AXE

The Rapid and Accurate Demultiplexer

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December 4, 2014

About Me

- Bioinformatician @ Borevitz Lab
  - TraitCapture Project Developer
  - Genomics (Low level Sequence Analysis)
  - Phenomics (Image analysis)
  - Sample tracking, data standards, HPC
- Starting PhD in Bioinformatics next year

In big data, binary goes up to 2. #eyenary

The High Throughput Problem

- Sequencing == firehose of data
- Need to put > 1 sample / lane
- Give BRF only one tube
- ∴ we need multiplexing
- ∴ de-multiplexing

The High Throughput Problem

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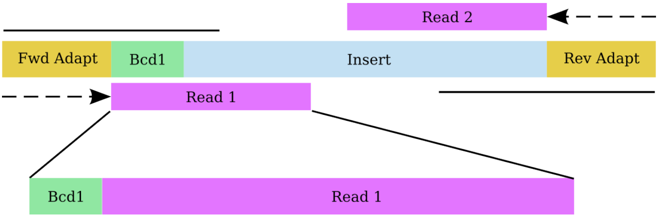
- $\therefore$ we need multiplexing
- $\therefore$ de-multiplexing

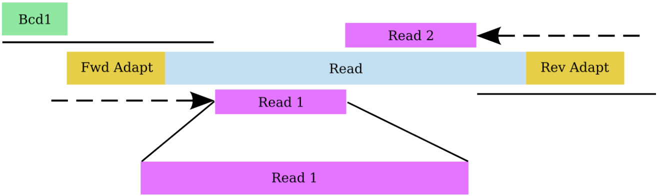
DNA/Molecular Barcoding

- DNA fragment contains per-sample unique seq.
- Sequenced, and "attached" to a read
- Must be balanced & staggered
- Hamming distance >2



So you need a demulitplexer?

- Some studies use kit protocols
- Most kits use index reads
- Illumina pipeline automatically demuxes these



So you need a demulitplexer?

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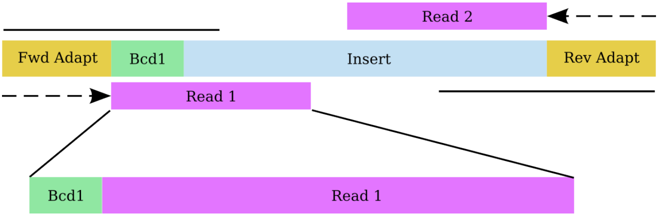
- Many advanced/homebrew protocols use "in-read"
- Must be demultiplexed by user



De-multiplex with `AXE`

- Barcoding scheme requires advanced de-multiplexing
- Trie-based lookup algorithm
- Fast (PE lane in 5-10 mins)
- Implemented in C
- CLI and `libaxe.so` + `axe.h`
- GNU GPL v3+

ACGTCATCGTAGCTGATCATGCTAGCTGACTGATCGATGCTAGCACAC
CACCGATCGATCGATGCTAGCTAGTCGATGCTAGTCGATGCTAGTCCA

Hamming distance

- Distance between two strings of equal length

```
ACTGTG
 x x  = 2
ACAGCG
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-
  ```python
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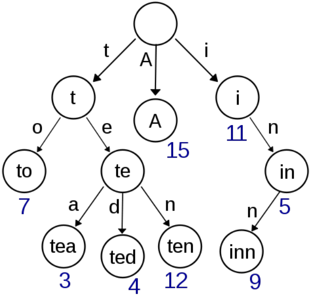
- `sum([0 if s1[i] == s2[i] else 1 for i in range(l)])`
- Good Enough™

A Forest of Tries?

- Trie is k-ary tree for k letter alphabet



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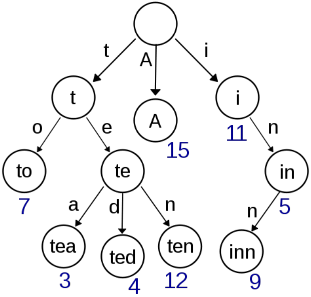

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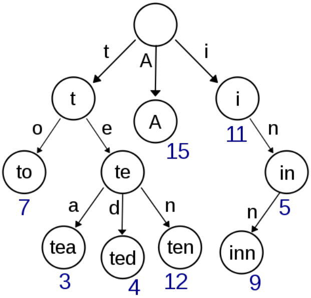

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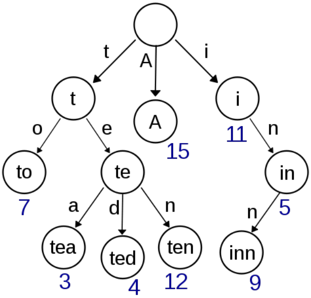

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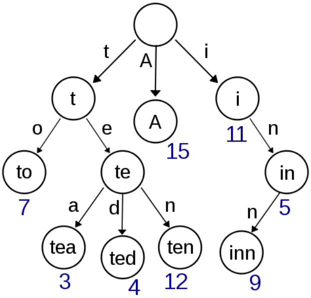
- Prefix lookups very fast



Hamming Mismatch Trie

- Pre-calculate all strings with Hamming dist *d* from search
- Make trie, do lookups
- Essentially a FSM

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CAAA
GAAA
TAAA
ACAA
AGAA
ATAA
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 | | | \-C
 | | |  -G
 | | |  -T
 | | \-C-A
 | |  -G-A
-| |  -T-A
 | \-C-A-A
 |  -G-A-A
 |  -T-A-A
 |-C-A-A-A
 |-G-A-A-A
 \-T-A-A-A
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The Algorithm

- Take read
- Walk trie w/ start of read
- Mark full-length matches
- Take longest match

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- Ok, time for an IPython Notebook

Thanks

- Justin Borevitz
- Sylvain Forêt
- Aaron Chuah
- Cam Jack
- Jared Streich & Collin Ahrens (β-testers)