Computational Pangenomics #CPANG19

Day 3 (September 11, 2018)

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Wrap up of day 2

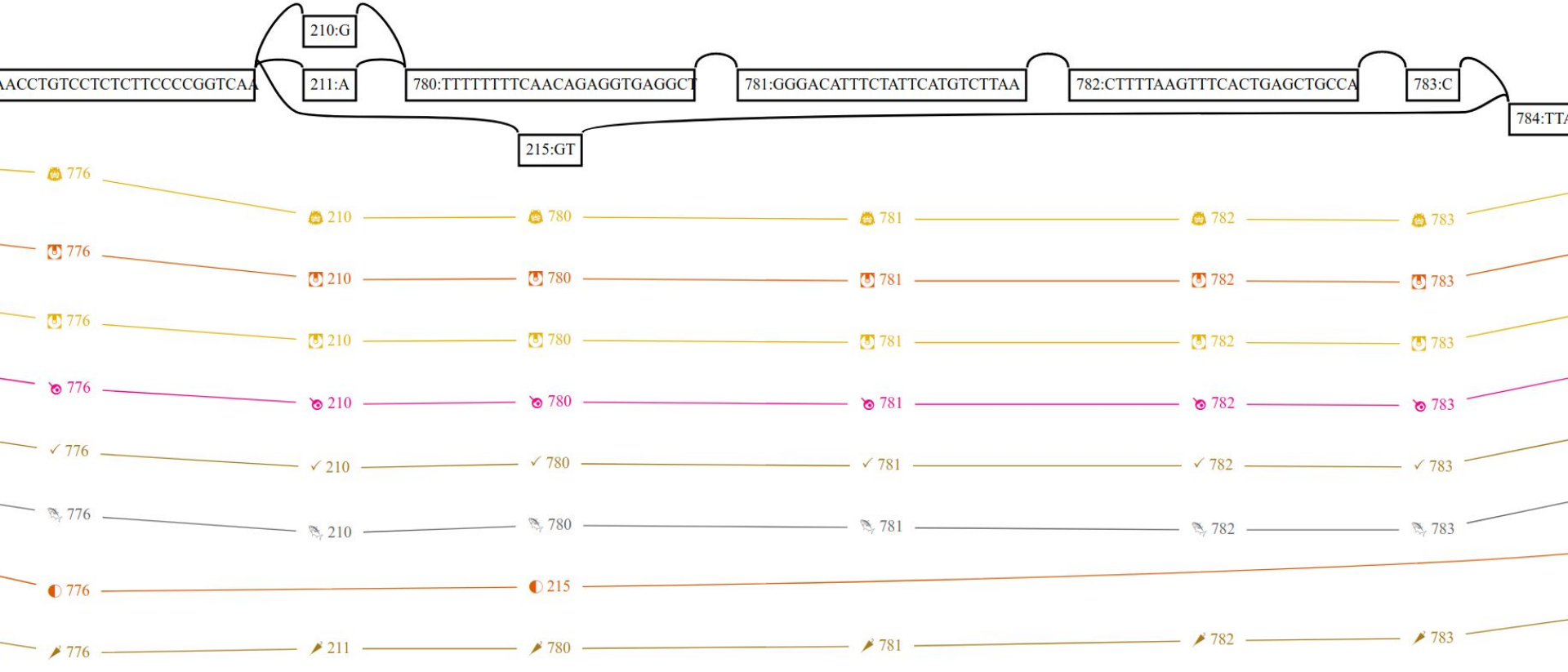
New commands in vg: msga, surject, vectorize, mod, prune, augment

New challenges: building and evaluating pangenome graphs for 5 HIV quasispecies

vg msga

```
vg msga -f GRCh38_alts/FASTA/HLA/L-3139.fa -D \
| vg mod -U 10 - | vg mod -X 32 -c - >L-3139.vg
```

```
vg view -dp L-3139.vg
```



vg surject

vg map -x z.xg -g z.gcsa -G z.sim | vg surject -d z.xg >aln.bam

or

vg map -d z -G z.sim --surject-to bam >aln.bam

Select the path to surject into with --into-path or --into-paths

vg vectorize

vg vectorize -f -x tiny.xg aln.gam

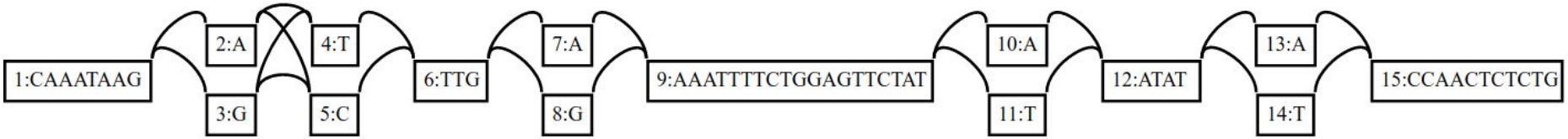
aln.name	node.1	node.2	node.3	node.4	node.5	node.6	node.7	node.8	node.9	node.10	node.11	node.12	node.13	node.14	node.15
d20030447889ddce	1	0	1	1	0	1	1	0	1	1	0	1	1	0	1
617e3f3871de4388	1	1	0	1	0	1	0	1	1	0	1	1	0	1	1
47747b2abe90ed0c	1	0	1	1	0	1	0	1	1	0	1	1	0	1	1
37b9b60a8a5213ff	1	1	0	1	0	1	0	1	1	1	0	1	0	1	1
e5d31d6cd282cf8d	1	0	1	1	0	1	0	1	1	0	1	1	0	1	1
57dda702eaeb82c9	1	0	1	0	1	1	1	0	1	1	0	1	1	0	1
08343878ae5b90f3	1	0	1	0	1	1	1	0	1	0	1	1	0	1	1
757b525e41d48830	1	1	0	1	0	1	1	0	1	1	0	1	0	1	1
cd17bf40552fc5a2	1	0	1	1	0	1	0	1	1	0	1	1	0	1	1
1b8e295543bed0e8	1	1	0	1	0	1	0	1	1	0	1	1	1	0	1

vg mod

MANY graph modification tools in one command line utility.

- Sorting
- Chopping
- Simplification
- Augmentation
- Unfolding/unrolling
- Path manipulation (add, remove, keep)
- … etc, etc

vg mod -pl / vg prune

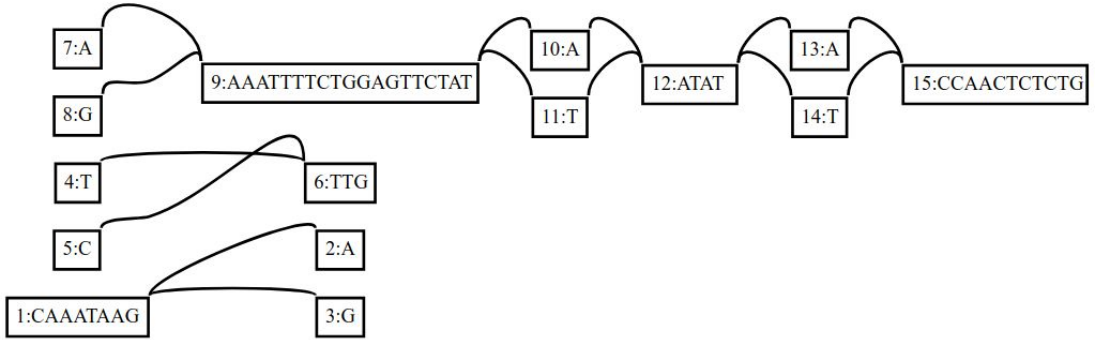


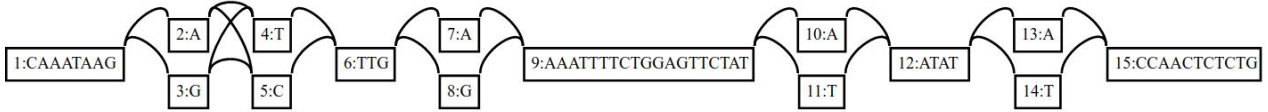
vg mod -pl 8 -e 2 tiny.vg

or

vg prune -k 8 -e 2 -s 0 tiny.vg

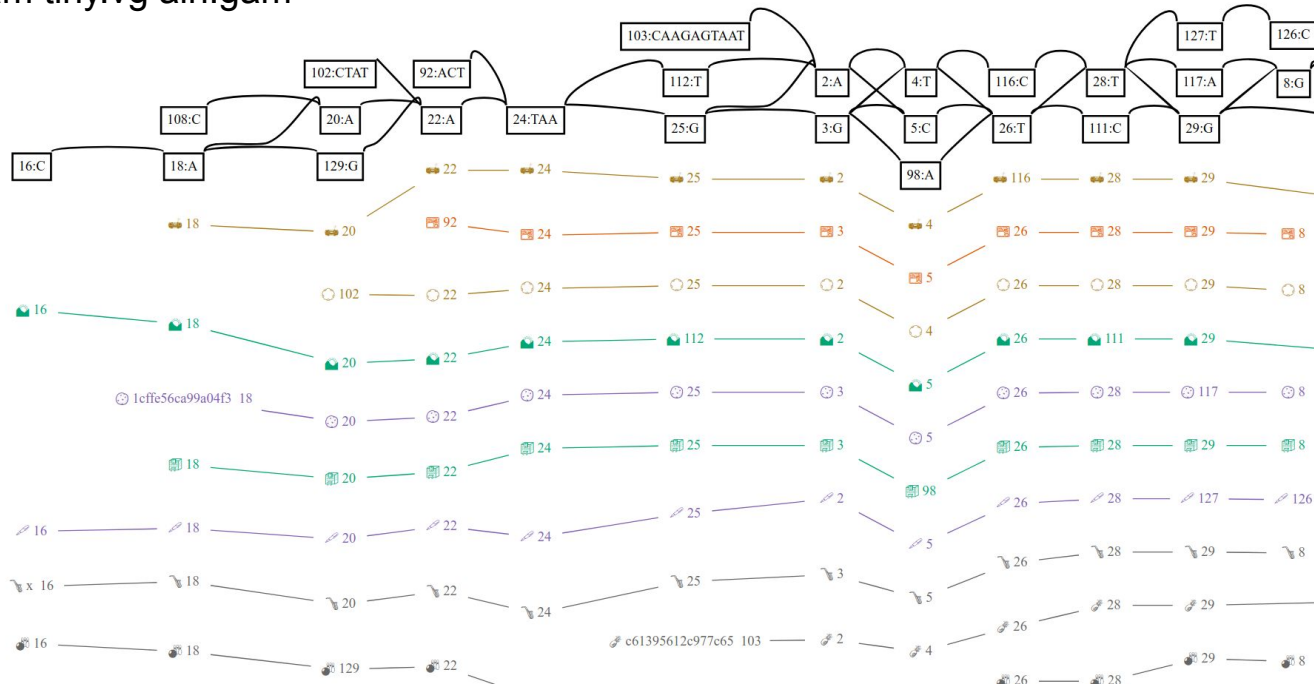
Removes edges for which we would have crossed 2 bifurcations in a path of 8 bases. (Used in indexing.)

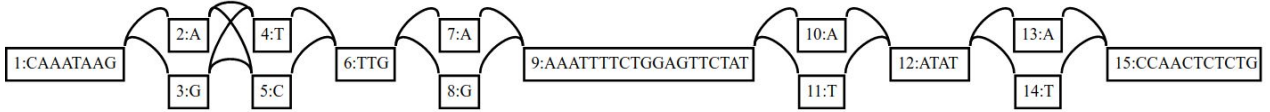




vg mod -i / vg augment

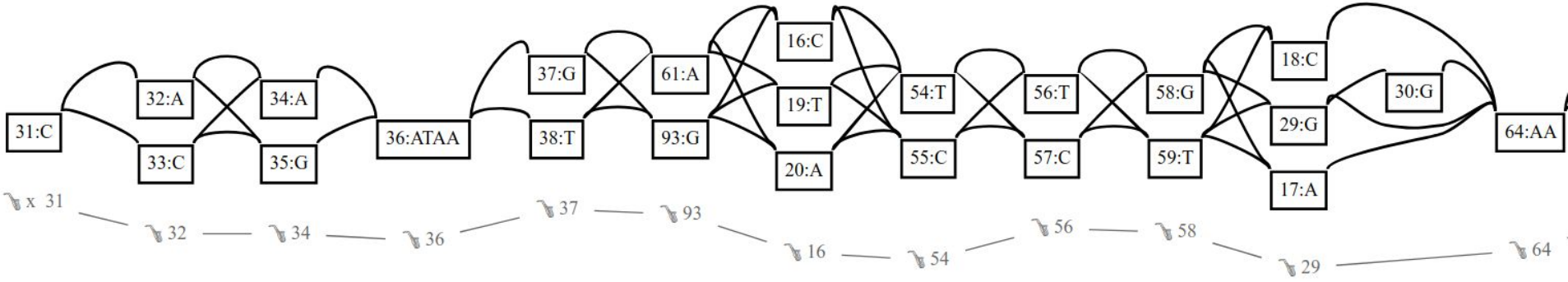
vg map -d tiny -G <(vg sim -n 10 -e 0.1 -i 0.05 -l 50 -a -x tiny.xg) >aln.gam
vg mod -i aln.gam tiny.vg >tiny+.vg
vg augment -g 1 -A aln+aug.gam tiny.vg aln.gam





vg mod -i / vg augment

vg map -d tiny -G <(vg sim -n 10 -e 0.1 -i 0.05 -l 50 -a -x tiny.xg) >aln.gam
vg mod -i aln.gam tiny.vg >tiny+.vg
vg augment -g 1 -A aln+aug.gam tiny.vg aln.gam



Questions

How confident are you with building your own workflows within vg framework?

How confident are you creating graphs using vg msga?

How confident are you with modifying graphs using vg mod?

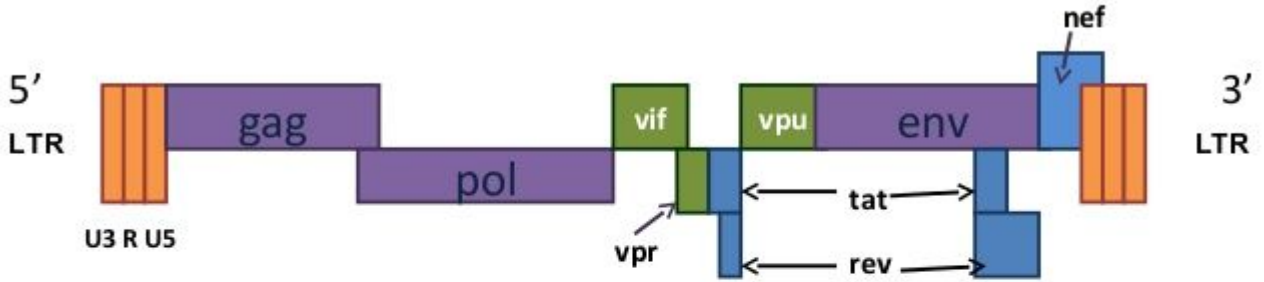
How confident are you with exploring the properties of mixed sequencing data sets using genome graphs?

How well do you understand algorithmic challenges that come with transitioning from linear reference genomes to graph genomes?

Presentations on HIV experiments

Automatic circularization of vg msga progressive assembly resulted from HIV's ~700bp LTR

HIV Genome



gag – core proteins (including p24)

pol – envelope glycoproteins

env – enzymes (RT, protease, Integrase)

tat, rev, nef, vif, vpu, vpr – proteins in the modification of host cell to enhance virus growth and regulate viral gene expression

LTR – Long Terminal Repeats- for initiation of transcription.

Maybe we’re at coffee break?

Classical (bacterial) pangenomics

New commands

index (of alignments), chunk, call, genotype, pack

vg index -a (start-node sorted alignment index)

vg construct -r small/x.fa -v small/x.vcf.gz >x.vg
vg index -x x.xg -g x.gcsa -k 16 x.vg
vg map -d x -G <(vg sim -n 100 -e 0.01 -i 0.005 -l 50 -a -x x.xg) >aln.gam
vg index -d aln.gam.idx -a aln.gam
vg index -d aln.gam.idx -D


```
{"key":"+a+26+0", "value":{"refpos": [{"is_reverse": true, "offset": 103, "name": "x"}], "identity
{"key":"+a+26+0", "value":{"refpos": [{"is_reverse": true, "offset": 103, "name": "x"}], "identity
{"key":"+a+32+0", "value":{"refpos": [{"is_reverse": true, "offset": 142, "name": "x"}], "identity
{"key":"+a+36+0", "value":{"refpos": [{"is_reverse": true, "offset": 172, "name": "x"}], "identity
{"key":"+a+42+0", "value":{"refpos": [{"offset": 186, "name": "x"}], "identity": 1.0, "sequence":
{"key":"+a+43+0", "value":{"refpos": [{"offset": 189, "name": "x"}], "identity": 1.0, "sequence":
{"key":"+a+46+0", "value":{"refpos": [{"offset": 201, "name": "x"}], "identity": 1.0, "sequence":
{"key":"+a+49+0", "value":{"refpos": [{"is_reverse": true, "offset": 204, "name": "x"}], "identity
{"key":"+a+52+0", "value":{"refpos": [{"offset": 219, "name": "x"}], "identity": 0.979999999999999
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{"key":"+a+55+0", "value":{"refpos": [{"is_reverse": true, "offset": 221, "name": "x"}], "identity
{"key":"+a+55+0", "value":{"refpos": [{"is_reverse": true, "offset": 221, "name": "x"}], "identity
{"key":"+a+55+0", "value":{"refpos": [{"offset": 255, "name": "x"}], "identity": 0.979999999999999
{"key":"+a+55+0", "value":{"refpos": [{"is_reverse": true, "offset": 221, "name": "x"}], "identity
{"key":"+a+55+0", "value":{"refpos": [{"is_reverse": true, "offset": 221, "name": "x"}], "identity
```

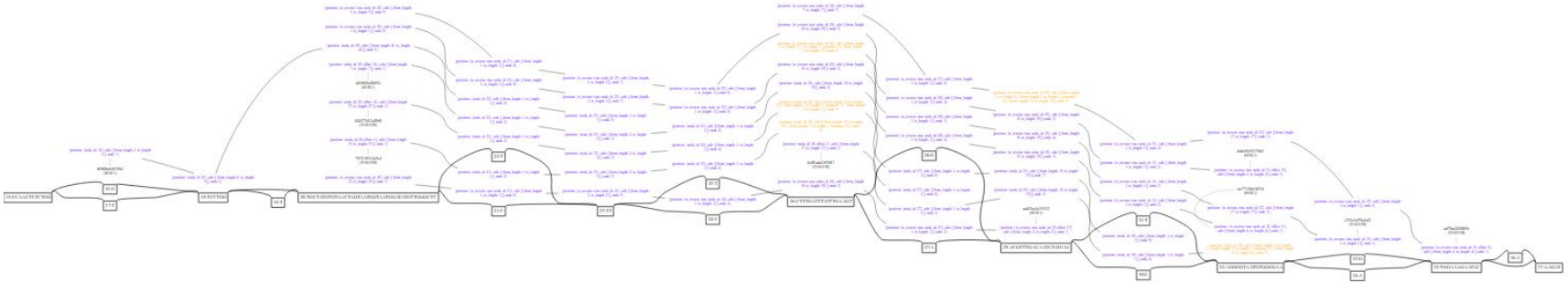
Sorting alignments (by start node id)

```
vg index -A -d aln.gam.idx | vg view -a -
vg index -A -d aln.gam.idx >aln.sort.gam
vg view -a aln.sort.gam | jq '.path.mapping[0].position.node_id' | head
```

```
16
18
20
20
20
22
16
16
32
32
….
```

vg index -N (node to alignment index)

```
vg index -N -d aln.sort.gam.idx aln.sort.gam
vg find -d aln.sort.gam.idx -o 24 | vg view -a - | wc -l
vg find -d aln.sort.gam.idx -o 23 | vg view -a - | wc -l
vg find -x x.xg -n 24 -c 1 >m.vg
vg view -dA  <(vg find -d aln.sort.gam.idx -A m.vg) <(vg find -x x.xg -G
<(vg find -d aln.sort.gam.idx -A m.vg))
```



vg explode (break graphs apart)

```
vg mod -pl 16 -e 3 x.vg | vg explode - parts
parts/component0.vg     x
parts/component1.vg     x
parts/component2.vg     x
parts/component3.vg     x
parts/component4.vg     x
parts/component5.vg
parts/component6.vg     x
parts/component7.vg     x
parts/component8.vg     x
parts/component9.vg     x
```

vg chunk (break graphs into pieces)

```
vg chunk -x x.xg -n 10
ls chunk*
```

```
chunk_0_ids_1_23.vg
chunk_1_ids_21_46.vg
chunk_3_ids_66_90.vg
chunk_5_ids_109_133.vg
chunk_7_ids_153_177.vg
chunk_9_ids_197_210.vg
chunk_0_ids_1_5_trace_annotate.txt
chunk_2_ids_43_68.vg
chunk_4_ids_88_112.vg
chunk_6_ids_131_155.vg
chunk_8_ids_175_200.vg
```

vg pack (graph coverage vectors)

vg pack -x x.xg -g aln.gam -d -n

```
0       0
1       0
2       1
3       0
4       1
5       1
6       2
7       2
8       0
9       2
10      2
11      0
12      2
….
```