Alignment-free de novo structural variations from pangenomes

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Project Information

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No data

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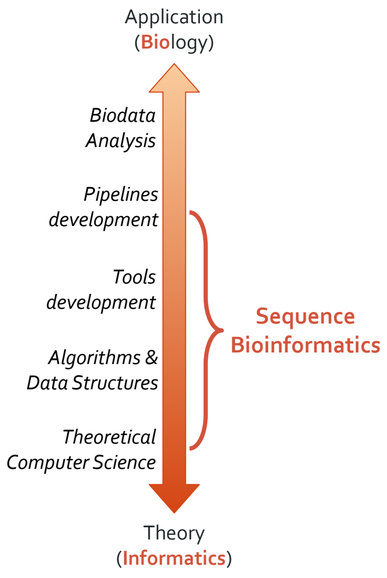
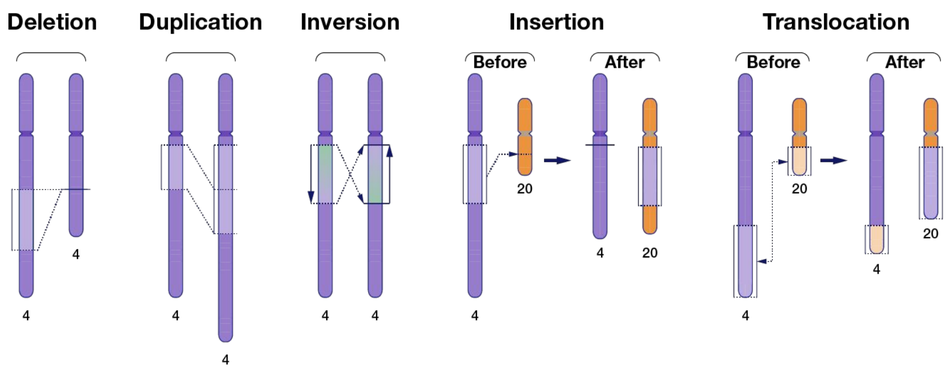
"Algorithms for Structural Variation Analysis in Challenging Genomic Regions"



Context

Structural Variation: big (≥50bp) chromosomal rearrangements



SVs account for **genetic disorders** *(autism, schizophrenia…)* and **cancer** *(melanoma, breast, prostate…)*

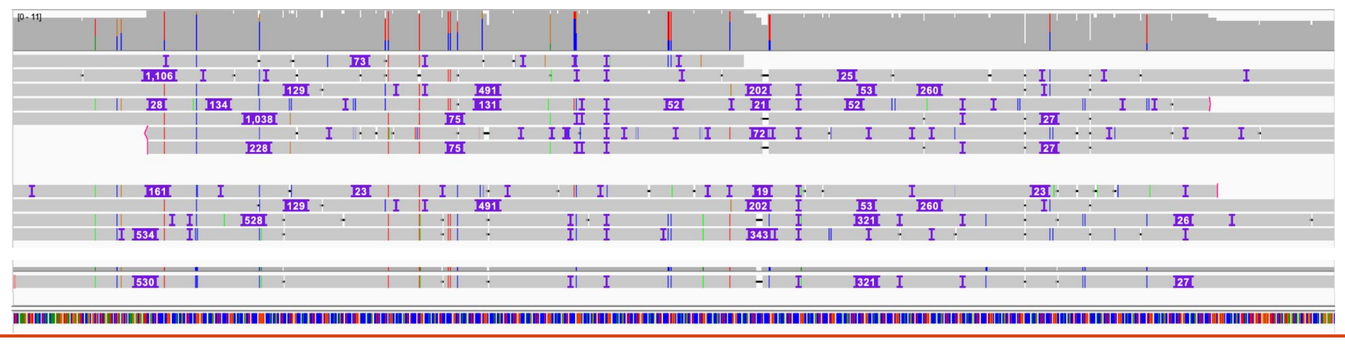
Image from https://www.genome.gov

State-of-the-art and CGR

A lot of ***reference-based*** approaches
- **short reads alignment (✗ inaccurate)**
  - …
- **long reads alignment (✗ "inaccurate")**
  - *SVIM [Bioinformatics, 2019]*
  - *cuteSV [Genome Biology, 2020]*
  - *SVDSS [Nature Methods, 2023]*
  - *sniffles2 [Nature Biotechnology, 2024]*
  - …
- **genome assembly (✗ expensive)**
  - *dipcall [Nature Methods, 2018]*
  - *PAV [Science, 2021]*
  - *VolcanoSV [Nature Communication, 2024]*
  - …

Few **pangenome-based** approaches **(✗ expensive)** *[bioRxiv, 2024]*

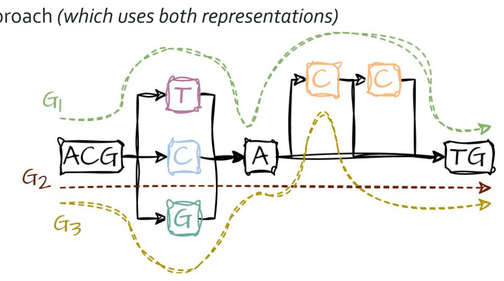
But what about Challenging Genomic Regions?



Proposal

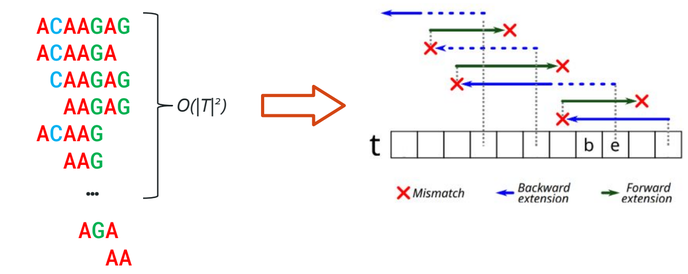
✓ **pangenome-based** approach *(which uses both representations)*

G_1 = ACGTACCTG
G_2 = ACGCATG
G_3 = ACGGACTG



✓ based on efficient FMD index (BWT-based) and **specific strings**

R = { ACATGAG }
T = { ACAAGAG }



✓ **mapping-free** approach *(does not rely on read alignments)*

Methods

(i) index pangenome

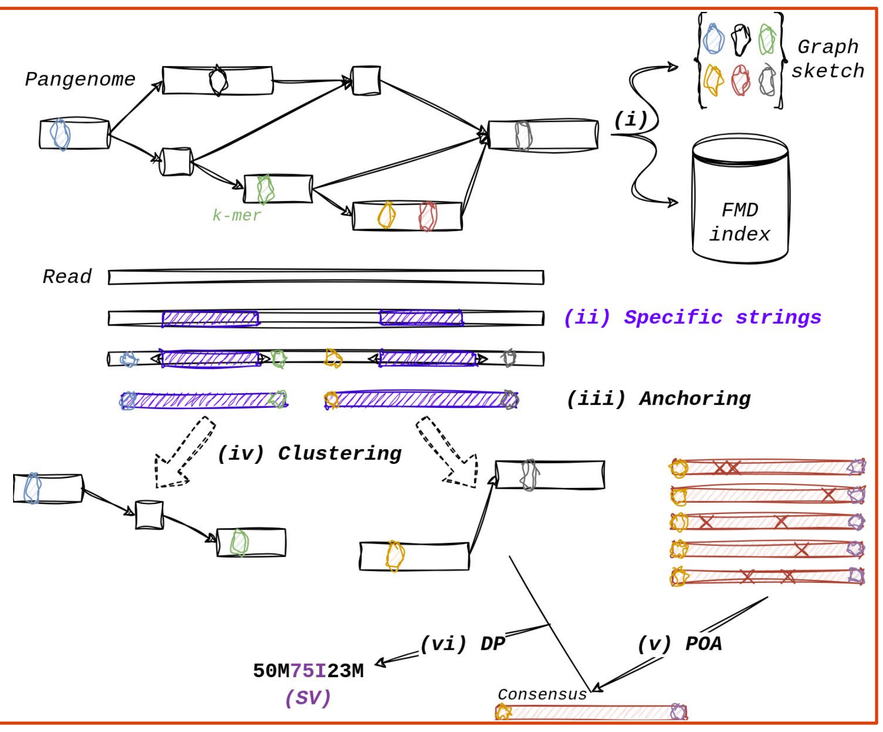
(ii) compute specific strings using the FMD-index

(iii) anchor specific strings to graph using the k-mer based sketches

(iv) assign clustering anchor specific strings to reduce graph complexity

(v) summarize information coming from different reads over the same locus

(vi) realign consensus back to local graph and get structural variation



Results & WIP

Currently testing a C++ prototype on chr21 from T2T, HPRC variant sets, and simulated PacBio HiFi data

Tool	Precision	Recall	F1
pansv	67.18	55.53	60.80
dipcall	80.46	60.88	69.32
sniffles2	69.07	54.59	60.99
cuteSV	72.23	51.46	60.09

→ improve approach
- enhance anchoring step
- replace POA with ad-hoc methodology that can exploit anchors

→ perform extensive experimental evaluation
- full-genome with genome stratification
- real data *(both PacBio and ONT)*

→ write the paper

https://github.com/ldenti/pansv

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