Celera Assembler: Adapting for the Future

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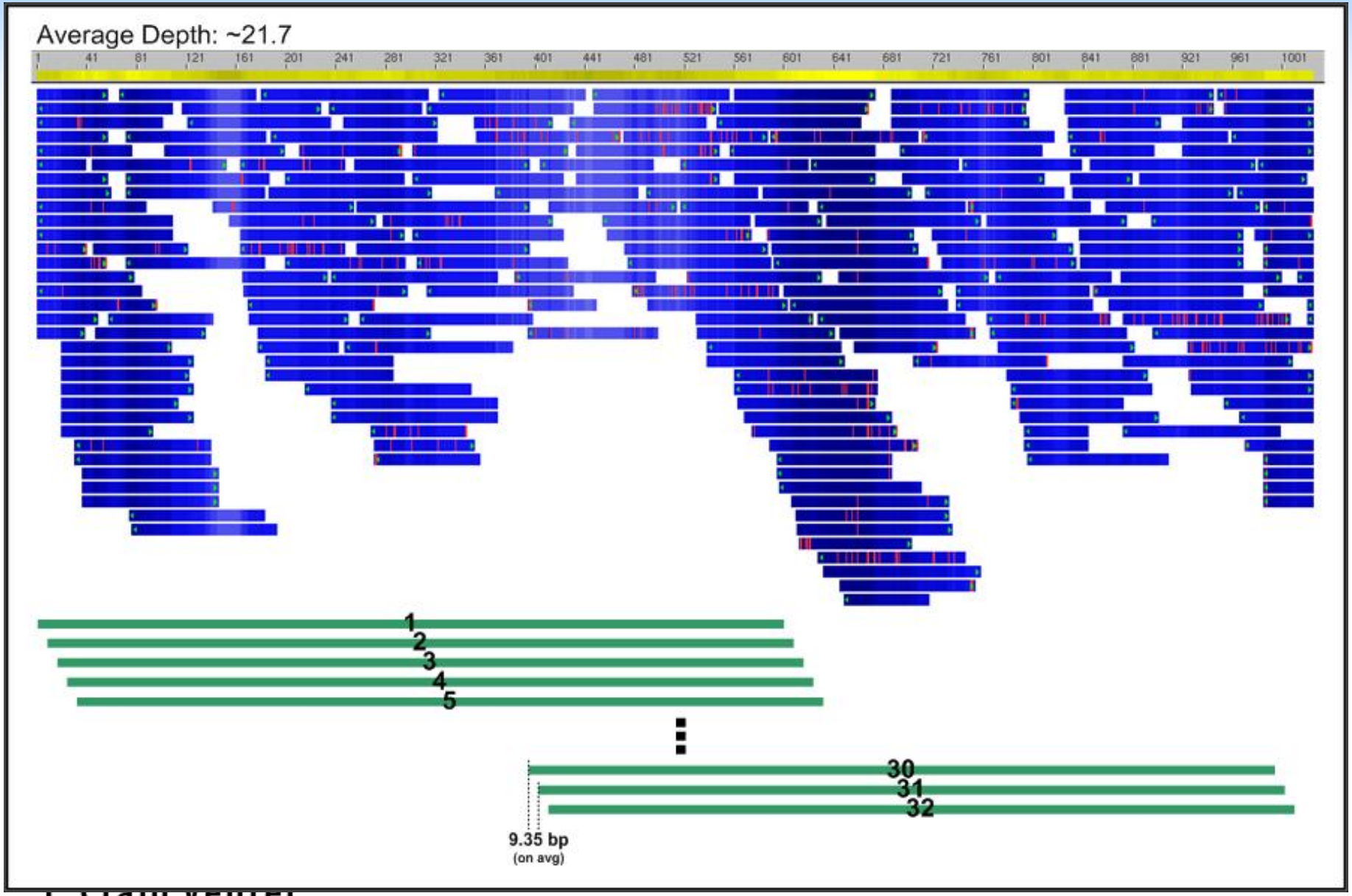
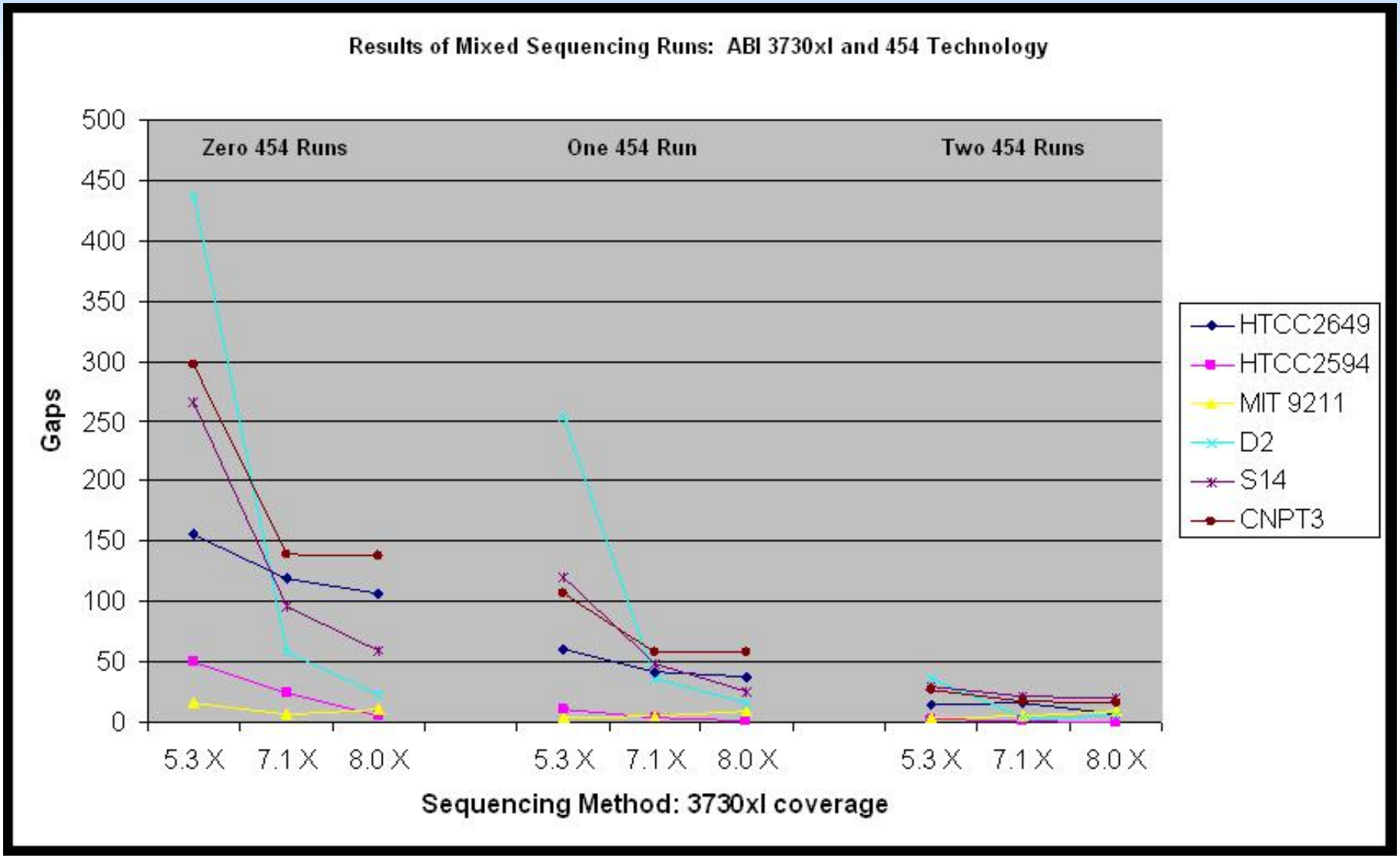
Celera Assembler

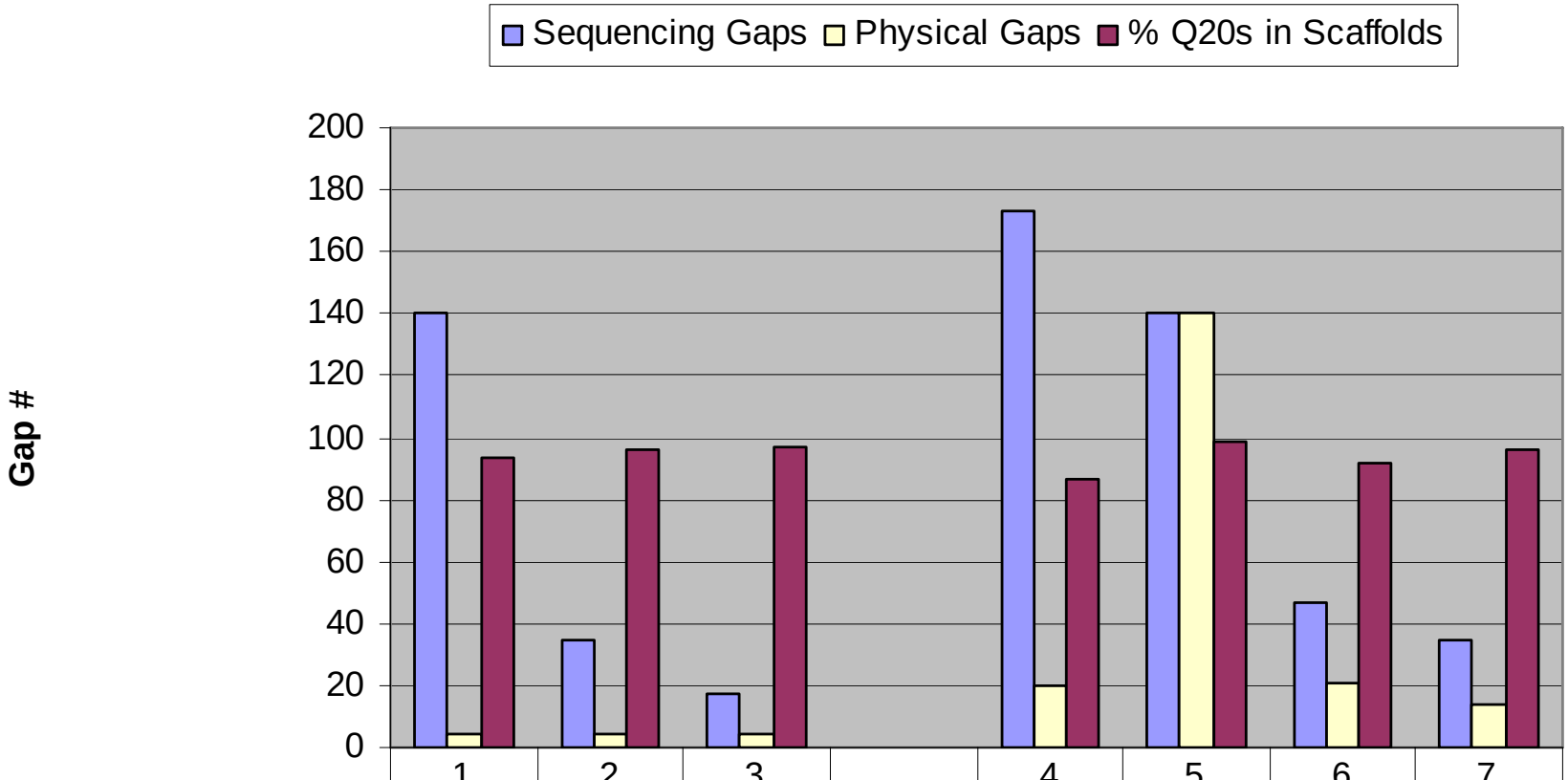
- Open source
- https://sourceforge.net/projects/wgs-assembler/
- Contact: Granger Sutton
- gsutton@jcvi.org

Current Hybrid Assembler

- Run Newbler
- Shred Newbler contigs in order to get longer fragments with fewer errors
- Input Sanger reads and shredded reads to Celera Assembler
- Maintain fragment depth of coverage
- Use low QVs for shreds so that Sanger reads dominate consensus


Average Depth: ~21.7
1
41
81
121
161
201
241
281
321
361
401
441
481
521
561
601
641
681
721
761
801
841
881
921
961
1001
1
2
3
4
5
30
31
32
9.35 bp
(on avg)


Results of Mixed Sequencing Runs: ABI 3730xl and 454 Technology
Zero 454 Runs
One 454 Run
Two 454 Runs
Gaps
500
450
400
350
300
250
200
150
100
50
0
5.3 X
7.1 X
8.0 X
5.3 X
7.1 X
8.0 X
5.3 X
7.1 X
8.0 X
Sequencing Method: 3730xl coverage
HTCC2649
HTCC2594
MIT 9211
D2
S14
CNPT3



	1	2	3		4	5	6	7
Sequencing Gaps	140	35	17		173	140	47	35
Physical Gaps	4	4	4		20	140	21	14
% Q20s in Scaffolds	93.67	95.91	97.05		86.35	98.86	92.03	96.06

Hybrid Assembly Strategy

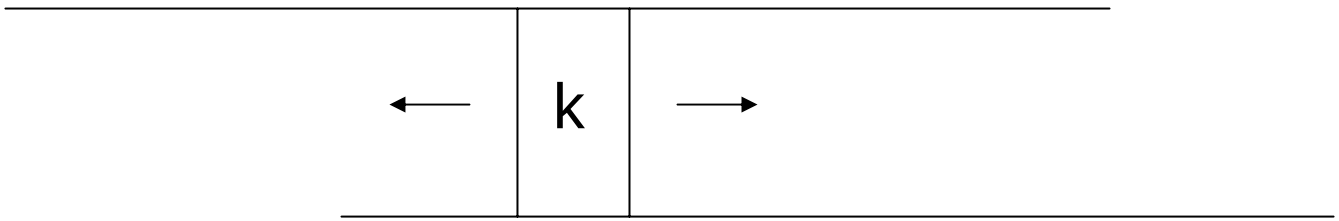
1. M063 - 0X Plasmid, .4X Fosmid, 1 FLX Run
2. M063 - 5.6X Plasmid, .4X Fosmid, 0 FLX Run
3. M063 - 5.6X Plasmid, .4X Fosmid, 1 FLX Run
4. lacto - 5X Plasmid - 0 FLX Run - 0 GS20 Run
5. lacto - 0X Plasmid - 1 FLX Run - 0GS20 Run
6. lacto - 5X Plasmid - 0 FLX Run - 1 GS20 Run
7. lacto - 5X Plasmid - 1 FLX Run - 0GS20 Run

New Hybrid Assembler

- Use 454 fragments directly
- Compress homopolymer runs for overlap detection
- Allow higher error rates in overlap extension
- Modify fragment error correction
- Modify repeat finding
- Modify consensus

Correcting k-mer Seeds

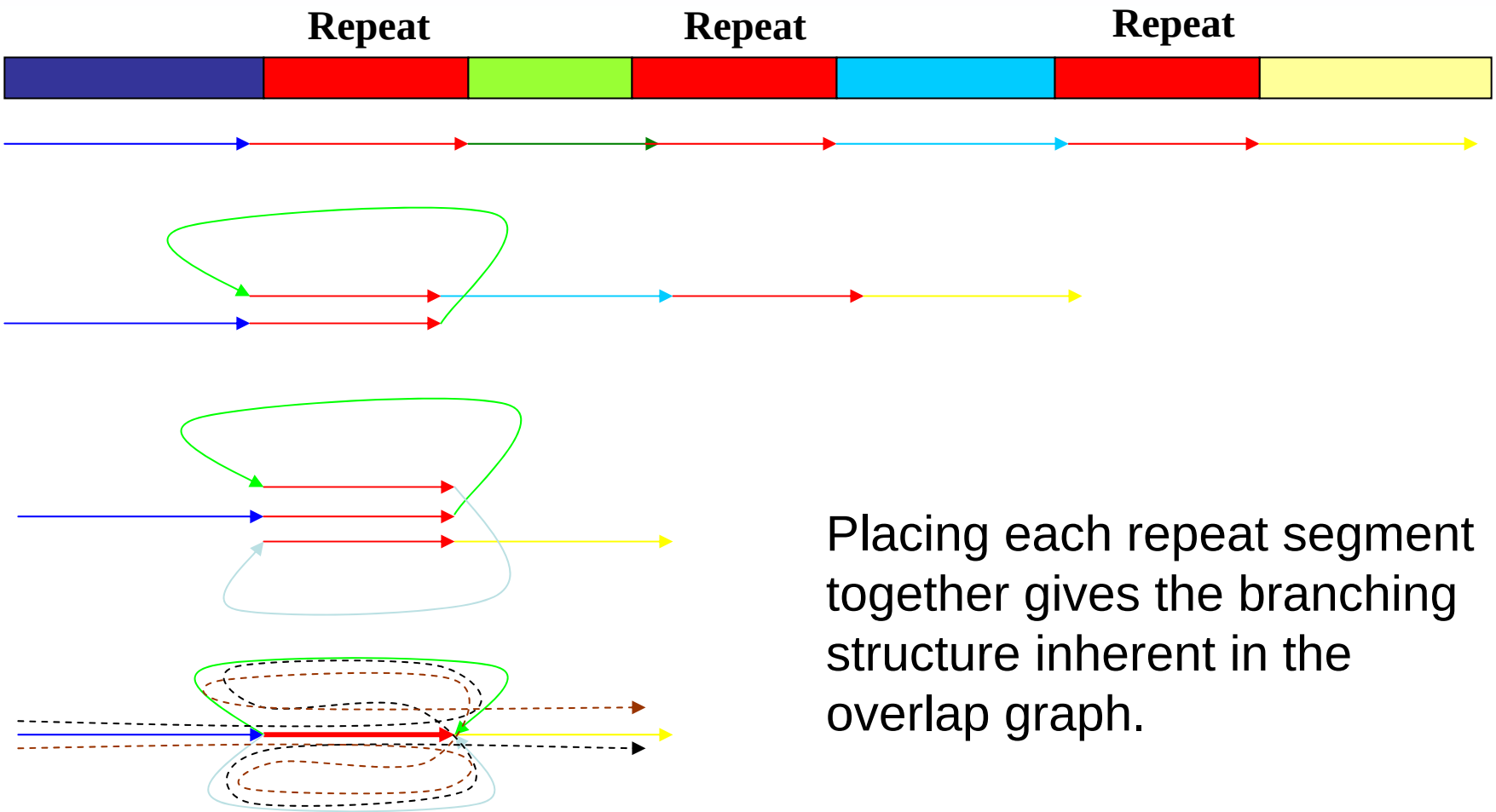
- Homopolymer run errors corrupt k-mers
- Truncate all homopolymer runs > t to length t
- Recompute k-mers to use for seeds
- Test on compressed D. willistoni fragments



Error Correction

```
1 ...AGT...AACT...TTACC...
2 ...AGT...AACT...TTACC...
3 ...AGT...AACT...TTACC...
4 ...AAT...AACT...TTACC...
5 ...AGT...AACT...TTACC...
-------------------------
6 ...AGT...AAAT...TGACC...
7 ...AGT...AAAT...TGACC...
8 ...AGT...AAAT...TGACC...
9 ...AGT...AAAT...TGACC...
```

Repeat / Chunk / Unitig / String Graph



Placing each repeat segment together gives the branching structure inherent in the overlap graph.

Consensus

A

```
...AGGCGA-TGAG...
...AGGCG-ATGAG...
...AGGCGA-TGAG...
...AGGCG-ATGAG...
...AGGCG-ATGAG...
...AGGCGA-TGAG...
...AGGCG-ATGAG...
...AGGCGAATGAG...
```

B

```
...AGGCGA-TGAG...
...AGGCGA-TGAG...
...AGGCGA-TGAG...
...AGGCGA-TGAG...
...AGGCGA-TGAG...
...AGGCGA-TGAG...
...AGGCGA-TGAG...
...AGGCGAATGAG...
```

Auto-Closure

- Will output gap or problematic region spanning clones
- Can design primers or output flanking sequence
- Can output consistently problematic mate pairs
- Established formats?

Leveraging Auto-Closure

- Assembler must respect constraints on finishing reads
- Assembler should allow and respect previously assembled contigs if desired
- Transposon mate pairs should be supported

Metagenomics

- Compilation macro and parameter settings for metagenomic assembly
- Shorter k-mers
- Higher error in overlaps allowed (10-12%)
- Significant increase in assembly for deep metagenomic data
- Significant increase in assembly for some polymorphic genomes like body louse

Celera Assembler

- https://sourceforge.net/projects/wgs-assembler/
- Granger Sutton gsutton@jcvi.org
- Generates .ace .agp files
- What other files needed?
- What other input must be supported?