Haplotype Assembly

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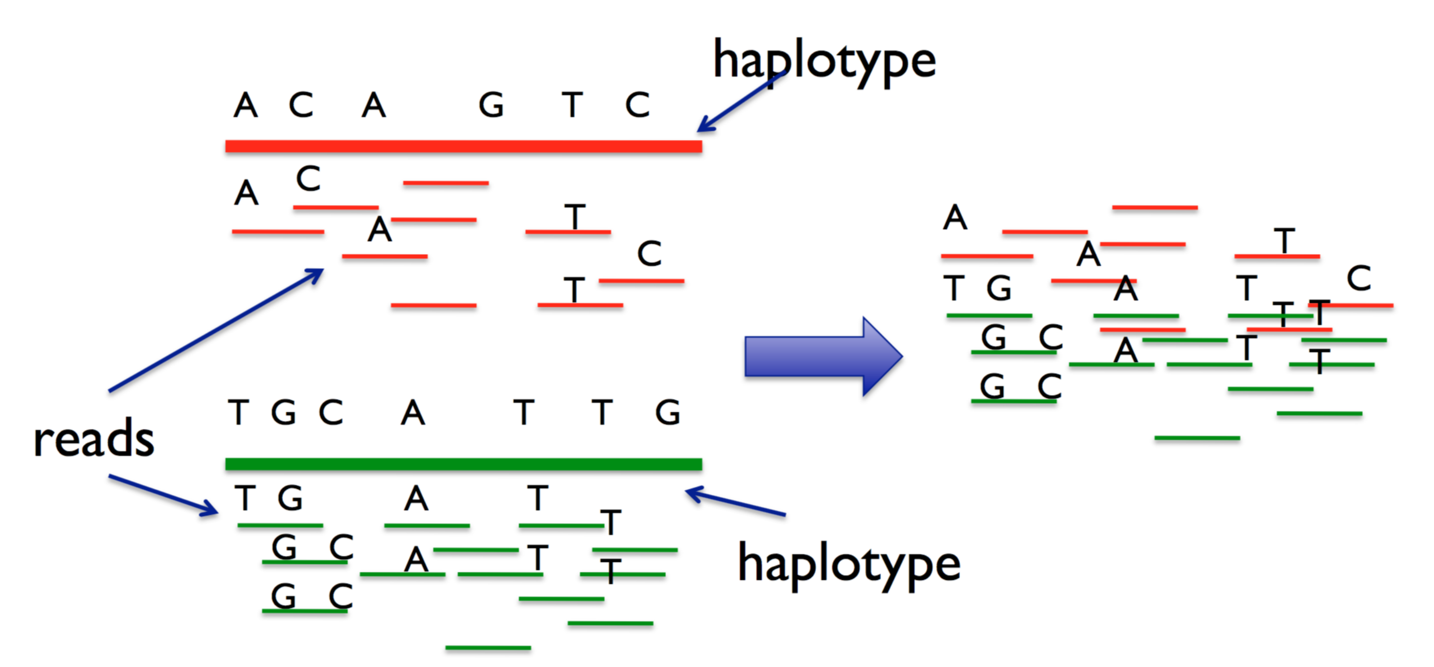
Motivate the Problem

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

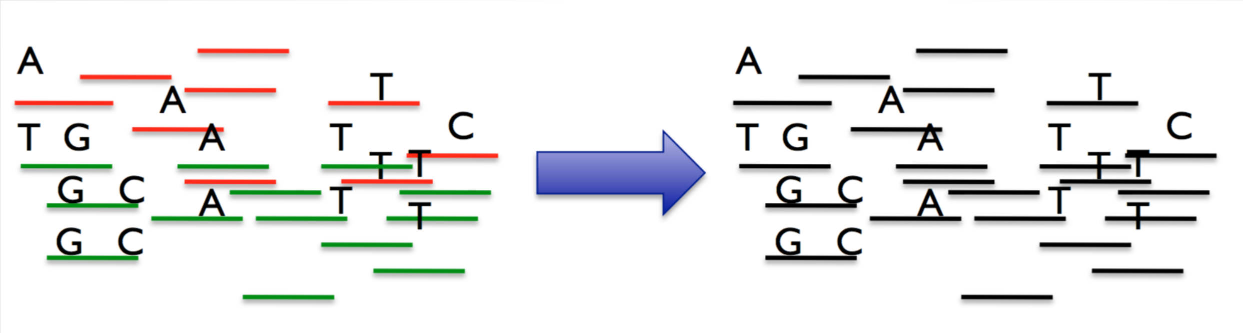
- Machines can read DNA to produce chunks of the haplotypes, but unsure which chromosome (which haplotype) a read is from

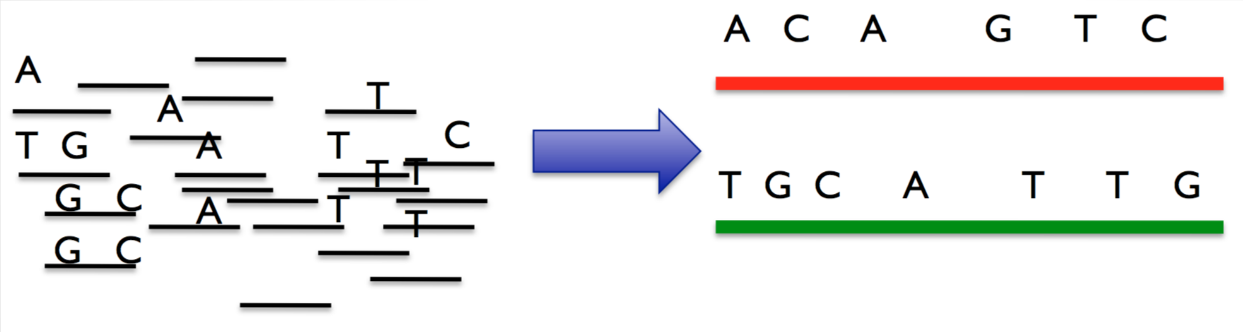
Motivate the Problem



Images from Dr. Eleazar Eskin, UCLA

Motivate the Problem

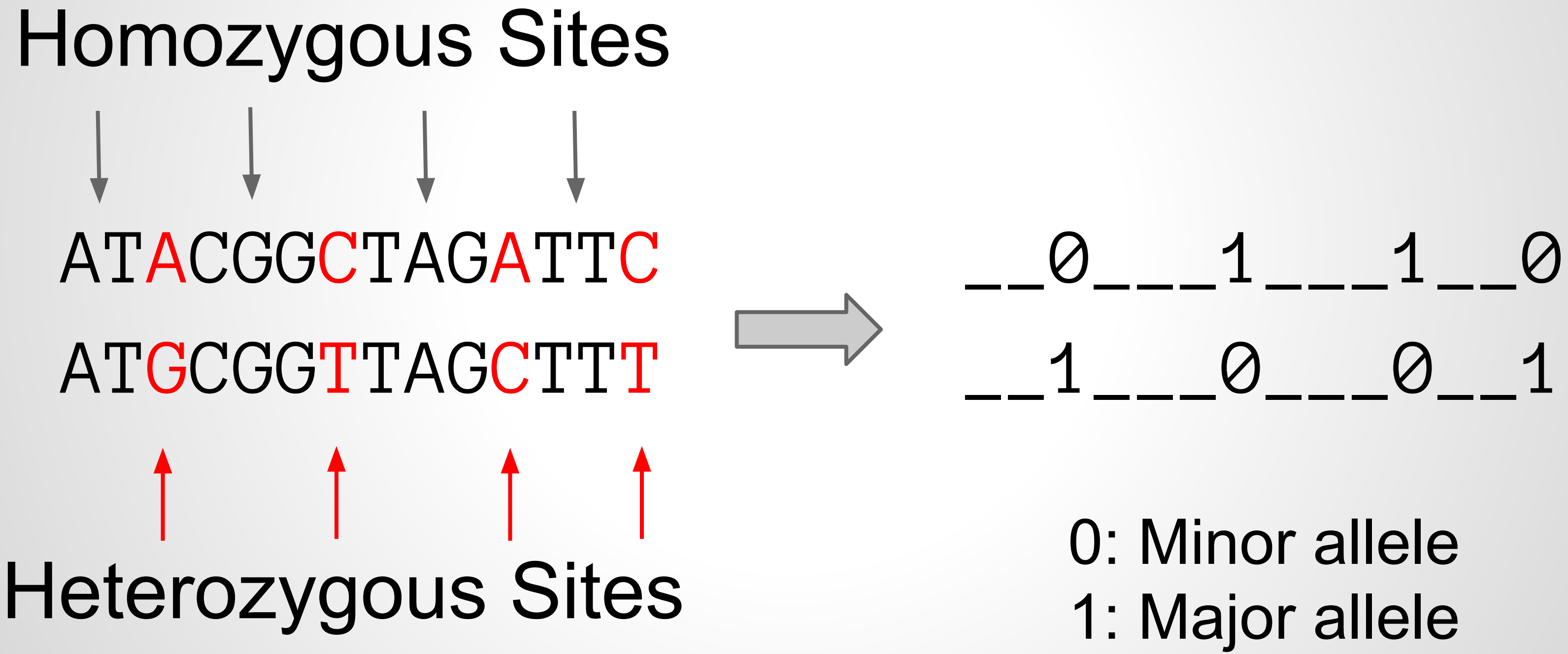




END GOAL!

Images from Dr. Eleazar Eskin, UCLA

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        0110…
                 →
__1___0___0__1        1001…
```

Not recording homozygous SNPs?

Computational Problem

How do we get from reads...

```
01101
 1101
 00101
  1010
   10100
...
```

→

to haplotypes?

```
01101011…
10010100…
```

Benchmarks

- Speed
- Accuracy (Switch Distance)

Baseline - Easy Project Algorithm

Assume no errors in reads

Go through all reads, placing them in the haplotype they match

=

Simple and fast!

Easy Algorithm Visualization

```
01101
 1101
   10110
   01001
     11011
```

H1:

H2:

Easy Algorithm Visualization

```
01101
 1101
   10110
   01001
     11011
```

H1: 01101

H2:

Easy Algorithm Visualization

```
⇨  01101                H1: 01101
    1101                H2: 10010
      10110
      01001
        11011
```

Easy Algorithm Visualization

```
    01101              H1: 01101
     1101              H2: 10010110
⇨      10110
       01001
         11011
```

Easy Algorithm Visualization

```
     01101
      1101
⇨       10110
        01001
          11011
```

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

Easy Algorithm Visualization

```
  01101
   1101
     10110
     01001
⇨        11011
```

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

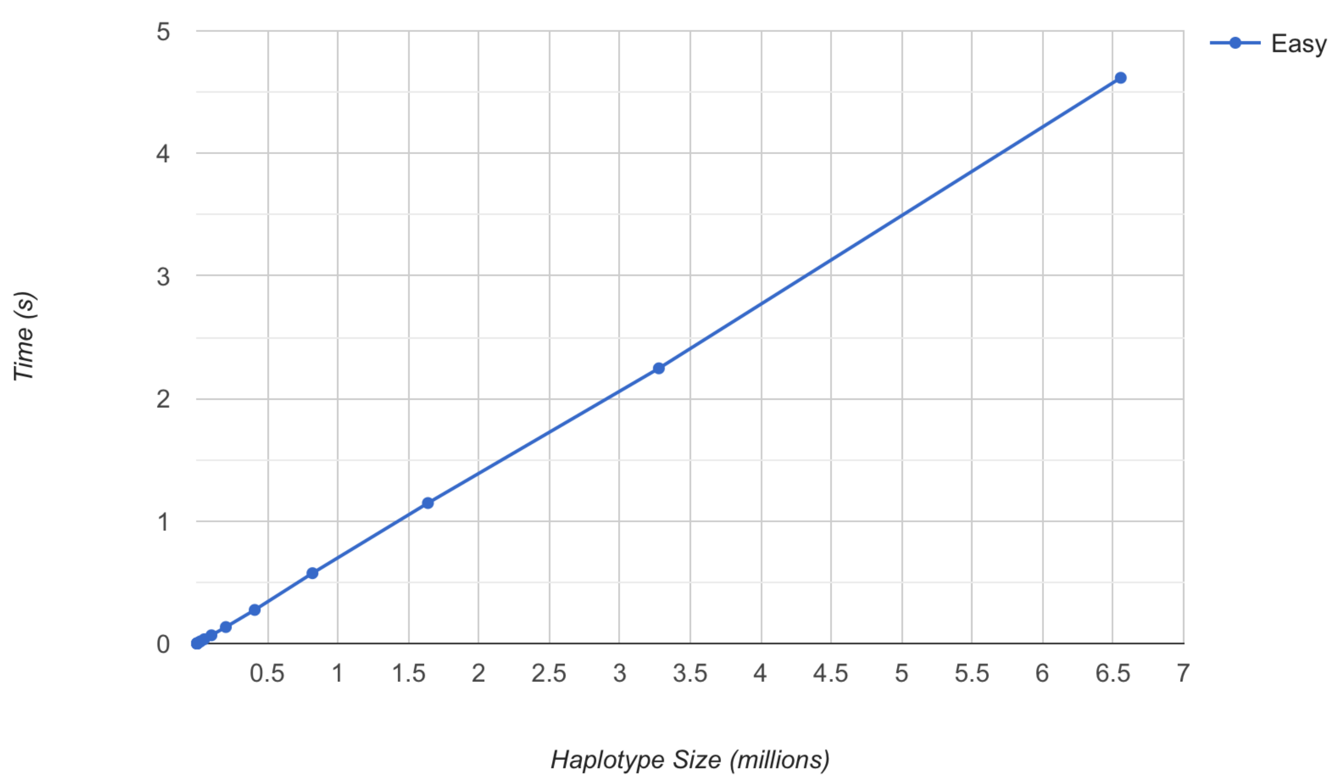
Easy Algorithm Visualization

```
01101
 1101
   10110
   01001
     11011
```

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

ALL DONE!

Easy Algorithm Runtime



Medium Project Algorithm

Allow for errors in reads

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

=

Accurate!

Medium Algorithm Visualization

```
A: 01101           H1:
B:  1100           H2:
C:   010110
D:    00000
E:      11011
F:       10101
```

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

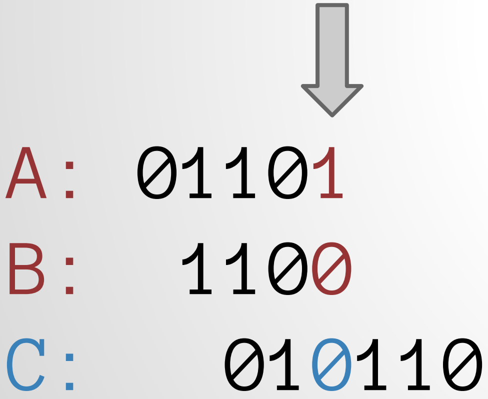
Example: SNP 5 on Haplotype 1

```
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

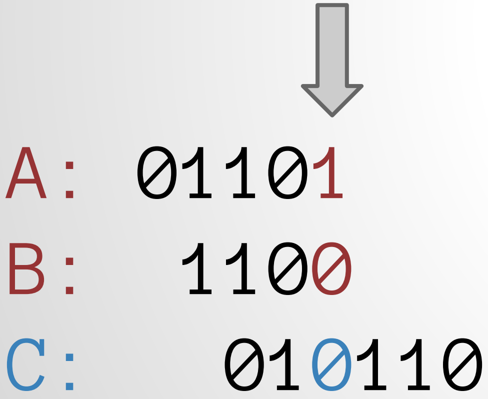
```
       ↓
A: 01101
B:  1100
C:   010110
```

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

Medium Algorithm Visualization

Now reassemble one haplotype, SNP by SNP

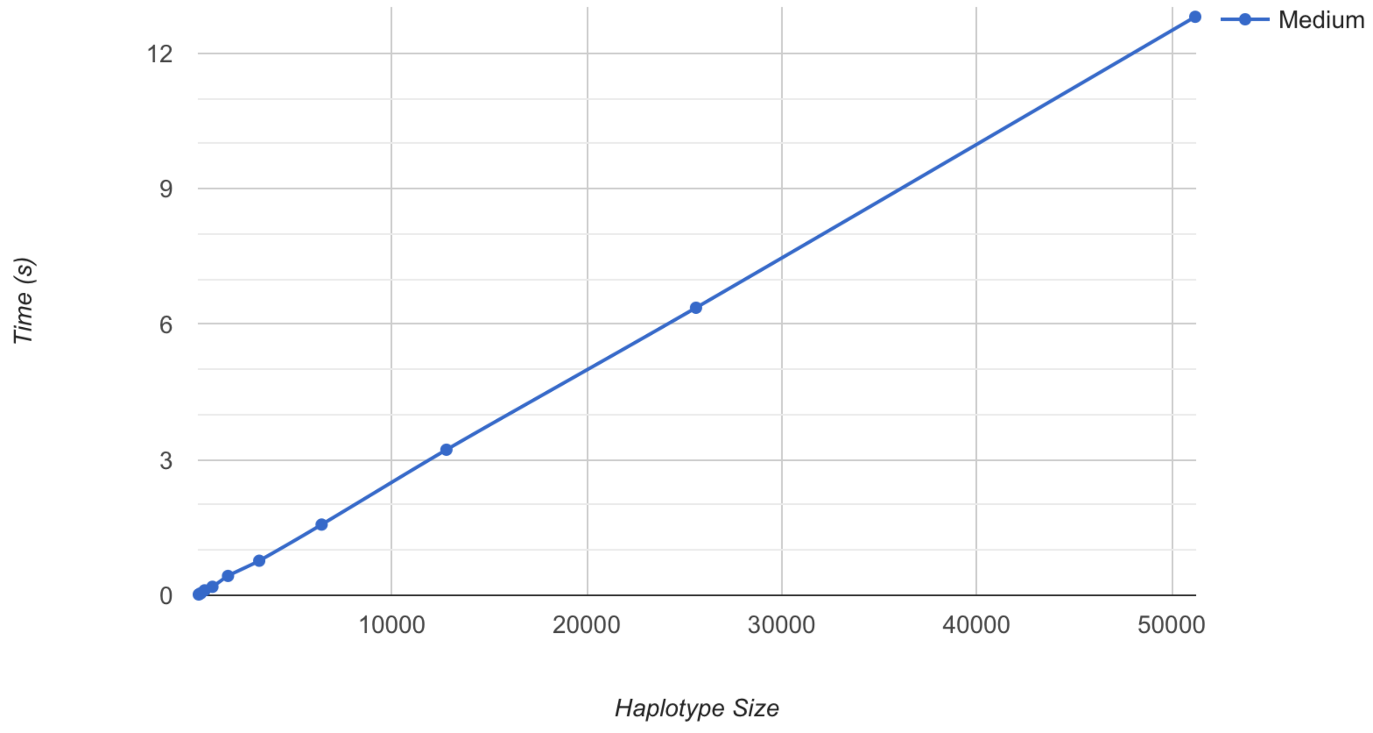
Example: SNP 5 on Haplotype 1



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

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

Medium Algorithm Runtime

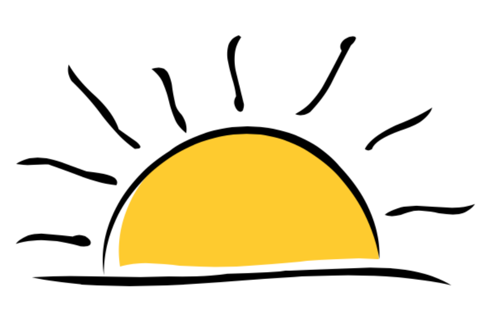


Time for Haplotype of Size 50,000

Easy: 0.035s

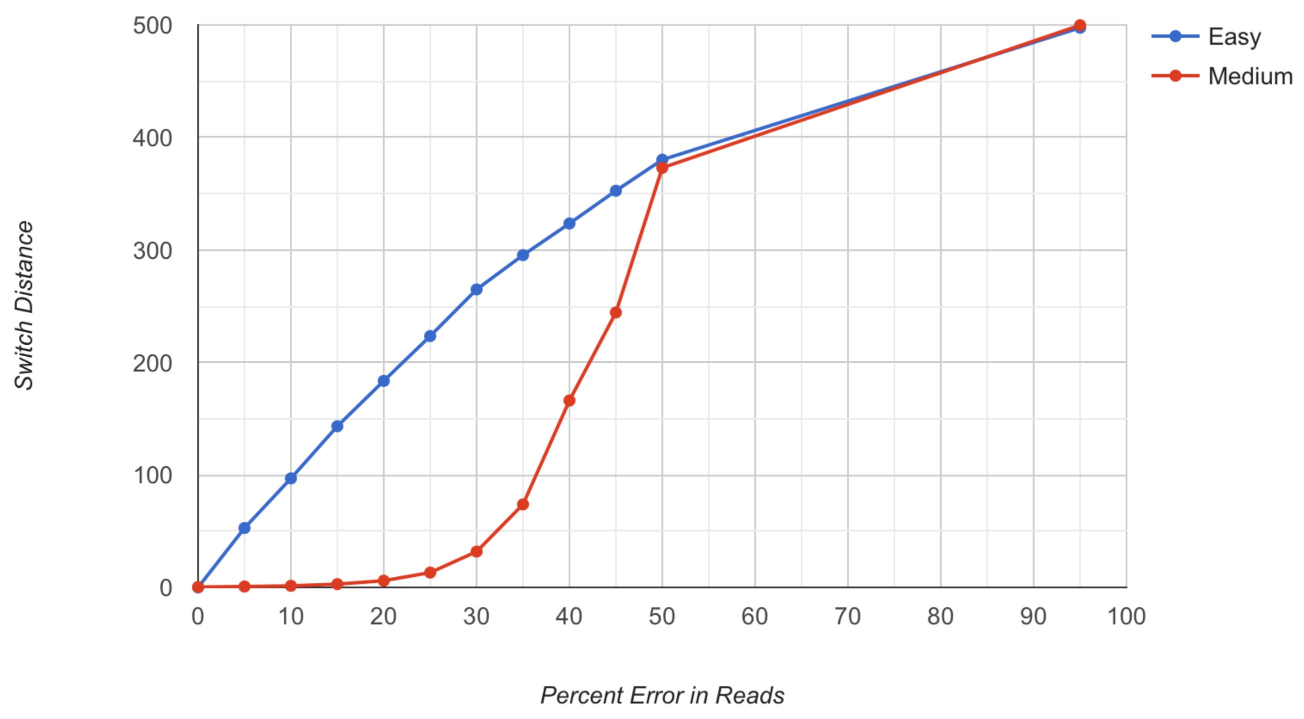
Medium: 12.8s

Medium is 365 times as slow as Easy



Accuracy - Easy vs Medium

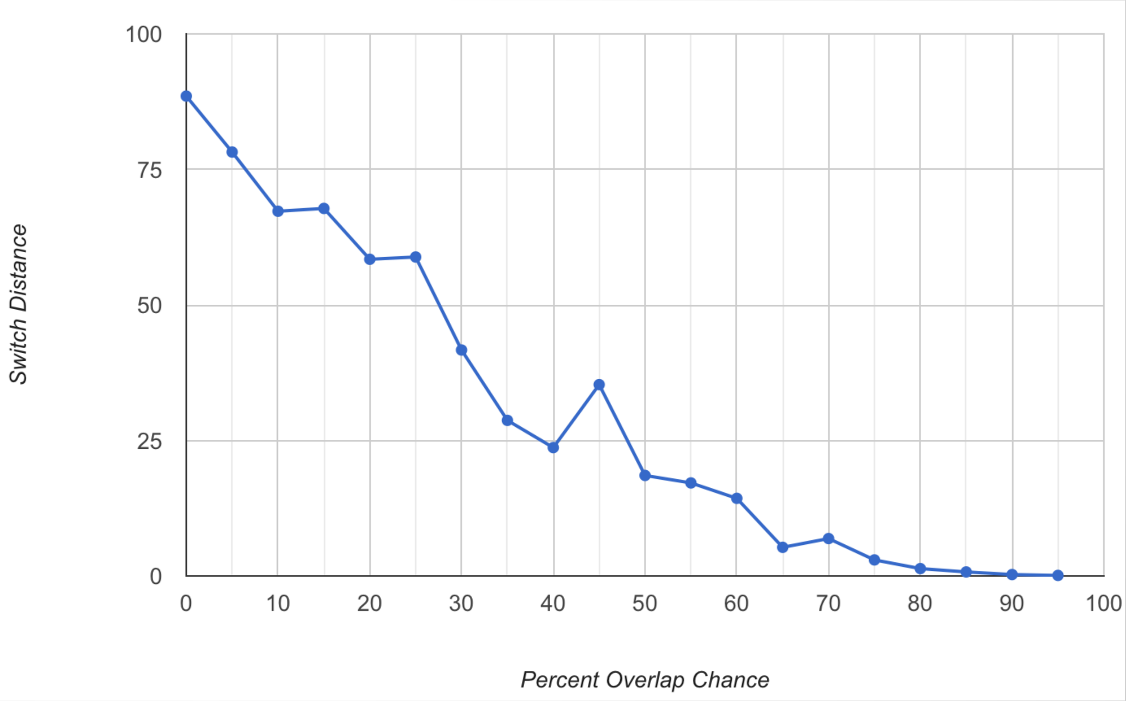
Haplotype length: 1000 SNPs



Overlap Chance in Reads

```
101101
0101
  00101
  011011
```

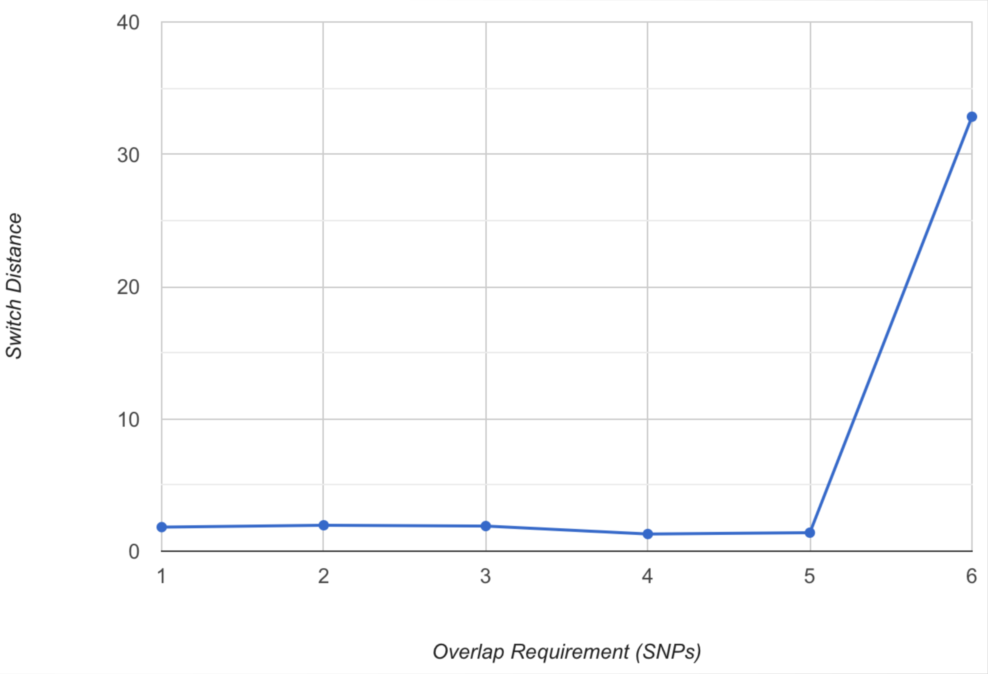
Overlap Chance
  = 50%



Overlap Requirement

```
101101
  100101
```

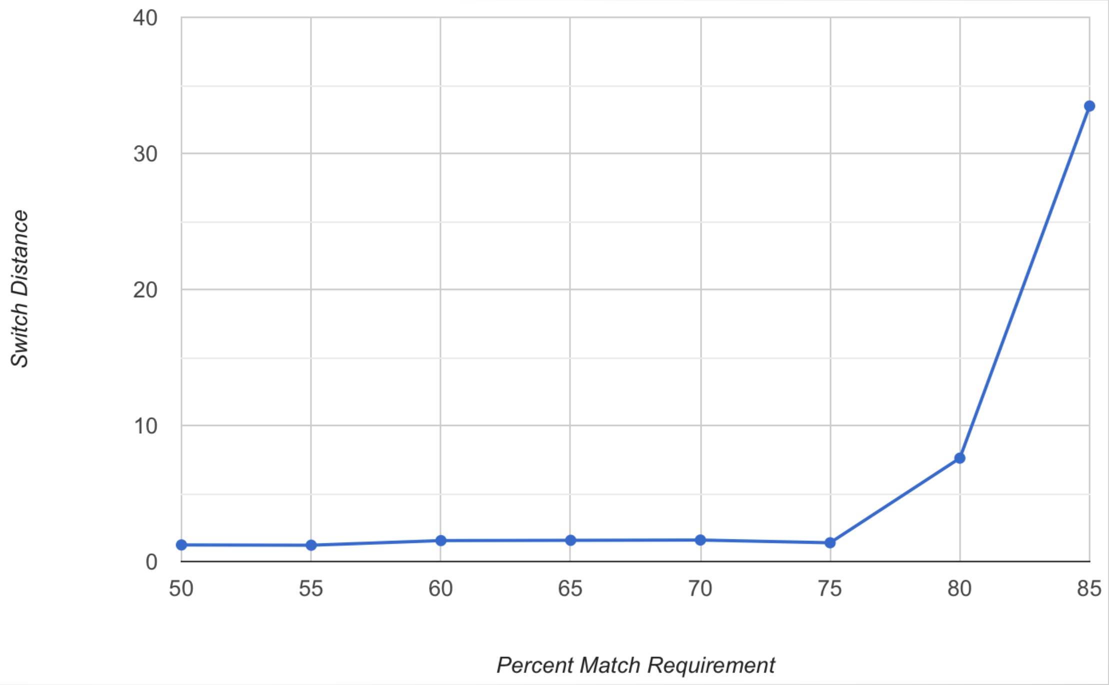
Overlap = 4



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!