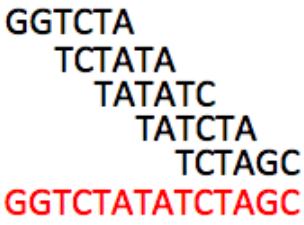
Series 2 - solution

Genomics and bioinformatics - Week 3 - October 2, 2012

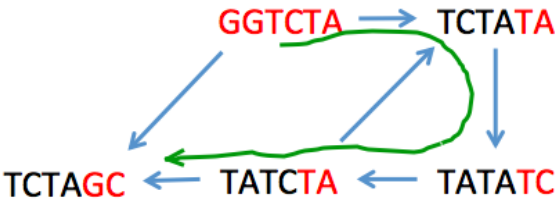
1 Overlap graphs

1. Just by looking manually at the overlaps (of size 4+):



2. The overlap (Hamiltonian) graph is build by taking the reads as vertices and adding an edge each time two reads have an overlap (of a chosen minimal size, here 4). Then find a path going through every vertex once and only once: this is called an Hamiltonian path. The contig is made of the first read plus, from each read in the path, its sub-sequence (in red below) that does not belong to the overlap. There may be several such paths; the number of them depends on the minimal overlap one chooses.

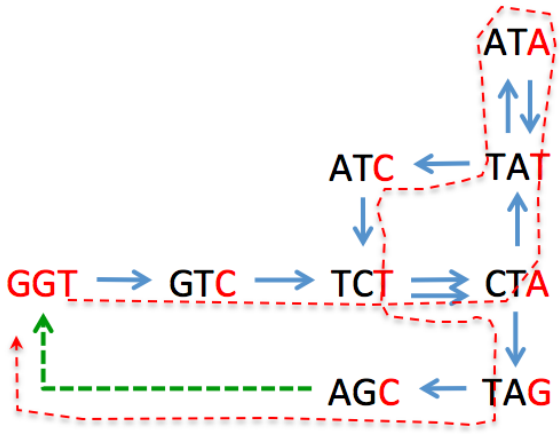
   As in part 1, one finds GGTCTATATCTAGC.



3. To build the "De Bruijn" graph, one proceeds as follows:

   - Choose an integer l (here $l = 4$ was given).
   - Build S_{l-1}, the set of all *unique* $l-1$-mers that the reads contain:
     $S_{l-1} = \{$GGT, GTC, TCT, CTA, TAT, ATA, ATC, TAG, AGC$\}$
     These are the vertices of the graph.
   - Build S_l, the set of all l-mers that the reads contain:
     $S_l =$ {GGTC, GTCT, TCTA,
     TCTA, CTAT, TATA,
     TATA, ATAT, TATC,
     TATC, ATCT, TCTA,
     TCTA, CTAG, TAGC}
     Those are the edges: GGTC binds GGT and GTC, etc.

- Then there are several ways to proceed:
  - Some duplicates in S_l are du to the overlaps between reads; some are really a repeat in the sequence of the contig itself. If you have an idea of which ones come from overlaps between reads (as we have here), discard only them. In this case,
    $S_l =$ {GGTC, GTCT, TCTA,
    ~~TCTA~~, CTAT, TATA,
    ~~TATA~~, ATAT, TATC,
    ~~TATC~~, ATCT, TCTA,
    ~~TCTA~~, CTAG, TAGC}
    We see that only TCTA is a real repeat.
  - Use only the unique edges, and artificially double some of the edges if necessary to make the graph Eulerian (in particular, cyclic, see below). Check however that the edges you add are at least among the duplicate reads you decided to discard from S_l when taking only the uniques.
  - In fact, duplicates are a real problem that is not so easily solved in practice. Real algorithms for example make estimates of the frequency of a repeat in the contig, and allow some errors.
- Close the graph by joining the starting vertex - the only one that has more outgoing than incoming edges - to the end vertex - with more incoming than out coming edges. This should make the graph Eulerian, i.e. cyclic, and every vertex having the same number of incoming and outgoing edges.
- Find a cycle that goes through each *edge* once and only once: this is called an Eulerian cycle. The contig is made of the first vertex, plus the last nucleotide of each vertex in the path.
  In the figure below, a green arrow joins the start and end, and the cycle is drawn in red.



As in part 1, one finds GGTCTATATCTAGC. Note the TCTA repeat in the sequence.