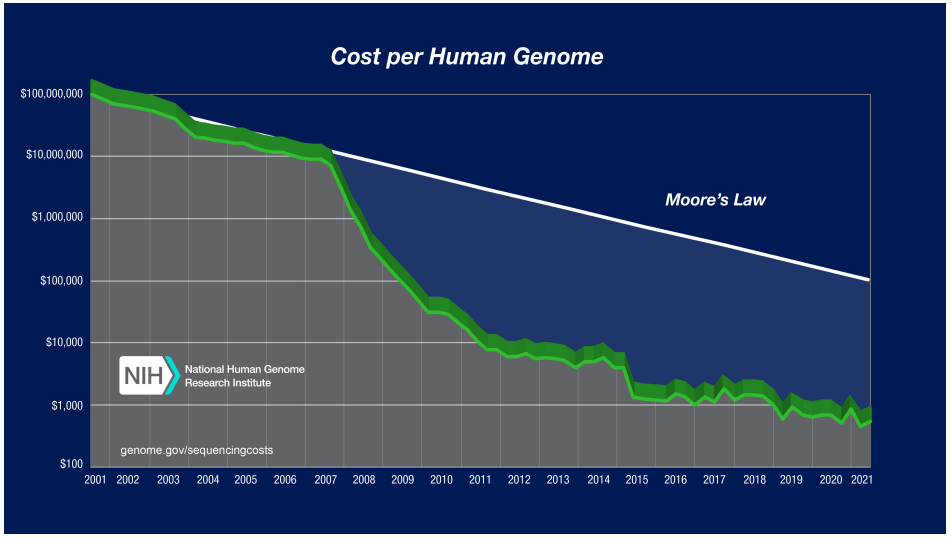
Genome Assembly



High Throughput Sequencing

Example applications:

- Sequencing a genome (DNA)
- Sequencing a transcriptome and gene expression studies (RNA)
- ChIP (chromatin immunoprecipitation)

Example platforms:

- 454
- Illumina
- SOLiD

Sequencing Output

- Hundreds of millions of sequencing reads, each ~200 nts in length
- We need to re-assemble the genome from these sequencing reads

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- ACGTAGTCGTAGTCGCTTACGATTCGTATGCGTACGTGTAGTCTACGTGTA
- CCGCGCGTACTCTCGATGTACGTGTCAGTTACGATGTACTGTAGTCAGTGT
- TTTGATCGTAGTGTCACTGAGCAAACACCATTACTTACTATCTTGGACATC
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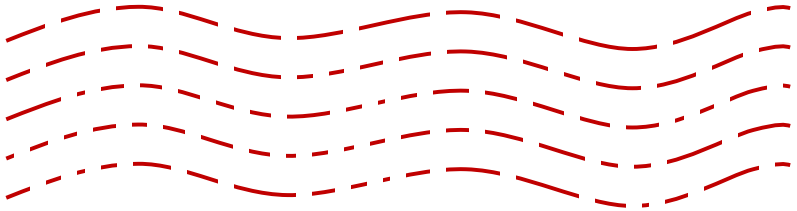
DNA Sequencing



DNA Sequencing

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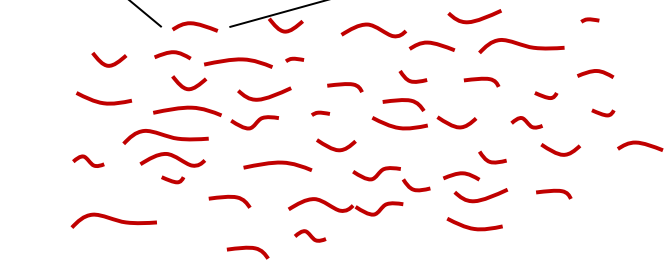

DNA Sequencing

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Assembly

>GGGCAGGC
>GGCTAGGG
>TAGGGCA

Assembly

>GGGCAGGC
>GGCTAGGG
>TAGGGCA

CTAG
GGGC
CAGG
GGCA
GCTA
AGGC
TAGG
AGGG
GCAG
GGCT
GGGC
TAGG
GGGC
AGGG

Assembly

>GGGCAGGC
>GGCTAGGG
>TAGGGCA

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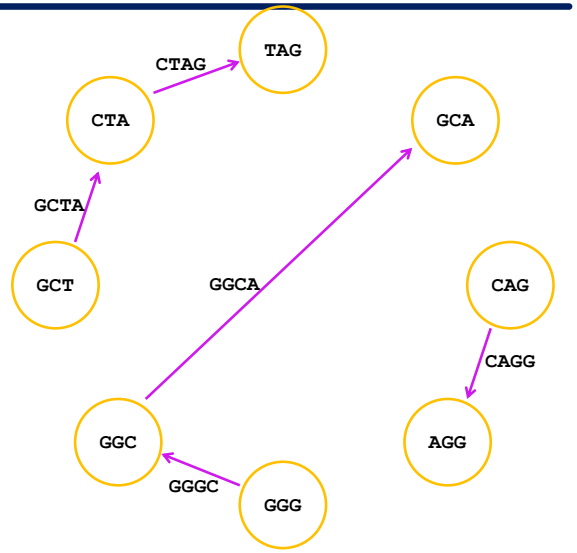

Assembly

>GGGCAGGC
>GGCTAGGG
>TAGGGCA

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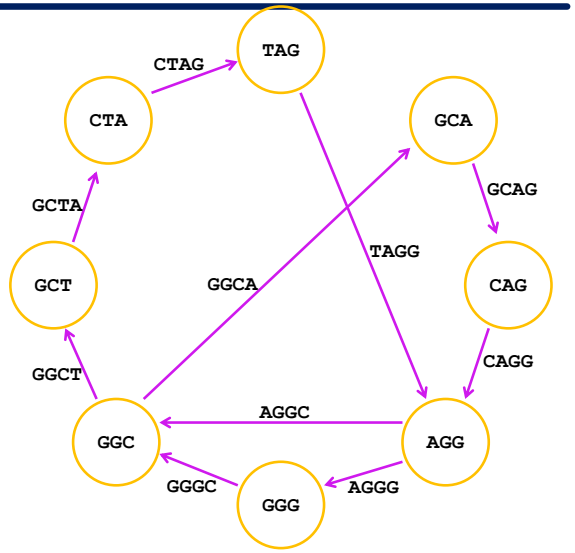

Assembly

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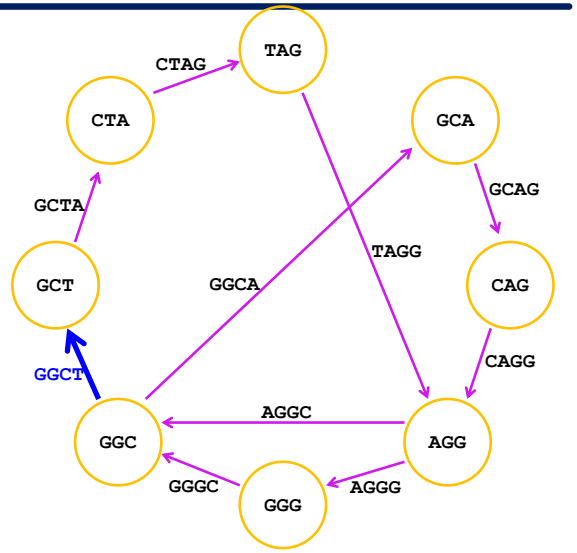

Assembly

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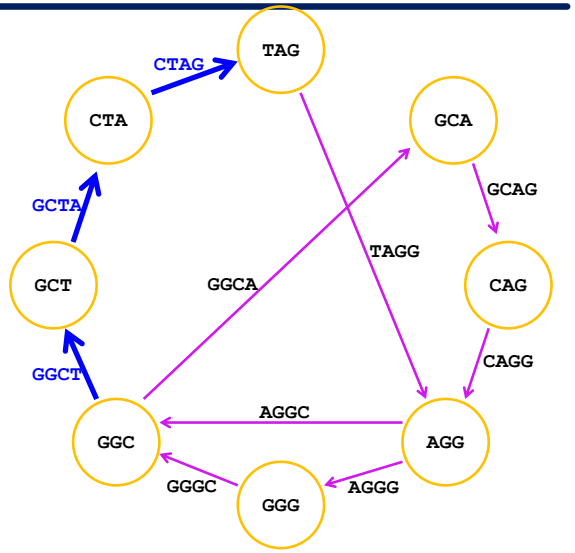

Assembly

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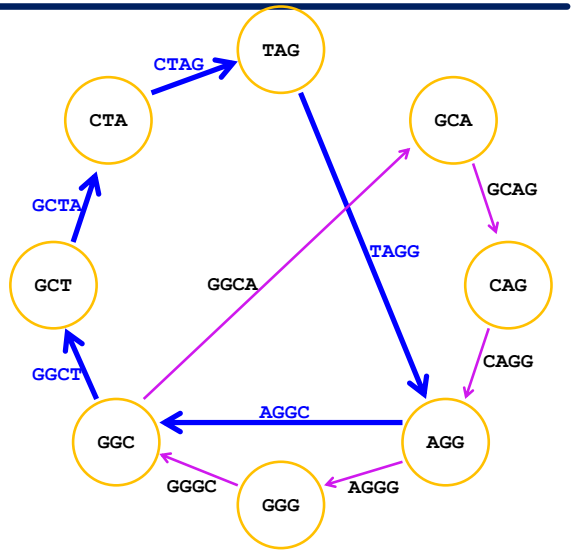

Assembly

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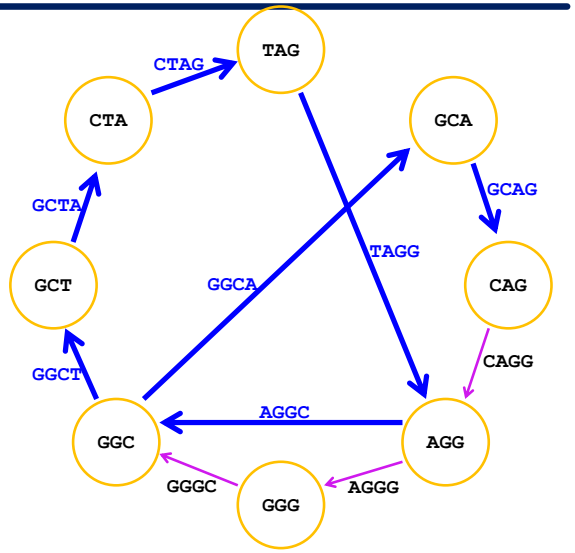
>GGGCAGGC
>GGCTAGGG
>TAGGGCA



Assembly

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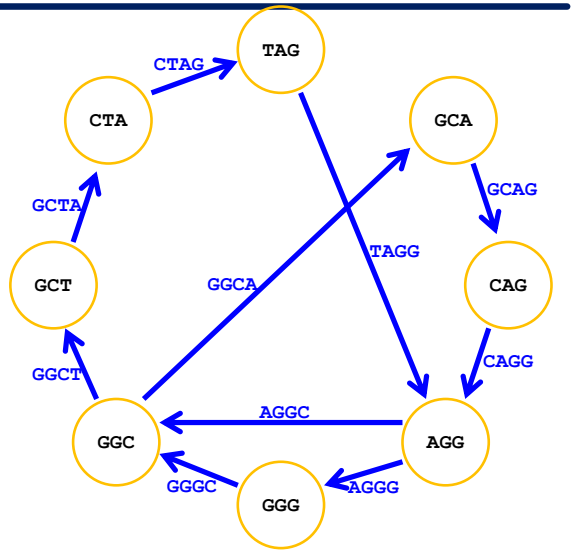
>GGGCAGGC
>GGCTAGGG
>TAGGGCA



Challenges

- Repeats
- Sequencing errors

Implementation

deBruijn graph can be implemented with a hash table

- Each entry in hash table corresponds to an edge in the graph (each key is a *k*-mer and each value is the number of occurrences of the *k*-mer).
- Nodes are stored implicitly.

Implementation

GGCT

Assembly corresponds to Euler path through graph

- Genome sequence starts with any *k*-mer (edge in the graph)
- Repeatedly extend genome sequence forward, one nucleotide at a time, until no further extensions are possible
  - The genome sequence is extended and a nucleotide added to its end if there exists a nucleotide (A, C, G, or T) that can be added to the end of the *k*-1 final nucleotides of the genome sequence to form a *k*-mer that is an edge in the graph.
  - If there are multiple individual nucleotides that can be added to the final *k*-1 nucleotides in the genome sequence to form *k*-mer edges in the graph, then the nucleotide resulting in the *k*-mer edge with the largest number of occurrences is chosen.
  - Each time the genome sequence is extended by a nucleotide, the corresponding *k*-mer edge is removed from the graph.

Implementation

GGCT

Assembly corresponds to Euler path through graph

- Genome sequence starts with any *k*-mer (edge in the graph)
- Repeatedly extend genome sequence backward, one nucleotide at a time, until no further extensions are possible
  - The genome sequence is extended and a nucleotide added to its front if there exists a nucleotide (A, C, G, or T) that can be added to the front of the *k*-1 first nucleotides of the genome sequence to form a *k*-mer that is an edge in the graph.
  - If there are multiple individual nucleotides that can be prepended to the first *k*-1 nucleotides in the genome sequence to form *k*-mer edges in the graph, then the nucleotide resulting in the *k*-mer edge with the largest number of occurrences is chosen.
  - Each time the genome sequence is extended by a nucleotide, the corresponding *k*-mer edge is removed from the graph.