\text{recognition site}} \overbrace{A}^{\text{spacer}} \overbrace{CGGT}^{\text{single standard}} \overbrace{5'}$

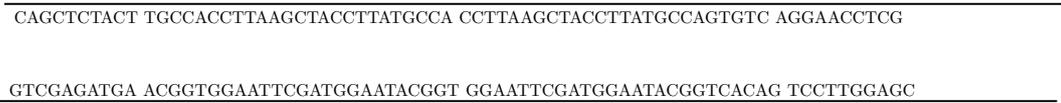
$T_8 : 5' CAGCTCT 3'$
 $3' GTCGAGAAATT 5'$
 $T_9 : 5' CAGCTCT 3'$
 $3' GTCGAGAATGG 5'$
 $T_{10} : 5' CAGCTCT 3'$
 $3' GTCGAGATACG 5'$

Out put detection molecule:

$T_{11} : 5' \overbrace{TA}^{\text{labeled bases}} 3'$
 $3' \overbrace{AACACA}^{\text{labeled bases}} 5'$

Mechanism of operation:

Initially the rules are considered to be in state q_0 . As the restriction enzyme recognizes the restriction site of the initiator the cleaving operation starts. Then the appropriate transition molecule splice with the cleaved site of the DNA sequence. After splicing the transition state occurs. We will select that particular sequence which will reach to the accepting state. It is our computational result. The restriction enzyme Ace III is used for cleaving the sequences which is of type IIS. The recognition site of this enzyme is $5' CAGCTC 3'$. Its cuts the sequences 7base per downstream from the non-palindromic asymmetric recognition sites.



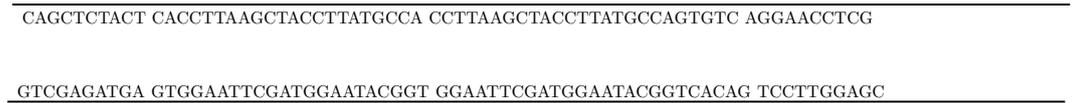
First of all an IFTM having the inside tape in above DNA sequences (initiator, medium, light and normal weight).



The initial state q_0 and the Inv (the back to back asymmetric restriction sites) are pointed in above DNA sequence.



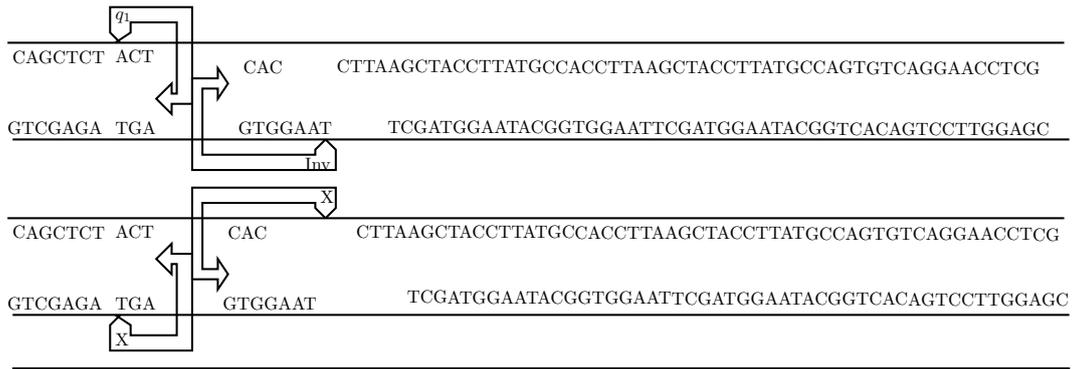
The symbol-excision enzyme cutter X are pointed in above DNA sequence and cut out from the DNA sequence.



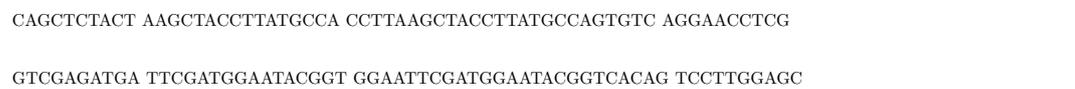
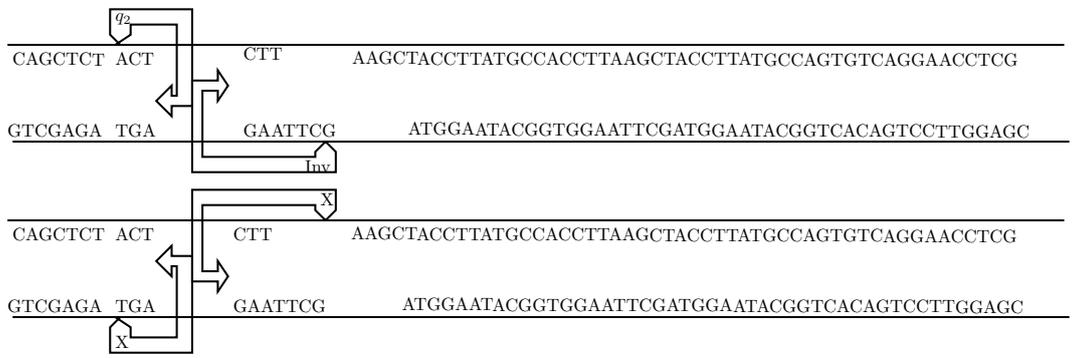
Finally insert the transition molecule T_1 , now getting the new DNA sequences.

$$\delta\left(q_0, \begin{matrix} ACTTGC \\ TGAACGGTGG \end{matrix}\right) = \left(q_1, \begin{matrix} ACT \\ TGAGTGG, S \end{matrix}\right)$$

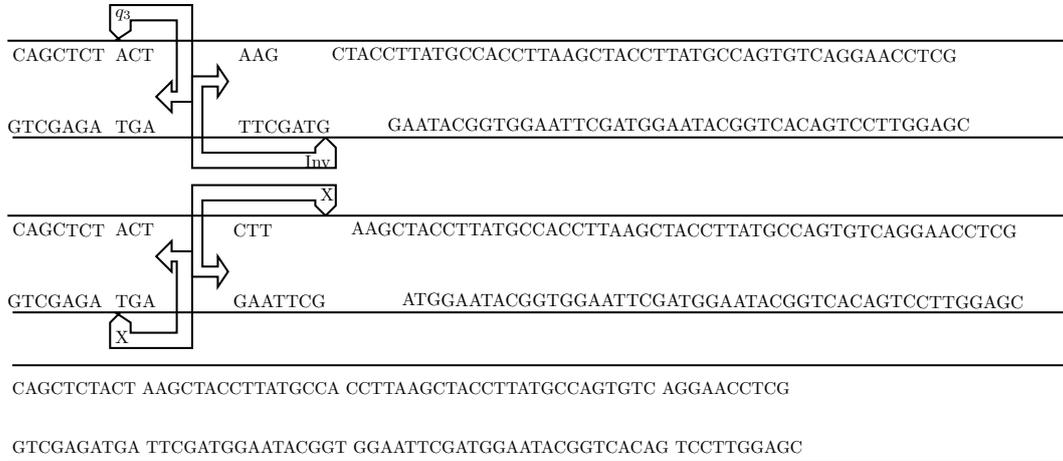
The header stay(S) that place but DNA sequences are cut(7 base per) and insert(transition molecule) getting new DNA sequences so the header point the new state. Similarly the above process are followed up to getting a resulting sequence of normal weight(that is up to state q_{11}).



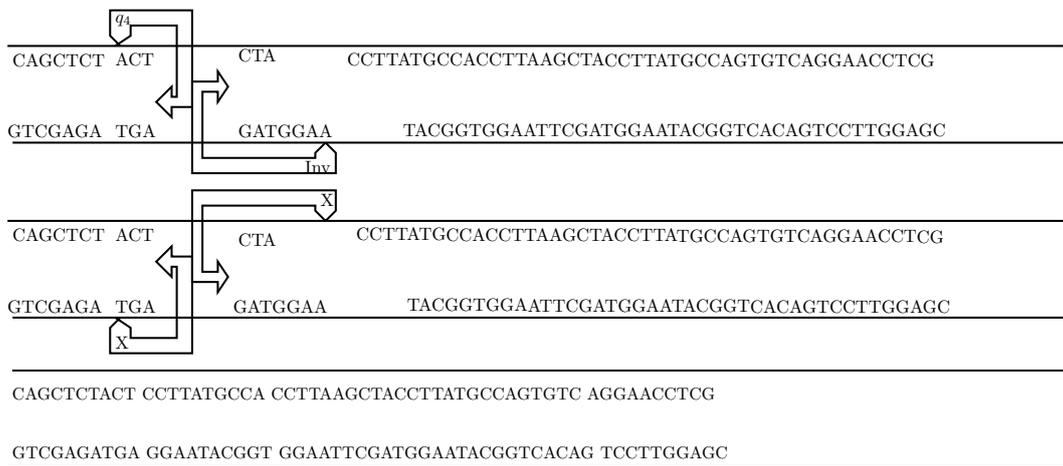
$$\delta\left(q_1, \begin{matrix} ACTCAG \\ TGAGTGGAAAT \end{matrix}\right) = \left(q_2, \begin{matrix} ACT \\ TGAGAAT, S \end{matrix}\right)$$



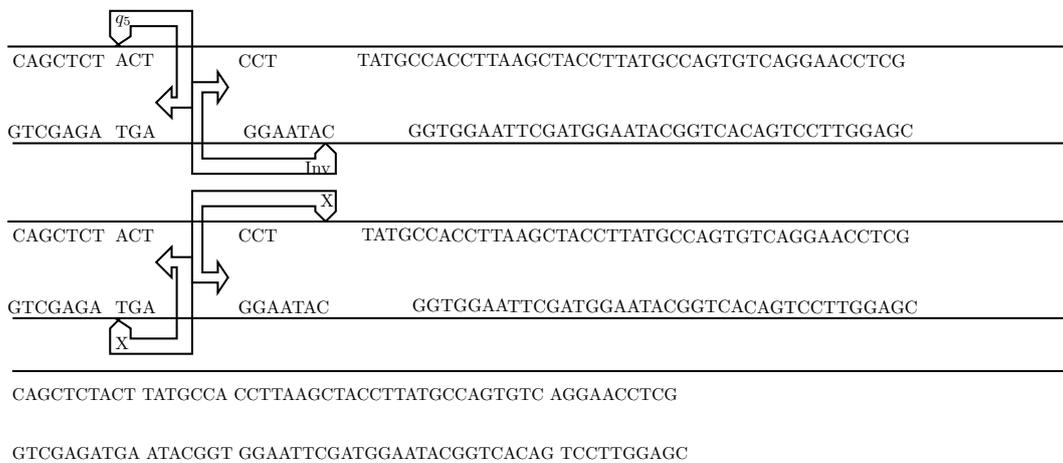
$$\delta(q_2, \begin{matrix} ACTCTT \\ TGAGAATTCTG \end{matrix}) = (q_3, \begin{matrix} ACT \\ TGATTCTG, S \end{matrix})$$



$$\delta(q_3, \begin{matrix} ACTAAG \\ TGATTCTGATG \end{matrix}) = (q_4, \begin{matrix} ACT \\ TGAGATG, S \end{matrix})$$



$$\delta(q_4, \begin{matrix} ACTCTA \\ TGAGATGGAA \end{matrix}) = (q_5, \begin{matrix} ACT \\ TGAGGAA, S \end{matrix})$$



$$\delta(q_5, \begin{matrix} CAGCTCTACTCCT \\ GTCGAGATGAGGAATAC \end{matrix}) = (q_6, \begin{matrix} CAGCTCTACT \\ GTCGAGATGAATAC, S \end{matrix})$$



$$\delta(q_6, \begin{matrix} CAGCTCTACTTAT \\ GTCGAGATGAATACGGT \end{matrix}) = (q_7, \begin{matrix} CAGCTCT \\ GTCGAGACGGT, S \end{matrix})$$



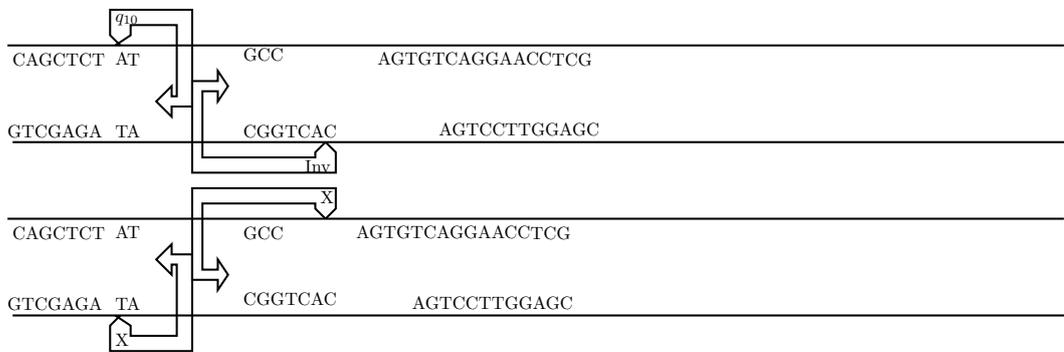
$$\delta(q_7, \begin{matrix} CAGCTCTGCCAAC \\ GTCGAGACGGTTGAATT \end{matrix}) = (q_8, \begin{matrix} CAGCTCT \\ GTCGAGAAATT, S \end{matrix})$$



$$\delta(q_8, \begin{matrix} CAGCTCTTTAAGC \\ GTCGAGAAATTCGATGG \end{matrix}) = (q_9, \begin{matrix} CAGCTCT \\ GTCGAGAATGG, S \end{matrix})$$



$$\delta\left(q_9, \begin{array}{l} CAGCTCTTACCTT \\ GTCGAGAATGGAATACG \end{array}\right) = \left(q_{10}, \begin{array}{l} CAGCTCT \\ GTCGAGATACG, S \end{array}\right)$$



$$\delta\left(q_{10}, \begin{array}{l} TATGCC \\ ATACGGTCAC \end{array}\right) = \left(q_{11}, \begin{array}{l} TAA \\ ATTCAC, H \end{array}\right)$$

The output detection molecule is radio-labeled. After the attachment of output detection molecule the transition to q_{11} occurs which is the accepting state(resulting state of DNA sequences). The output molecule can be detected by performing gel electrophoresis. The last ten bases of the consequence is **AGGAACCTCG** which represents the primary intuitionistic fuzzy set **normal weight**. The result of problem is height=5.4' and weight=45kg then body mass index is denoted as **normal weight**.

6. CONCLUSION

In this work, we suggest some mechanisms to find the body mass index using the operations of class II and class IIS restriction endonucleases. We considered real DNA sequences to our schematic BB-3 Turing machine that could be used with commercially available enzymes to implement a Turing machine in lab. We propose an intuitionistic fuzzy Turing machine based on splicing theory and find results of our wet lab experiment. In this work we have used intuitionistic fuzzy DNA to handle the imprecision of input data which are very essential for our real life applications.

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