Haplotype Assembly

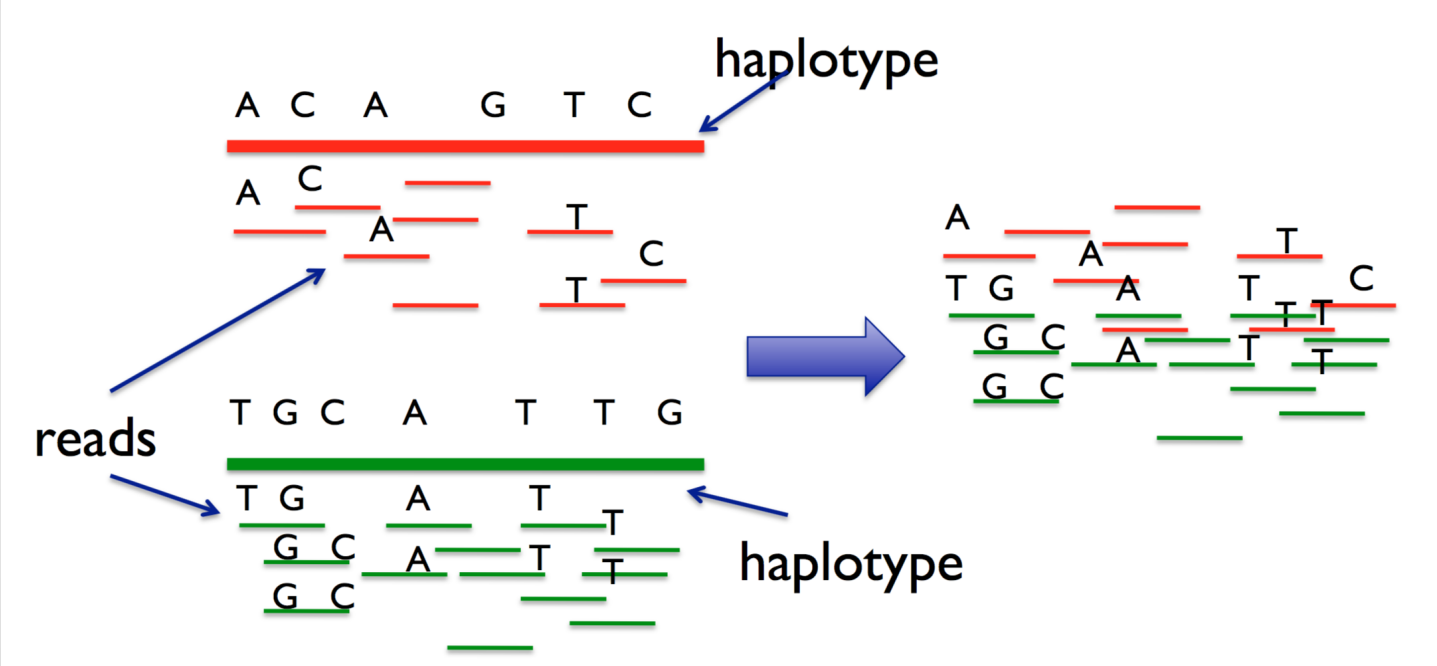
Daniel Norman

Motivate the Problem

- Haplotype information is needed
  - Haplotypes differentiate humans from each other

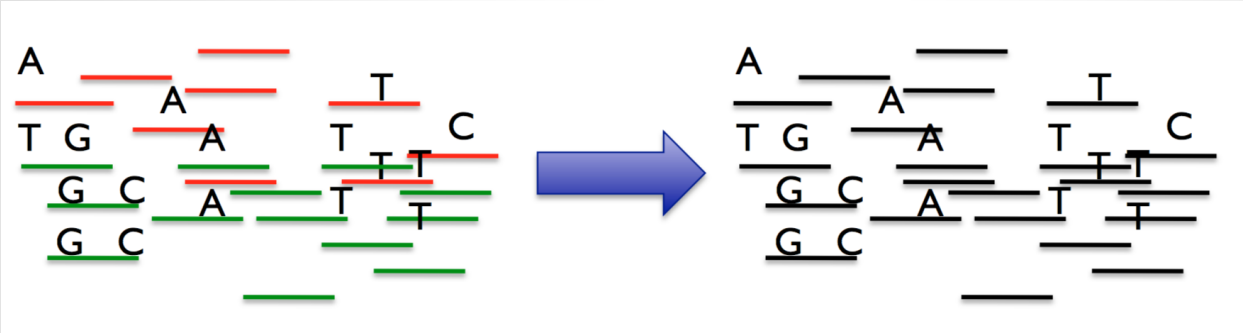
- Machines can read DNA to produce chunks of the haplotypes, but unsure which chromosome (which haplotype) a read is from

Motivate the Problem



Images from Dr. Eleazar Eskin, UCLA

Motivate the Problem



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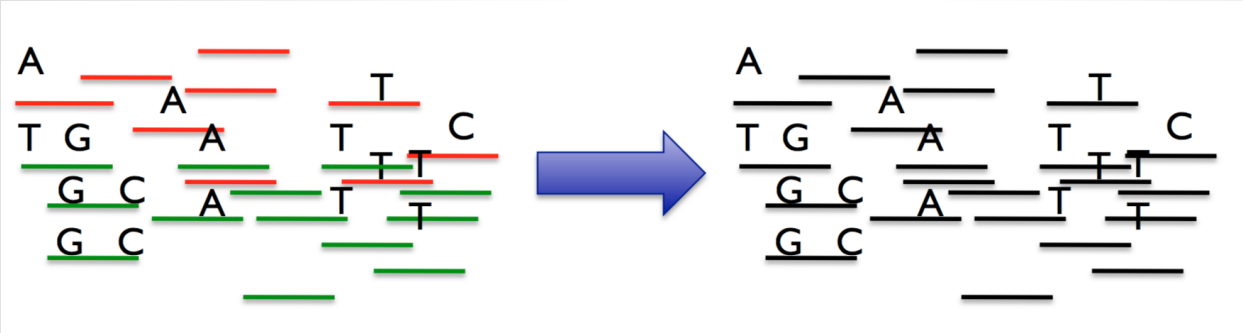

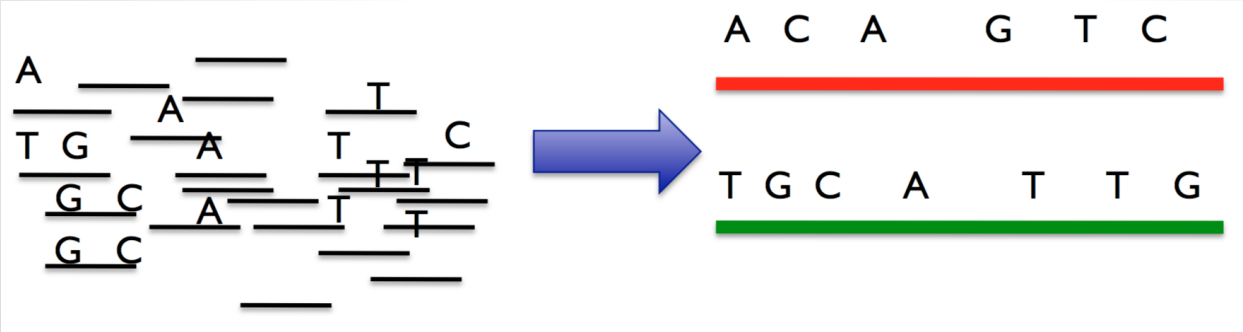

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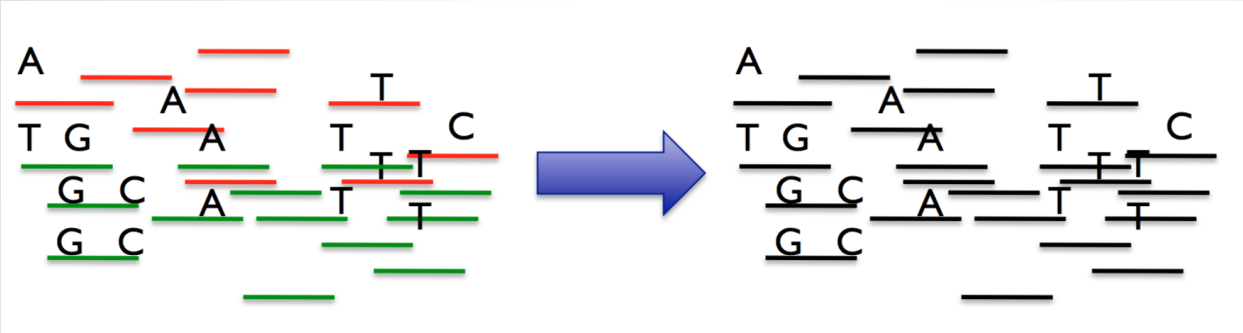
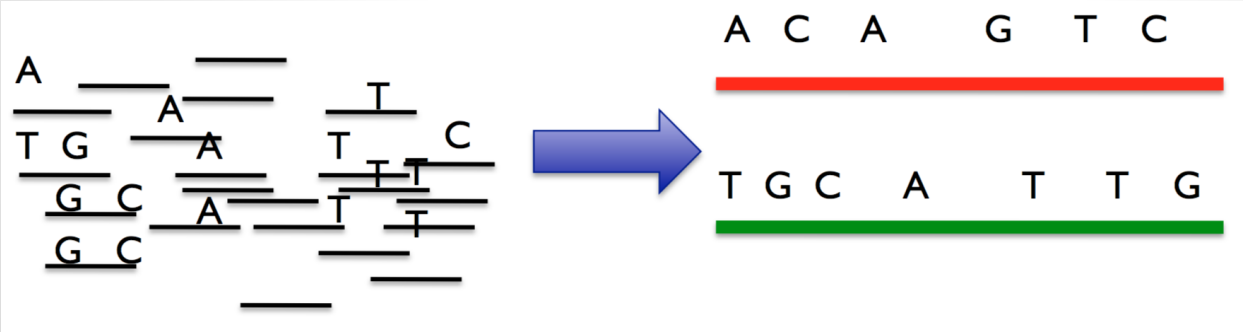




END GOAL!

Images from Dr. Eleazar Eskin, UCLA

Computational Problem

Homozygous Sites

ATACGGCTAGATTC

ATGCGGTTAGCTTT

Heterozygous Sites

Computational Problem

Homozygous Sites

```
ATACGGCTAGATTC
ATGCGGTTAGCTTT
```

Heterozygous Sites

```
__0___1___1__0
__1___0___0__1
```

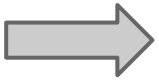
0: Minor allele
1: Major allele

Computational Problem

```
__0___1___1__0
__1___0___0__1
```

Computational Problem

```
__0___1___1__0
__1___0___0__1
```



```
0110…
1001…
```

Not recording homozygous SNPs?

Computational Problem

How do we get from reads...

```
01101
 1101
 00101
  1010
   10100
```

...

Computational Problem

How do we get from reads...

```
01101
 1101
 00101
  1010
   10100
```

...

to haplotypes?

```
01101011...
10010100...
```

Benchmarks

- Speed
- Accuracy (Switch Distance)

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Baseline - Easy Project Algorithm

Assume no errors in reads

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Go through all reads,
placing them in the
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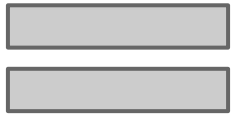


Simple and fast!

Easy Algorithm Visualization

```
01101                H1:
 1101                H2:
   10110
   01001
     11011
```

Easy Algorithm Visualization

```
01101
 1101
   10110
   01001
     11011
```

```
H1: 01101
H2:
```

Easy Algorithm Visualization

```
01101
 1101
   10110
   01001
     11011
```

H1: 01101

H2: 10010

Easy Algorithm Visualization

```
01101
 1101
   10110
   01001
     11011
```

```
H1: 01101
H2: 10010110
```

Easy Algorithm Visualization

```
01101
 1101
   10110
   01001
     11011
```

```
H1: 01101001
H2: 10010110
```

Easy Algorithm Visualization

```
01101
 1101
   10110
   01001
     11011
```

```
H1: 01101001
H2: 1001011011
```

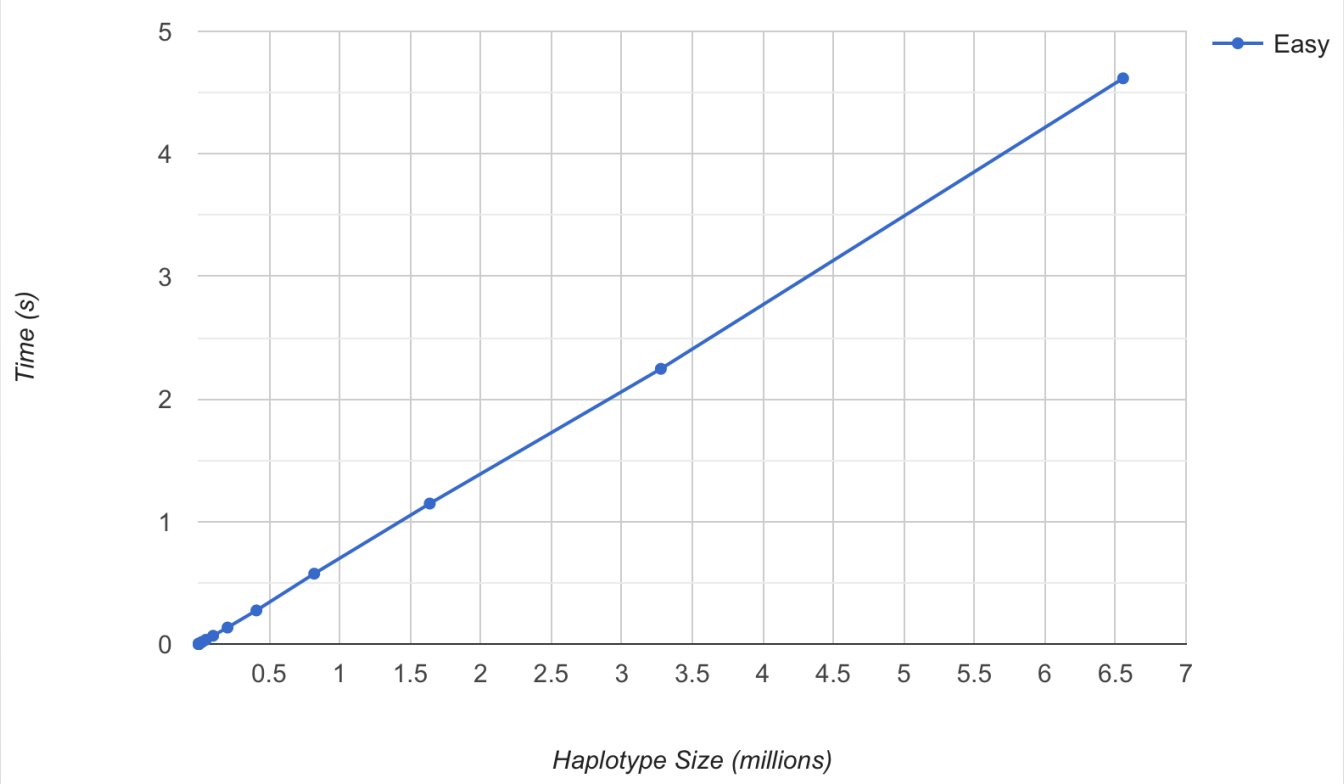
Easy Algorithm Visualization

```
01101
 1101
   10110
   01001
     11011
```

```
H1: 0110100100
H2: 1001011011
```

ALL DONE!

Easy Algorithm Runtime



Medium Project Algorithm

Allow for errors in reads

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Partition reads into two distinct groups based on a matching criteria, then reassemble

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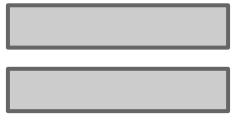


Accurate!

Medium Algorithm Visualization

```
A: 01101
B:  1100
C:   010110
D:    00000
E:      11011
F:       10101
```

H1:

H2:

Medium Algorithm Visualization

```
A: 01101
B:  1100
C:   010110
D:    00000
E:      11011
F:       10101
```

H1: A

H2:

Medium Algorithm Visualization

```
A: 01101
B:  1100
C:   010110
D:    00000
E:      11011
F:       10101
```

H1: A, B

H2:

Medium Algorithm Visualization

```
A: 01101
B:  1100
C:   010110
D:     00000
E:       11011
F:        10101
```

```
H1: A, B
H2: C
```

Medium Algorithm Visualization

```
A: 01101
B:  1100
C:   010110
D:     00000
E:       11011
F:        10101
```

H1: A, B

H2: C

Medium Algorithm Visualization

```
A: 01101
B:  1100
C:   010110
D:     00000
E:       11011
F:        10101
```

```
H1: A, B
H2: C, E
```

Medium Algorithm Visualization

```
A: 01101
B:  1100
C:   010110
D:     00000
E:       11011
F:        10101
```

```
H1: A, B
H2: C, E, F
```

Medium Algorithm Visualization

Now reassemble one haplotype, SNP by SNP

Example: SNP 5 on Haplotype 1

```
A: 01101          H1, SNP 5:
B:  1100
C:   010110
```

Medium Algorithm Visualization

Now reassemble one haplotype, SNP by SNP

Example: SNP 5 on Haplotype 1

```
A:  01101
B:   1100
C:    010110
```

```
H1, SNP 5:
  = [1+0+flip(0)]/3
```

Medium Algorithm Visualization

Now reassemble one haplotype, SNP by SNP

Example: SNP 5 on Haplotype 1

```
A:  01101          H1, SNP 5:
B:   1100            = [1+0+flip(0)]/3
C:    010110         = [1+0+1]/3
```

Medium Algorithm Visualization

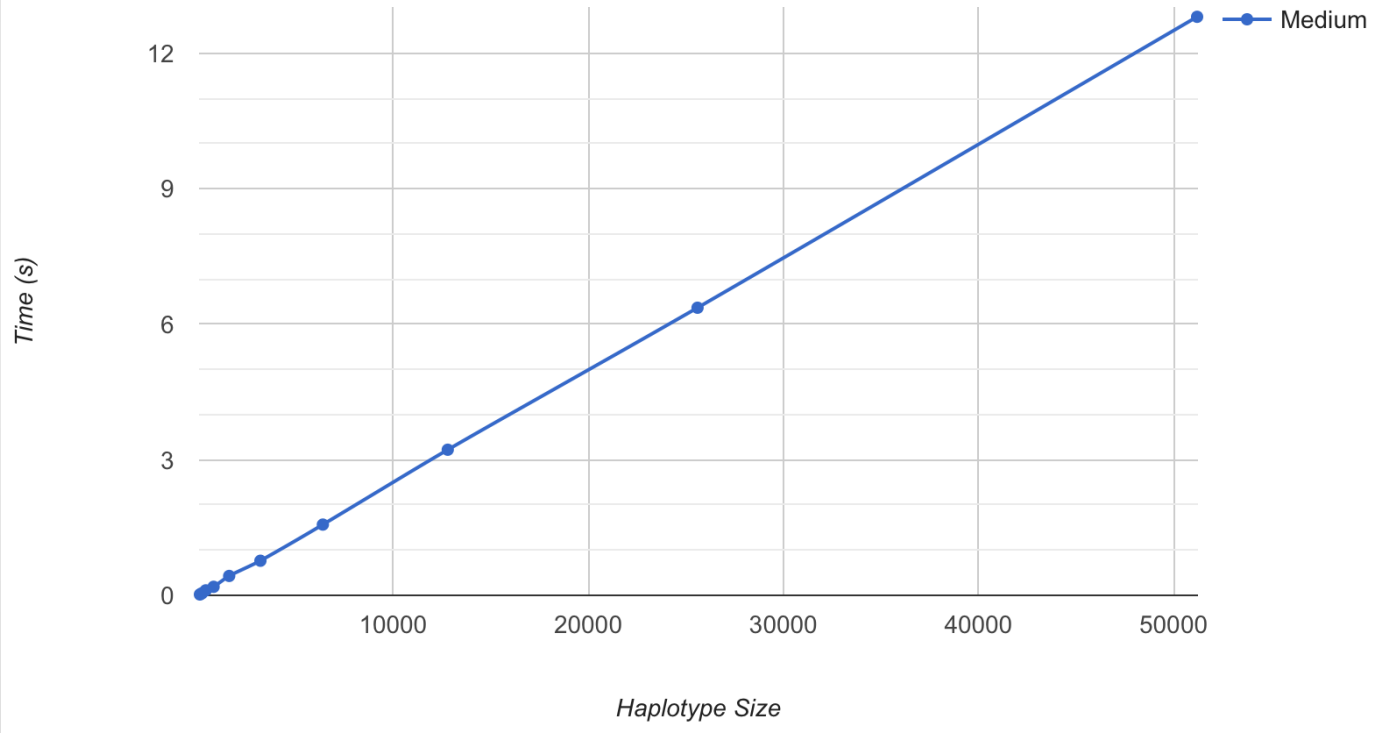
Now reassemble one haplotype, SNP by SNP

Example: SNP 5 on Haplotype 1

```
A:  01101
B:   1100
C:    010110
```

```
H1, SNP 5:
   = [1+0+flip(0)]/3
   = [1+0+1]/3
   = 1
```

Medium Algorithm Runtime



Time for Haplotype of Size 50,000

Easy: 0.035s

Medium: 12.8s

Time for Haplotype of Size 50,000

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Medium is 365 times as slow as Easy

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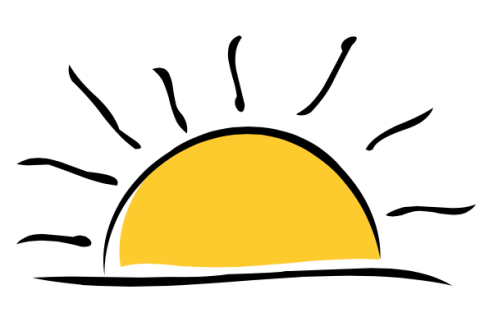
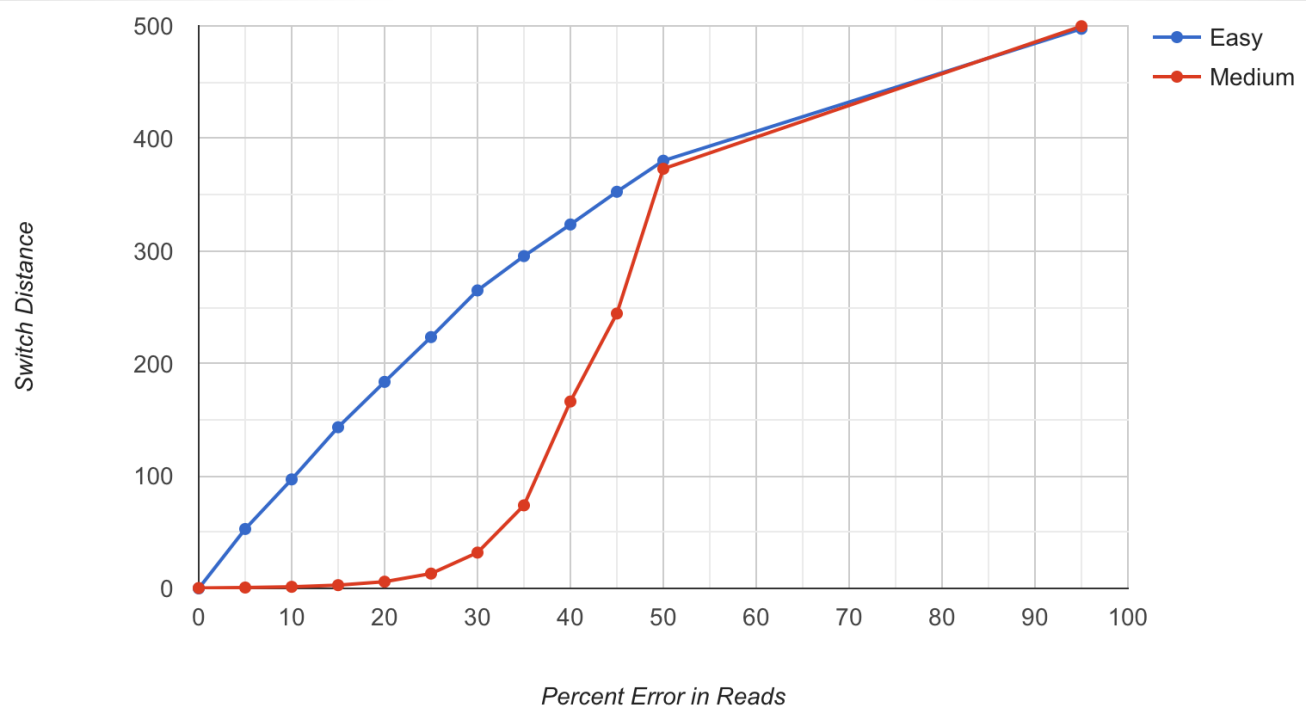


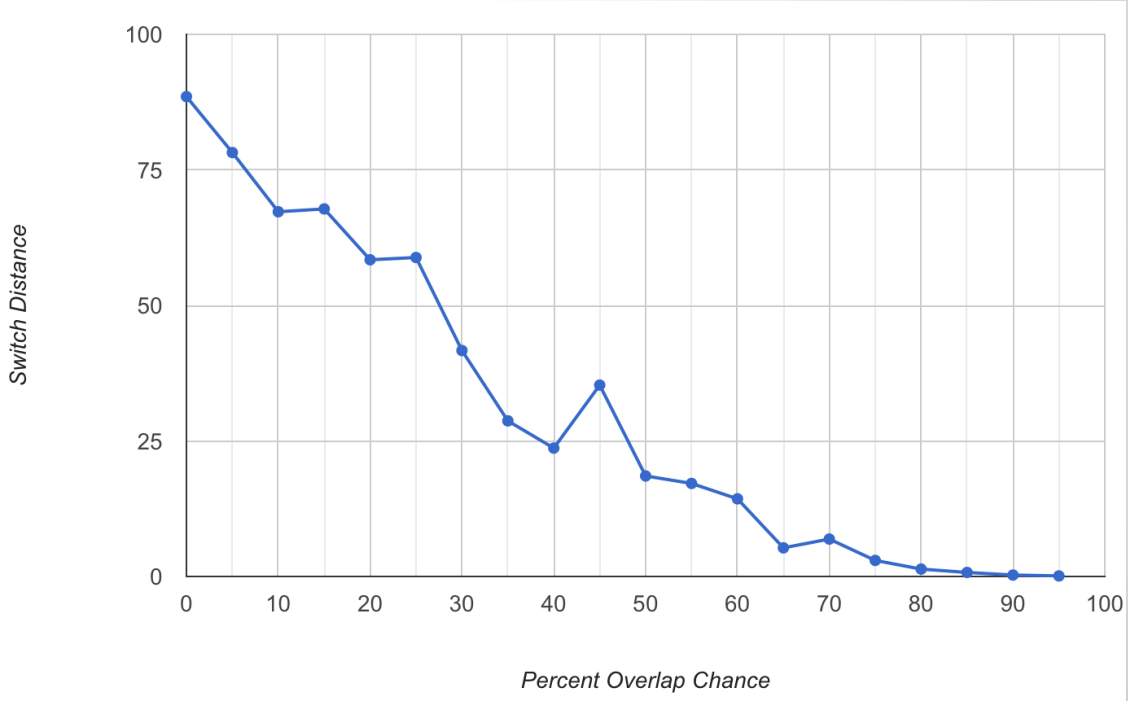
Accuracy - Easy vs Medium

Haplotype length: 1000 SNPs



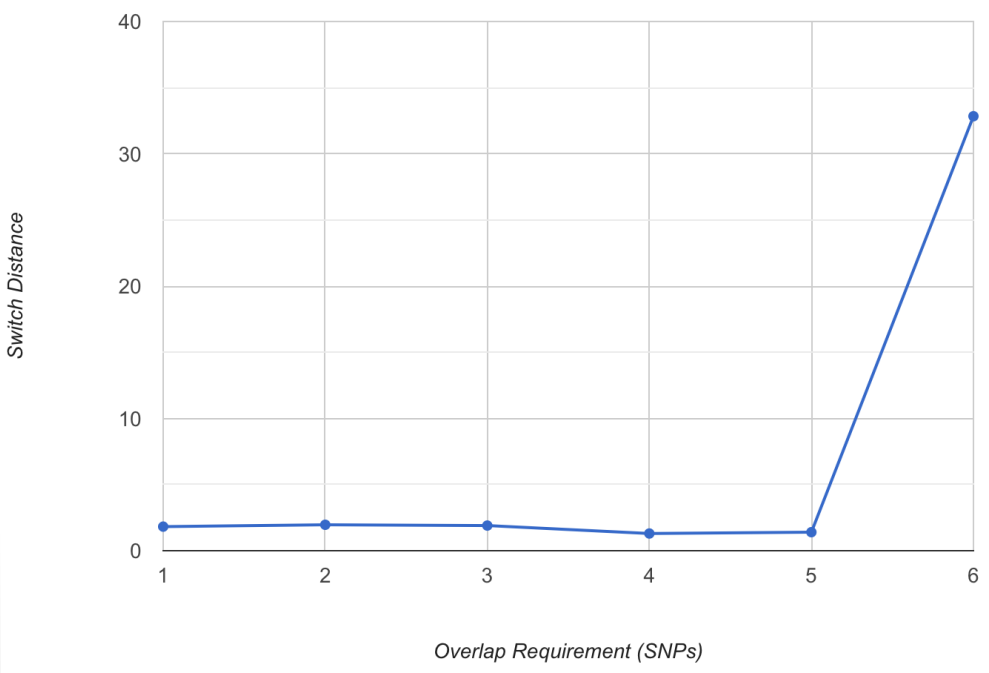
Overlap Chance in Reads

```
101101
0101
  00101
  011011

Overlap Chance
  = 50%
```



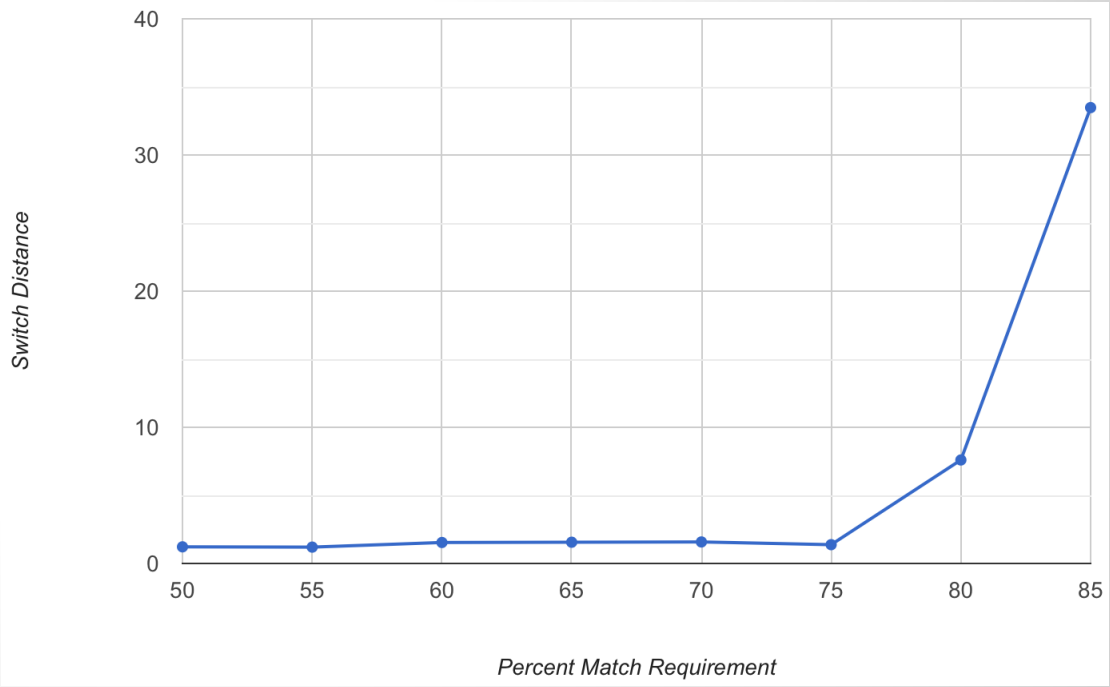
Overlap Requirement

```
101101
  100101

Overlap = 4
```



Match Requirement

```
101101
  100101

Matches = 75%
```



Something Interesting

- Medium gets slightly worse accuracy than Easy at very high error rates
  - Medium requires reads to meet match criteria
  - If few meet criteria, it has to guess often
  - Easy will place reads into a haplotype no matter what

- Hard algorithm working
  - Requires very low error rate and lots of overlap

Thank You!