Algorithmic Approaches for Biological Data, Lecture #17

Katherine St. John

City University of New York
American Museum of Natural History

6 April 2016

Outline

- Recap: Recursion

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- Assembling Sequence Reads

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- Reframing Biology Questions

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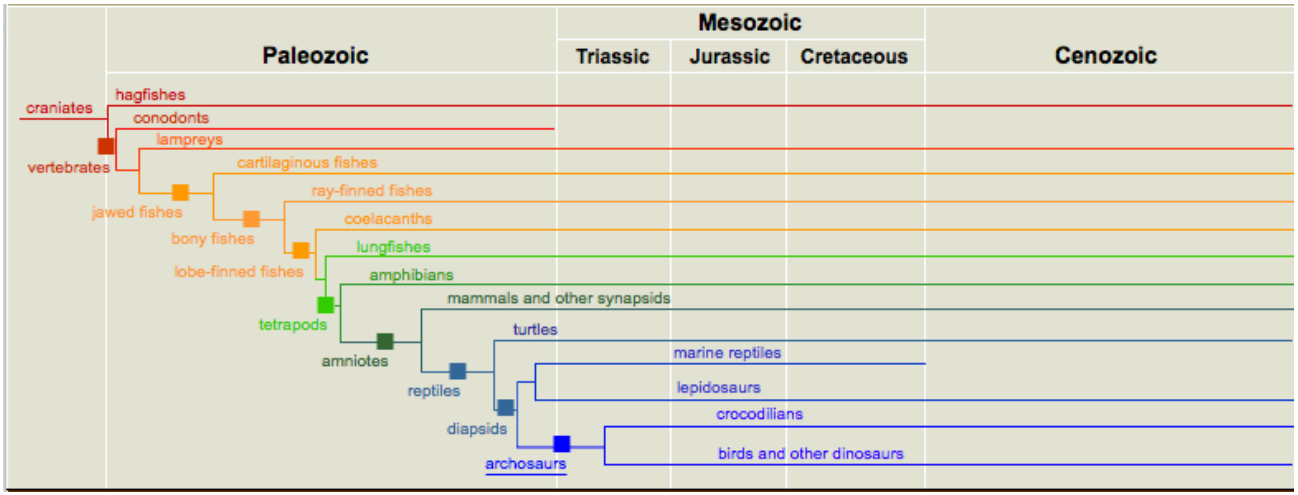
- Overlap & Hamiltonian Graphs
- Hamiltonian & Eulerian Paths

Recap: Recursion



Smithsonian Institute

- Works well for problems that break into pieces that can be solved independently

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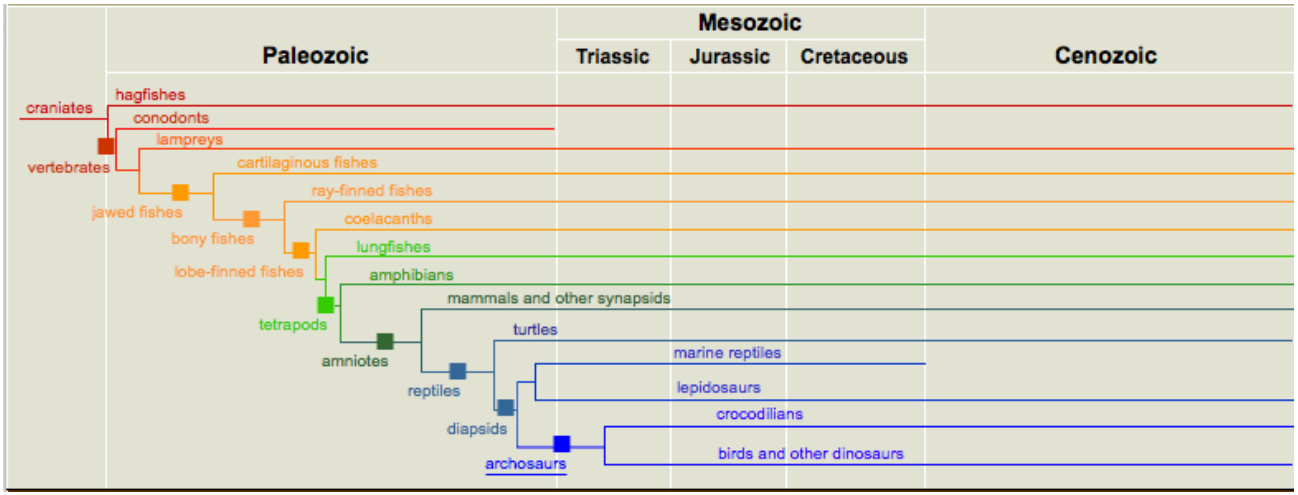

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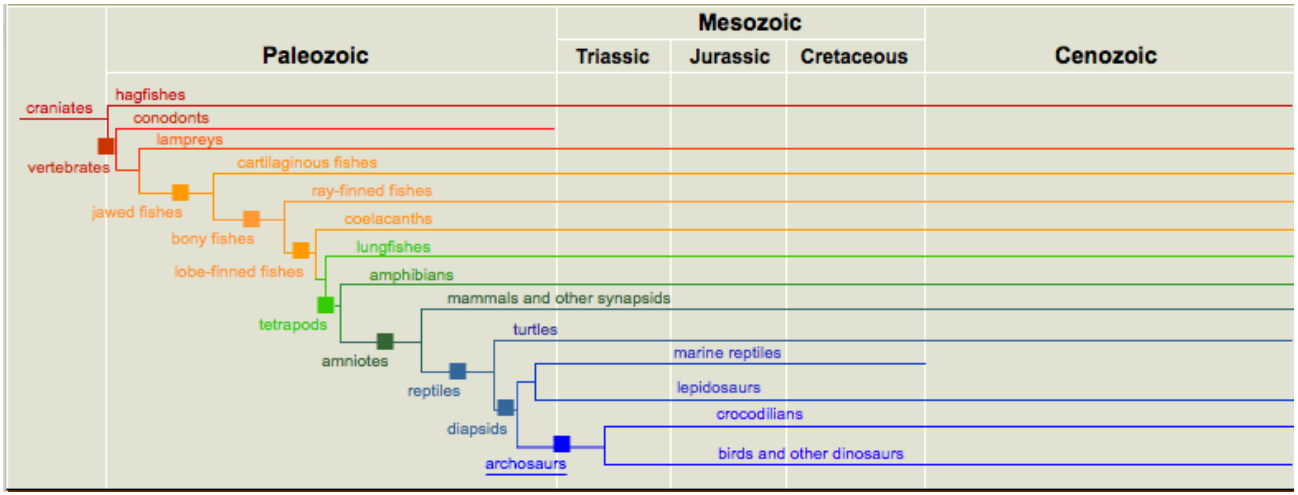

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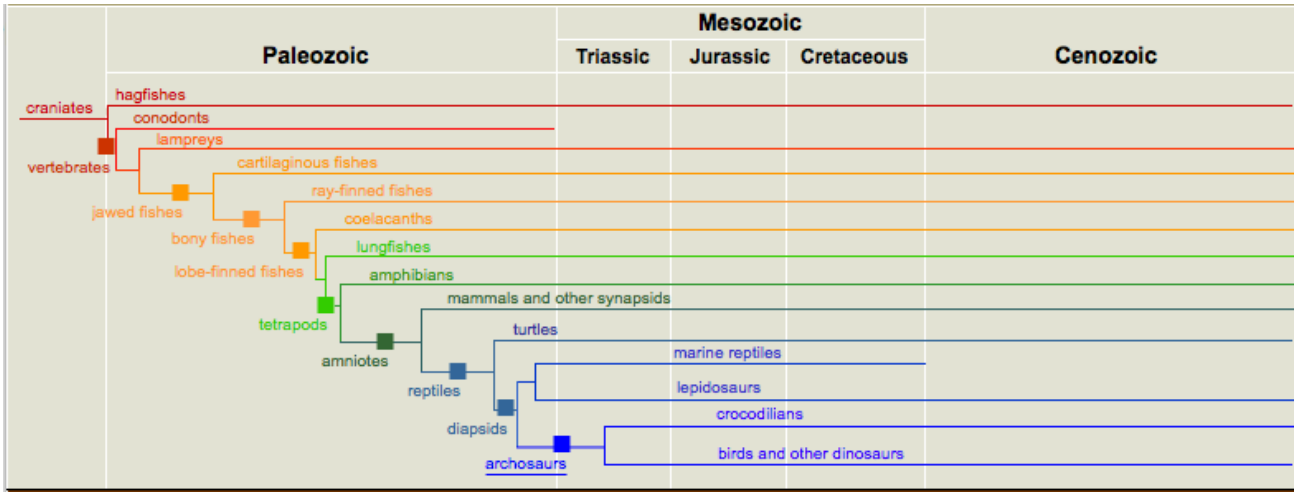
- Two parts:
  - Base Case: smallest possibility

Recap: Recursion



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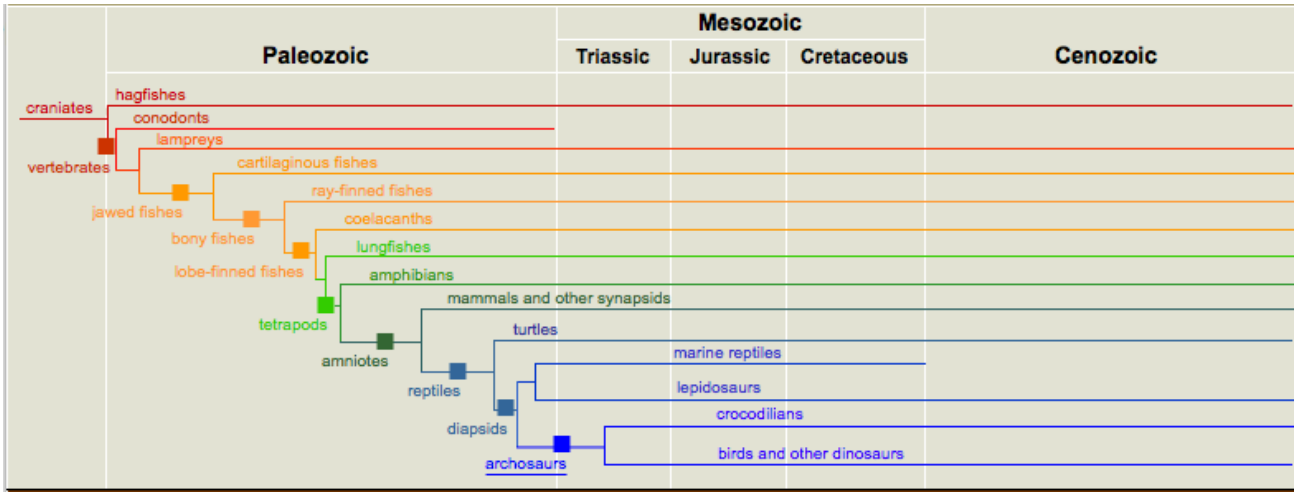

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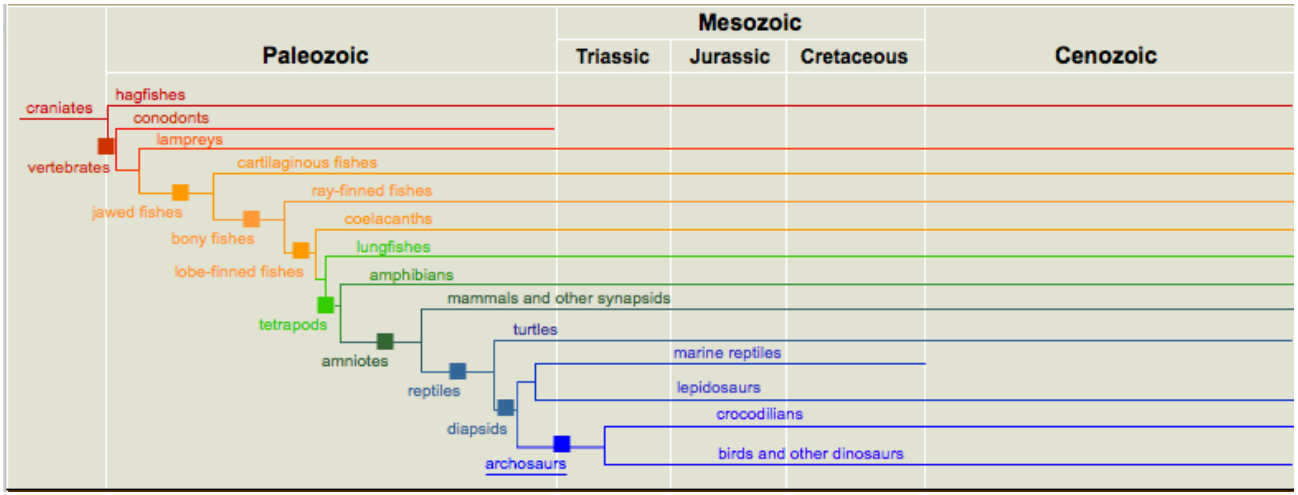

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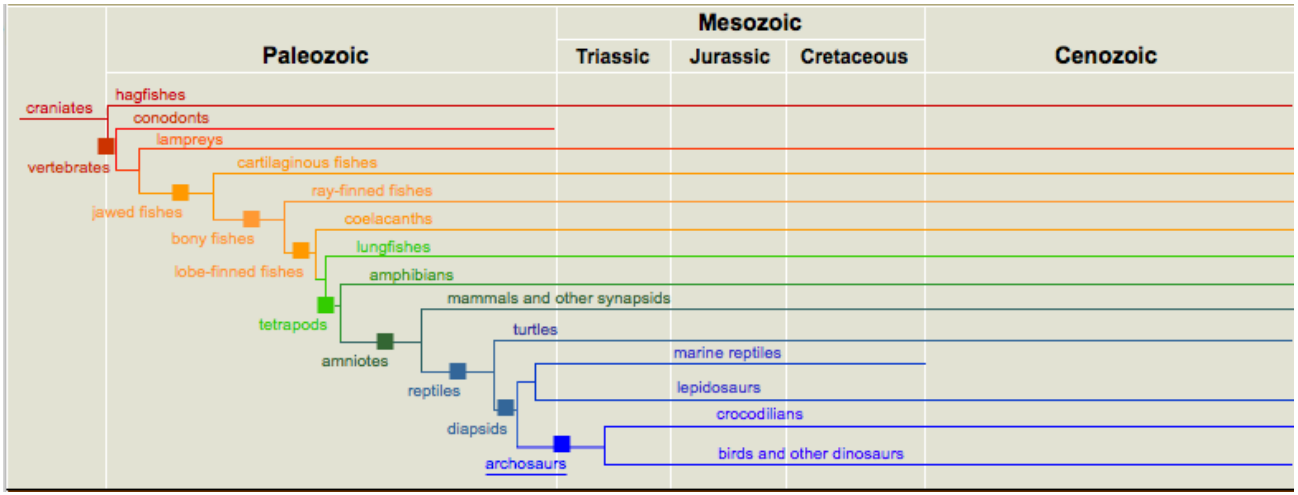

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- Two parts:
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    (for trees: internal nodes)
- *PythonTutor Demo*

Assembling Sequence Reads

Multiple identical copies of a genome

Shatter the genome into reads

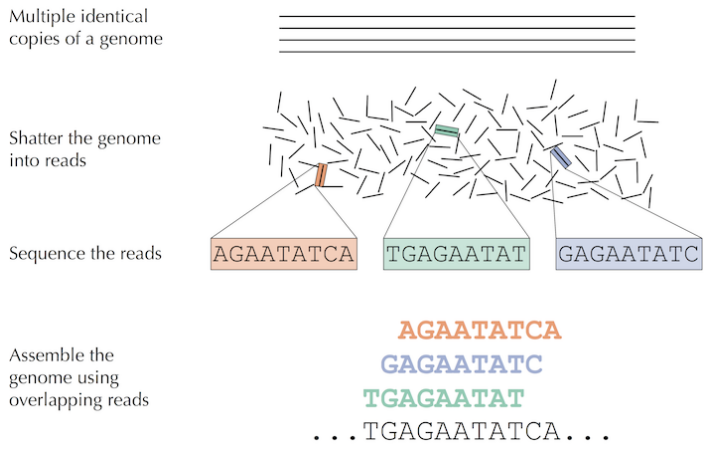
Sequence the reads

Assemble the genome using overlapping reads

AGAATATCA
GAGAATATC
TGAGAATAT
...TGAGAATATCA...

Compeau & Pevzner, Vol 1, Chapter 3

Assembling Sequence Reads



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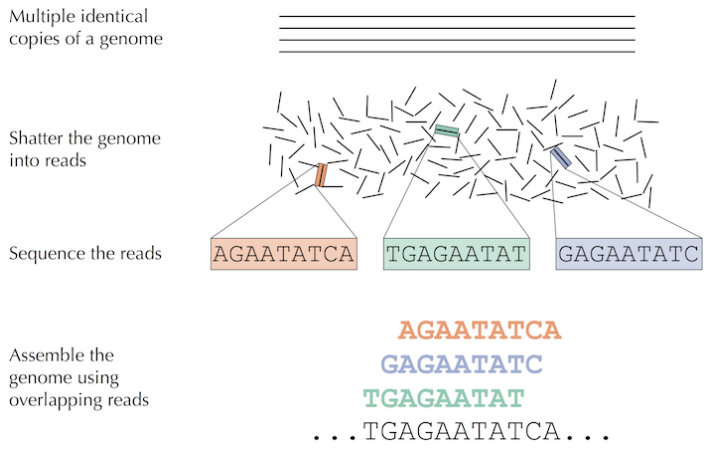
- Given a bunch of sequence reads (of length k), how do you assembly them?

Assembling Sequence Reads



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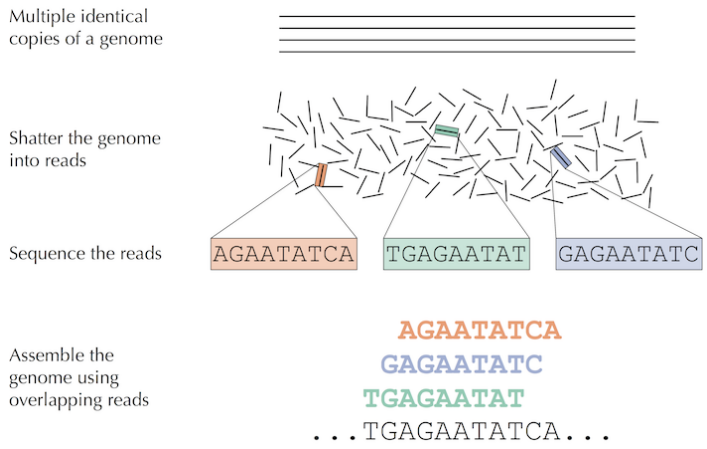
Assembling Sequence Reads



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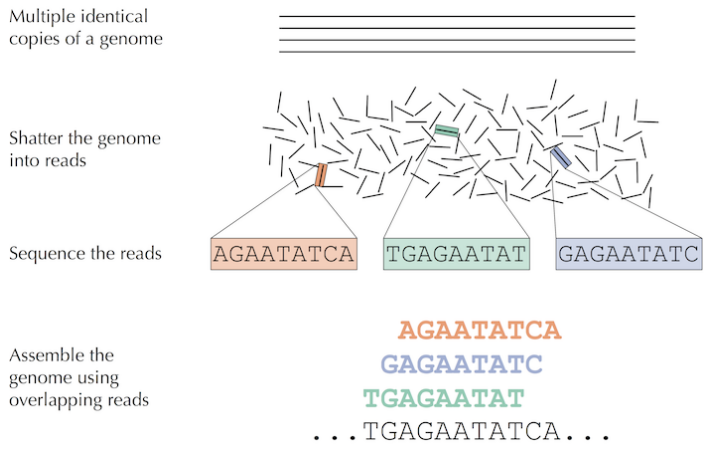
  - 10 copies of a single-stranded sequence

Assembling Sequence Reads



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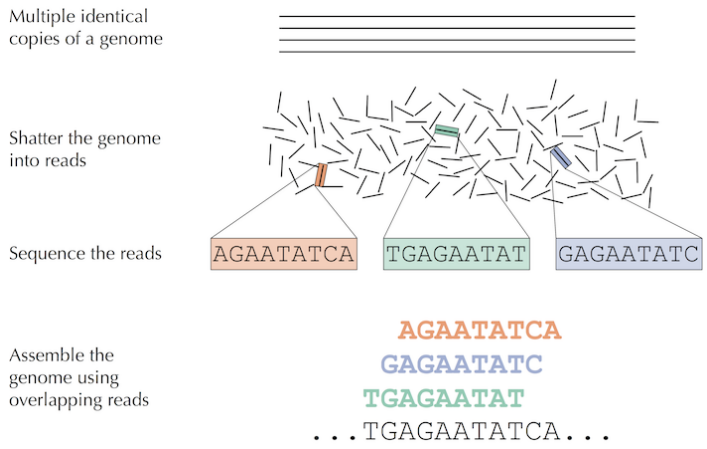
  - k=4

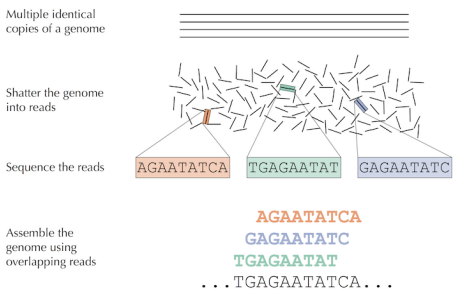
Assembling Sequence Reads



Compeau & Pevzner, Vol 1, Chapter 3

- Given a bunch of sequence reads (of length k), how do you assembly them?
- In pairs/triples:
  - 10 copies of a single-stranded sequence
  - k=4
  - Some errors in sequencing.

Reframing Biology Questions



- How can we store the information in the computer?

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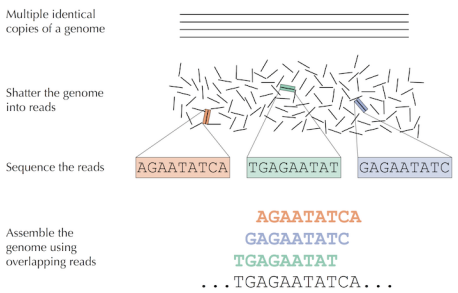

- How can we store the information in the computer?
- What additional information and what structures do we need?

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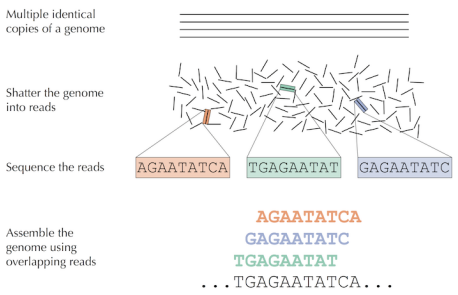
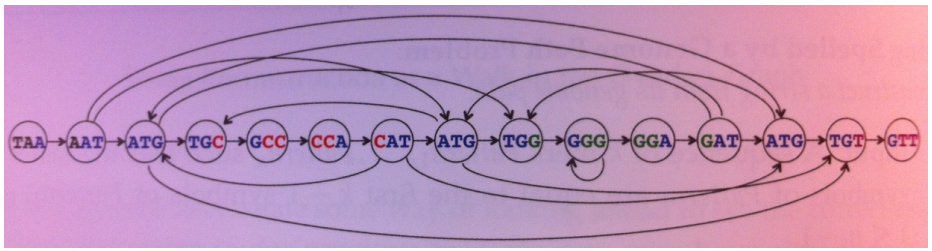
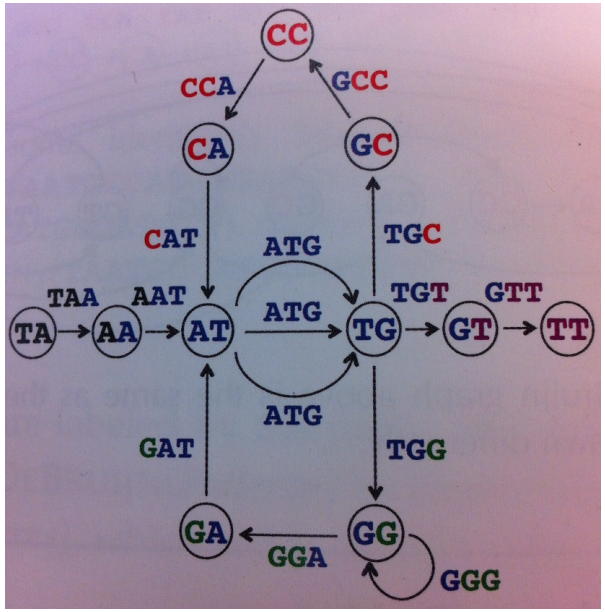


- How can we store the information in the computer?
- What additional information and what structures do we need?
- How do you represent overlaps in a graph?

Useful Graphs: Overlap & deBruijn



overlap graph



deBruijn graph

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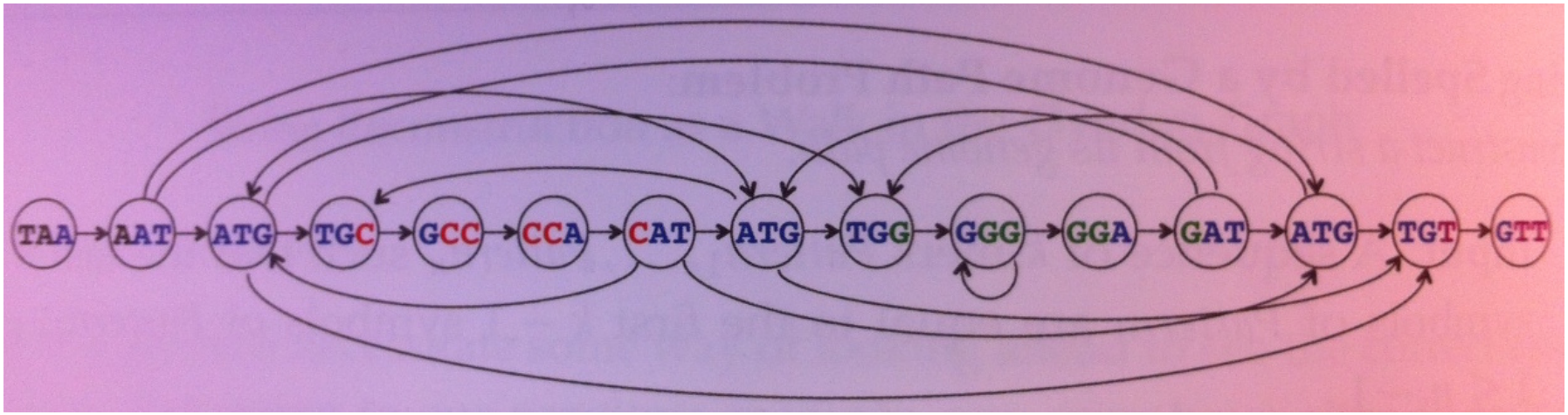

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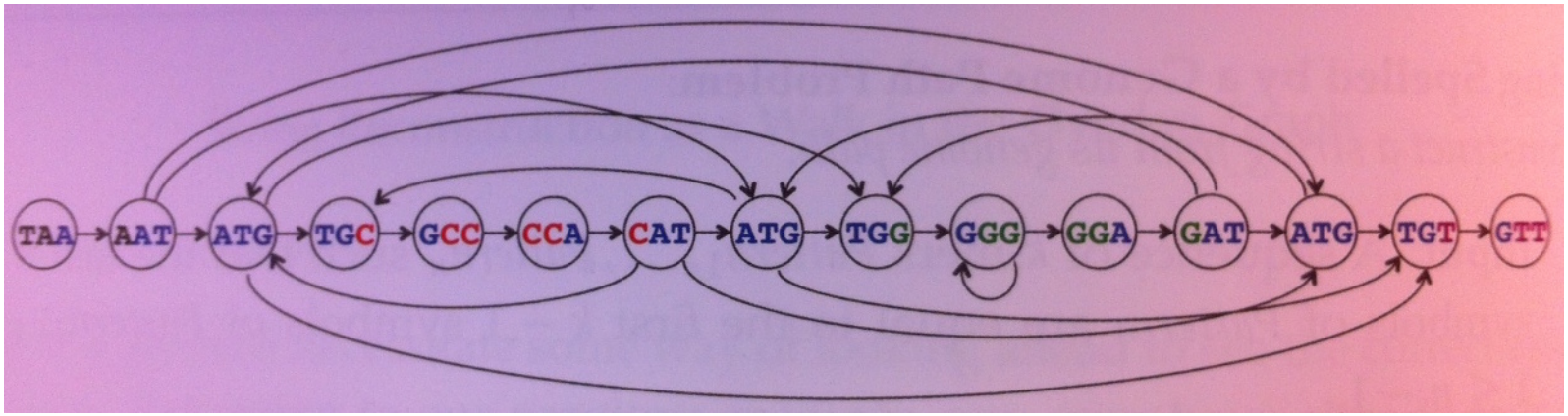
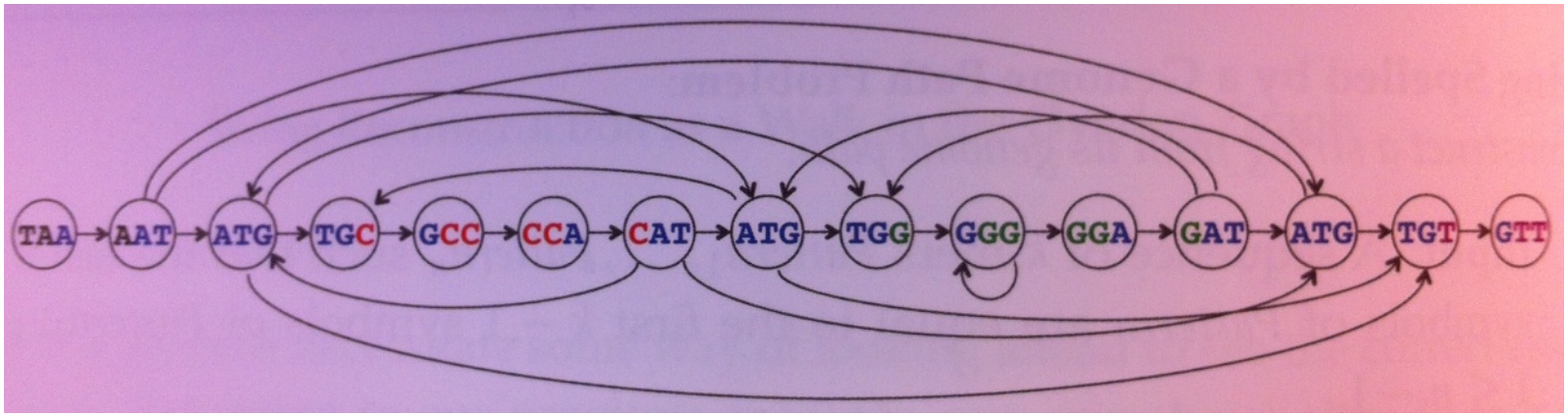


- The vertices are the reads.

Overlap Graphs



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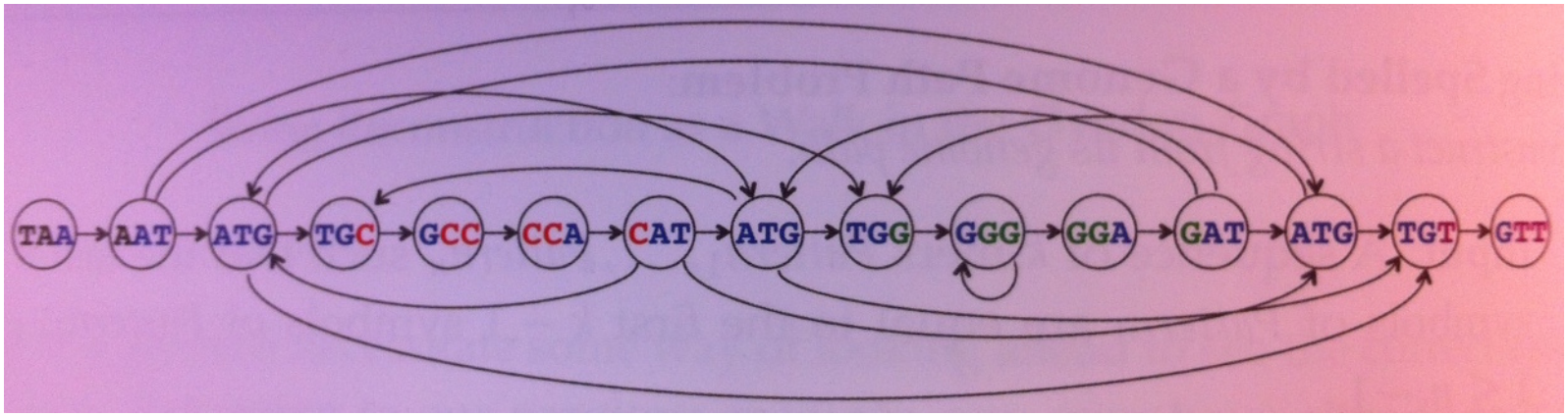

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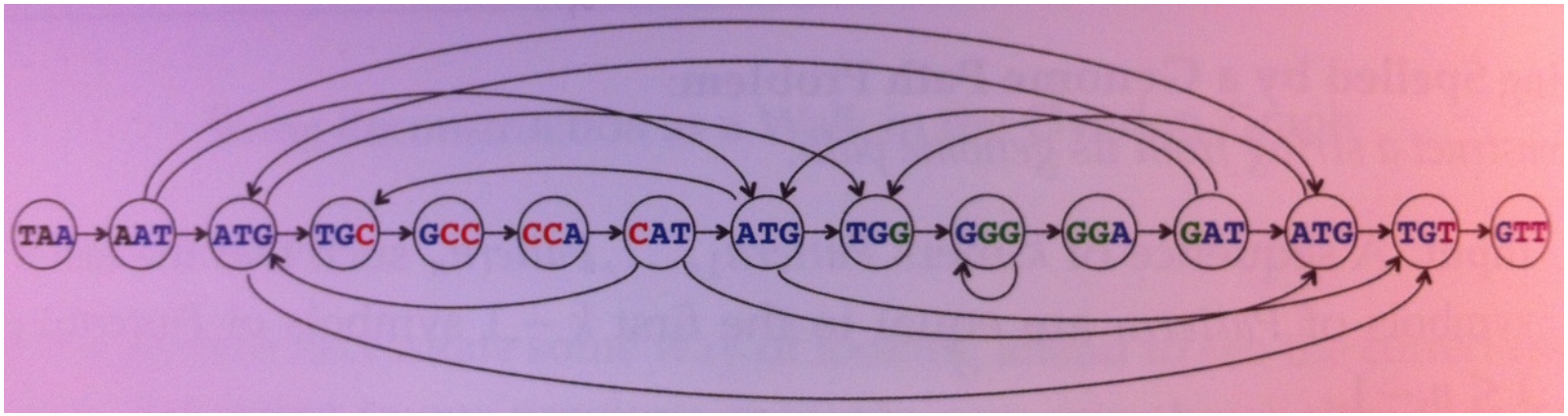

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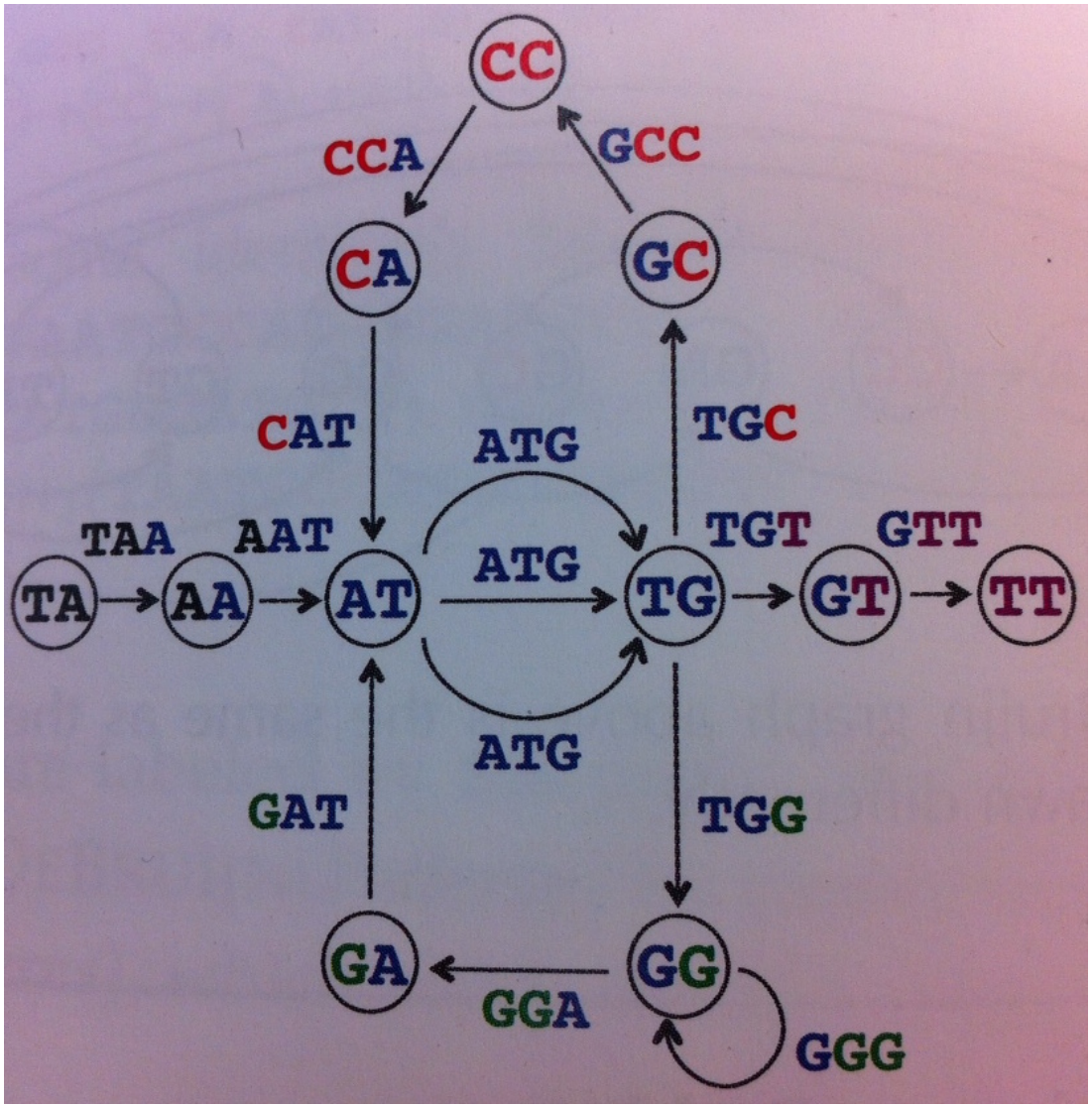
- Each read came from the original sequence, so, should be in the final sequence.
- Final sequence corresponds to a path that visits all the vertices (called Hamiltonian path).

deBruijn Graphs



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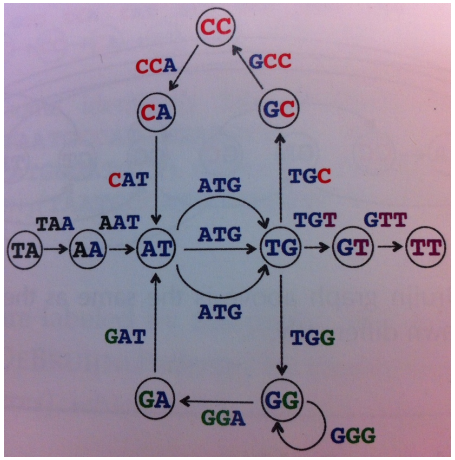
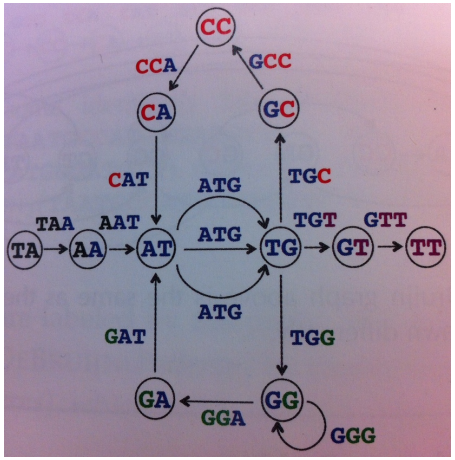


- Label edges by k-mers.

deBruijn Graphs



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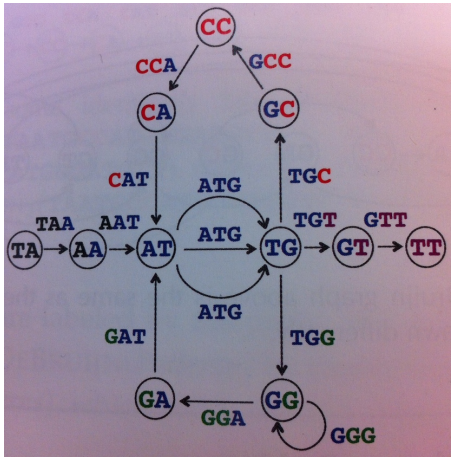

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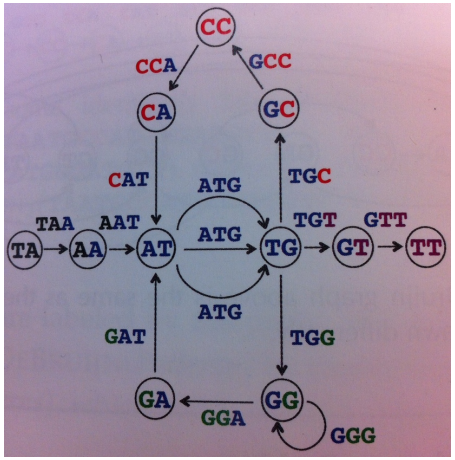

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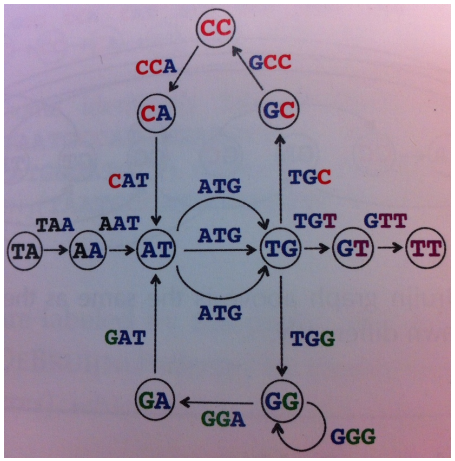
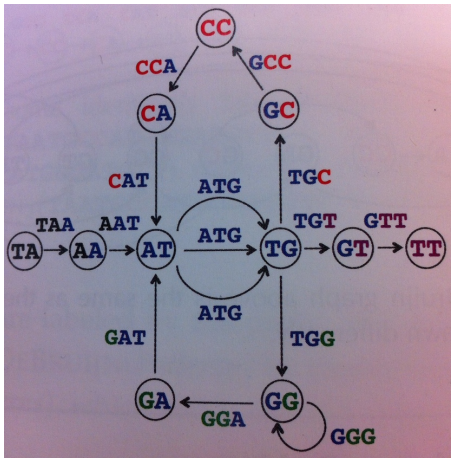
- The completed sequence is one of the Eulerian paths of the graph.

Computational Questions



- Finding Hamiltonian paths is NP-hard.

Computational Questions



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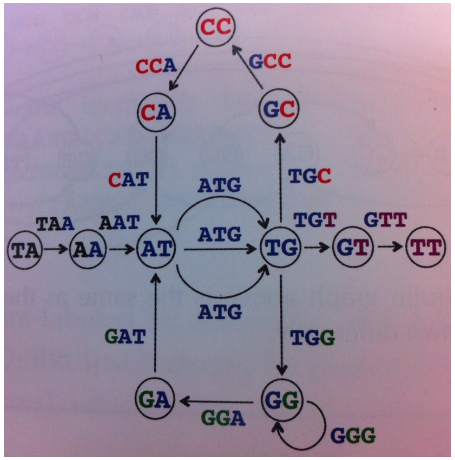

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- Since tractable, will compute Eulerian paths.

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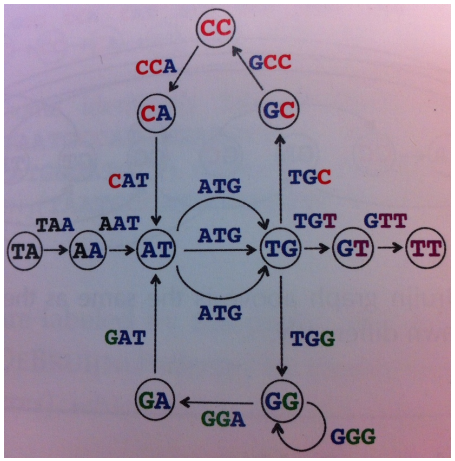
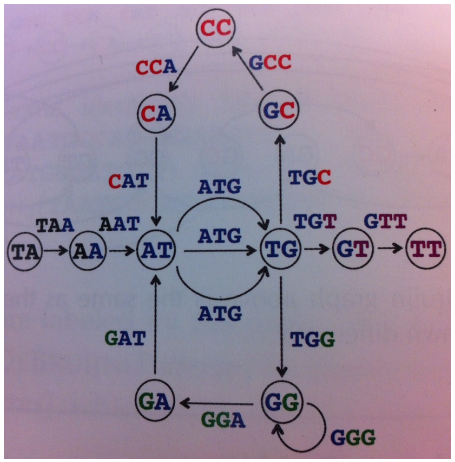


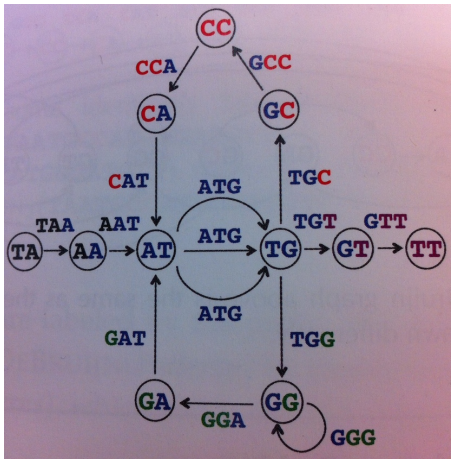
- Finding Hamiltonian paths is NP-hard.
- Eulerian paths exist if the out-degree = in-degree for every vertex.
- Since tractable, will compute Eulerian paths.
- And then, if more than one, choose (using additional information).

Building deBruijn Graphs



- Input: Reads of multiple sequences

Building deBruijn Graphs



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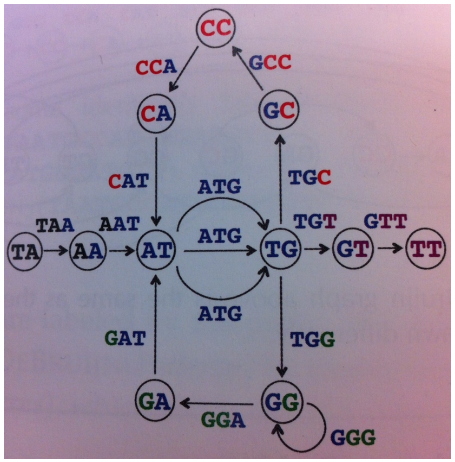
- Make k-mers of the reads.

Building deBruijn Graphs



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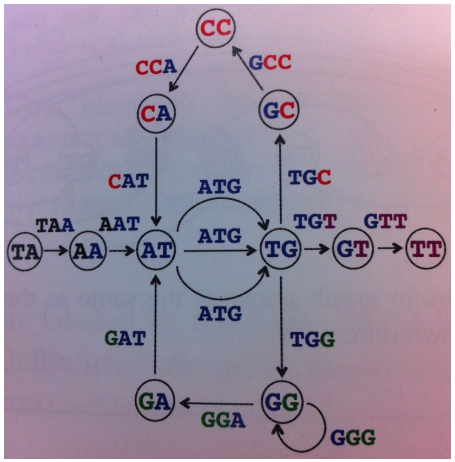

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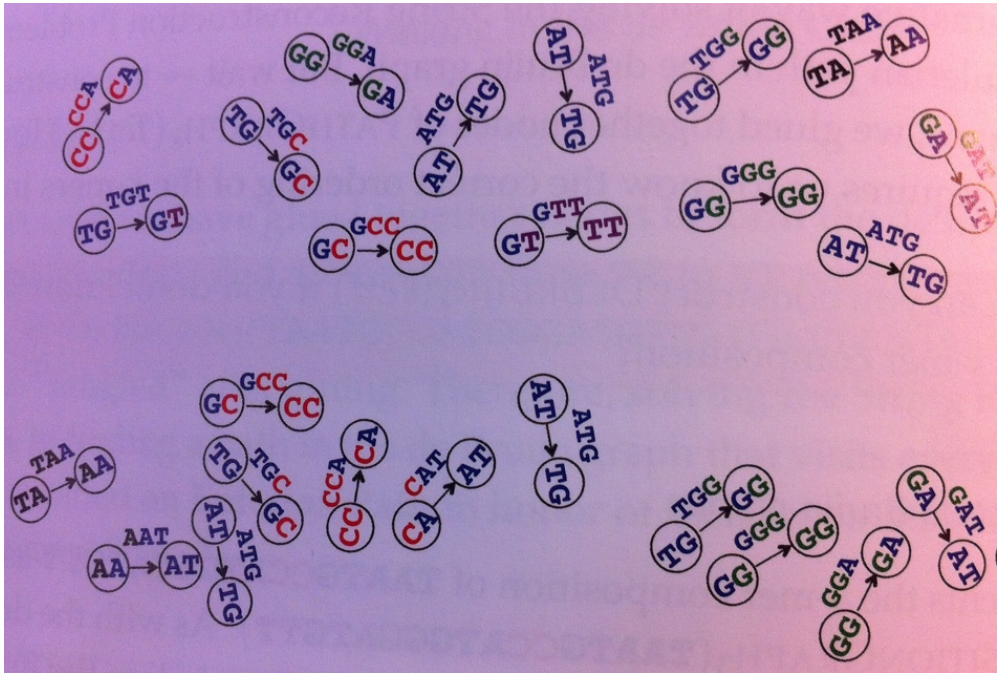
- Make k-mers of the reads.
- Build deBruijn graphs from the reads.
- (Find Eulerian paths...)

Recap



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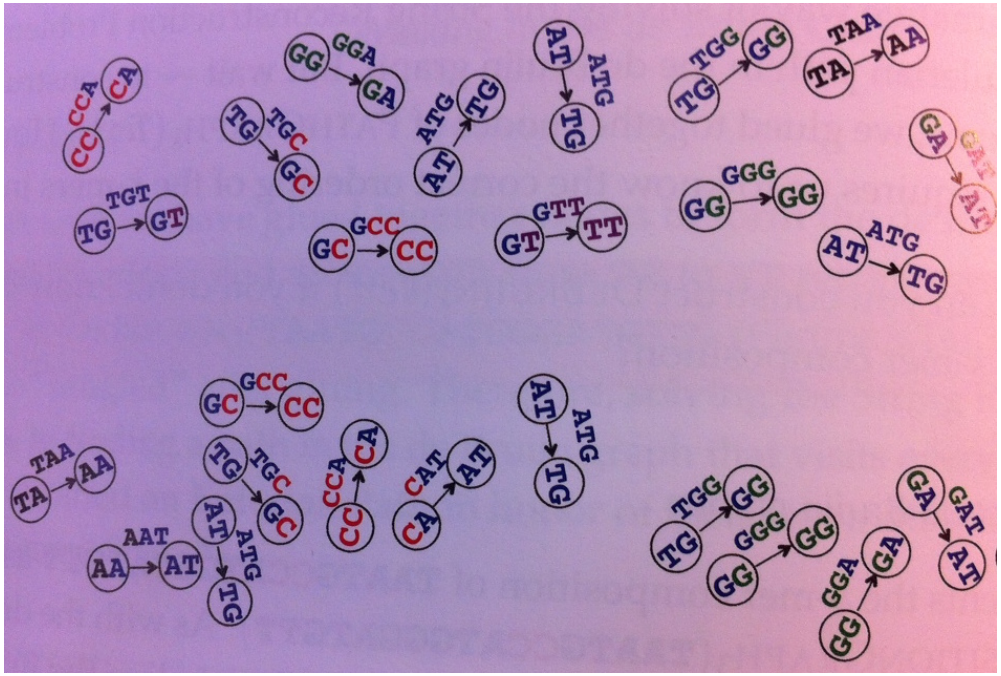

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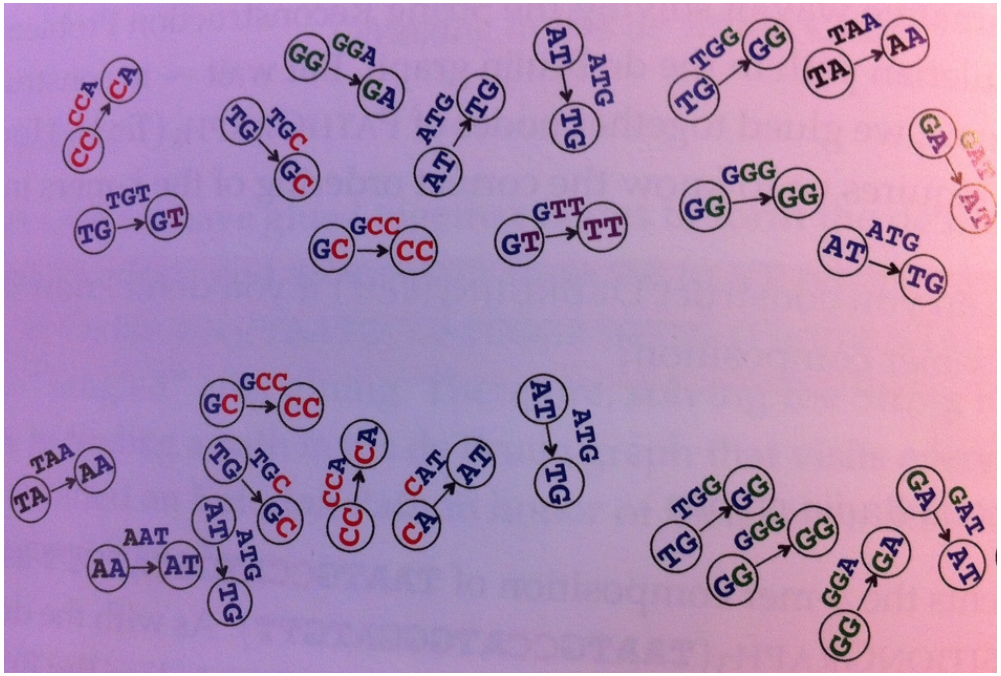

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