Indexing Finite Language Representation of Population Genotypes

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JOINT WORK WITH
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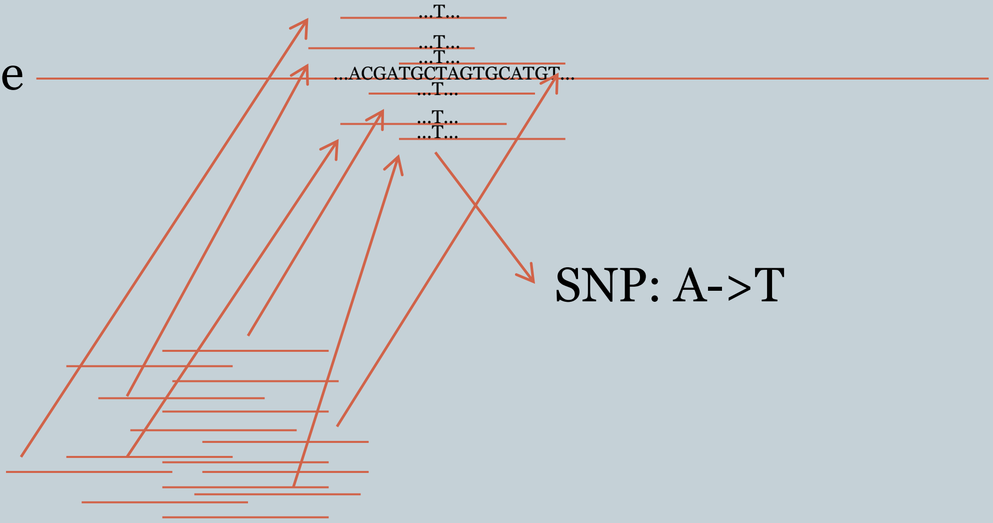
Variation calling



short DNA reads aligned to same region

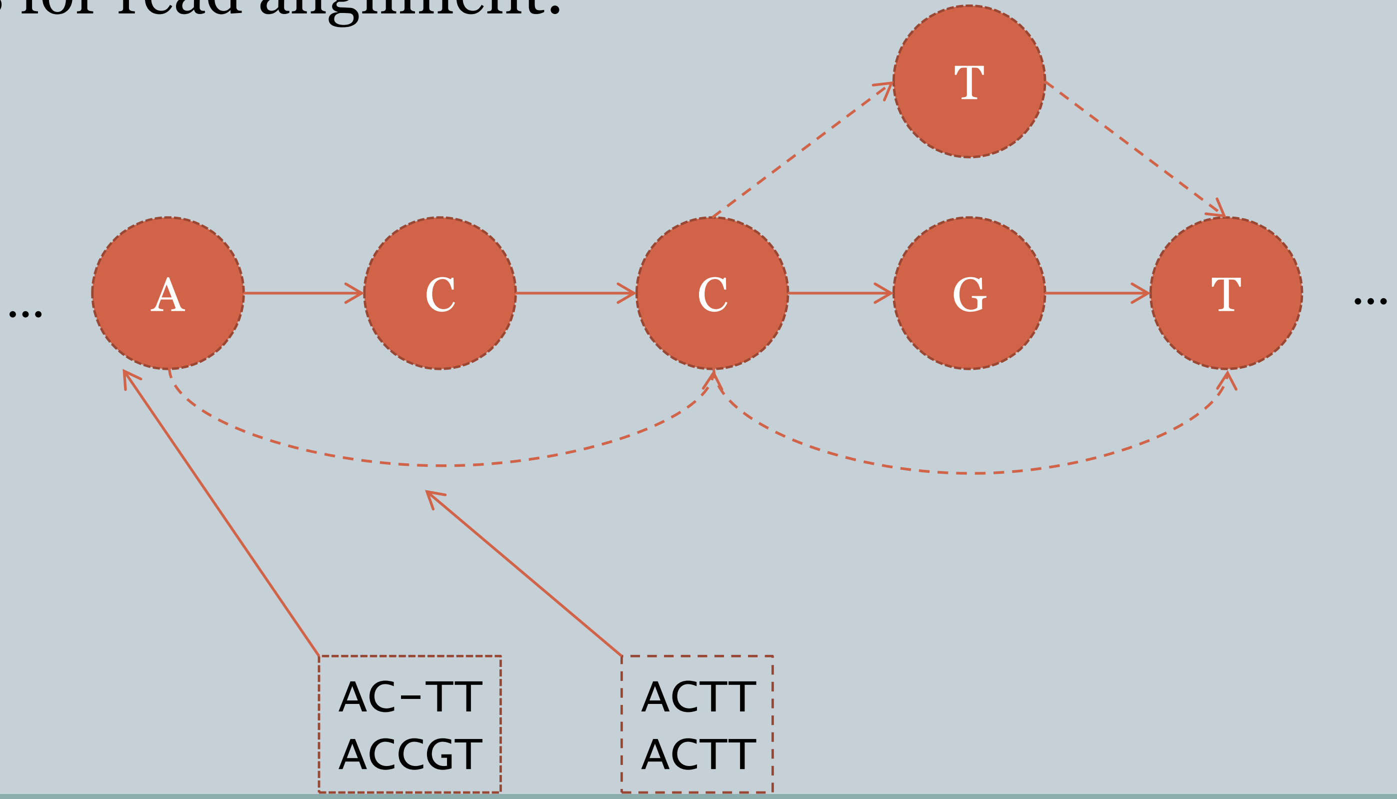
...T...
...T...
...T...
reference genome ...ACGATGCTAGTGCATGT...
...T...
...T...
...T...

SNP: A->T

millions of short DNA reads

Enhanced variation calling

- Why always only one reference is used?
- We propose to use reference + known variations as the basis for read alignment:

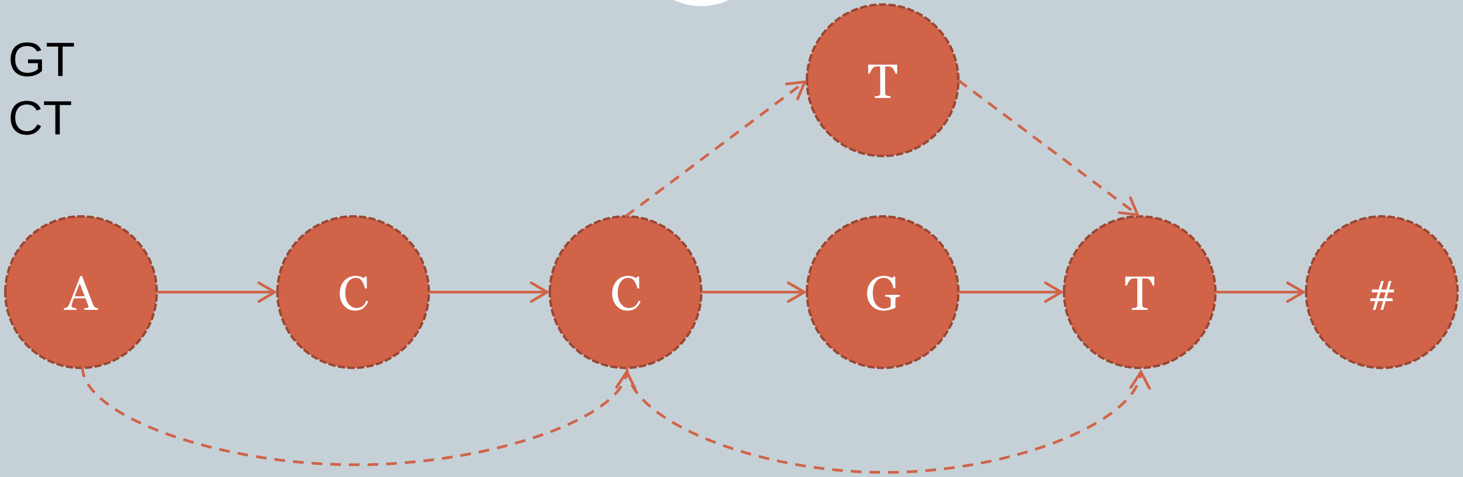


Enhanced variation calling

- Sirén, Välimäki, Mäkinen. Indexing Finite Language Representation of Population Genotypes. *WABI 2011*.
  - Generalization of Burrows-Wheeler transform for finite automata
    - Based on our work in RECOMB 2009 for multiple genomes.
  - Supports alignment of reads alike the other read aligners
    - Given a pattern P of length m, one can count the paths starting with P in O(m) time
    - Locate using the standard sampling mechanism.
    - Extends to approximate search with the general backtracking & branch-and-bound mechanism.
  - Similar space usage as for other read aligners
    - Less than 70 MB for multiple alignment of 4 assemblies of human chromosome 18 each about 76 Mbp long

Some insights

Search GT
Search CT



		GBWT	Distinguishing prefixes	Edges
		T	#	1
		#	A	2
	0 G	A	CC	1
1 G	2 C	AC	CG	1
4 C			CT	2
		C	G	1
		CGT	T#	1
		C	TT	1

All paths in lex order

#
ACCGT#
ACCTT#
ACGT#
ACTT#
CCGT#
CCTT#
CGT#
CT#
CTT#
GT#
T#
TT#

Summary

- Make finite automaton from reference + SNP data or from multiple alignment.
- Make it reverse deterministic (skipped details).
- Sort distinguishing prefixes (prefix doubling, radix sort, others?)
- Output GBWT.
- Read alignment almost identical to normal BWT read aligners.

What now?

- Index construction for human genome + SNPs requires really much RAM (terabytes)
- Summer 2011->now : Distributed construction algorithm almost ready
  - Choose p pivot prefixes, and let p machines sort their parts independently.
  - Each machine needs to access the whole automaton:
    - Compressed graph representation required.
- Aiming to release first version of the index with HG+simple common SNPs still this year.

Thanks for listening!

QUESTIONS?
COMMENTS?
NEW IDEAS?