Locality sensitive hashing for the edit distance

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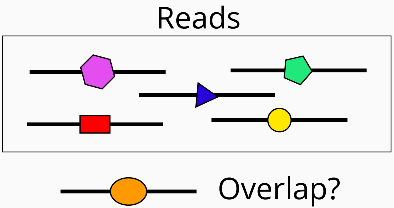
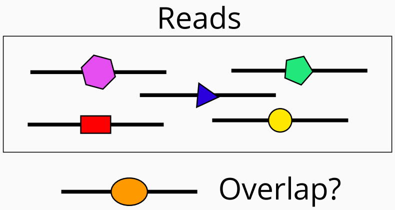
Overlap computation

- Compute overlaps between reads (HMAP)
- Instance of "Nearest Neighbor Problem" for edit distance
- Use multiple hash tables
- Need meaningful hash collisions



Overlap computation



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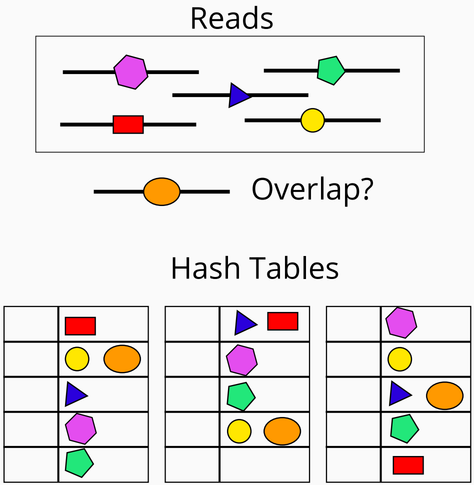

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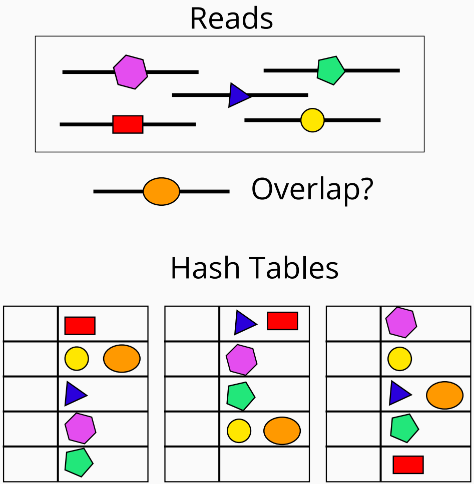

Locality Sensitive Hashing

Pick h at random from $\mathcal{H}$:

$$\Pr[h(\bigcirc) = h(\circ)] > \Pr[h(\bigcirc) = h(\blacktriangleright)]$$

Locality sensitive hash family

Family $\mathcal{H}$ of hash functions where similar elements are more likely to have the same value than distant elements.

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$$\Pr[h(\bigcirc) = h(\bigcirc)] > \Pr[h(\bigcirc) = h(\blacktriangleright)]$$

$$\mathrm{Sketch}(\bigcirc) = \{h_1(\bigcirc), \ldots, h_m(\bigcirc)\}$$

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Locality Sensitive Hashing

The family $\mathcal{H}$ is sensitive for distance D if there exists $d_1 < d_2$, $p_1 > p_2$ such that for all $x, y \in \mathcal{U}$

$$\mathrm{D}(x,y) \leq d_1 \implies \Pr_{h \in \mathcal{H}}[h(x) = h(y)] \geq p_1$$

$$\mathrm{D}(x,y) \geq d_2 \implies \Pr_{h \in \mathcal{H}}[h(x) = h(y)] \leq p_2$$

- **Low distance** $\iff$ **High collisions**
- **High distance** $\iff$ **Low collisions**

Locality sensitive hash family

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LSH for the edit distance

How to design an LSH for edit distance?

- LSH for Jaccard distance (minHash) used as proxy
- Jaccard distance is **significantly different** than edit distance

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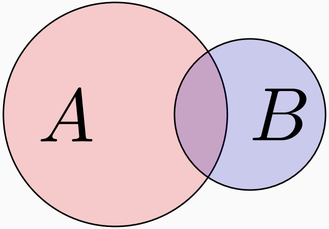
Jaccard distance

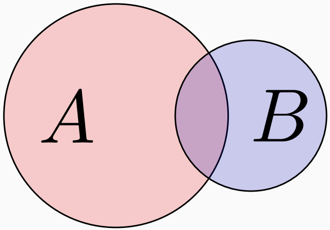
Jaccard distance between sets A, B:



$$\mathrm{J}(A, B) = 1 - \frac{|A \cap B|}{|A \cup B|}$$

Jaccard distance

Jaccard distance between sets A, B:



$$\mathrm{J}(A, B) = 1 - \frac{|A \cap B|}{|A \cup B|}$$

Jaccard between sequences x, y:
Jaccard distance of their k-mer sets

$$\mathrm{J}(x, y) = \mathrm{J}(\mathcal{K}(x), \mathcal{K}(y))$$

- Low $\mathrm{D}(x, y) \implies$ Low $\mathrm{J}(x, y)$
- High $\mathrm{D}(x, y) \not\Rightarrow$ High $\mathrm{J}(x, y)$

Jaccard ignores k-mer repetition

$$x = \overbrace{\texttt{AAAAAAAAAAAAAAA}}^{n-k}\overbrace{\texttt{CCCCC}}^{k}$$

$$y = \underbrace{\texttt{AAAAA}}_{k}\underbrace{\texttt{CCCCCCCCCCCCCCC}}_{n-k}$$

Jaccard ignores k-mer repetition

$$x = \overbrace{\texttt{AAAAAAAAAAAAAAA}}^{n-k}\overbrace{\texttt{CCCCC}}^{k} \quad \rightarrow \{\texttt{AAAAA}, \texttt{AAAAC}, \texttt{AAACC}, \texttt{AACCC}, \texttt{ACCCC}, \texttt{CCCCC}\}$$

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Jaccard distance $\mathrm{J}(x, y) = 0$ Edit distance $\mathrm{D}(x, y) \geq 1 - \frac{2k}{n}$

Identical k-mer content and high edit distance

Weighted Jaccard handles repetitions

$$x = \overbrace{\texttt{AAAAAAAAAAAAAAA}}^{n-k}\overbrace{\texttt{CCCCC}}^{k} \to \left\{ \begin{array}{c} (\texttt{AAAAA},1),(\texttt{AAAAA},2),\ldots,(\texttt{AAAAA},11) \\ (\texttt{AAAAC},1),(\texttt{AAACC},1),(\texttt{AACCC},1),(\texttt{ACCCC},1),(\texttt{CCCCC},1) \end{array} \right\}$$

$$y = \underbrace{\texttt{AAAAA}}_{k}\underbrace{\texttt{CCCCCCCCCCCCCCC}}_{n-k} \to \left\{ \begin{array}{c} (\texttt{AAAAA},1),(\texttt{AAAAC},1),(\texttt{AAACC},1),(\texttt{AACCC},1),(\texttt{ACCCC},1), \\ (\texttt{CCCCC},1),(\texttt{CCCCC},2),\ldots,(\texttt{CCCCC},11) \end{array} \right\}$$

Weighted Jaccard $\mathrm{J^w}(x,y) = 1 - \frac{k+2}{n}$ Edit distance $\mathrm{D}(x,y) \geq 1 - \frac{2k}{n}$

Weighted Jaccard $=$ Jaccard for multi-sets

Jaccard and weighted Jaccard ignore relative order

$$x = \texttt{CCCCACCAACACAAAACCC}$$

$$y = \texttt{AAAACACAACCCCACCAAA}$$

Jaccard and weighted Jaccard ignore relative order

$$x = \texttt{CCCCACCAACACAAAACCC} \quad \rightarrow \left\{ \begin{matrix} \texttt{AAAA,AAAC,AACA,AACC,ACAA,ACAC,ACCA,ACCC} \\ \texttt{CAAA,CAAC,CACA,CACC,CCAA,CCAC,CCCA,CCCC} \end{matrix} \right\}$$

$$y = \texttt{AAAACACAACCCCACCAAA} \quad \rightarrow \left\{ \begin{matrix} \texttt{AAAA,AAAC,AACA,AACC,ACAA,ACAC,ACCA,ACCC} \\ \texttt{CAAA,CAAC,CACA,CACC,CCAA,CCAC,CCCA,CCCC} \end{matrix} \right\}$$

x, y: de Bruijn sequences,
contain all 16 possible 4-mers once

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x, y: de Bruijn sequences,
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$$\mathrm{J}(x, y) = \mathrm{J}^{\mathrm{w}}(x, y) = 0 \qquad \mathrm{D}(x, y) = 0.63$$

Jaccard is different from edit distance

Unlike edit distance, Jaccard is insensitive to:

1. k-mer repetitions
2. relative positions of k-mers

OMH: Order Min Hash

- minHash is an LSH for Jaccard
- OMH is a refinement of minHash
- OMH is sensitive to
  - repeated k-mers
  - relative order of k-mers

minHash & OMH sketches

$x = \texttt{AGTTGAGCGGAAGGTG}$, $k = 2$

$$x = \texttt{AGTTGAGCGGAAGGTG},\ k = 2$$

Order: permutation of Σ^k

AT
AG
GT
CG
GT
TT
GG
CA
TG
TC
AA
AC
TA
GA
GC
CT

AG
GT
CG
TT
GG
TG
AA
GA
GC

minHash & OMH sketches

$$x = \texttt{AGTTGAGCGGAAGGTG},\ k = 2,\ m = 6$$

1	2	3	4	5	6
AG	GG	CG	AA	TG	TT
GT	GA	GA	AG	TT	GG
CG	CG	TG	TT	GG	AG
TT	AG	AG	GT	CG	GC
GG	GC	GC	TG	AA	GA
TG	GT	GG	GC	GT	AA
AA	AA	TT	GA	AG	CG
GA	TT	AA	CG	GC	TG
GC	TG	GT	GG	GA	GT

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AG	GG	CG	AA	TG	TT
GT	GA	GA	AG	TT	GG
CG	CG	TG	TT	GG	AG
TT	AG	AG	GT	CG	GC
GG	GC	GC	TG	AA	GA
TG	GT	GG	GC	GT	AA
AA	AA	TT	GA	AG	CG
GA	TT	AA	CG	GC	TG
GC	TG	GT	GG	GA	GT

minHash & OMH sketches

$x = \texttt{AGTTGAGCGGAAGGTG}, k = 2, m = 6$

Order: permutation of $\Sigma^k \times \{1, \ldots, n\}$

1	2	3	4	5	6
AG	GG	CG	AA	TG	TT
GT	GA	GA	AG	TT	GG
CG	CG	TG	TT	GG	AG
TT	AG	AG	GT	CG	GC
GG	GC	GC	TG	AA	GA
TG	GT	GG	GC	GT	AA
AA	AA	TT	GA	AG	CG
GA	TT	AA	CG	GC	TG
$\boxed{\text{GC}}$	$\boxed{\text{TG}}$	$\boxed{\text{GT}}$	$\boxed{\text{GG}}$	$\boxed{\text{GA}}$	$\boxed{\text{GT}}$

GA, 4
TG, 3
AG, 5
GT, 1
GT, 13
AA, 10
AG, 11
TT, 2
AG, 0
CG, 7
GG, 12
GC, 6
TG, 14
GG, 8
GA, 9

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1	2	3	4	5	6
AG	GG	CG	AA	TG	TT
GT	GA	GA	AG	TT	GG
CG	CG	TG	TT	GG	AG
TT	AG	AG	GT	CG	GC
GG	GC	GC	TG	AA	GA
TG	GT	GG	GC	GT	AA
AA	AA	TT	GA	AG	CG
GA	TT	AA	CG	GC	TG
GC	TG	GT	GG	GA	GT

1	2	3	4	5	6
GA, 4	CG, 7	GT,13	AG, 0	AA,10	GA, 9
TG, 3	TG,14	GA, 4	TT, 2	GT,13	GG, 8
AG, 5	AG, 0	GA, 9	AG,11	GA, 9	GC, 6
GT, 1	GA, 9	TG, 3	AG, 5	GT, 1	TG,14
GT,13	AG, 5	AG, 5	AA,10	AG, 5	GT,13
AA,10	AG,11	CG, 7	GT,13	TT, 2	TT, 2
AG,11	GA, 4	TT, 2	CG, 7	GA, 4	AA,10
TT, 2	GT,13	AA,10	GG, 8	CG, 7	AG, 0
AG, 0	TT, 2	GG,12	GA, 4	AG, 0	CG, 7
CG, 7	TG, 3	GG, 8	GA, 9	TG, 3	GG,12
GG,12	GG, 8	TG,14	TG,14	GG, 8	AG,11
GC, 6	AA,10	GT, 1	TG, 3	GG,12	TG, 3
TG,14	GG,12	AG,11	GC, 6	GC, 6	GT, 1
GG, 8	GT, 1	GC, 6	GT, 1	AG,11	GA, 4
GA, 9	GC, 6	AG, 0	GG,12	TG,14	AG, 5

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CG	CG	TG	TT	GG	AG
TT	AG	AG	GT	CG	GC
GG	GC	GC	TG	AA	GA
TG	GT	GG	GC	GT	AA
AA	AA	TT	GA	AG	CG
GA	TT	AA	CG	GC	TG
GC	TG	GT	GG	GA	GT

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GA, 4	CG, 7	GT,13	AG, 0	AA,10	GA, 9
TG, 3	TG,14	GA, 4	TT, 2	GT,13	GG, 8
AG, 5	AG, 0	GA, 9	AG,11	GA, 9	GC, 6
GT, 1	GA, 9	TG, 3	AG, 5	GT, 1	TG,14
GT,13	AG, 5	AG, 5	AA,10	AG, 5	GT,13
AA,10	AG,11	CG, 7	GT,13	TT, 2	TT, 2
AG,11	GA, 4	TT, 2	CG, 7	GA, 4	AA,10
TT, 2	GT,13	AA,10	GG, 8	CG, 7	AG, 0
AG, 0	TT, 2	GG,12	GA, 4	AG, 0	CG, 7
CG, 7	TG, 3	GG, 8	GA, 9	TG, 3	GG,12
GG,12	GG, 8	TG,14	TG,14	GG, 8	AG,11
GC, 6	AA,10	GT, 1	TG, 3	GG,12	TG, 3
TG,14	GG,12	AG,11	GC, 6	GC, 6	GT, 1
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GT	GA	GA	AG	TT	GG
CG	CG	TG	TT	GG	AG
TT	AG	AG	GT	CG	GC
GG	GC	GC	TG	AA	GA
TG	GT	GG	GC	GT	AA
AA	AA	TT	GA	AG	CG
GA	TT	AA	CG	GC	TG
GC	TG	GT	GG	GA	GT

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GA, 4	CG, 7	GT, 13	AG, 0	AA, 10	GA, 9
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AG, 5	AG, 0	GA, 9	AG, 11	GA, 9	GC, 6
GT, 1	GA, 9	TG, 3	AG, 5	GT, 1	TG, 14
GT, 13	AG, 5	AG, 5	AA, 10	AG, 5	GT, 13
AA, 10	AG, 11	CG, 7	GT, 13	TT, 2	TT, 2
AG, 11	GA, 4	TT, 2	CG, 7	GA, 4	AA, 10
TT, 2	GT, 13	AA, 10	GG, 8	CG, 7	AG, 0
AG, 0	TT, 2	GG, 12	GA, 4	AG, 0	CG, 7
CG, 7	TG, 3	GG, 8	GA, 9	TG, 3	GG, 12
GG, 12	GG, 8	TG, 14	TG, 14	GG, 8	AG, 11
GC, 6	AA, 10	GT, 1	TG, 3	GG, 12	TG, 3
TG, 14	GG, 12	AG, 11	GC, 6	GC, 6	GT, 1
GG, 8	GT, 1	GC, 6	GT, 1	AG, 11	GA, 4
GA, 9	GC, 6	AG, 0	GG, 12	TG, 14	AG, 5

GC GA AG GG AG TG

OMH is a LSH for edit distance

Theorem: OMH is a LSH for edit distance

There exists (d_1, d_2, p_1, p_2) such that OMH is sensitive for the edit distance.

Conclusion

- OMH:
  - improvement on minHash
  - easy to compute
  - locality sensitive for edit distance
- LSH for other alignment scores?
- Smallest “gap” achievable?

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