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VLSI Design and Implementation DNA Sequence Alignment for Hardware Based Applications

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ABSTRACT

In this paper we are going to propose a new approach to map the DNA sequences using Smith waterman algorithm with Gotoh algorithm. In general Bio medical applications sequence mapping plays a major role for identifying various issues regarding diseases, mutations etc. can be analyzed and identified. As the mapping process is the most time consuming process here we are going to resolve it by introducing divide and conquer based approach and implement parallelism for mapping the sequences and we can enhance the performance of mapping sequence process. The proposed implementation is suitable for FPGA hardware utilization which is the prime factor of our suggested implementation. The synthesis and simulation of the proposed implementation can be done using CAD tools & MATLAB for extracting the DNA data.

Keywords : DNA sequence, Sequence Alignment, Smith waterman algorithm, gotoh, FPGA, D & C principle.

I. INTRODUCTION

In bio science studies DNA plays a vital compound to retrieve the data about its specifications and species. This particular DNA sequence describes the functionality and features etc., information related to particular creature is known and the data related will be comprised in it. This sequence mainly consists of four different nucleotide structures that can be defined as A, T, G and C. theses can further abbreviated as A for Adenine, and T for thymine, C for cytosine and G for guanine. By aligning them altogether in various forms constitutes the DNA structure of a particular species. The alignment of the resultant sequence of DNA will be in a structure called helical that is utilized for getting its features and characteristics of that unique species. For a wide of applications this DNA matching is widely employed to analyze and extract the data which makes use of a method called mapping among two different sequnces.

Scientists use two methods to solve the mapping problem: - heuristic methods and exact methods. Heuristic methods solve the mapping problem more rapidly than accurate methods do. However, such methods like BLAST and FASTA, suffer from accuracy. Therefore, bioinformatics researchers use

dynamic programming, which is more efficient; an algorithm called smith waterman is very widely employed algorithm for the determination of correlation among two different data sequences..

Sequence:

The four major elements of DNA with a wide range of combinations among these nucleotides can be simply defined as a sequence.

Sequencing:

Sequencing is a method or approach to determining the fragments of DNA.

Sequence alignment:

The comparability lies in structuring of the collection of nucleotide sequences for detecting homology sections amongst those fragments. These can be utilised for examining and evaluating that whether there exists any relationship between query (which is our input sequence that need to analyzed) and database (simply it can be a known sequence for reference from cloud or any data base system). To determine the resemblance between the known and unknown fragments of DNA data of sequence, here the methodology uses dynamic way of programming which includes the break-down of the whole sequence of nucleotides into simpler, non-interdependent subsets of sequences. That gets the scoring for every search of resemblance to find the congruence with further more realistically.

Sequence Alignment methods:

The congruence can be classified into majorly in two ways:

Global Alignment:

Composition wise similar strings of DNA possessing identical number of nucleotides can be considered as best suitable sequences this type of alignment/congruency. This way of alignment can be processed from start to end by identifying the appropriate and most practically suitable alignment match of nucleotide.

Local Alignment:

Local matching of data is mostly applied for getting comparison of data which is assumed as that may be similar or completely unique data. This uncovers local systems with significant degree of correlation.

Separate algorithms describe these two alignment approaches, which employ scoring matrices to align the two different series of letters or patterns (sequences). For aligning two distinct sequences, the two alternative alignment algorithms are primarily described by the Dynamic programming methodology.

II. RELATED WORKS

BLASTN:

The most basic and widely utilized data sequence correlation finder in the field of molecular biology is BLATN which is specifically for DNA data. It is employed to efficiently locate biologically significant comparable areas between two sequences. As the amount of genome sequences grows, so does the time required for BLAST to do a thorough genomic database search. As a result, it is necessary to expedite the search process. This method is employed in various scenarios such as when there is a need for determining the correlation amongst huge amount of genomic datasets with respect to the query (unknown/input) sequence. BLASTN method is the extraction from BLAST technique but completely dedicated to DNA data. This method is majorly consisting of various stages such as matching of words where the determination of matching can be analysed followed by extensions of both un-gapped and gapped as next following stage.

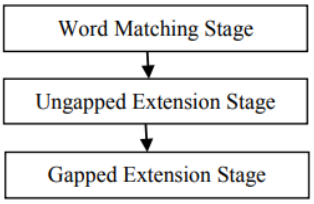


Fig.1: basic steps or stages involved in BLAST

The input for the Word Matching step is a string of DNA bases that commonly comprises A, C, G, and T. The database is searched for brief precise matches of a specific length between the query and the topic sequence. This brief precise match is referred to as the seed. Each seed is extended in both directions during the Ungapped Extension step, permitting replacement. When two sequences of equal length are split and their alignment scores surpass the threshold value, such pairs are referred to be high scoring pairs (HSP). At the end, such HSPs are obtained. Dynamic programming algorithms are utilised to expand the HSPs during the Gapped Extension step. It supports insertions and removals. The fundamental concept of involved in this particular blast method is the concept of filtering. Though every stage of this method of pipelining results in increasingly complex, it is critical to limit the quantity of data that must be processed owing to the exponential rise in data volume. Filtration is a process that discards unimportant fractions as soon as feasible, reducing total computing time. Each level of BLASTN needs a varying amount of processing time. After analysing each stage, it becomes clear that the word matching stage is the most time intensive. As a result, to improve BLASTN's overall performance, the calculation time of this step should be sped up.

Dynamic Programming:

The needleman-Wunsch and Smith-Waterman data of DNA correlation methods comes under this dynamic programming approach. In 1981 scientists named Temple F. Smith and Michael S. Waterman are the persons to propose a sequence alignment algorithm known as Smith Waterman. it gives conserved regions of correlation amongst the sequences, and may line up 2 partially overlapping fragments of data sequences. the framed sub segments of aligned fragments can also be applied for checking the similarity between the known and unknown sequences. this S-W varied from the N-W as it will have any negative scoring only for un-matched conditions any value is negative n the matrix fill it will mark it to zero (consider max value in comparison with '0').

III. PROPOSED METHOD

SYSTOLIC ARRAY ALIGNMENT:

The Systolic Arrays can be determined by whether they are included with local data transmission and parallel processing. Processing Elements can be placed in a 2-d format, which is as follows Fig. 3.1(a), linear, as shown in Fig. 3.1(b), or some other random shapes structures like hexagonal, as shown in Fig. 3.1(c), which is here implemented as a circuit with data flowing in 3 various directions. in the very conventional or tradition process[7], it can be designed by starting with the problems in the flow and after that following with these stages: 1) as a first step/stage DG which means a dependent graph which is the generation of flow in a graphical way including nodes that reciprocates the evaluation part and the edges represent the dependency of data that is provided; 2) the next thing is the generation of SFG which is a signal flow graph which is the reduced one axis of DG.

Subsequently,an SFG has a dimensionless than the correspondent DG; this is because in a DG each node represents one simple computation, while in the SFG a node is a processing unit, that should be reused in successive time steps, and for this reason nodes of a line in a DG can be mapped to a single node in the SFG; and 3) array processor design, that consists in designing the internal structure of each PE.

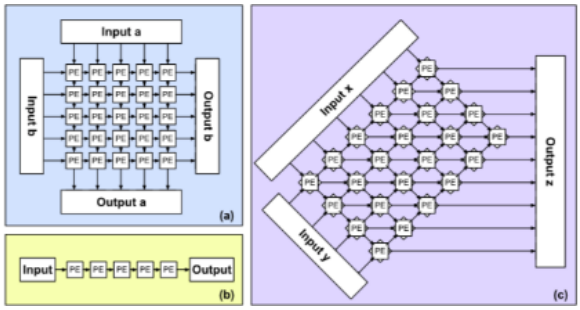


Figure 3.1 Systolic Array

SEQUENCE ALIGNMENT

Sequence comparison is a fundamental operation that allows biologists to find any functional correlations.

Sequence alignment is the most computational intensive task during comparison and providing alignment score that represents similarity index amongst unknown which is query can be defined as Qry and known sequence which is obtained from database here referred as Sbj.

If there is a match or a substitution the value of the scoring must be updated using the value coming from a substitutional matrix: given the two AAs Qry(i) and Sbj(j), this matrix returns a value s(Qry(i),Sbj(j)) that represents the probability that an AA(amino acids) is substituted with another during evolution [21]. When a deletion or an insertion occurs, the alignment score must be updated using instead a gap penalty.

The most used penalty is the affine one (γaff) in which two different values, called gap_open d and gap_extension e, are used to encourage one large gap rather than many small ones, since the former condition is more likely. In the following equation, g represents the length of the gap [22]:

γaff =– d–(g–1)·e. (1)

for the analysis and extraction of correlated sequences, the widely utilized method of alignment tool is "S-W" [23].

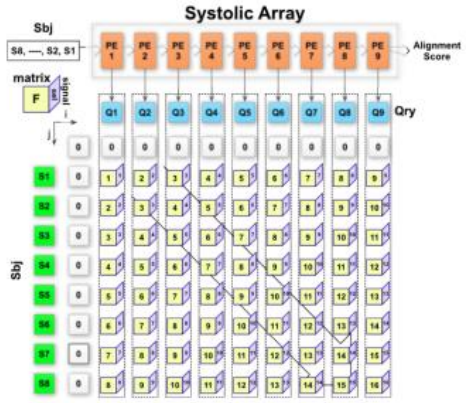


Figure 3.2 DGS_S-W algorithm matrix alignment

DGS_S-W algorithm

S-W is a dynamic programming approach that uses a score matrix F(i, j) to record correlation values at every moment, as seen in the lower section of Fig. 3.2. The scope of this study does not allow for a full discussion of the S-W algorithm. Here, we describe briefly its architecture and to do so, we introduce its working mechanism at a glance. It is important to highlight that adopting the gap affine model, each cell is required to evaluate three different values.

Recently, this algorithm has been optimized for the SA implementation is allowing faster and lighter computations. The main idea of this optimization is to use a sel signal that can be either 0 or 1 to choose on-the-fly between gap_open and gap_extension and for this reason it is called dynamic gap selector (DGS): this substitutes the usage of two gap matrices that are provided by the original algorithm, that required a higher computation effort and an increased complexity. S-W algorithm is divided into three steps. 1) Initialization: first row and first column of the matrix, respectively, F(i,0) and F(0, j), are initialized to 0. 2) Score Matrix filling: each cell is filled with a value of F(i, j); in the case of DGS_S-W, this value is evaluated .

Traceback: the maximum score represents the starting point for the best local alignment that is found tracing back till the first 0 is found.

Interleaving in SAs

In this process of sequencing correlation, systolic array structure has been involved. Here we are going to elaborate about assigning the interleaving to PE level and the extension of it to the entire SA. These can be further categorized as 1) with WIL and 2) without having the internal loop; this thing is again extended to the segmentation of sub divisions as 1) results storing in cells and 2) those with extension of results over cells to get WIL-PT. The DGS S-W SA falls within this category.

The major benefits of bit based matching process are as follows:

- In hardware, RNA rules and DNA patterns are stored in nonvolatile memory. In bit based matching each FSM states holds only one bit. Significant speed improvements and area reduction is obtained using FSM based state transitions.
- Parallel computation is accomplished with multiple sub patterns that stored in different

FSM machines and synchronized through PMV vectors.

- Bit wise FSM state transitions fail even with one bit mismatch during string matching process and successive payloads are bypassed without making any further FSM state transition and matching process.

And the key issues related to the DNA biological sequence matching includes lack of parallel processing during similarity measure and scoring, selection of core processing element for lesser power and to exploits high scalability.

Therefore, all the factors discussed so far gives a complete scenario of the factors that are required to improve the throughput rate of pattern matching system for RNA system and biological pattern analyzes. The various factors that are motivated this research are:

- The data pattern correlation algorithm leads to high amount of propagation time that is effected in a greater extent to a wide range of nucleotides together as a pattern along with its complexity. In this case, longer incursions should be broken into many sub patterns and matched in parallel.
- Scalability and reconfigurable nature of the memory elements used to store the patterns for matching units is essential to update and include the new patterns and also for realizing the parallelism.
- The only possible way to reduce power consumption in any RNA system is dynamic power management (DPM) through data transition reduction controller.
- FPGA-based systems provide higher flexibility and re-configurability compared to ASIC based solutions with satisfactory processing throughput without causing latency problem.
- Integration of the entire patterns matching system using ADPLL will provide fully synchronous matching process for RNA for different kind of network traffic rate.

Bit Based String Matching Methodologies

The statistical nature of RNA rule sets and matrix evaluation of dynamic programming in DNA sequence alignment bit based string matching methodology is proposed as shown in Fig m which works across RNA patterns with different traffic rate, correlation and gab penalty measure of various DNA sequences .Here, the idea is to process string as a sequence of bits and to handle rule set updating and data base changes using reconfigurable hardware devices. In this a particular number of fragments are required for finding the correlation among the complete data sequence each having its own storage cell of memory which is a vital thing to consider here.

PAIR-WISE DNA SEQUENCE ALIGNMENT

Sequence alignment by pairs Dynamic programming is always more accurate than heuristic programming at sequence alignment. However, it has the disadvantage of being computationally complicated and time-consuming. As a result, because DP techniques are exhaustive in nature, optimising them to enhance speed is challenging

DGS_SW is well known Dynamic programming method to explore the correlation level between the sequences through score matrix generated dynamically during matching process. If the gap is arise during matching process in matrix, dynamic programming is used to align the gaps by assigning some unified score values.

Here to increase the through put of PE, pipelining was merged into it.

DGS_SW : Dynamically selection of Gap in Smith-Waterman

This is the approach which is most widely utilized for the congruency of data sequences and here we further implemented a technique called pipelining in systolic array approach.

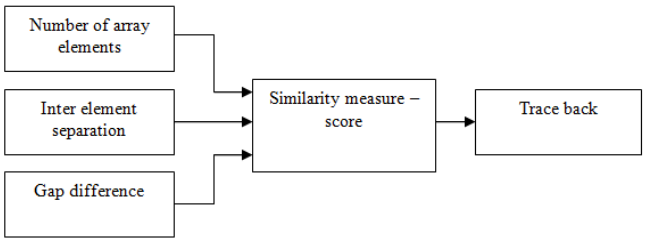


Fig. 3.4. dual data fragments correlation using smith waterman technique

Here two segments of whole data are correlated obtained from the matrix PE for performing the congruency operation as shown in Fig 4. Utilizing SA based pipelining amongst the PE blocks. Finally score assignments is done for analyzing the amount of correlation and penalty gap amongst unknown input and reference input. DGS_SW is a dynamic programming based algorithm that determines a score matrix F (i, j) during the correlation determining process as shown in Fig 5.

Smith-Waterman Algorithm

1. Converting the raw data to bits of "0" & "1"
2. Generating a L length systolic matrix array
3. Segmenting the L into sub sequences

Assigning 2 as match score if condition is satisfied or else assigning zero as gap difference

Once this is satisfied we can directly go to 5th step.

4. Escalate the score numbers to preceding rows &b columns for every new task of nucleotide matching.
5. By utilizing max driven point sin array we have trace back the sequence of data
6. Finally need to make the decision of the process

The result indicates that dynamic programming has the efficiency to operate at high frequency and shows a clear improvement in hardware utilization rate with significant hardware complexity reduction.

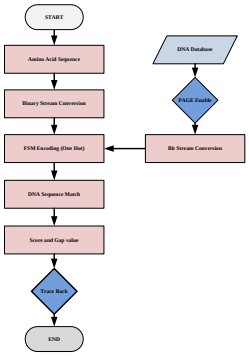


Fig. 3.5. Architecture for sequence alignment using FSM machines

Though the sequence alignment of biological sequence matching is data dependence algorithm here with FSM based bit holding method constraint it over a maximum number of PEs required to match the total query sequence in the database and the problem over trade off complexity over incoming protein sequences lengths is solved.

During the hardware synthesis it was observed that,

- When compared to an ASCII-based matching procedure, the number of comparisons and bit transitions is significantly reduced.
- The maximum number of PEs in FSM based architecture is set with pre-defined pattern lengths.

The bit wise FSM state transitions shares the same features that of an RNA system hence it is essential for high speed DNA matching process. Consequently, all these observations, advantages were analyzed and in the subsequent section detailed explanation is given about FSM machines proposed for RNA and DNA biological sequence matching process.

IV. RESULTS AND DISCUSSION

Fig. known and unknown DNA

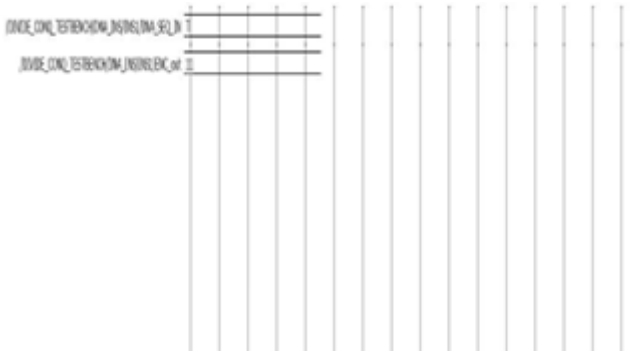


Fig. Encoded output

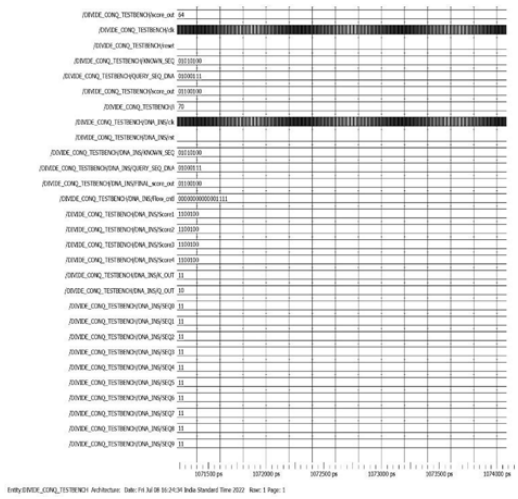
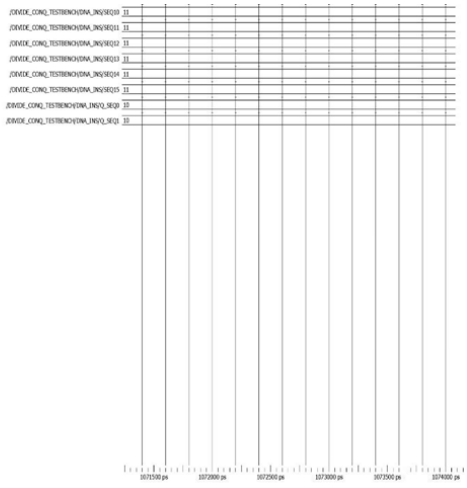


Fig. Score value generation



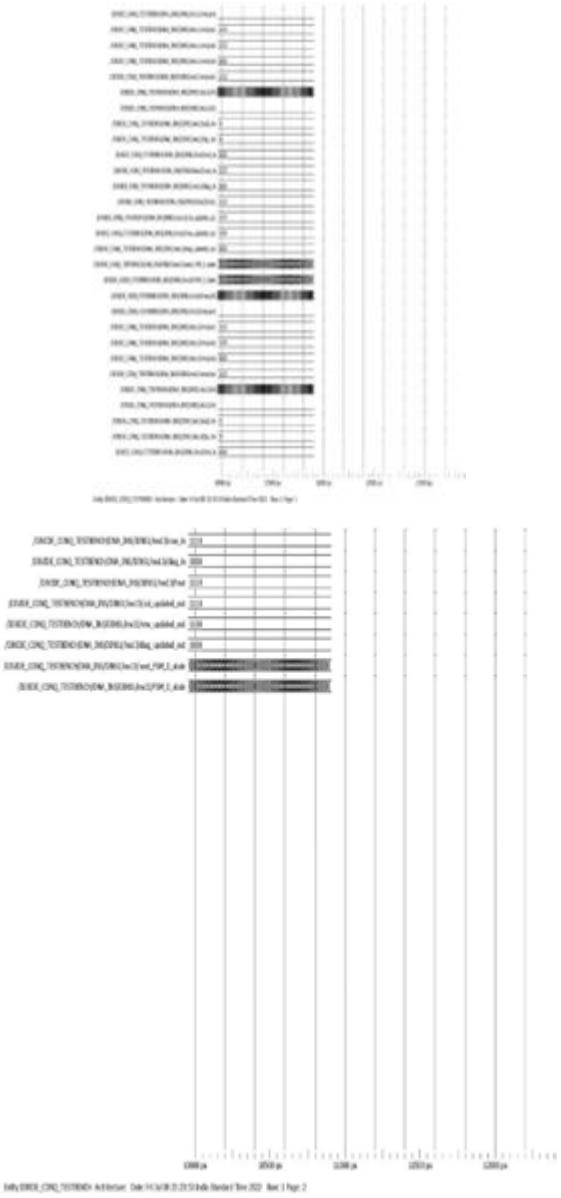


Fig. FSM State values

Date: July 10, 2022 Project: final

Flow Status	Successful - Sun Jul 10 13:28:01 2022
Quartus II Version	9.1 Build 222 10/21/2009 SJ Web Edition
Revision Name	final
Top-level Entity Name	DNA_TOP
Family	Stratix II
Met timing requirements	No
Logic utilization	1 %
Combinational ALUTs	102 / 12,480 (< 1 %)
Dedicated logic registers	136 / 12,480 (1 %)
Total registers	136
Total pins	26 / 343 (8 %)
Total virtual pins	0
Total block memory bits	0 / 419,328 (0 %)
DSP block 9-bit elements	0 / 96 (0 %)
Total PLLs	0 / 6 (0 %)
Total DLLs	0 / 2 (0 %)
Device	EP2S15F484C3
Timing Models	Final

Page 1 of Revision: final

Fig. Logical elements of proposed system

Date: July 10, 2022 Project: privious

Flow Status	Successful - Sun Jul 10 13:29:27 2022
Quartus II Version	9.1 Build 222 10/21/2009 SJ Web Edition
Revision Name	privious
Top-level Entity Name	DNA_TOP
Family	Stratix II
Met timing requirements	Yes
Logic utilization	1 %
Combinational ALUTs	93 / 12,480 (< 1 %)
Dedicated logic registers	125 / 12,480 (1 %)
Total registers	125
Total pins	26 / 343 (8 %)
Total virtual pins	0
Total block memory bits	0 / 419,328 (0 %)
DSP block 9-bit elements	0 / 96 (0 %)
Total PLLs	0 / 6 (0 %)
Total DLLs	0 / 2 (0 %)
Device	EP2S15F484C3
Timing Models	Final

Page 1 of Revision: privious

Fig. Logical elements of existing system

Date: July 10, 2022 Project: privious

PowerPlay Power Analyzer Status	Successful - Sun Jul 10 13:32:38 2022
Quartus II Version	9.1 Build 222 10/21/2009 SJ Web Edition
Revision Name	privious
Top-level Entity Name	DNA_TOP
Family	Stratix II
Device	EP2S15F484C3
Power Models	Final
Total Thermal Power Dissipation	324.38 mW
Core Dynamic Thermal Power Dissipatio	0.00 mW
Core Static Thermal Power Dissipation	302.98 mW
I/O Thermal Power Dissipation	21.40 mW
Power Estimation Confidence	Low: user provided insufficient toggle rate data

Fig. Power Analyzer report of proposed system

Fmax Summary

	Fmax	Restricted Fmax	Clock Name	Note
1	304.69 MHz	304.69 MHz	clk	

Fig. Power Analyzer report of existing system

Fmax Summary

	Fmax	Restricted Fmax	Clock Name	Note
1	306.65 MHz	306.65 MHz	clk	

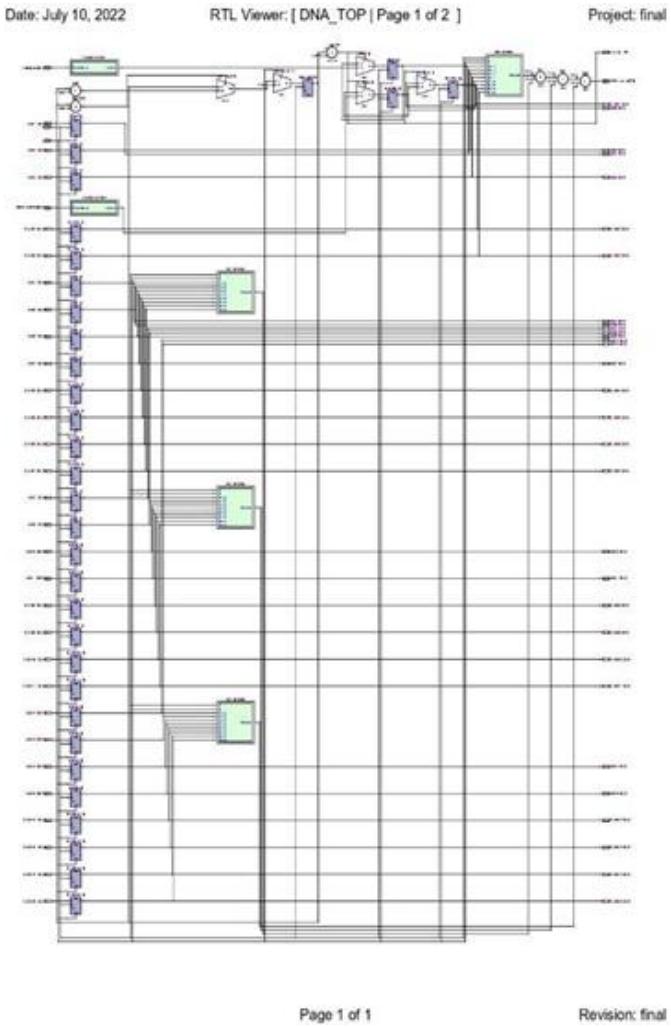
Fig. Time Analyzer report of proposed system

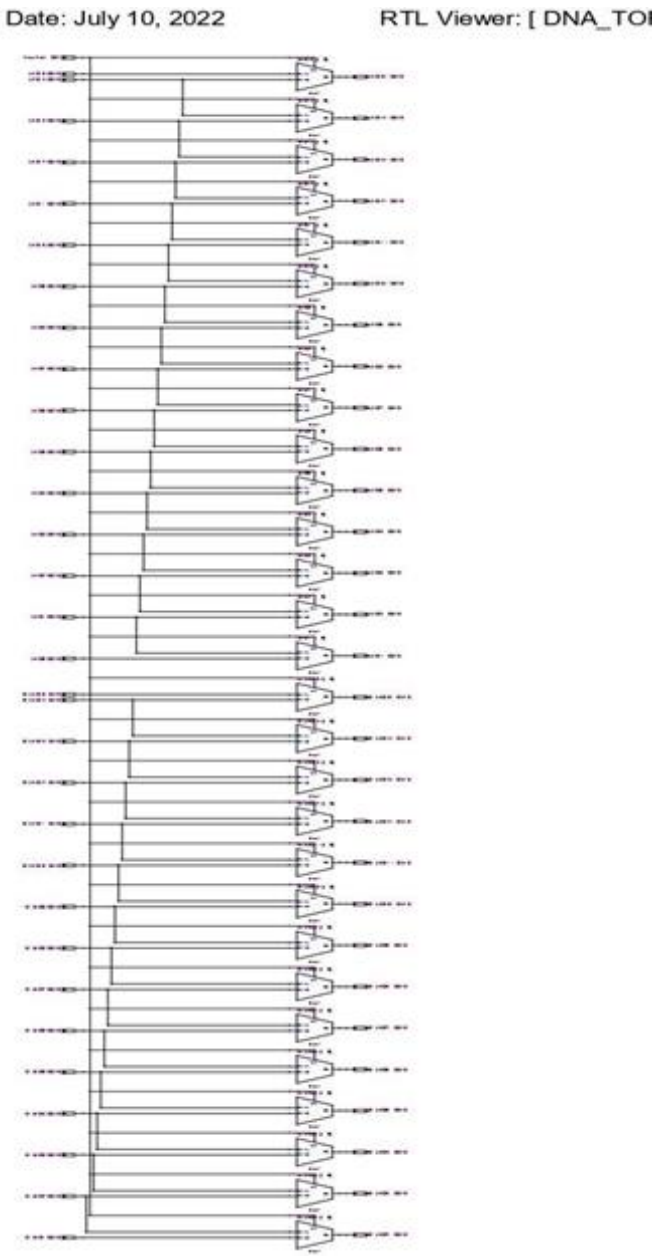
Type used	LE's used	Fmax(MHz)	Power (mW)
Core processing	93 logical	306.65	302.98

element	elements		
FSM based array element	102 logical elements	302.98	302.98

Here for DNA grouping arrangement recreation is done to decide the malignant growth types in view of succession arrangements on an enormous data set where various examples of different disease types are sorted. Here thorough test seat is mad e with a succession of different protein arrangements and recognition is likewise conveyed after the match score is assessed.

RTL VIEW OF COMPLETE SYSTEM





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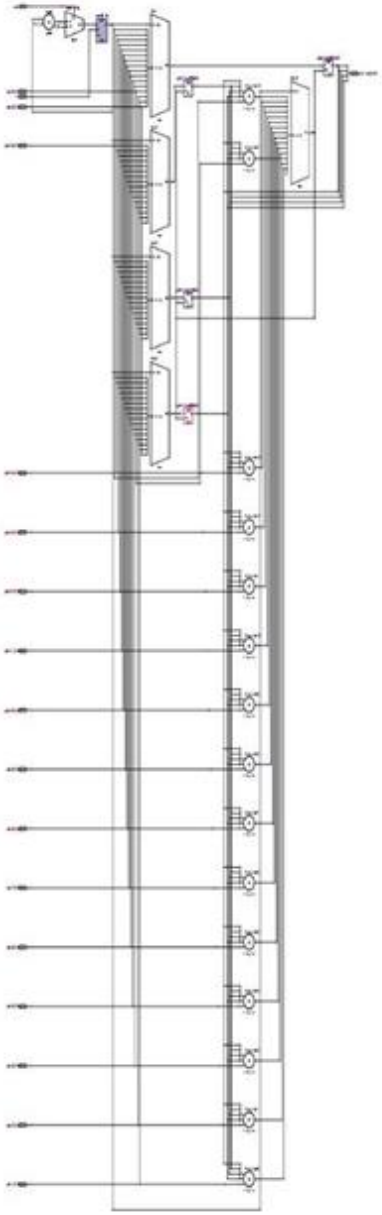

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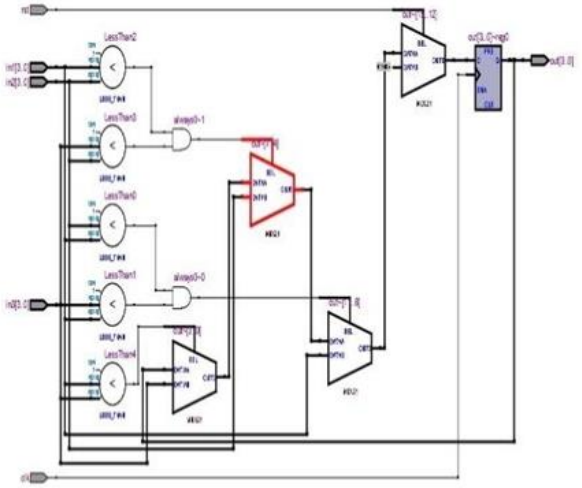

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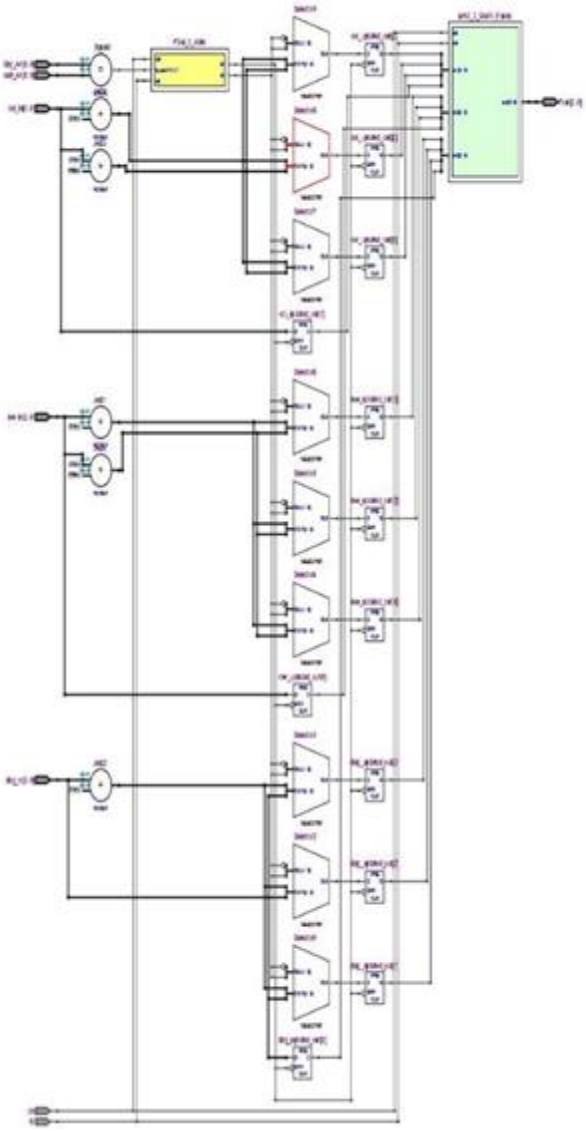

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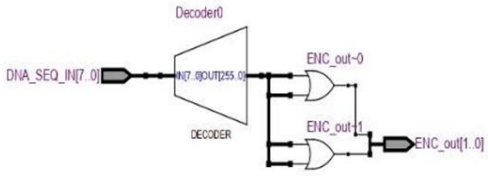

III. CONCLUSION

Because several sequences are matched in parallel, it is clearly demonstrated that the deconstructed systolic array technique always delivers extremely good performance. However, flexibility to optimise the power over DGS SW algorithm is not available. The only approach to approximate matching without using any power reduction strategies is to address distinct regions of PEs. However, this will have a substantial impact on performance. A systolic array-based matrix calculation is used to calculate the similarity score between DNA sequences in order to efficiently extract the gap penalty.

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