

Constructing a Fast Bioinformatics Algorithm to Solve Cancer Genome Assembly Using Enhanced Euler Path on Constructed De Bruijn Bioinformatics Graph

Michael Shan-Hui Ho, Kun-Yu Hung, Paul Pin-Shuo Huang, Jack Dao-Jie Li and Dio Feng-Yu Chung

Abstract—Cancer is defined as a disease that involves changes or mutations in the cell genome. Cancer genome sequencing has been recognized as a NP problem. Cancer genome sequencing includes cancer genome assembly and cancer genome alignment is through early detection improving survival opportunity of cancer patients. In this research, a bioinformatics approach uses a proposed modified Euler path on a constructed De Bruijn cancer genome graph for solving cancer genome assembly. This fast DNA algorithm fully utilizes parallelism to conquer time complexity bottleneck, and improves any cancer genome Assembly more efficient. The experimental results of cancer genome reassemble is estimated in $O(n^3)$ polynomial bound.

Keywords—Cancer Genome Assembly; Cancer Genome Alignment; De Bruijn Graphs; Euler Path

I. Introduction

Cancer is an important public health concern around the world. Cancer is defined as a disease that involves changes or mutations in the cell genome. These changes (mutations) produce proteins that disrupt the delicate cellular balance between cell division and quiescence, resulting in cells that keep dividing to form cancers. The underlying cause of mutations leading to cancer is DNA damage.

DNA damage In human cells, the estimated average number of DNA damages occurring per hour is about 800, and the number per day is about 19,200[1]. Under normal circumstances, healthy cells repair virtually all of these damages. Damages that are not repaired are termed mutations. When a single cell acquires enough mutations in the DNA sequence of relevant ‘cancer gene(s)’ it begins to behave in an abnormal way characteristic of cancer.

Michael Shan-Hui Ho

Department of Electrical Engineering, NTPU,
New Taipei City, Taiwan, ROC

Kun-Yu Hung

Department of Information Management, MCU
Taoyuan Country, Taiwan, ROC

Paul Pin-Shuo Huang

Department of Electrical Engineering, NTPU,
New Taipei City, Taiwan, ROC

Jack Dao-Jie Li

Department of Electrical Engineering, NTPU,
New Taipei City, Taiwan, ROC

Dio Feng-Yu Chung

Department of Electrical Engineering, NTPU,
New Taipei City, Taiwan, ROC

Cancer genome sequencing includes cancer genome assembly and cancer genome alignment is through early detection improving survival opportunity of cancer patients.

A. Cancer Genome Assembly

For the last 30 years, fragment assembly followed the “overlap–layout–consensus” paradigm[2]. Although this approach proved to be useful in assembling clones, it faces difficulties in genomic shotgun assembly: the algorithms often unable to resolve repeats even in prokaryotic genomes. So, in the past decade, there has been a new approach: instead of “overlap–layout–consensus” paradigm, the new algorithm is based on the notion of the De Bruijn graph and transforms the cancer genome assembly problem into an Euler super path problem [3].

B. The Euler Path Problem

The Euler path problem can be traced back 300 years, to the Prussian city of Königsberg (Kaliningrad, Russia). In Königsberg city, seven bridges crossed four parts of the city. Residents enjoyed strolling through their city, and they wondered if every part of the city could be visited by walking across each of the seven bridges exactly once and returning to one’s starting location.

A mathematician, Leonhard Euler [4], proposed a solution in 1735; it made a conceptual breakthrough that would solve this “Bridges of Königsberg” problem. First, Euler assumes each landmass represents a point (also called vertex) and each bridge denotes a line segment (also called edge) connecting two points/ vertices. This creates a network graph of vertices connected by edges. By describing a procedure for determining whether an arbitrary graph contains a path that visits every edge exactly once. This solution, called the Euler path, is based on the concept of an undirected graph. The De Bruijn graph is a kind of digraph, for a digraph, Euler path not only to traverse all the edges, but also follows the correct direction. In a more rigorous description, there exists a path which can traverse the graph without repeating all the edges and visits them by directed edges along the direction.

C. De Bruijn Graph

Dutch mathematician Nicolaas De Bruijn finds a cyclic sequence of letters taken from a given alphabet for which



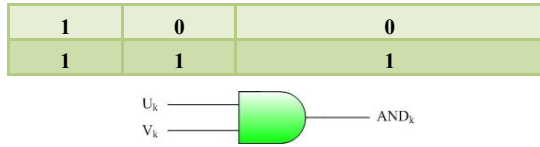


Figure 3: Logic circuitry of parallel AND on one bit

ParallelOneBitAND(T_0, U_k, V_k, AND_k)
 $T_1^{U=1} = +(T_0, U_k^1)$ and $T_1^{U=0} = -(T_0, U_k^1)$.
 $T_2^{U=1, V=1} = +(T_1^{U=1}, V_k^1)$ and $T_2^{U=1, V=0} = -(T_1^{U=1}, V_k^1)$
 $T_2^{U=0, V=1} = +(T_1^{U=0}, V_k^1)$ and $T_2^{U=0, V=0} = -(T_1^{U=0}, V_k^1)$
If (Detect($T_2^{U=1, V=1}$)) == “yes” **then**
 Append-head($T_2^{U=1, V=1}, AND_k^1$) **EndIf**
If (Detect($T_2^{U=1, V=0}$)) == “yes” **then**
 Append-head($T_2^{U=1, V=0}, AND_k^0$) **EndIf**
If (Detect($T_2^{U=0, V=1}$)) == “yes” **then**
 Append-head($T_2^{U=0, V=1}, AND_k^1$) **EndIf**
If (Detect($T_2^{U=0, V=0}$)) == “yes” **then**
 Append-head($T_2^{U=0, V=0}, AND_k^0$) **EndIf**
 $T_0 = \cup(T_2^{U=1, V=1}, T_2^{U=1, V=0}, T_2^{U=0, V=1}, T_2^{U=0, V=0})$
EndAlgorithm

Figure 4: Parallel AND operation on one bit algorithm

B. OR Operation on Bioinformatics Computing

The OR operation of a bit with two input Boolean variables U and V produces a result of 1 or 0. The logic circuitry of parallel OR on one bit is shown in Figure 5. The corresponding truth table of the one-bit OR is shown in Table 3.

Table 3: The truth table of the one-bit OR

| Input | | Output |
|-------|-------|-----------------------|
| U_k | V_k | $OR_k = U_k \vee V_k$ |
| 0 | 0 | 0 |
| 0 | 1 | 1 |
| 1 | 0 | 1 |
| 1 | 1 | 1 |



Figure 5: Logic circuitry of parallel OR on one bit

ParallelOneBitOR(T_0, U_k, V_k, OR_k)
 $T_1^{U=1} = +(T_0, U_k^1)$ and $T_1^{U=0} = -(T_0, U_k^1)$.
 $T_2^{U=1, V=1} = +(T_1^{U=1}, V_k^1)$ and $T_2^{U=1, V=0} = -(T_1^{U=1}, V_k^1)$
 $T_2^{U=0, V=1} = +(T_1^{U=0}, V_k^1)$ and $T_2^{U=0, V=0} = -(T_1^{U=0}, V_k^1)$
If (Detect($T_2^{U=1, V=1}$)) == “yes” **then**
 Append-head($T_2^{U=1, V=1}, OR_k^1$) **EndIf**
If (Detect($T_2^{U=1, V=0}$)) == “yes” **then**
 Append-head($T_2^{U=1, V=0}, OR_k^0$) **EndIf**
If (Detect($T_2^{U=0, V=1}$)) == “yes” **then**
 Append-head($T_2^{U=0, V=1}, OR_k^1$) **EndIf**
If (Detect($T_2^{U=0, V=0}$)) == “yes” **then**
 Append-head($T_2^{U=0, V=0}, OR_k^0$) **EndIf**
 $T_0 = \cup(T_2^{U=1, V=1}, T_2^{U=1, V=0}, T_2^{U=0, V=1}, T_2^{U=0, V=0})$
EndAlgorithm

Figure 6: Parallel OR operation on one bit algorithm

C. XOR Operation on Bioinformatics Computing

The Exclusive-OR (XOR) operation of a bit which can generate an output of 1 or 0. The logic circuitry of parallel XOR on one bit is shown in Figure 7. The corresponding truth table of the one-bit XOR is shown in Table 4:

Table 4: The truth table of the one-bit XOR

| Input | | Output |
|-------|-------|--------------------------|
| U_k | V_k | $XOR_k = U_k \oplus V_k$ |
| 0 | 0 | 0 |
| 0 | 1 | 1 |
| 1 | 0 | 1 |
| 1 | 1 | 0 |



Figure 7: Logic circuitry of Parallel XOR on one bit

ParallelOneBitXOR(T_0, U_k, V_k, XOR_k)
 $T_1^{U=1} = +(T_0, U_k^1)$ and $T_1^{U=0} = -(T_0, U_k^1)$.
 $T_2^{U=1, V=1} = +(T_1^{U=1}, V_k^1)$ and $T_2^{U=1, V=0} = -(T_1^{U=1}, V_k^1)$
 $T_2^{U=0, V=1} = +(T_1^{U=0}, V_k^1)$ and $T_2^{U=0, V=0} = -(T_1^{U=0}, V_k^1)$
If (Detect($T_2^{U=1, V=1}$)) == “yes” **then**
 Append-head($T_2^{U=1, V=1}, XOR_k^0$) **EndIf**
If (Detect($T_2^{U=1, V=0}$)) == “yes” **then**
 Append-head($T_2^{U=1, V=0}, XOR_k^1$) **EndIf**
If (Detect($T_2^{U=0, V=1}$)) == “yes” **then**
 Append-head($T_2^{U=0, V=1}, XOR_k^1$) **EndIf**
If (Detect($T_2^{U=0, V=0}$)) == “yes” **then**
 Append-head($T_2^{U=0, V=0}, XOR_k^0$) **EndIf**
 $T_0 = \cup(T_2^{U=1, V=1}, T_2^{U=1, V=0}, T_2^{U=0, V=1}, T_2^{U=0, V=0})$.
EndAlgorithm

Figure 8: Parallel XOR operation on one bit algorithm

D. Bio-arithmetic Parallel Comparator on n Bits

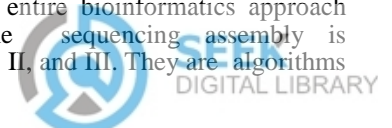
The following algorithm, ParallelComparator (T_0, T_0 overlay, T_a, T_b, m, n, g, b), is an n-bit comparator. Algorithm for parallel execution is shown in Figure 11.

ParallelComparator($T_0, T_0^{overlay}, T_a, T_b, m, n, g, b$)
For $d=0$ to $\text{Min}(n-m, b-g)$
For $p=n$ **downto** m
OneBitComparator($T_0^{\bar{}}$, $T_a, T_b, p, g+d$)
If (Detect($T_0^{\bar{}}$)) == “yes” **then**
 Append($T_0^{overlay}, O_{p, g+d}^1$)
 Discard($T_0^{\bar{}}$) **EndIf**
EndFor
EndFor
If (Detect($T_0^{overlay}$)) == “yes” **then**
 $T_0 = \cup(T_0, T_0^{overlay})$ **EndIf**
 Discard($T_0^{overlay}$)
EndAlgorithm

Figure 9: Parallel comparator on n bits

V. Fast Bioinformatics Parallel Algorithms for Solving Cancer Genome Sequencing Assembly

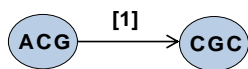
In this research, the entire bioinformatics approach for solving cancer genome sequencing assembly is accomplished by algorithms I, II, and III. They are algorithms



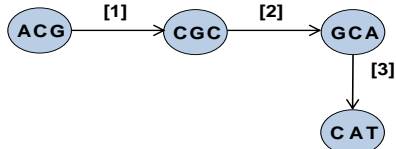

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    End If
    Discard( $T_{15}, T_{16}$ )
    End For
     $T_{DBGraph} = \cup(T_{13}, T_{14})$ 
    End For
    EndAlgorithm
    
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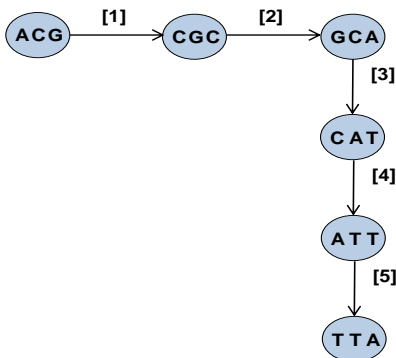
Figure 20: Parallel modified euler path algorithm



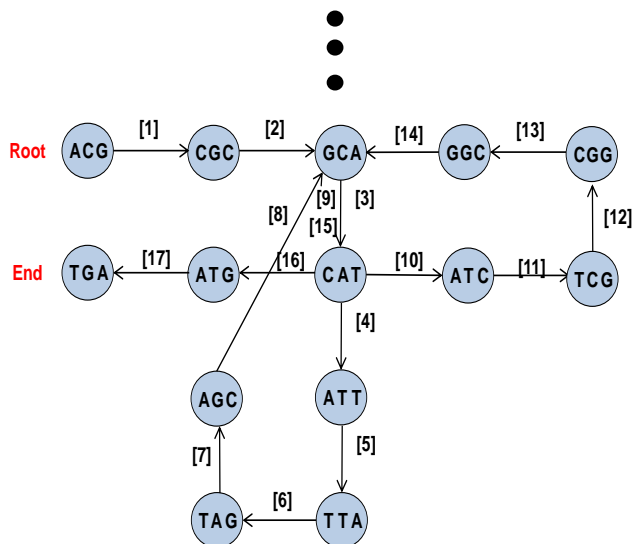
(a) The root is vertex 'ACG'. Add vertex 'CGC' to the root and from path [1] between them.



(b) Add vertex 'GCA' and 'CAT' to travel paths [2] and [3].



(c) Add vertex 'ATT' and 'TTA' to travel paths [4] and [5].



(d) construction of the modified Euler path.

Figure 21: Example of the modified Euler path construction

VI. Complexity Analysis

- (1) The time complexity of **Algorithm I** to construct the De Bruijn graph is estimated in $O(n^3)$ polynomial bound.
- (2) The time complexity of **Algorithm II** to append stickers is estimated in $O(3n-1)$ polynomial bound.
- (3) The time complexity of **Algorithm III** for parallel modified euler path in De Bruijn is estimated in $O(n^3)$ polynomial bound.
- (4) The time complexity of total algorithm is in $O(n^3)$ polynomial bound.

VII. Conclusion

Taking into account efficiency and accuracy, this paper uses a fast bioinformatics method to construct a De Bruijn graph along with a modified Euler path in order to solve a cancer genome assembly problem. The research utilizes parallelism to make executions with greater efficiency. We hope that this research demonstrates that bioinformatics computing is a technology worth pursuing, and should thus attract more scholars into this domain.

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