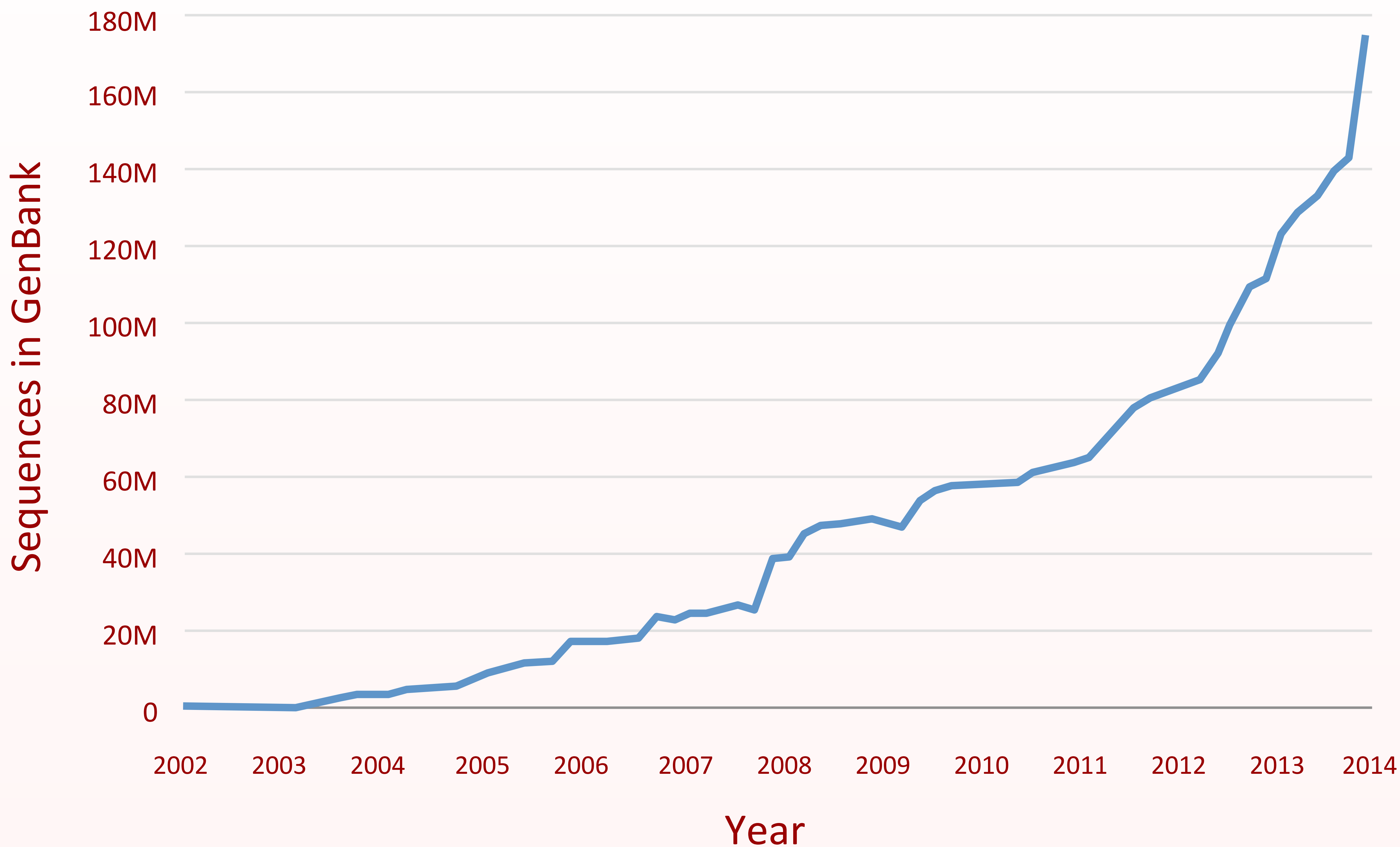
Genomic Compression: Storage, Transmission, and Analytics

Noah M. Daniels
Bonnie Berger

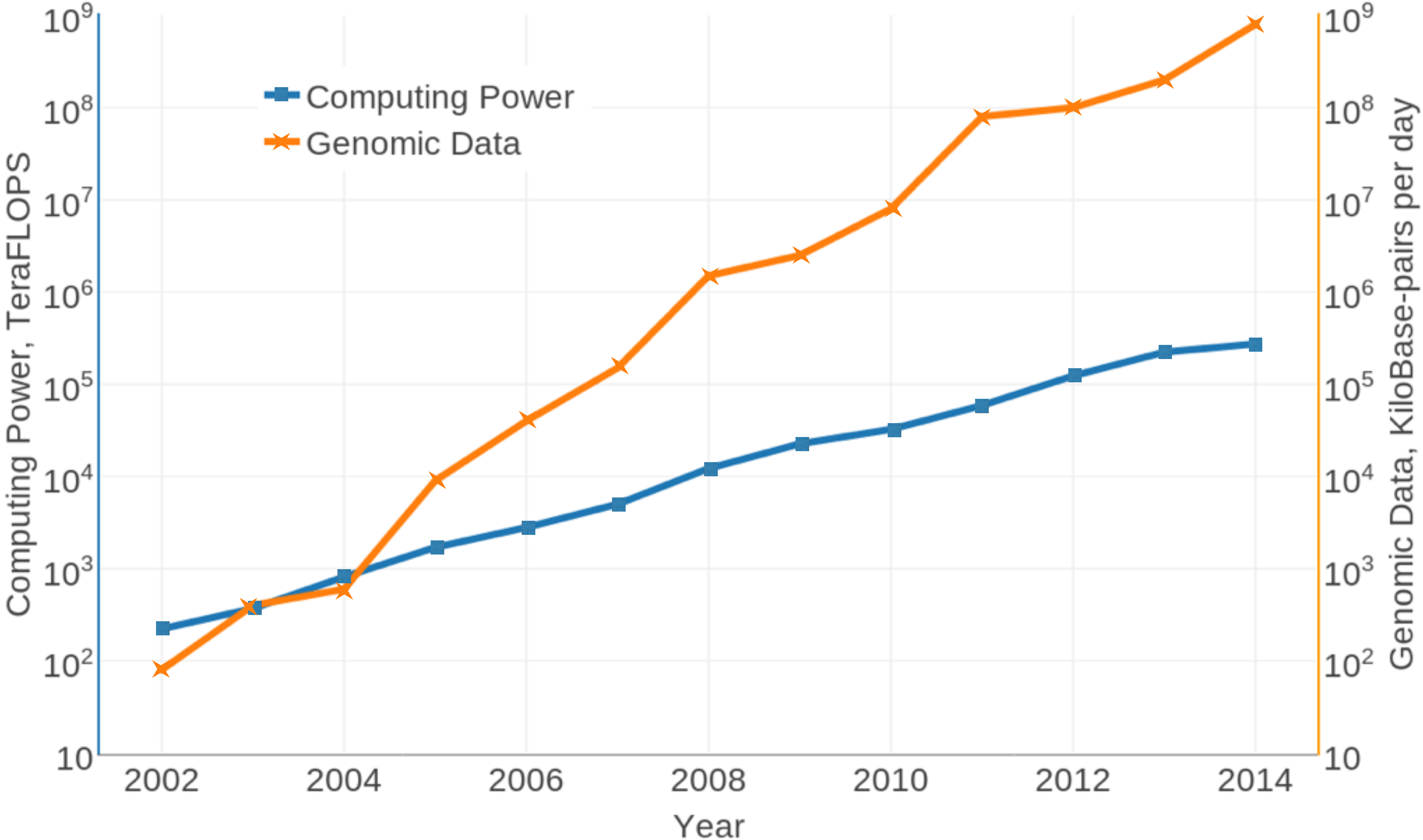
Genomic data are growing exponentially



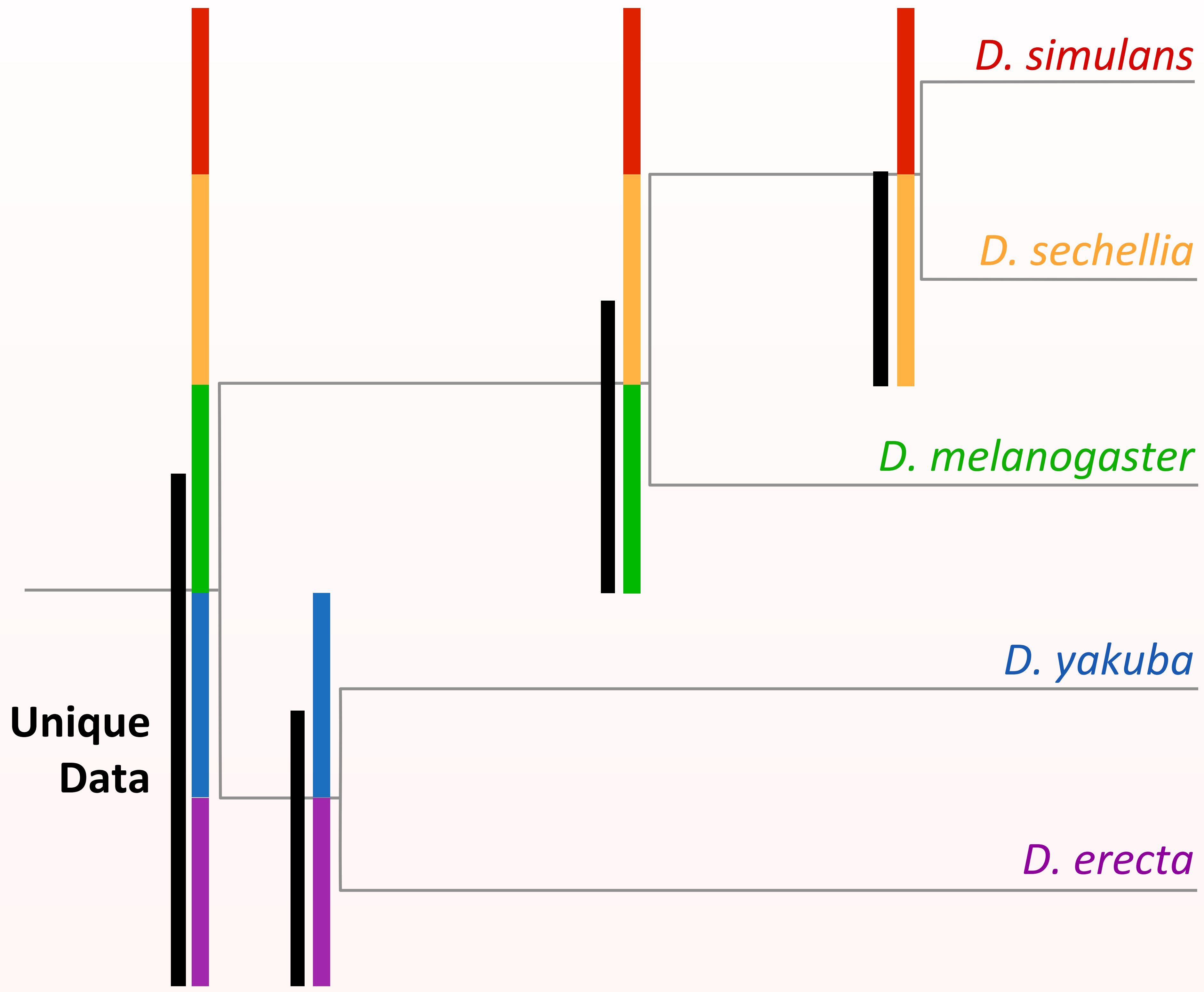

A bigger cloud?


A bigger cloud?
Still constrained by Moore

Genomic data are growing exponentially



Redundancy in data



Outline

Compression background

Storage and transmission

Analysis

Limits to compression

Source coding theorem [Shannon, 1948]

N i.i.d. random variables from source X

each with entropy $H(X)$

cannot be compressed into fewer than $NH(X)$ bits without loss of information

$$\mathrm{H}(X) = -\sum_{i} \mathrm{P}(x_i) \log_b \mathrm{P}(x_i)$$

What can we do?

Approach Shannon limit as efficiently as possible (fast, lossless compression)

Be willing to throw away information (*lossy* compression)

Approaching Shannon limit

Huffman coding [1952]

Arithmetic coding [Rissanen 1976]

Lempel-Ziv [1977]

Burrows-Wheeler Transform [1994]

Huffman coding

Huffman coding

Variable-length prefix code

Huffman coding

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More frequent symbols take fewer bits

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DNA (A,C,T,G)

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2 bits/symbol: 00, 01, 10, 11

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Suppose AT bias

Huffman coding

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DNA (A,C,T,G)

2 bits/symbol: 00, 01, 10, 11

Suppose AT bias

P. falciparum 20% GC

A

T

C

G

A	0.4
T	0.4
C	0.1
G	0.1

A 0.4

T 0.4

C 0.1

G 0.1

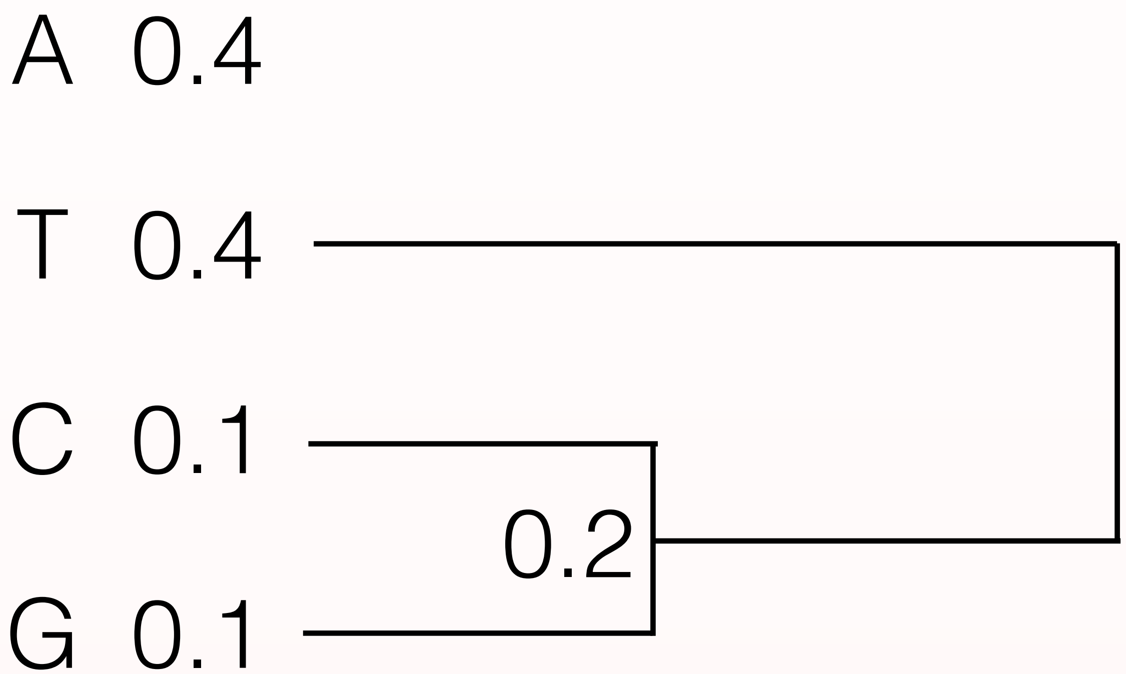
A 0.4

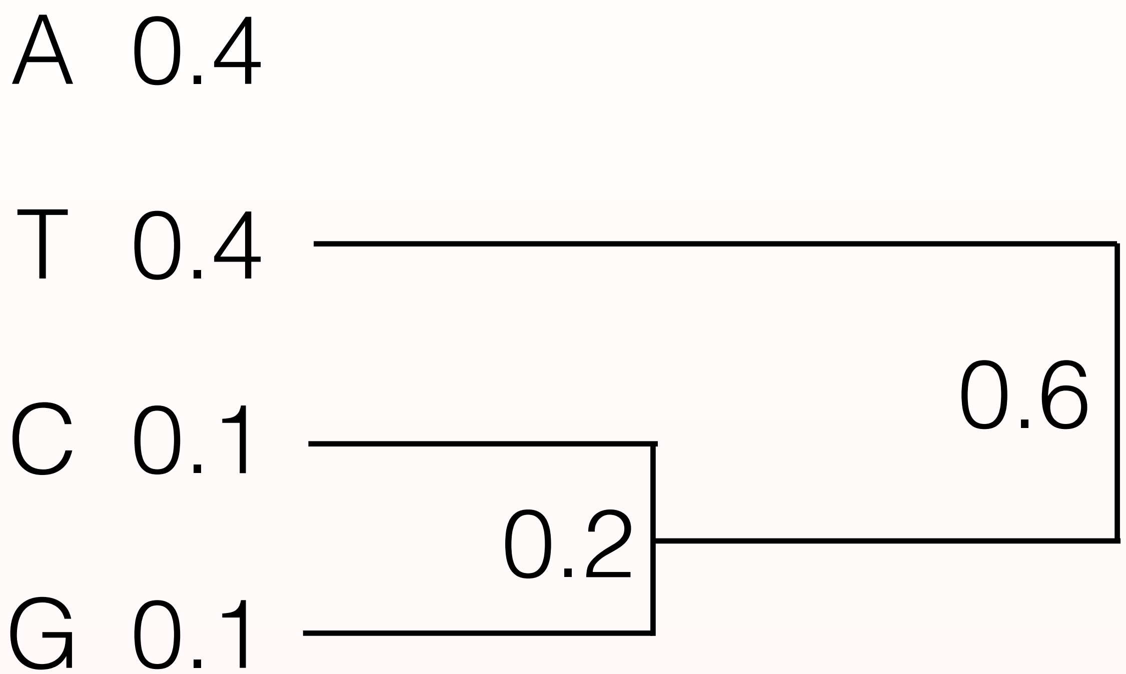
T 0.4

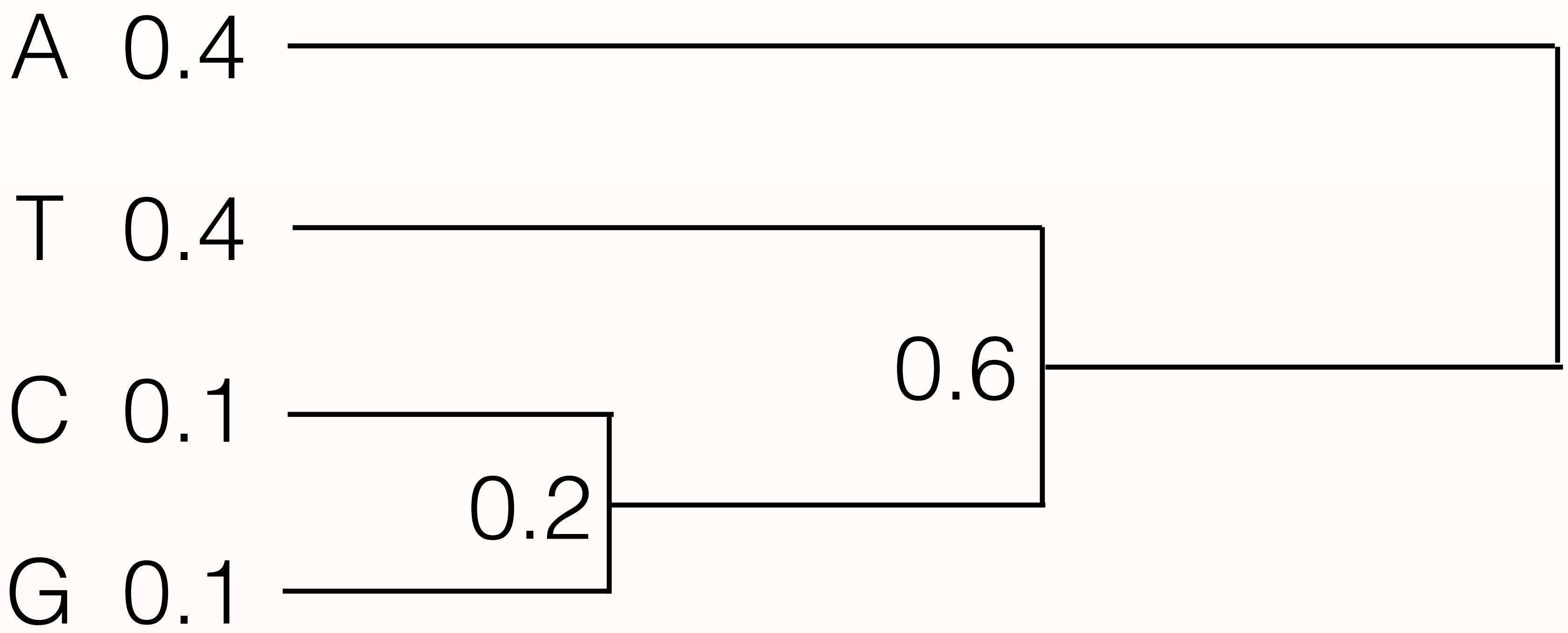
C 0.1

0.2

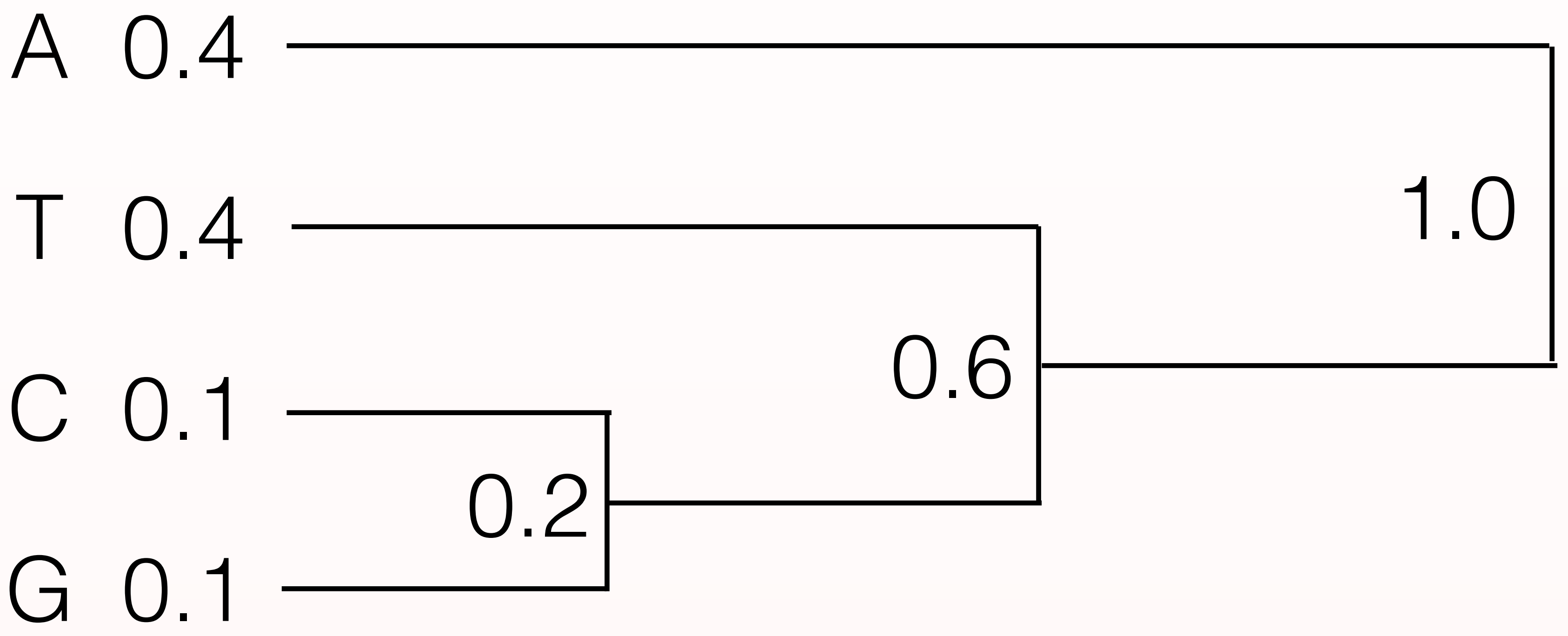
G 0.1

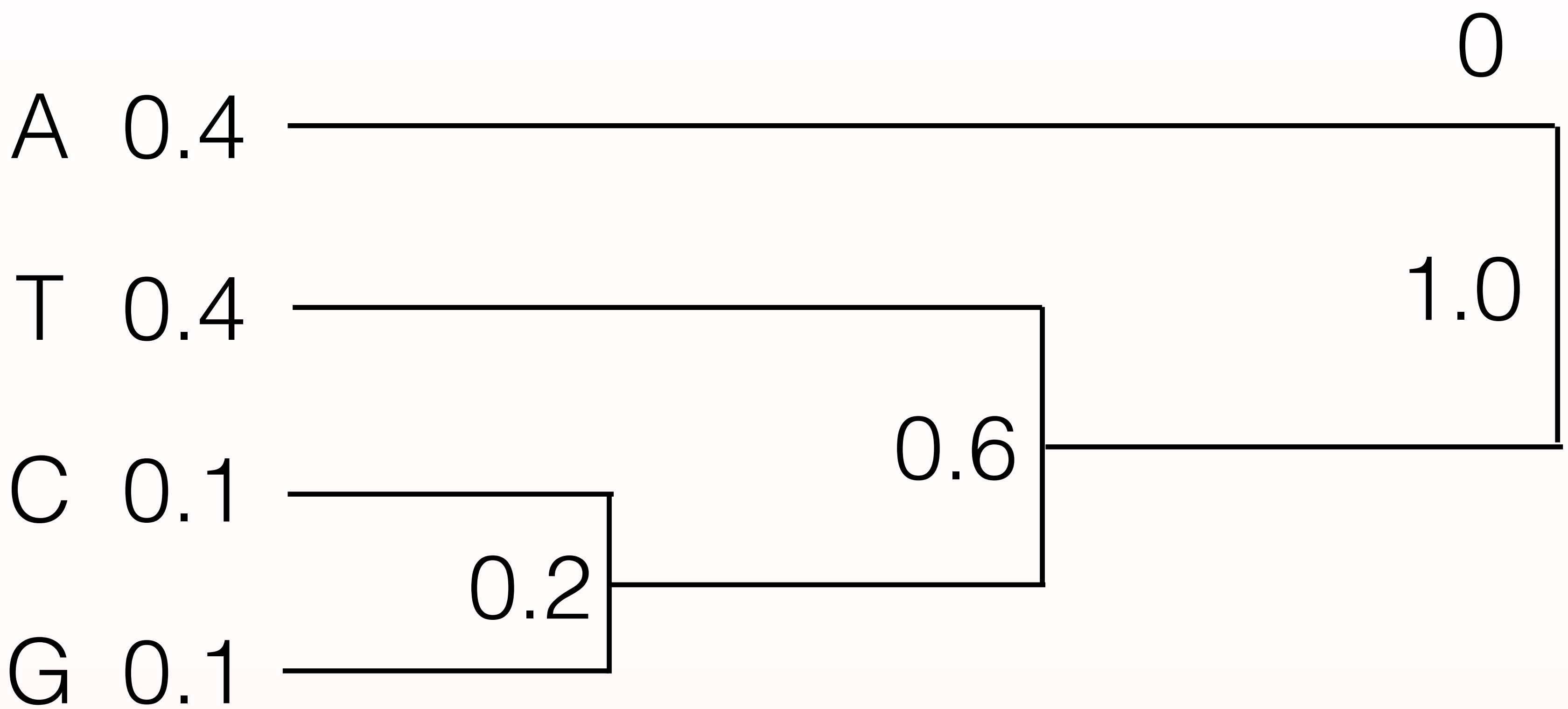

A 0.4
T 0.4
C 0.1
G 0.1
0.2

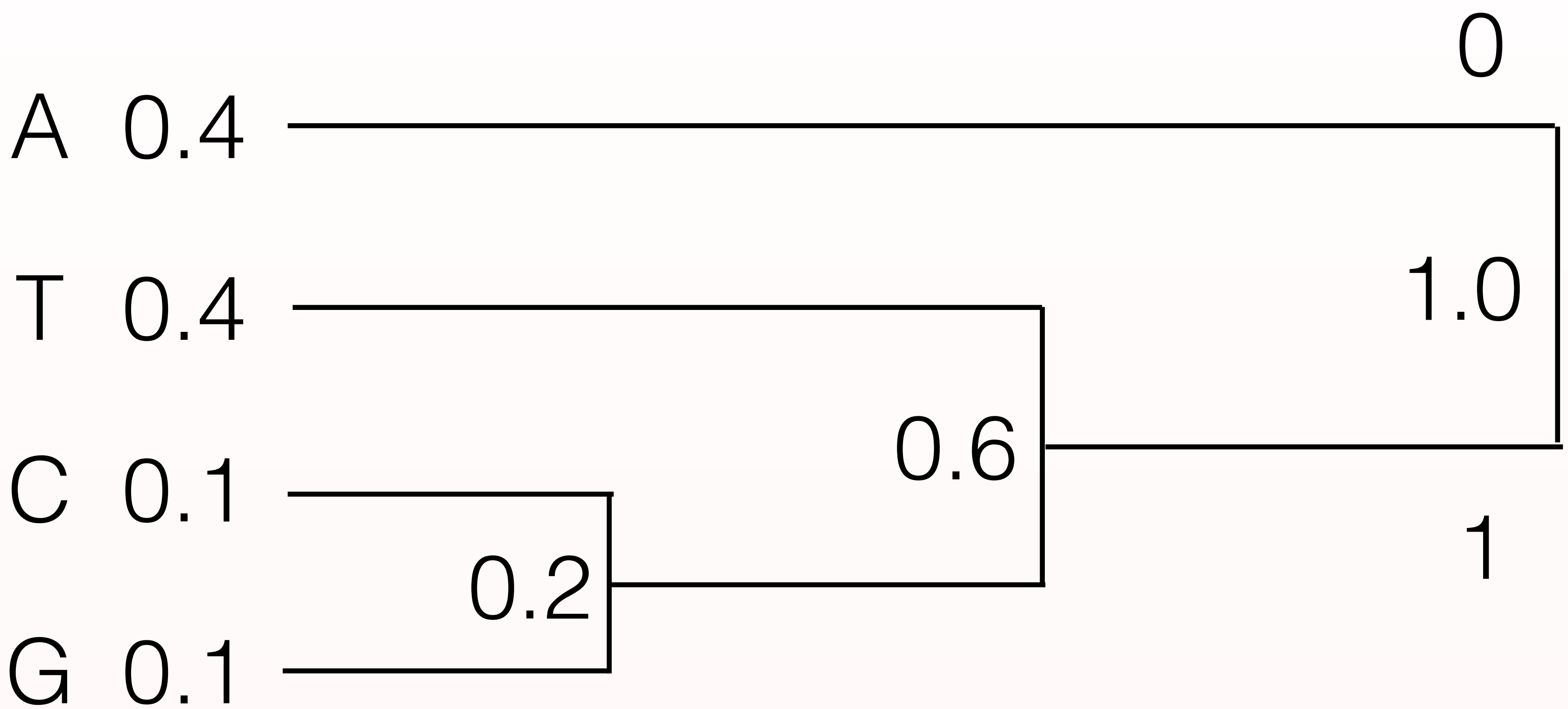

A 0.4
T 0.4
C 0.1
G 0.1
0.2
0.6

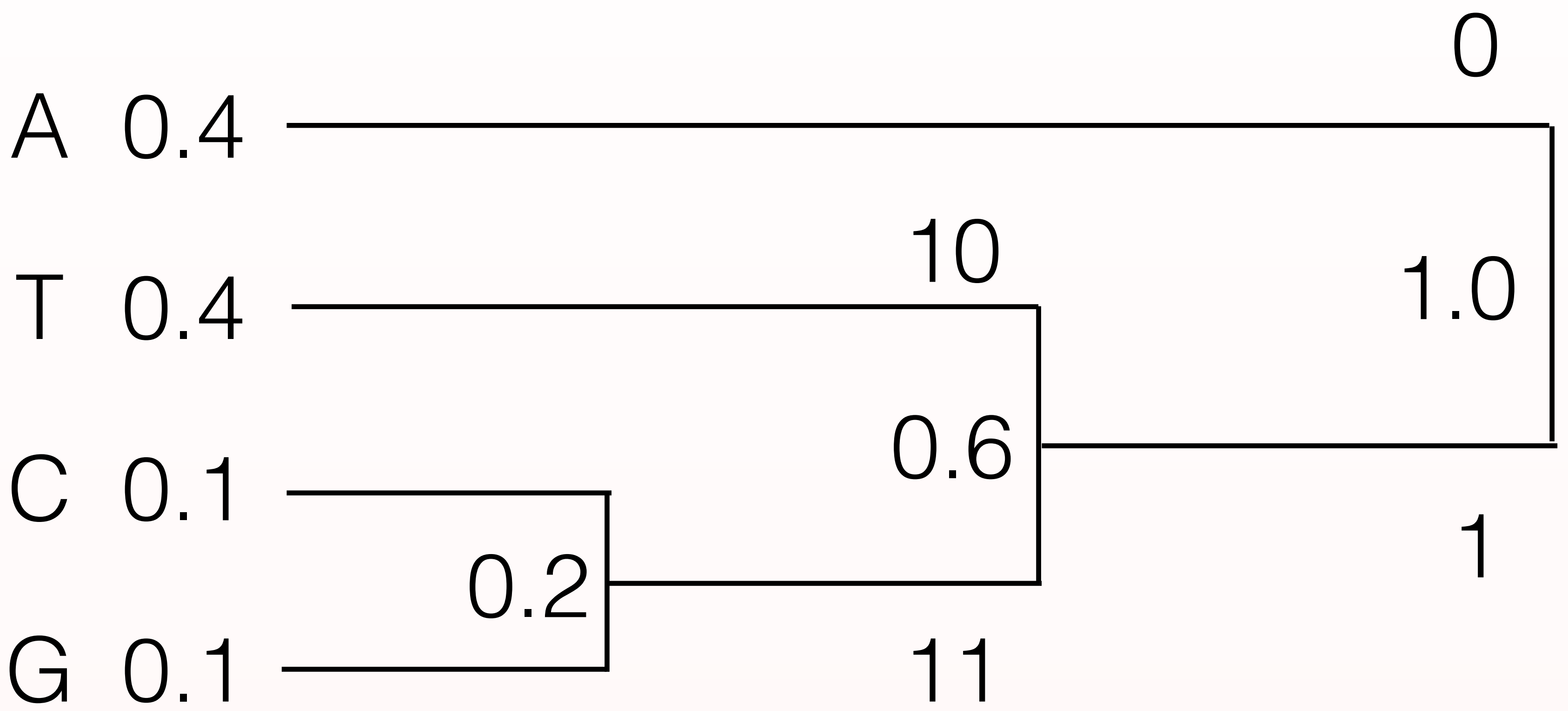


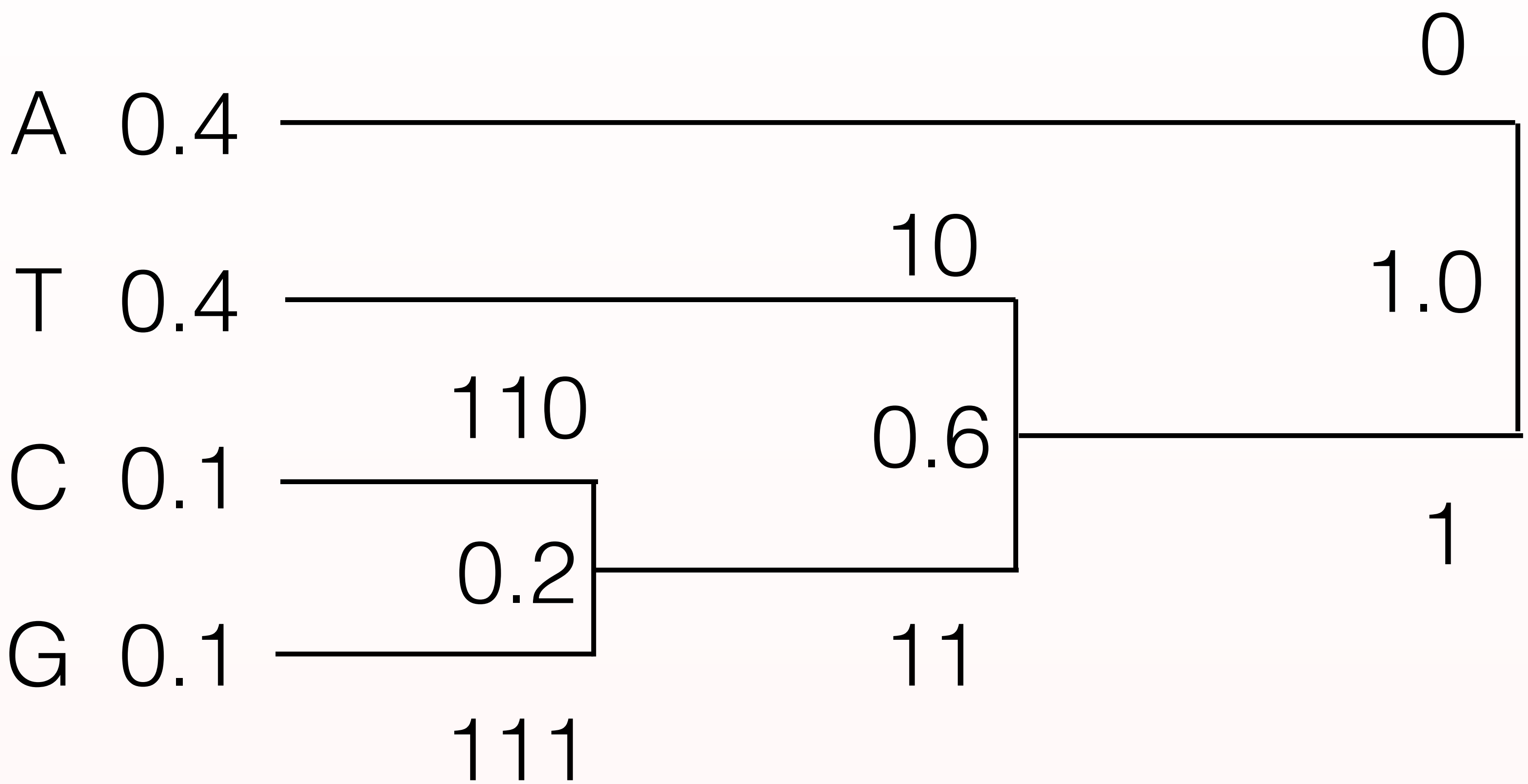
A 0.4
T 0.4
C 0.1
G 0.1
0.2
0.6


A 0.4
T 0.4
C 0.1
G 0.1
0.2
0.6
1.0


A 0.4
T 0.4
C 0.1
G 0.1
0.2
0.6
1.0
0


A 0.4
T 0.4
C 0.1
G 0.1
0.2
0.6
1.0
0
1


A 0.4
T 0.4
C 0.1
G 0.1
0.2
0.6
1.0
0
10
11
1



A 0.4
T 0.4
C 0.1
G 0.1
0
10
1.0
110
0.6
0.2
1
11
111

Huffman coding

Naive encoding: 2 bits/base

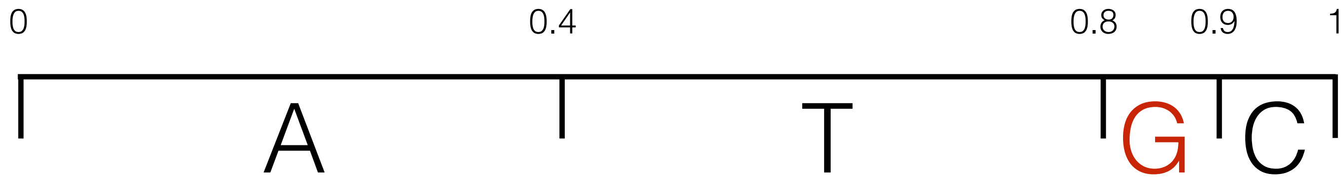
Huffman coding: 1.8 bits/base

	A	T	G	C
F	0.4	0.4	0.1	0.1
Codeword	0	10	110	111
Bits	1	2	3	3
Avg Bits	0.4	0.8	0.3	0.3

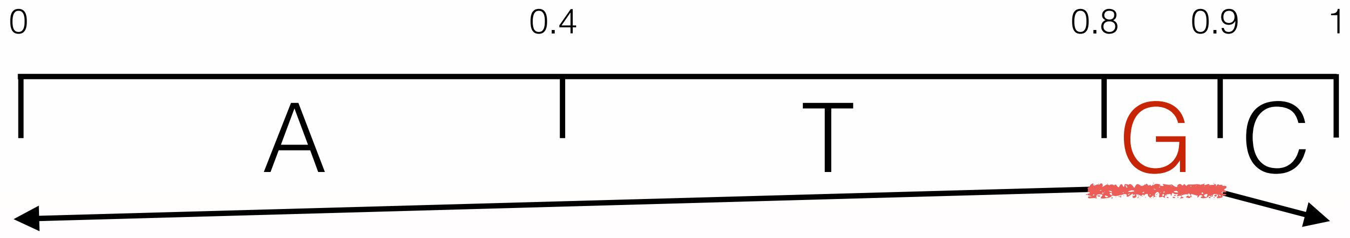
Arithmetic coding

Encode entire message as a number

	A	T	G	C
F	0.4	0.4	0.1	0.1
Interval	[0,0.4)	[0.4,0.8)	[0.8,0.9)	[0.9,1)



GATTACA



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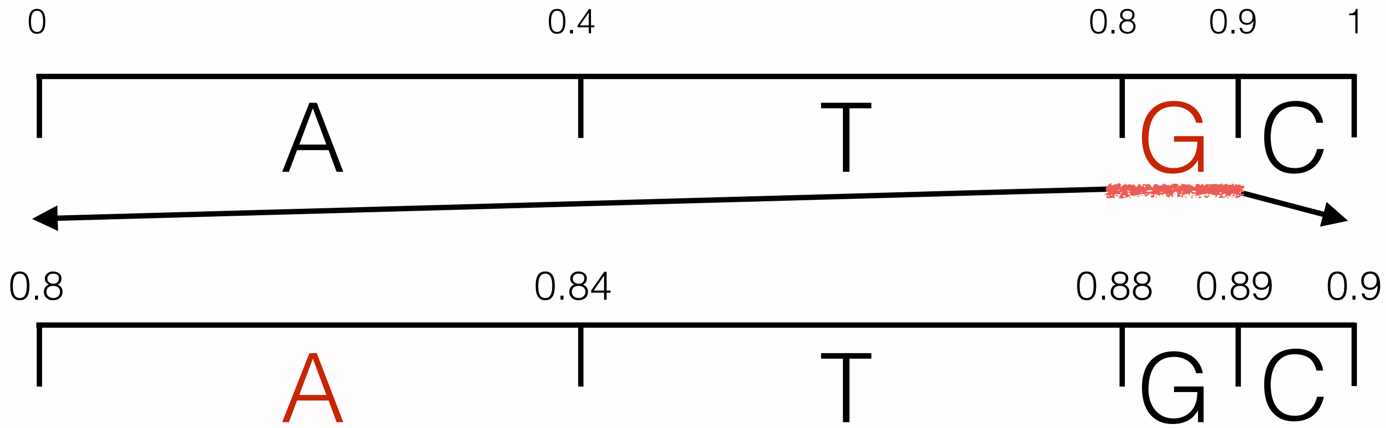

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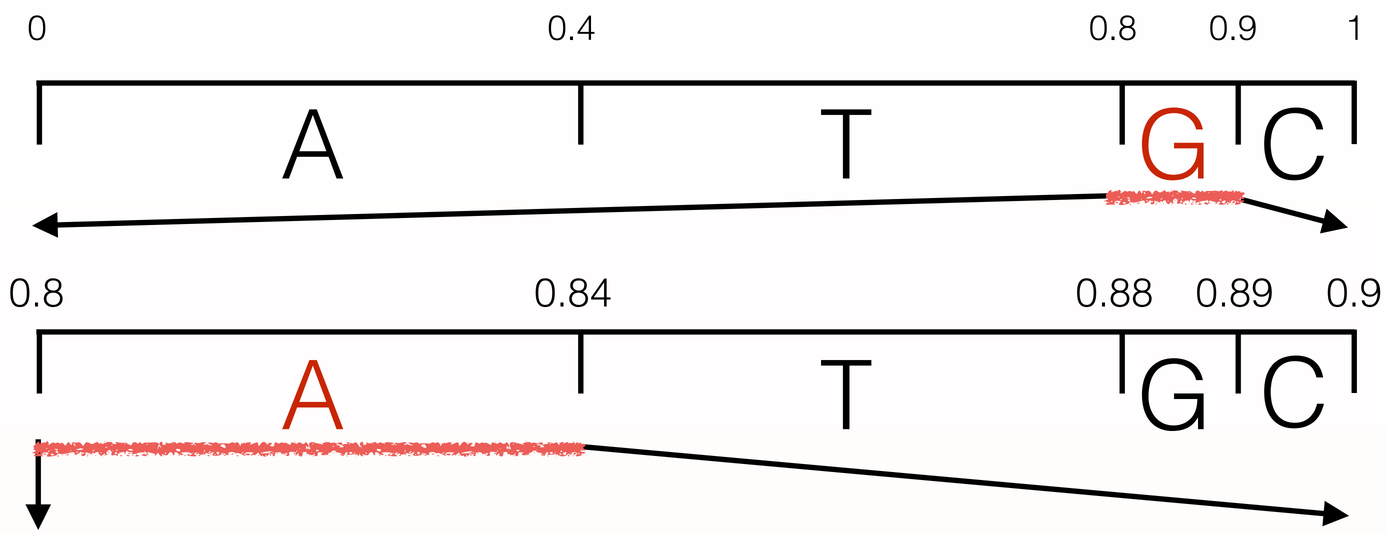
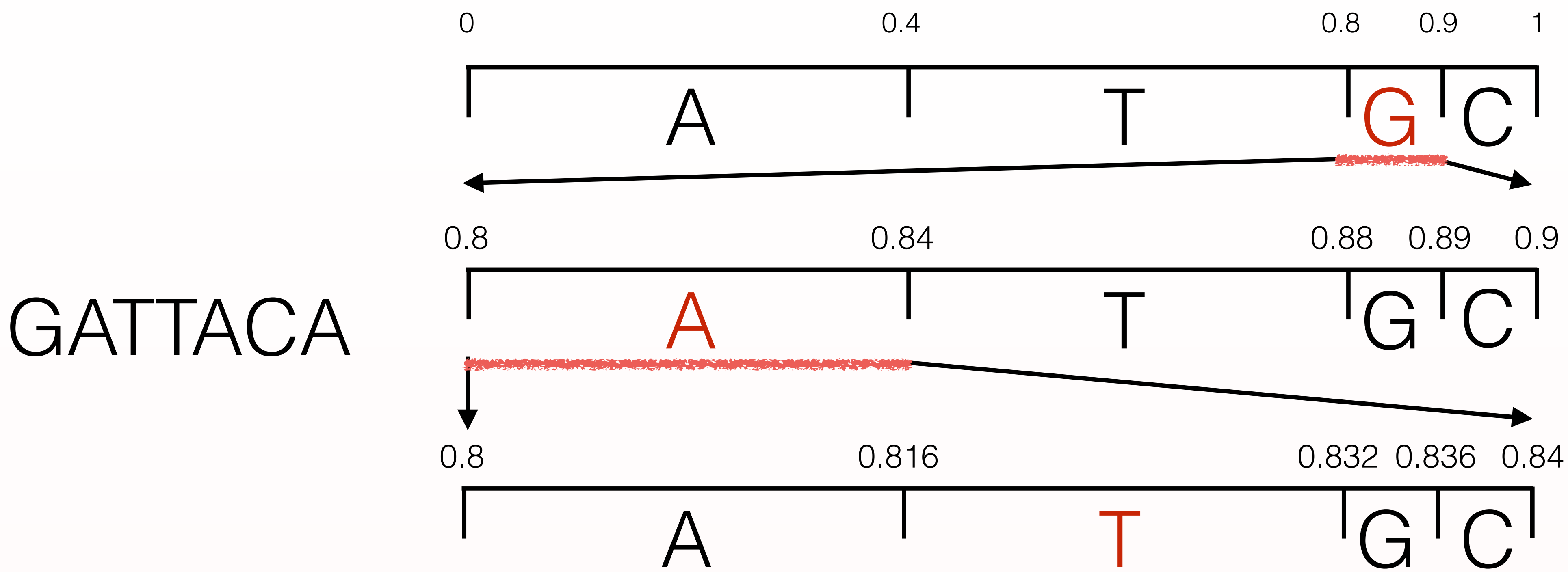
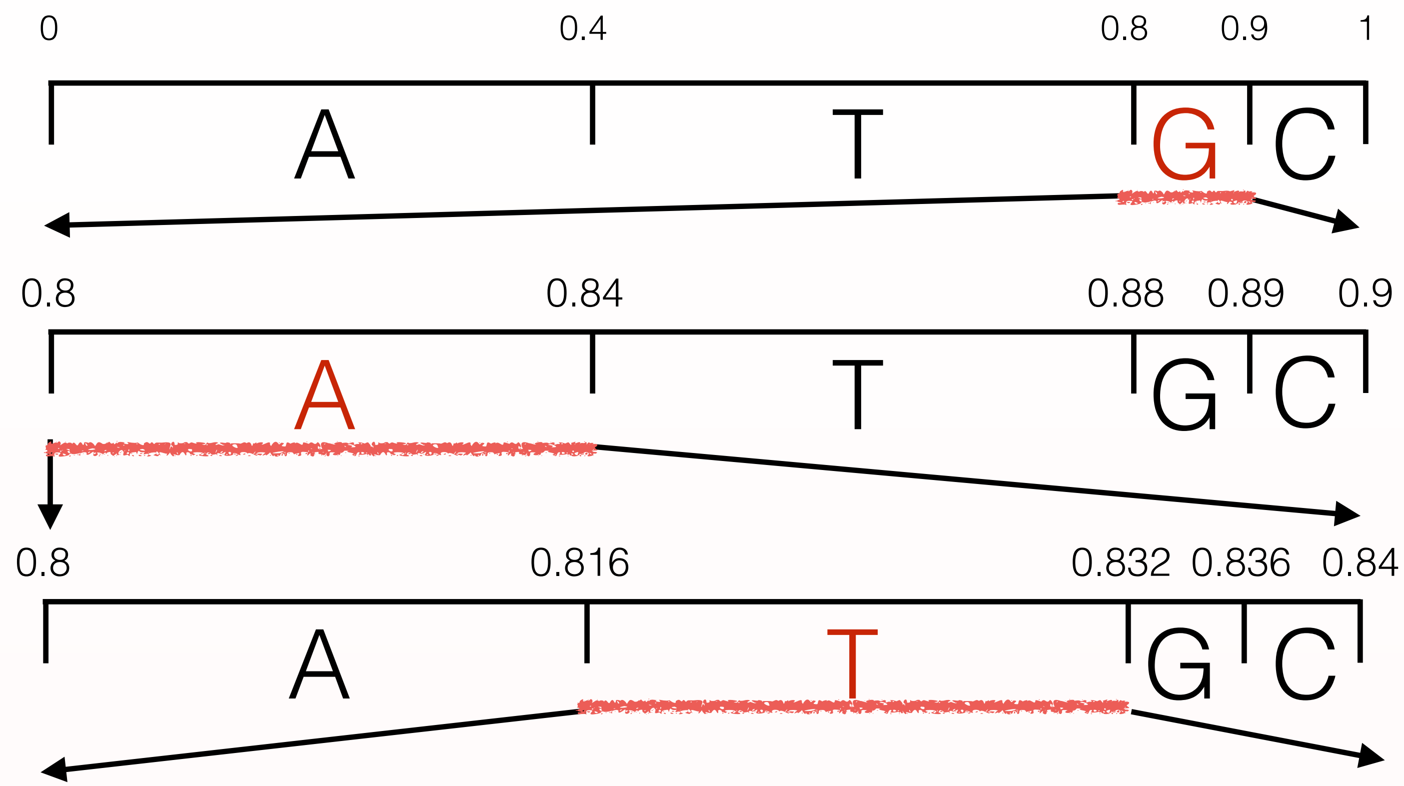




GATTACA
0
0.4
0.8
0.9
1
A
T
G
C
0.8
0.84
0.88
0.89
0.9
A
T
G
C
0.8
0.816
0.832
0.836
0.84
A
T
G
C

GATTACA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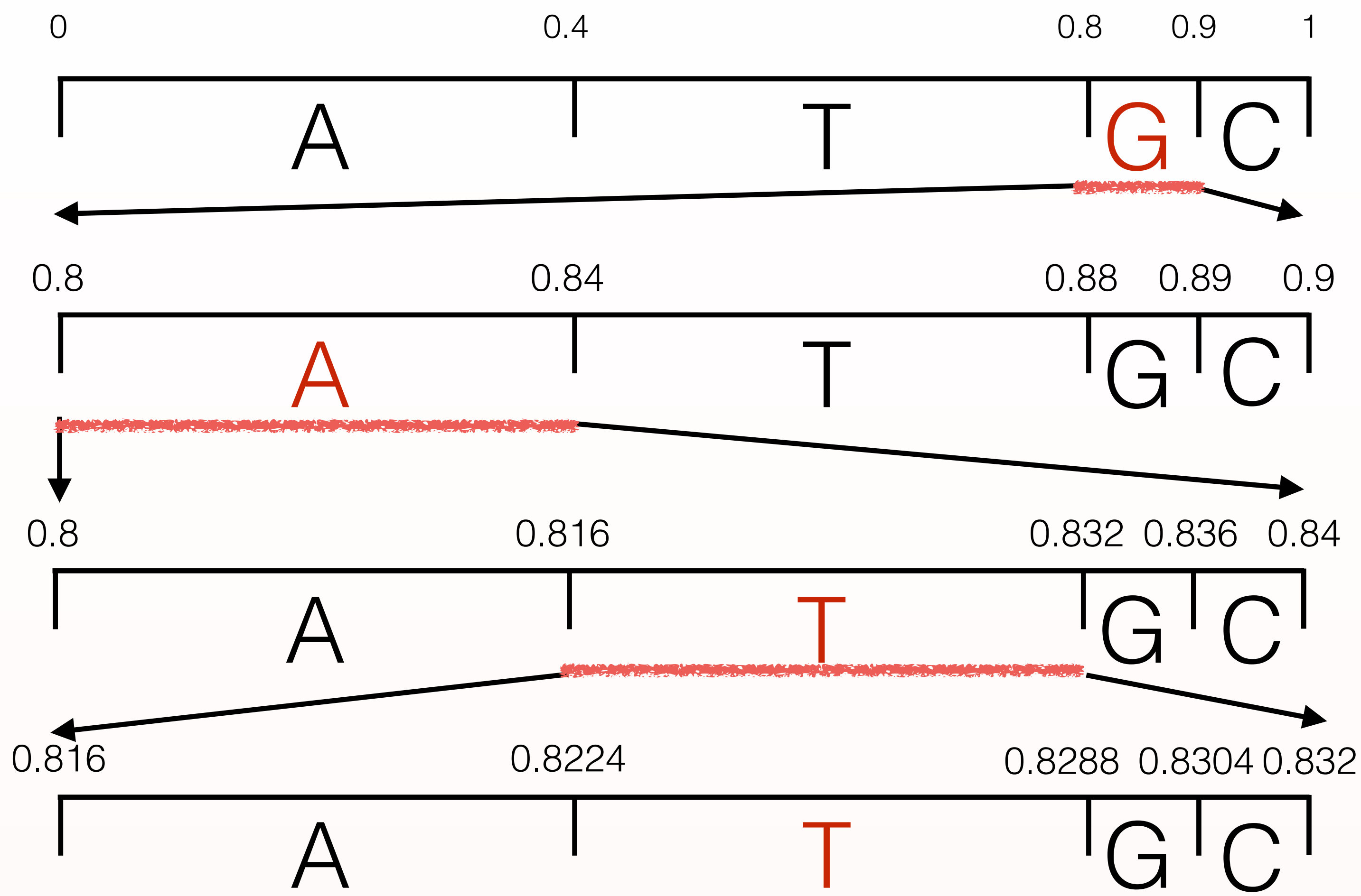
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0.816
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0.836
0.84
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C
0.816
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0.8288
0.8304
0.832
A
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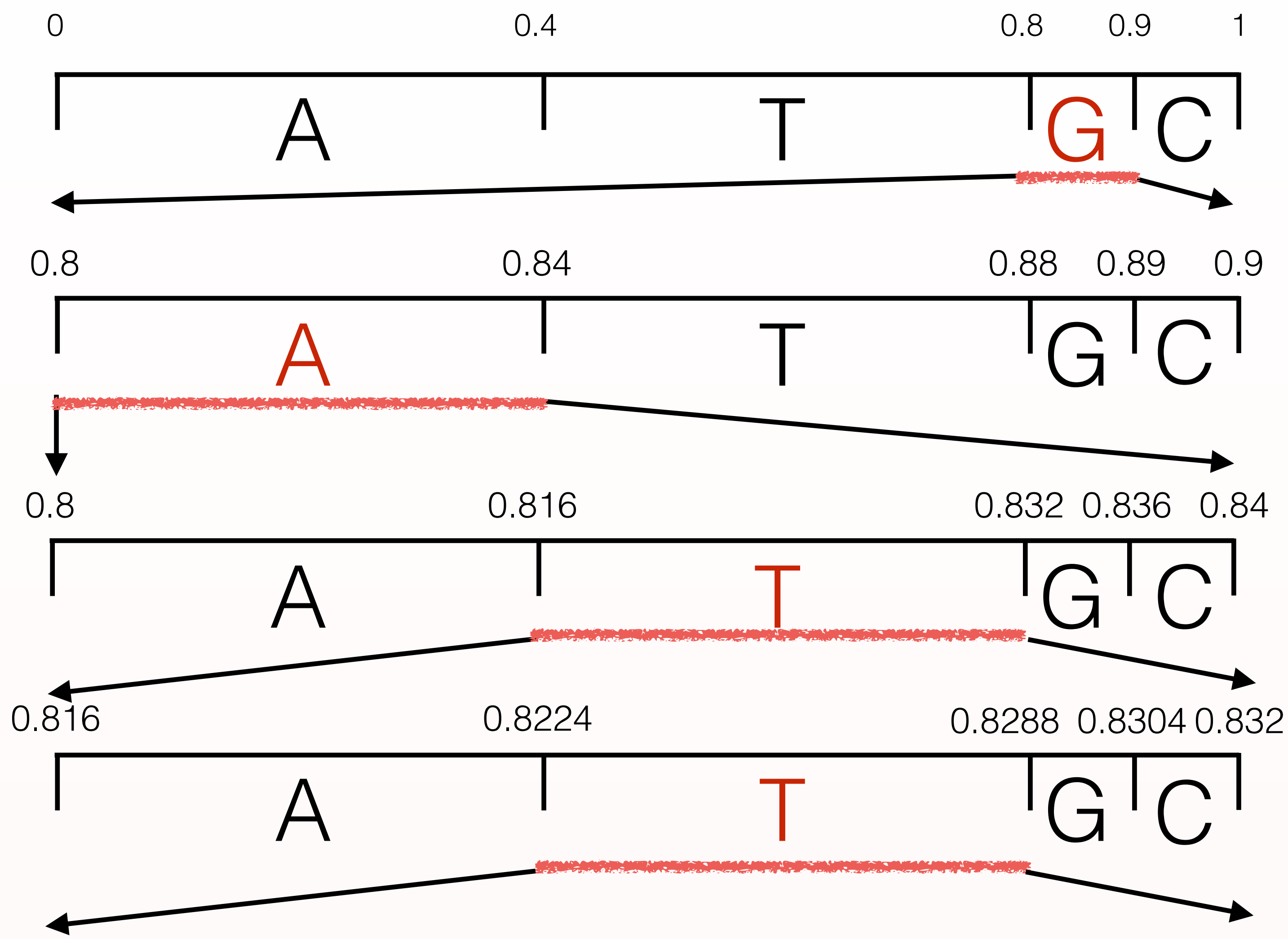
C

GATTACA



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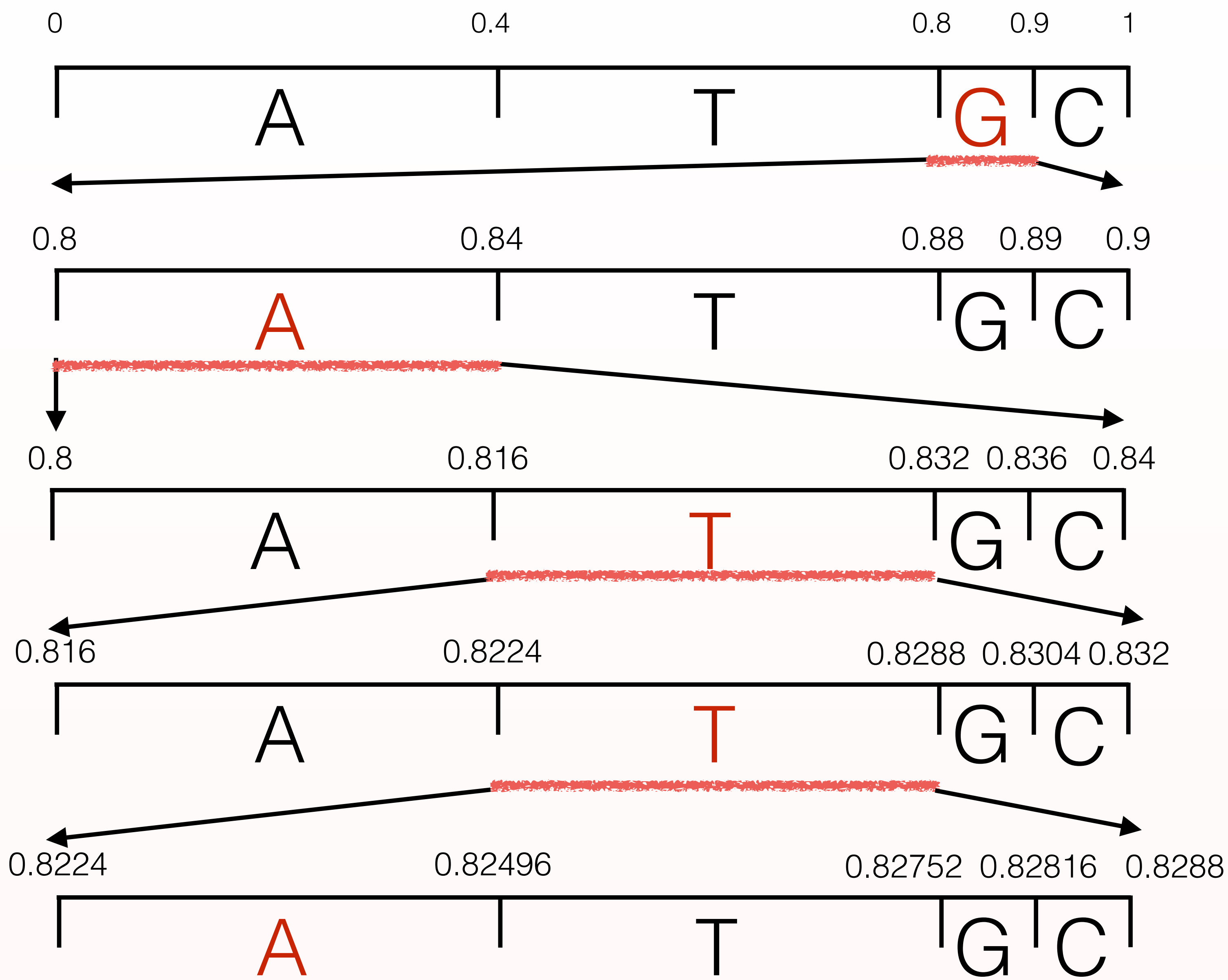

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0.82752
0.82816
0.8288
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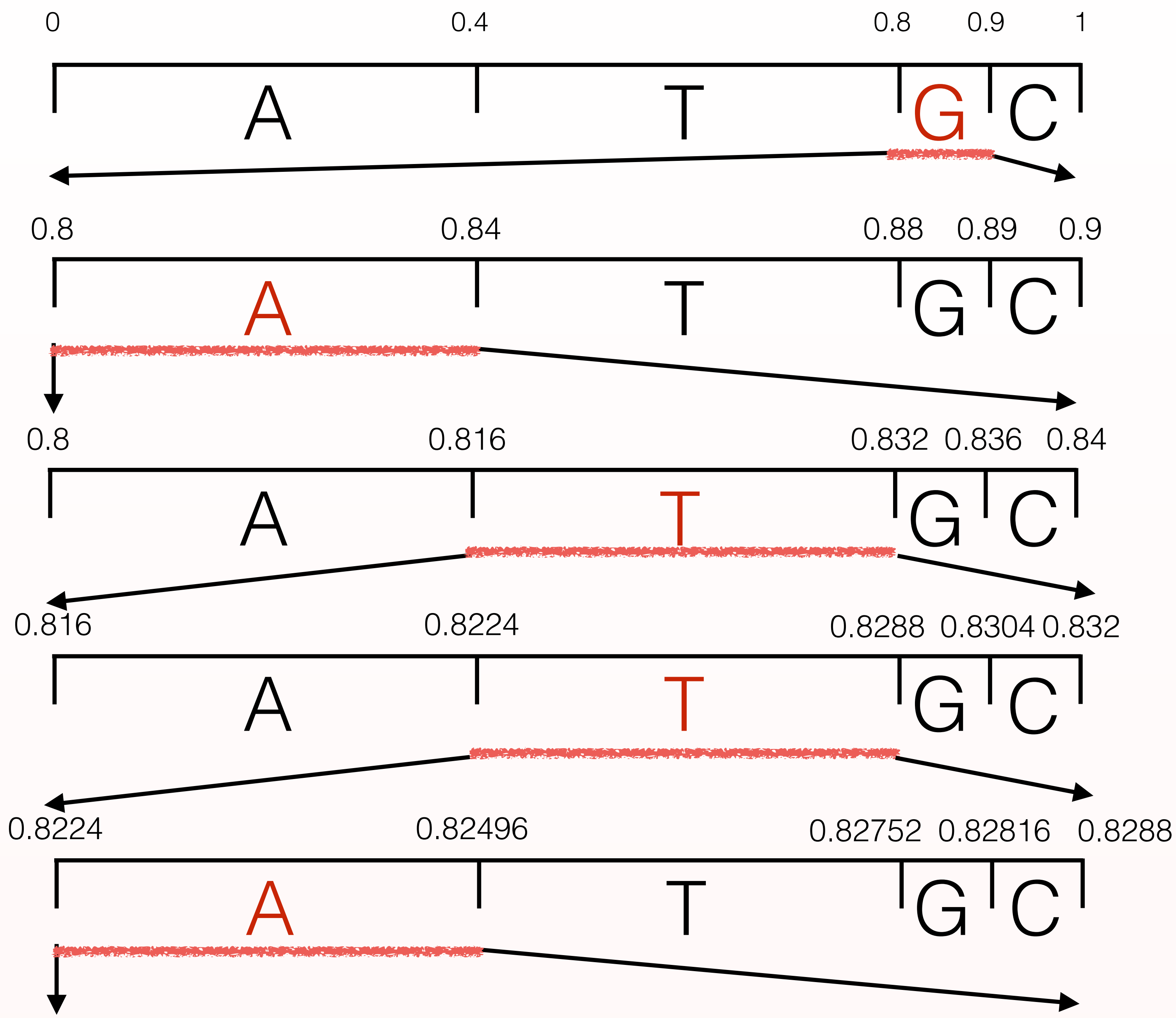
C

GATTACA



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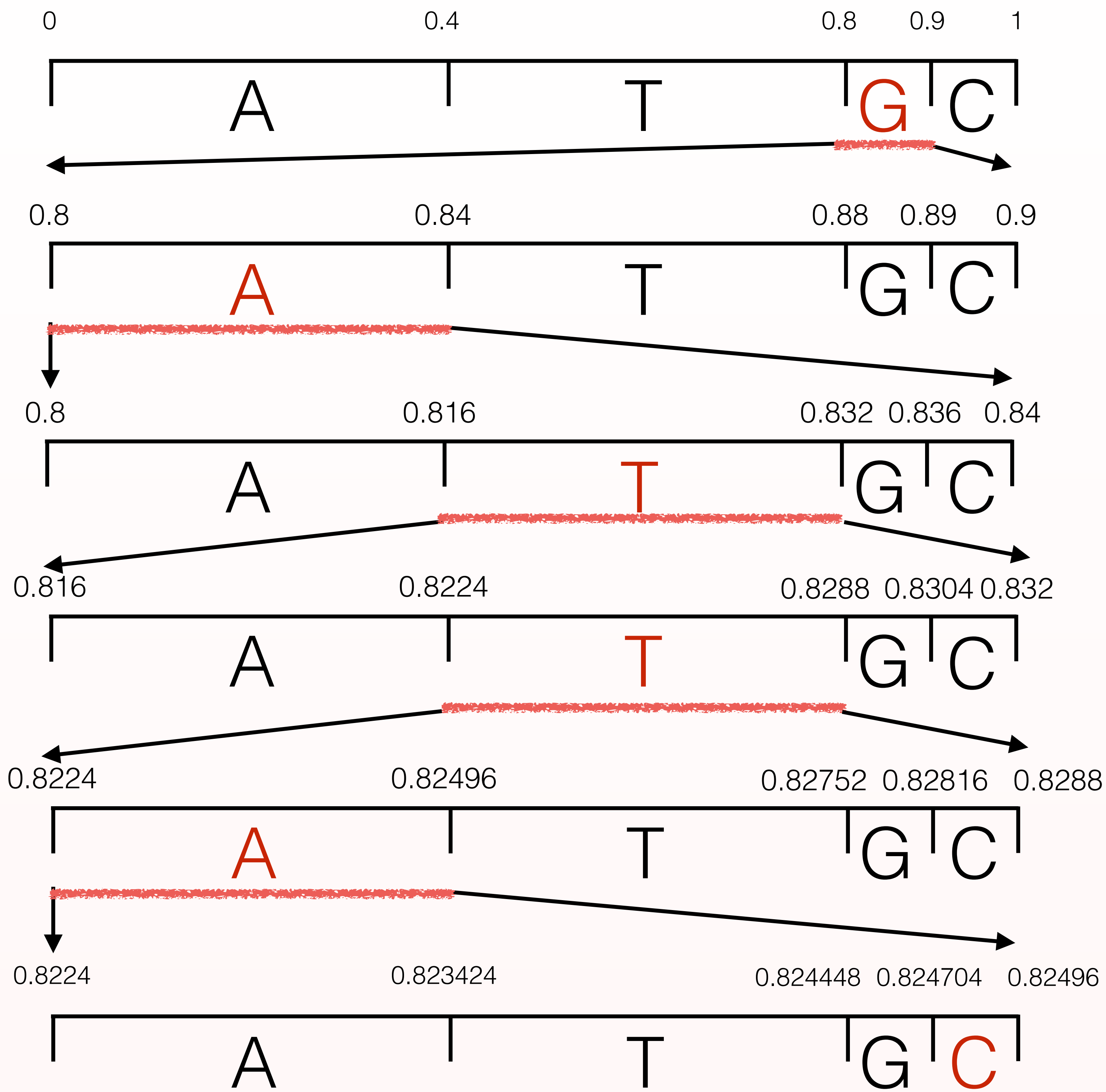
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A
T
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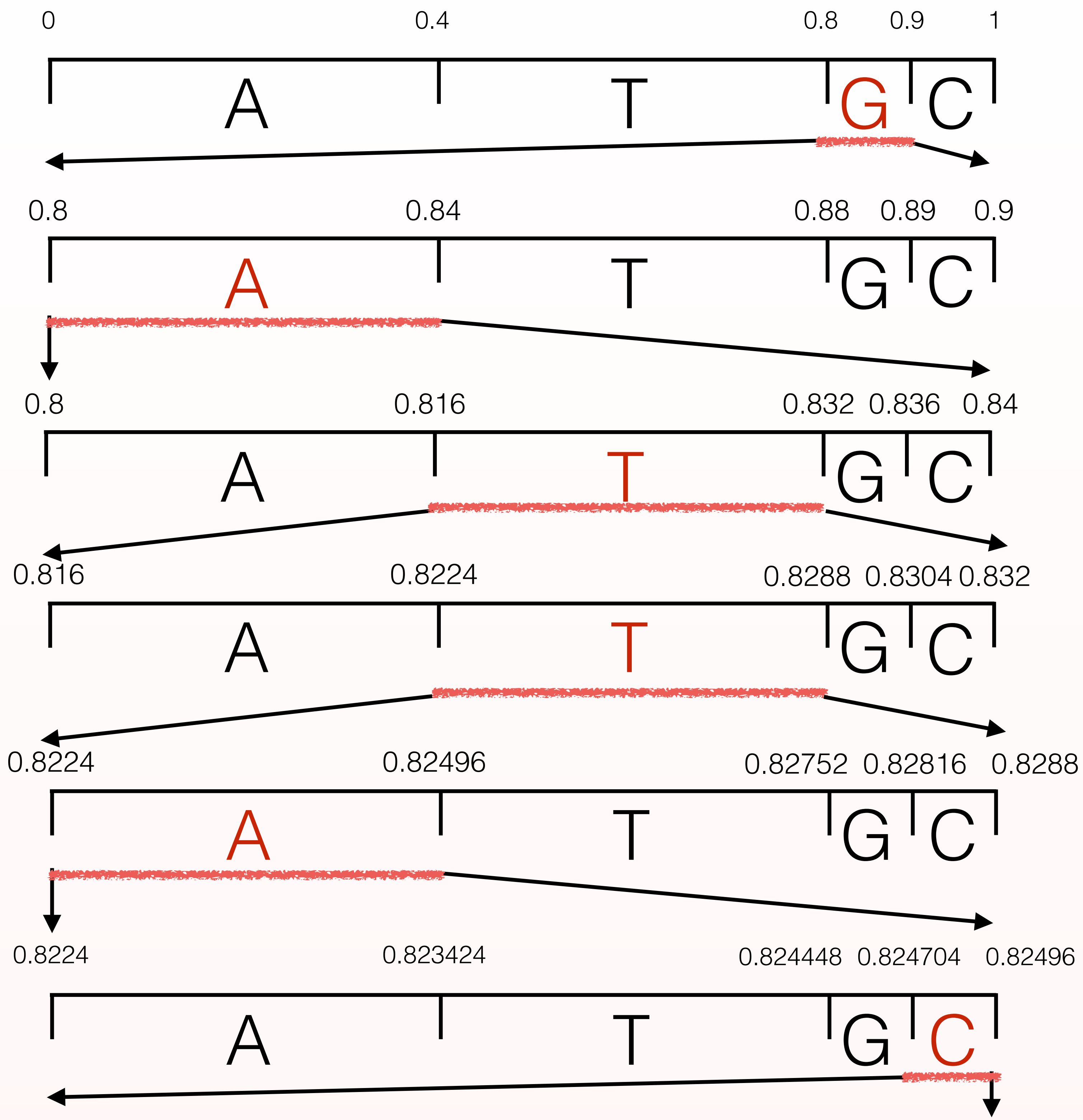
C
0.8224
0.82496
0.82752
0.82816
0.8288
A
T
G
C
0.8224
0.823424
0.824448
0.824704
0.82496
A
T
G
C

GATTACA



0
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A
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T
G
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0.8224
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T
G
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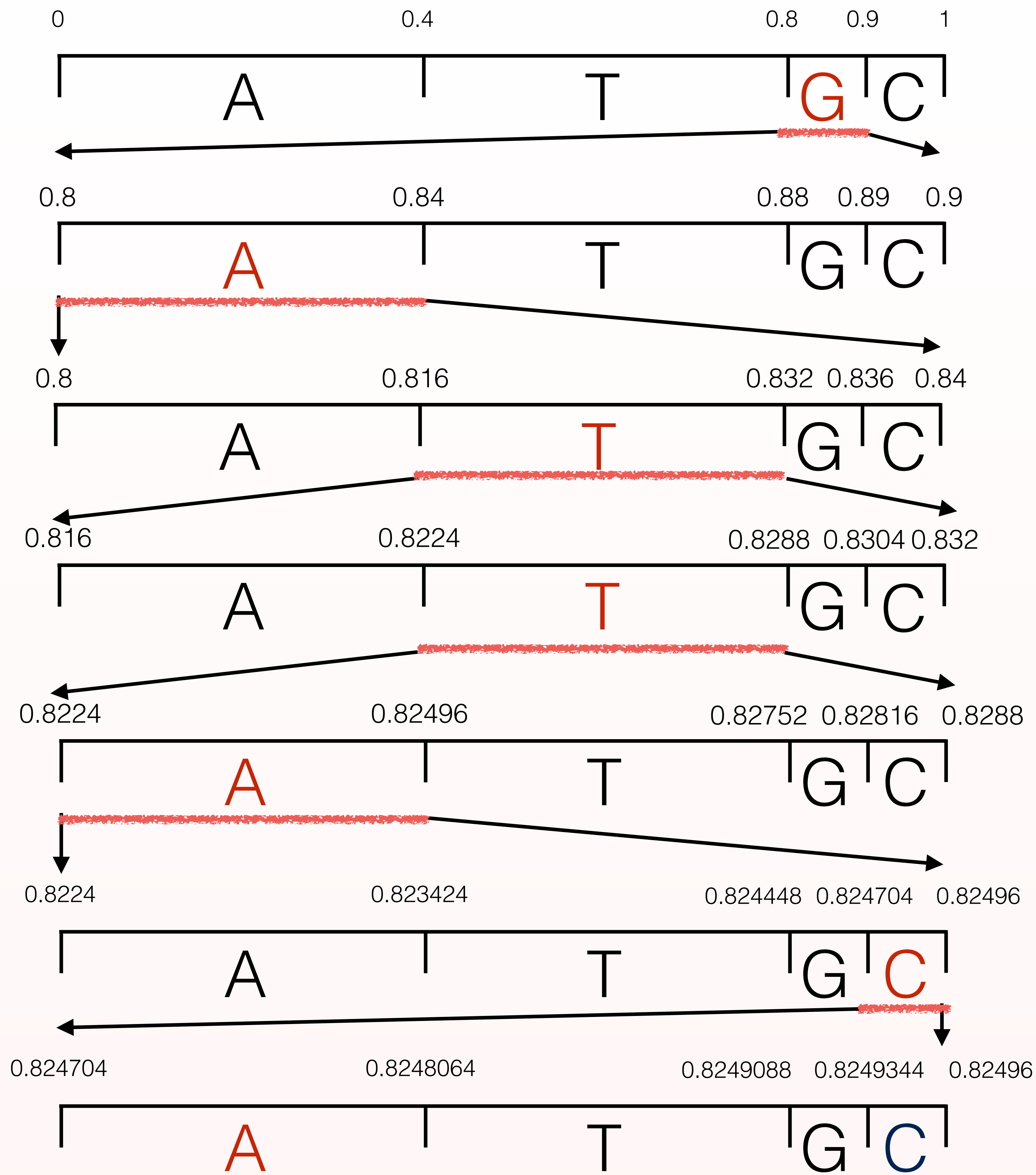

0
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0.9
1
A
T
G
C
0.8
0.84
0.88
0.89
0.9
A
T
G
C
0.8
0.816
0.832
0.836
0.84
A
T
G
C
0.816
0.8224
0.8288
0.8304
0.832
A
T
G
C
0.8224
0.82496
0.82752
0.82816
0.8288
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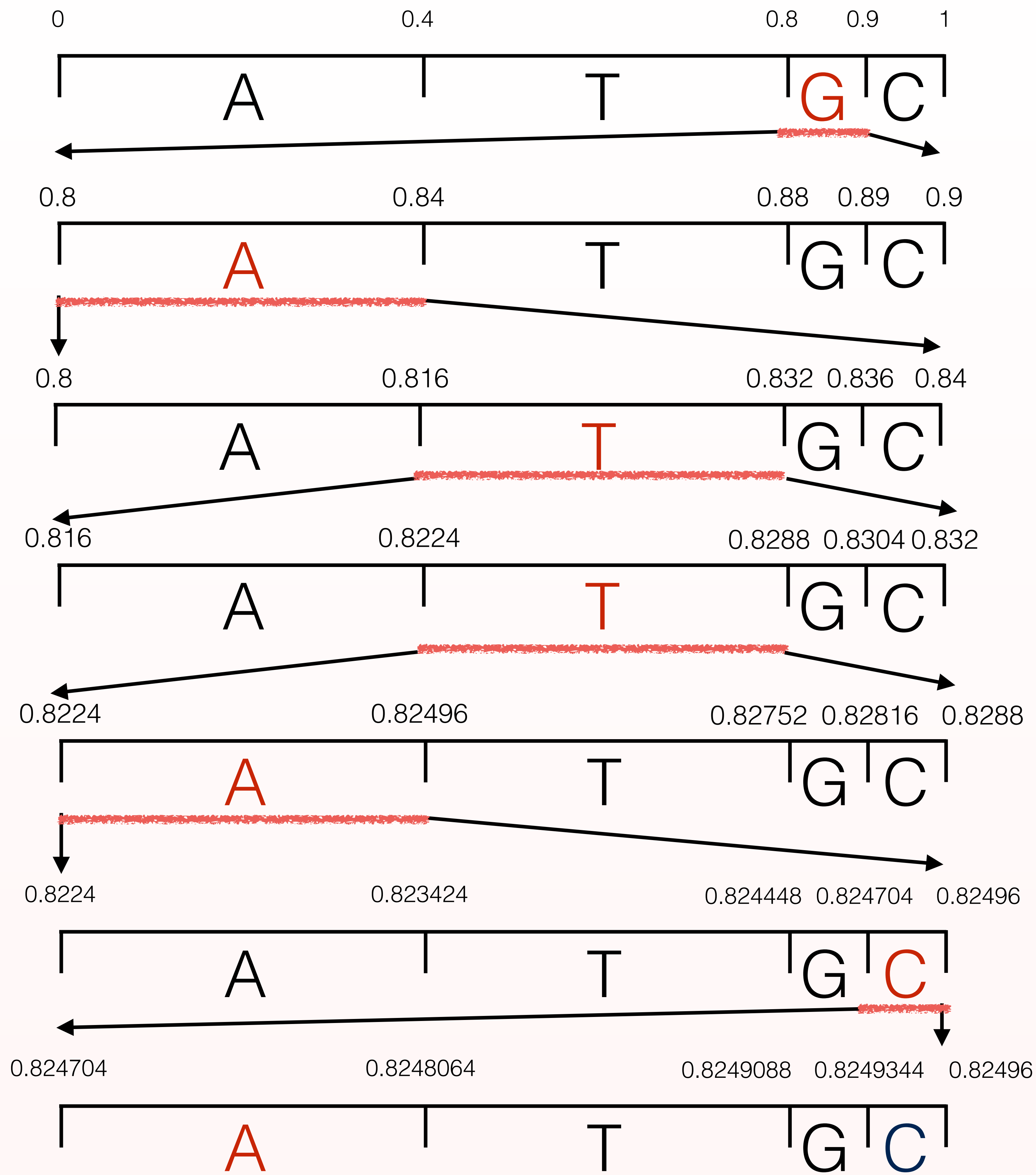
T
G
C
0.8224
0.823424
0.824448
0.824704
0.82496
A
T
G
C
0.824704
0.8248064
0.8249088
0.8249344
0.82496
A
T
G
C

GATTACA



0.824704

Arithmetic coding

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How do we know when the message ends?

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I lied; we need a stop symbol

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Bigger problem: floating point precision

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Rodionov & Volkov, 2007 & 2010 (p-adic arithmetic)

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Integer version

Rodionov & Volkov, 2007 & 2010 (p-adic arithmetic)

Huffman coding is a specialized case, less likely to be optimal

Lempel-Ziv

Slide a fixed-length window along sequence

Replace already-seen patterns (of some maximum length)

Used by gzip (& others)

`GATTACATTA`

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```
GATTACATTA

GATTAC<1,4>
```

Lempel-Ziv

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GATTACATTA

GATTAC<1,4>

Pointer

Lempel-Ziv

Slide a fixed-length window along sequence

Replace already-seen patterns (of some maximum length)

Used by gzip (& others)

GATTACATTA

GATTAC<1,4>

Pointer Length

Burrows-Wheeler Transform (BWT)

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block-sorting compression

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not itself a compressor, but a way to sort input, reversibly

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Genomic compressors

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Why not just gzip it?

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sequence

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quality scores (one per base)

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sequence: 4-letter alphabet

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Why not just gzip it?

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quality scores (one per base)

sequence: 4-letter alphabet

quality scores: 40-value range

sequence: must be lossless

quality scores: lossy might be ok

Genomic compressors

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Take advantage of structure

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Store differences from a **reference**

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Cluster similar reads (**reference-free**)

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Take advantage of structure

Store differences from a **reference**

Cluster similar reads (**reference-free**)

don’t have references for all species

SCALCE [Hach et al. 2012]

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Reference-free

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Reference-free

Locally Consistent Encoding

SCALCE [Hach et al. 2012]

Reference-free

Locally Consistent Encoding

Buckets reads by substrings

SCALCE [Hach et al. 2012]

Reference-free

Locally Consistent Encoding

Buckets reads by substrings

improves LZ77 runtime AND compression

SCALCE [Hach et al. 2012]

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Identify local maxima

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Identify local maxima
Identify local minima

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Partition at each side

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Extend L and R to “core blocks”

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X0X

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X0X

2 1 3 1 2 0 3 2 1 0 2 0 2 1 3 1 2 0 3 2 1 0 2

SCALCE [Hach et al. 2012]

Identify local maxima
Identify local minima
Partition at each side
Extend L and R to “core blocks”

XOX

2 1 **3** 1 **2** 0 **3** 2 1 0 **2** 0 **2** 1 **3** 1 **2** 0 **3** 2 1 0 2

SCALCE [Hach et al. 2012]

Identify local maxima

Identify local minima

Partition at each side

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X0X

2 1 **3** 1 **2** 0 **3** 2 1 0 **2** 0 **2** 1 **3** 1 **2** 0 **3** 2 1 0 2

| 2 1 **3** | 1 **2** | 0 **3** | 2 1 0 **2** | 0 **2** | 1 **3** | 1 **2** | 0 **3** | **2** 1 0 2 |

SCALCE [Hach et al. 2012]

Identify local maxima
Identify local minima
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X0X

21**3**1**2**0**3**210**2**0**2**1**3**1**2**0**3**2102

|21**3**|1**2**|0**3**|210**2**|0**2**|1**3**|1**2**|0**3**|**2**102|

2131,3**12**0,2**032**,3**2102**0,2**02**1,2**13**1,
3**12**0,2**03**2,3**2102**

SCALCE [Hach et al. 2012]

Core blocks between 8 & 20

99% of all HTS reads of length ≥50

include at least one core of length ≤14

Identify overlapping reads by core blocks

Reorder reads to favor LZ77

DeeZ [Hach, et al. 2014]

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Given a mapping (reads to reference)

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Build contig covering all reads within a block

Encode locus for each read within contig

Encode rare differences (sequencing errors)

DeeZ [Hach, et al. 2014]

```
           GTCGTCTACA T
          CGTCGTCTACA
        AACCTCGTCTAC
              GTCTACA TCTA
ACGTGCTAAACGTCGTTTACAGTCTACAGA
```

DeeZ [Hach, et al. 2014]

```
           GTCGTCTACA T
          CGTCGTCTACA
        AACCTCGTCTAC
              GTCTACA TCTA
ACGTGCTAAACGTCGTTTACAGTCTACAGA

ACGTGCTAAACGTCGTCTACA TCTACAGA
```

DeeZ [Hach, et al. 2014]

```
           GTCGTCTACA T
          CGTCGTCTACA
        AACCTCGTCTAC
              GTCTACA TCTA
ACGTGCTAAACGTCGTTTACAGTCTACAGA

ACGTGCTAAACGTCGTCTACA TCTACAGA
```

DeeZ [Hach, et al. 2014]

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Tokenization of read names

DeeZ [Hach, et al. 2014]

Tokenization of read names

LZ77

DeeZ [Hach, et al. 2014]

Tokenization of read names

LZ77

Lossy QS compression from SCALCE

DeeZ [Hach, et al. 2014]

Tokenization of read names

LZ77

Lossy QS compression from SCALCE

Random access

PathEnc [Kingsford & Patro 2015]

Reference-based

- but no aligning
- statistical, generative model of reads

For RNA-seq data (but need not be)

PathEnc [Kingsford & Patro 2015]

GAUU

GAUUAGAUUG

PathEnc [Kingsford & Patro 2015]

GAUU

$\downarrow$

AUUA

GAUUAGAUUG

PathEnc [Kingsford & Patro 2015]

$$\begin{tikzcd} \text{GAUU} \arrow[d] \\ \text{AUUA} \arrow[d] \\ \text{UUAG} \end{tikzcd}$$

GAUUAGAUUG

PathEnc [Kingsford & Patro 2015]

GAUU

↓

AUUA

↓

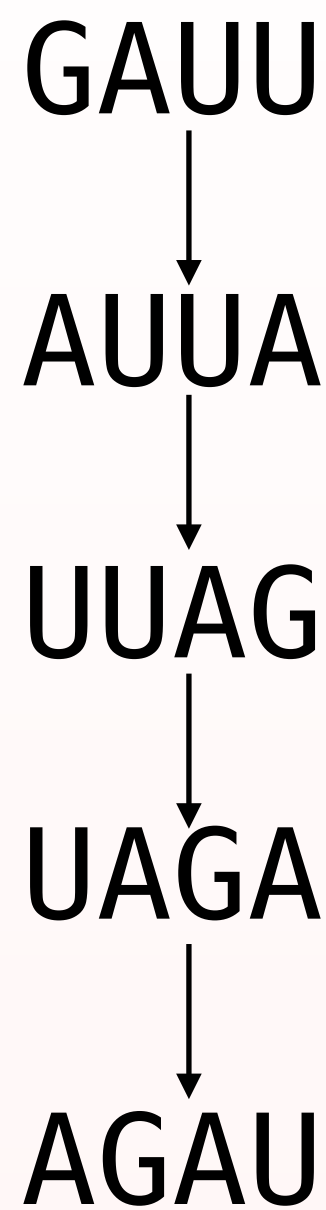
UUAG

↓

UAGA

GAUUAGAUUG

PathEnc [Kingsford & Patro 2015]



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GAUU

↓

AUUA

↓

UUAG

↓

UAGA

↓

AGAU

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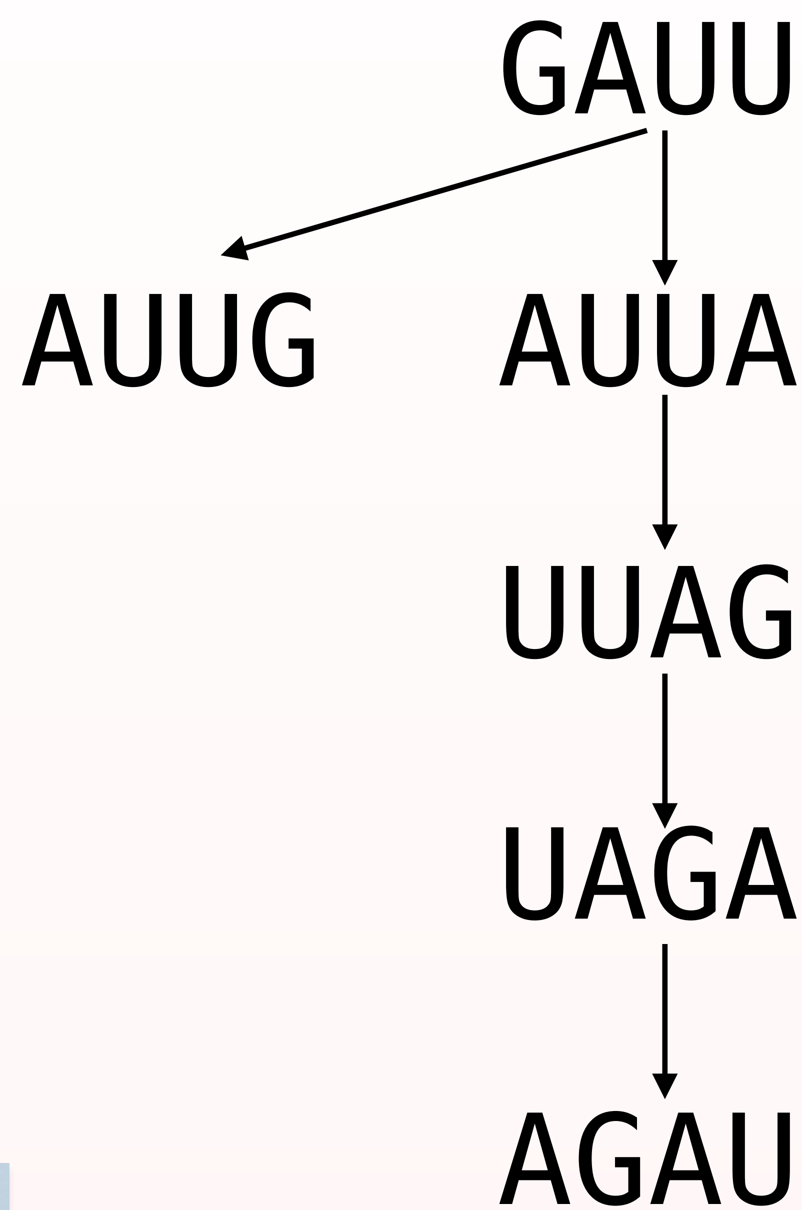

GAUUAGAUUG

PathEnc [Kingsford & Patro 2015]

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Path encoding in graph G

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1 node per k-mer

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edge between k-mers *(u,v)* if *v* follows *u*

PathEnc [Kingsford & Patro 2015]

Path encoding in graph G

1 node per k-mer

edge between k-mers *(u,v)* if *v* follows *u*

Each read encoded as a path in G

PathEnc [Kingsford & Patro 2015]

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1st node of each read path (read head)

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edges removed for nonexistent k-mers

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resulting bit string gzipped

PathEnc [Kingsford & Patro 2015]

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remaining nodes (read tails)

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arithmetic coding

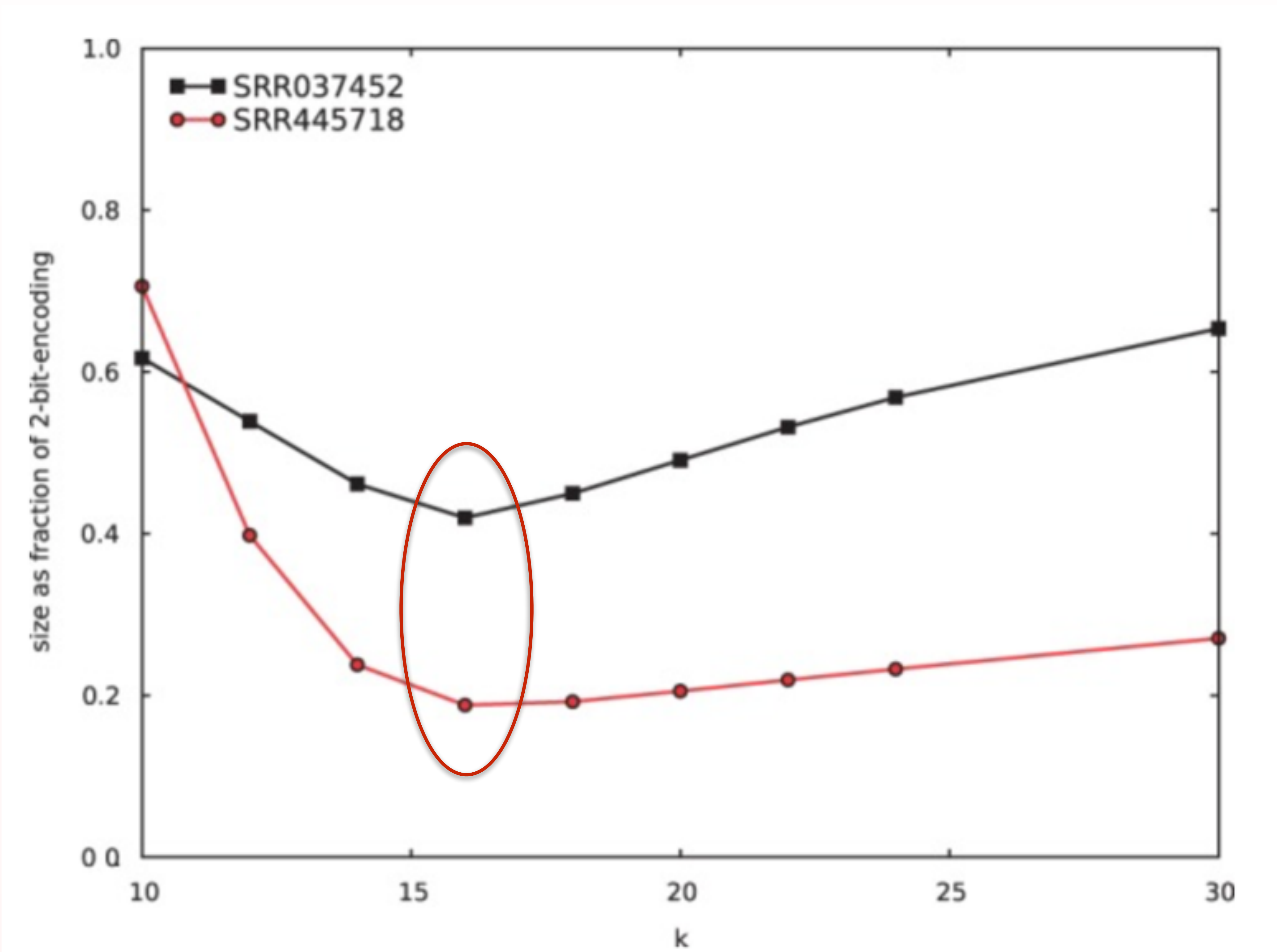
PathEnc [Kingsford & Patro 2015]

remaining nodes (read tails)

arithmetic coding

probability distribution per node in G

PathEnc [Kingsford & Patro 2015]



MINCE [Patro & Kingsford 2015]

MINCE [Patro & Kingsford 2015]

Reference-free

MINCE [Patro & Kingsford 2015]

Reference-free

Buckets reads based on *k*-mers (k=15)

MINCE [Patro & Kingsford 2015]

Reference-free

Buckets reads based on *k*-mers (*k*=15)

Replace common *k*-mer with pointer

MINCE [Patro & Kingsford 2015]

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Buckets reads based on *k*-mers (*k*=15)

Replace common *k*-mer with pointer

Reorder reads within each bucket

MINCE [Patro & Kingsford 2015]

Reference-free

Buckets reads based on *k*-mers (*k*=15)

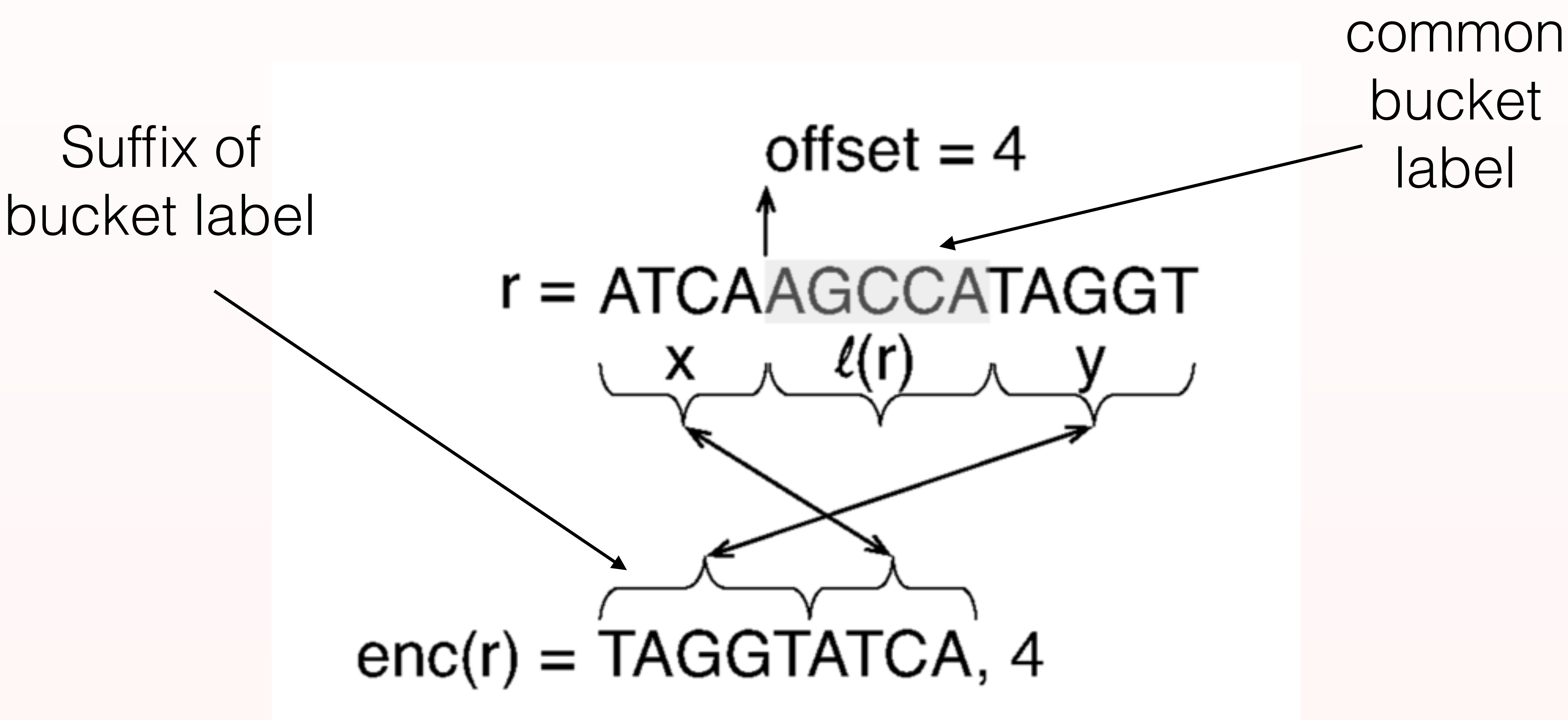
Replace common *k*-mer with pointer

Reorder reads within each bucket

This boosts lzip performance

MINCE [Patro & Kingsford 2015]

Split-swap read transformation

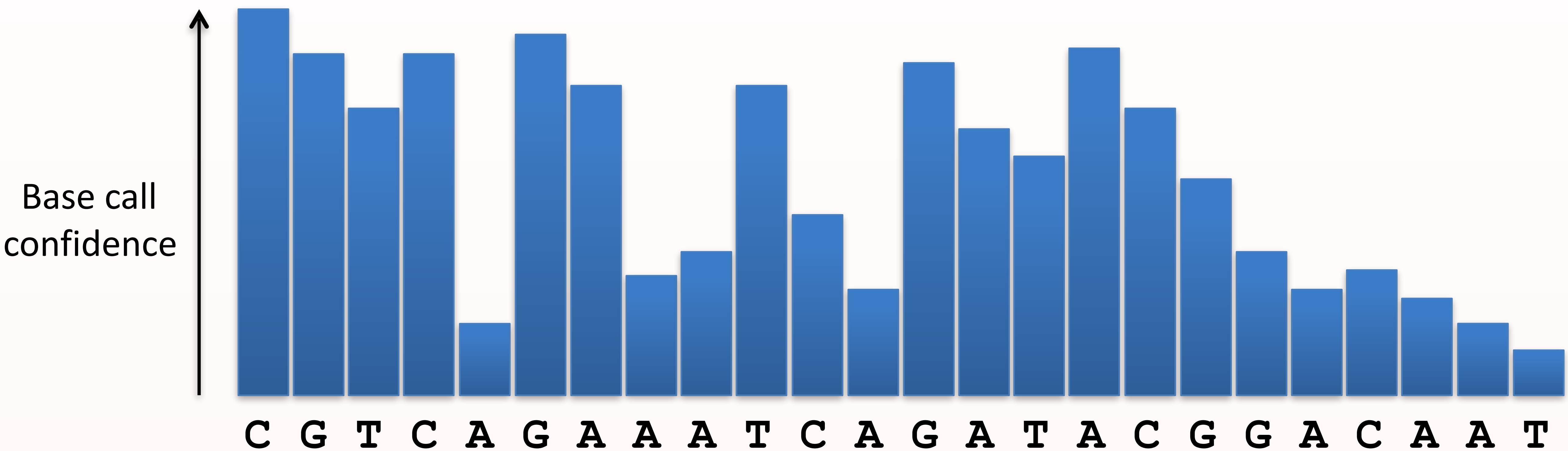


The Quality Score Problem

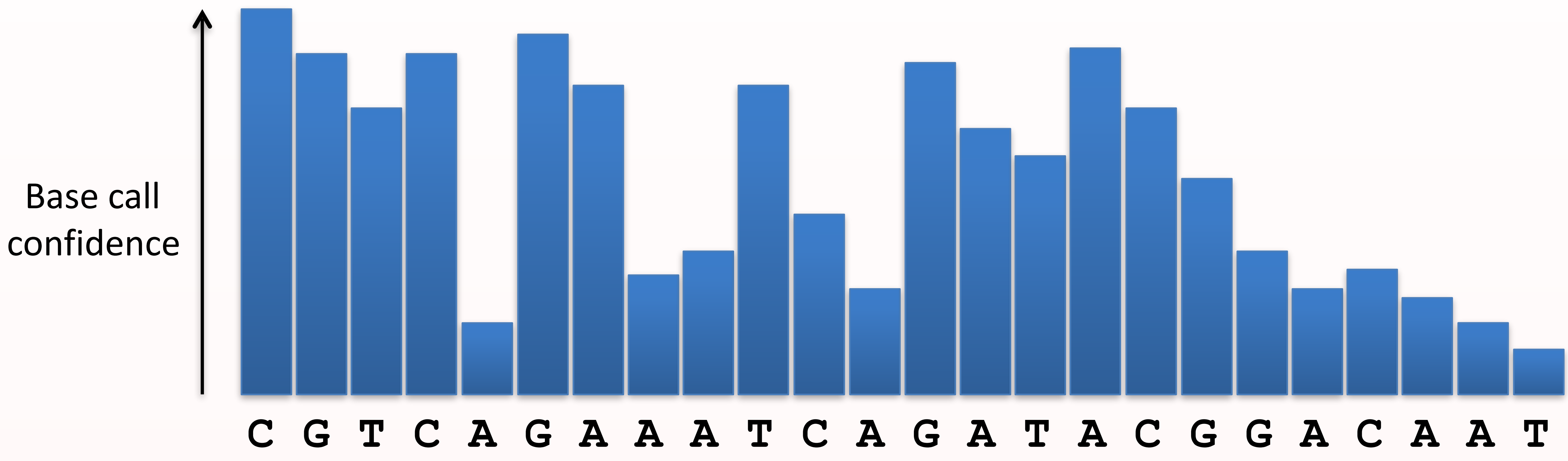
The Quality Score Problem

C G T C A G A A A T C A G A T A C G G A C A A T

The Quality Score Problem



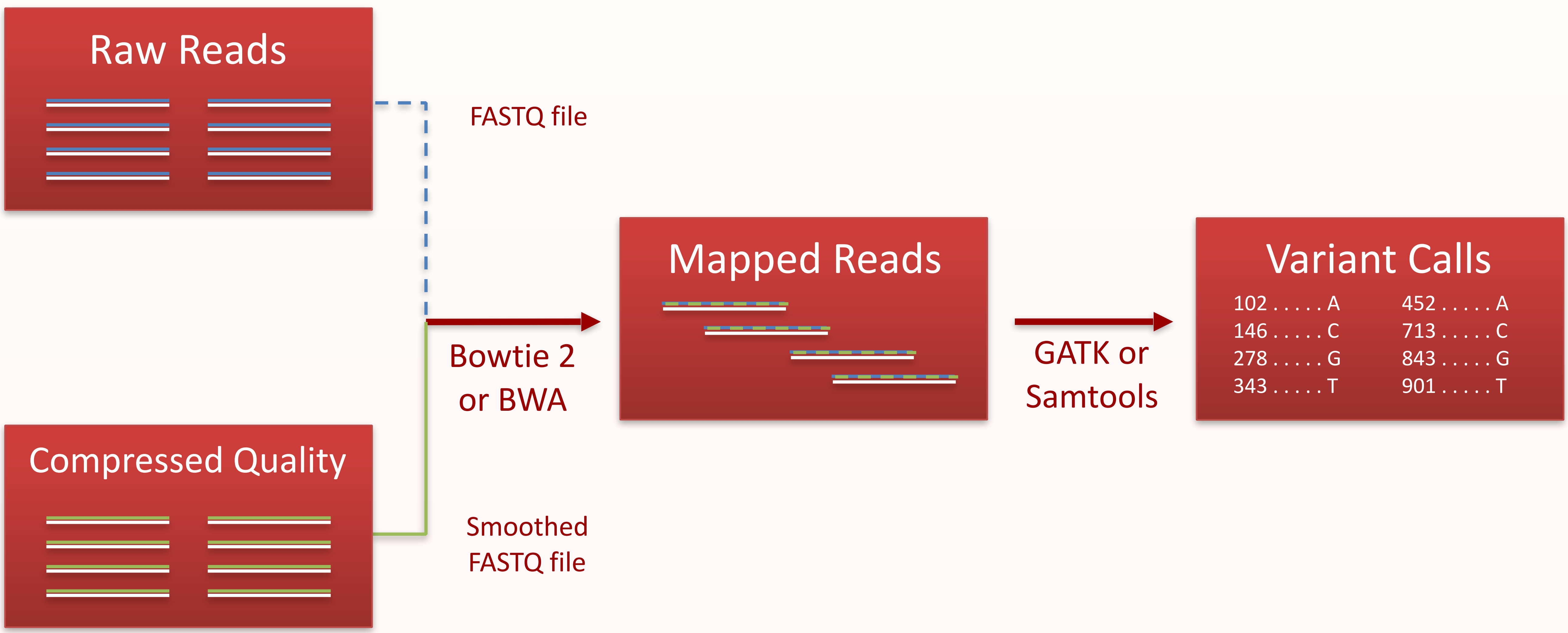
The Quality Score Problem



Given reads from a genome, can we **efficiently** compress quality scores while maintaining or even improving accuracy?

Quality scores in SNP-calling

Quality scores in SNP-calling



Quality score compressors

Quality score compressors

Greater dynamic range than sequence

Quality score compressors

Greater dynamic range than sequence

Can be lossless or lossy

Quality score compressors

Greater dynamic range than sequence

Can be lossless or lossy

Focus here on lossy

8-binning [Illumina]

Universally collapse dynamic range 40 => 8

Small effect on SNP calling error

Available in CRAM

QS bins	New value
N (no call)	N (no call)
2-9	6
10-19	15
20-24	22
25-29	27
30-34	33
35-39	37
≥40	40

SCALCE [Hach et al. 2012]

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Lossy compression of quality scores

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Lossy compression of quality scores

Neighboring QSs often similar

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Reduce dynamic range

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SCALCE [Hach et al. 2012]

Lossy compression of quality scores

Neighboring QSs often similar

Reduce dynamic range

Arithmetic coding

Small loss (<0.1%) of SNP calling accuracy

QVZ [Malysa, et al. 2015]

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Based on rate-distortion theory

Discard as little information as possible for a desired bit rate

Key insight: neighboring QSs are likely to be correlated

Illumina reads often have lower QSs at end

QVZ [Malysa, et al. 2015]

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1. Compute the empirical transition probabilities of a Markov-1 model

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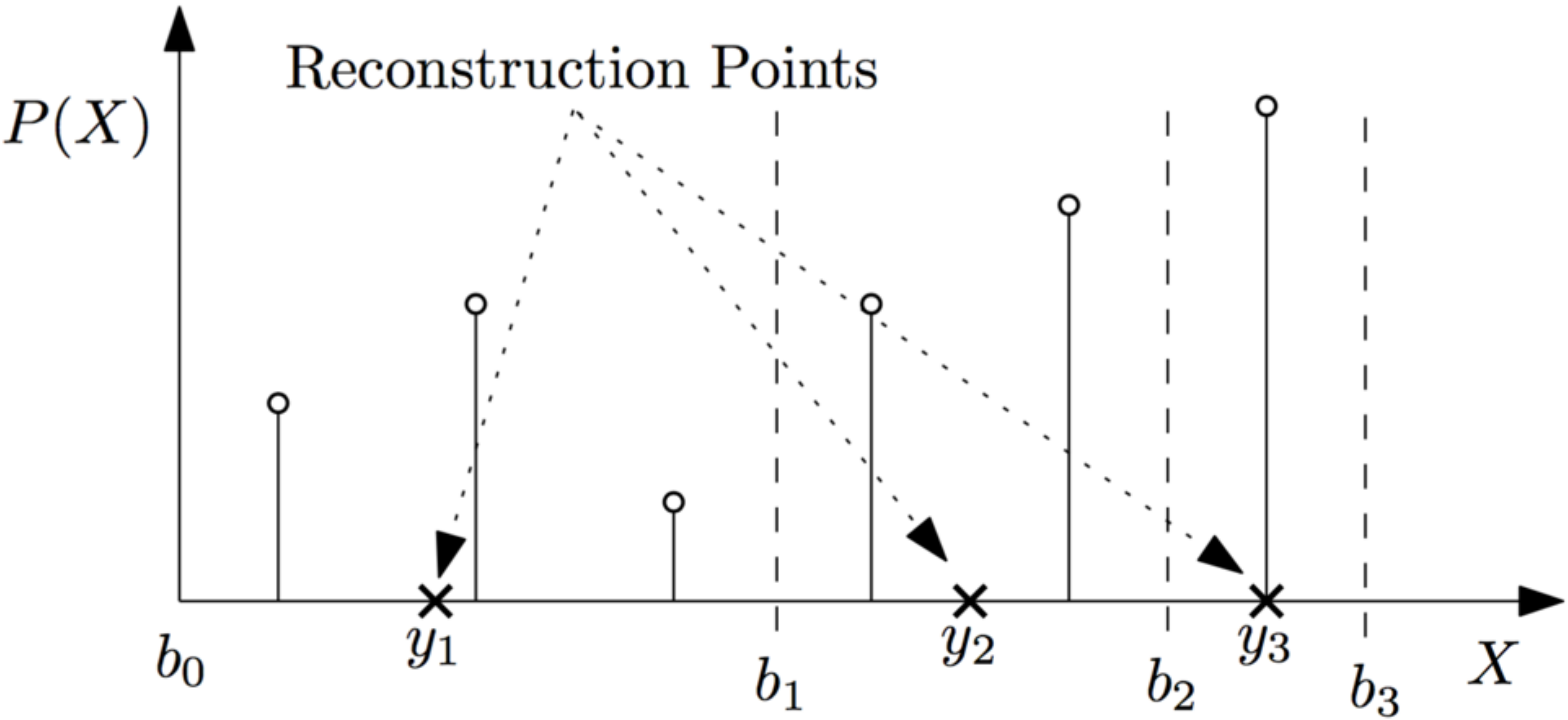
2. Construct a codebook using the Lloyd-Max algorithm

3. Quantize the input using the codebook, use arithmetic encoder

QVZ [Malysa, et al. 2015]



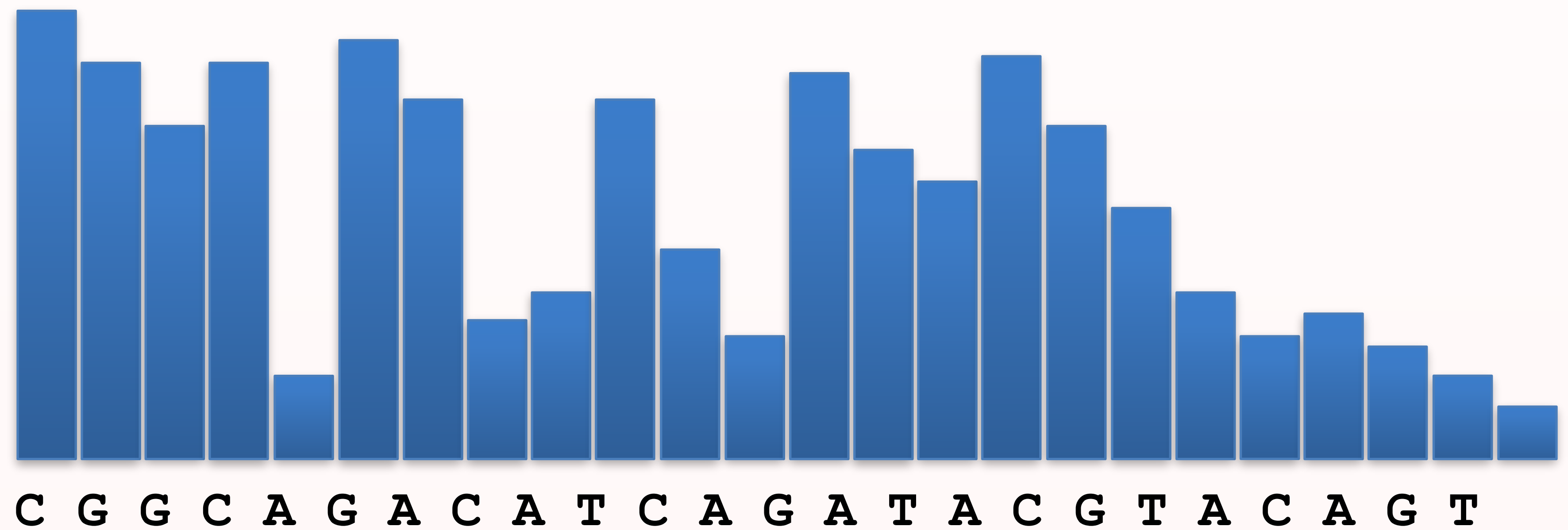
Quartz [Yu, et al. 2015]

Preprocessing

Quartz [Yu, et al. 2015]

Preprocessing

Compression



Quartz [Yu, et al. 2015]

Preprocessing

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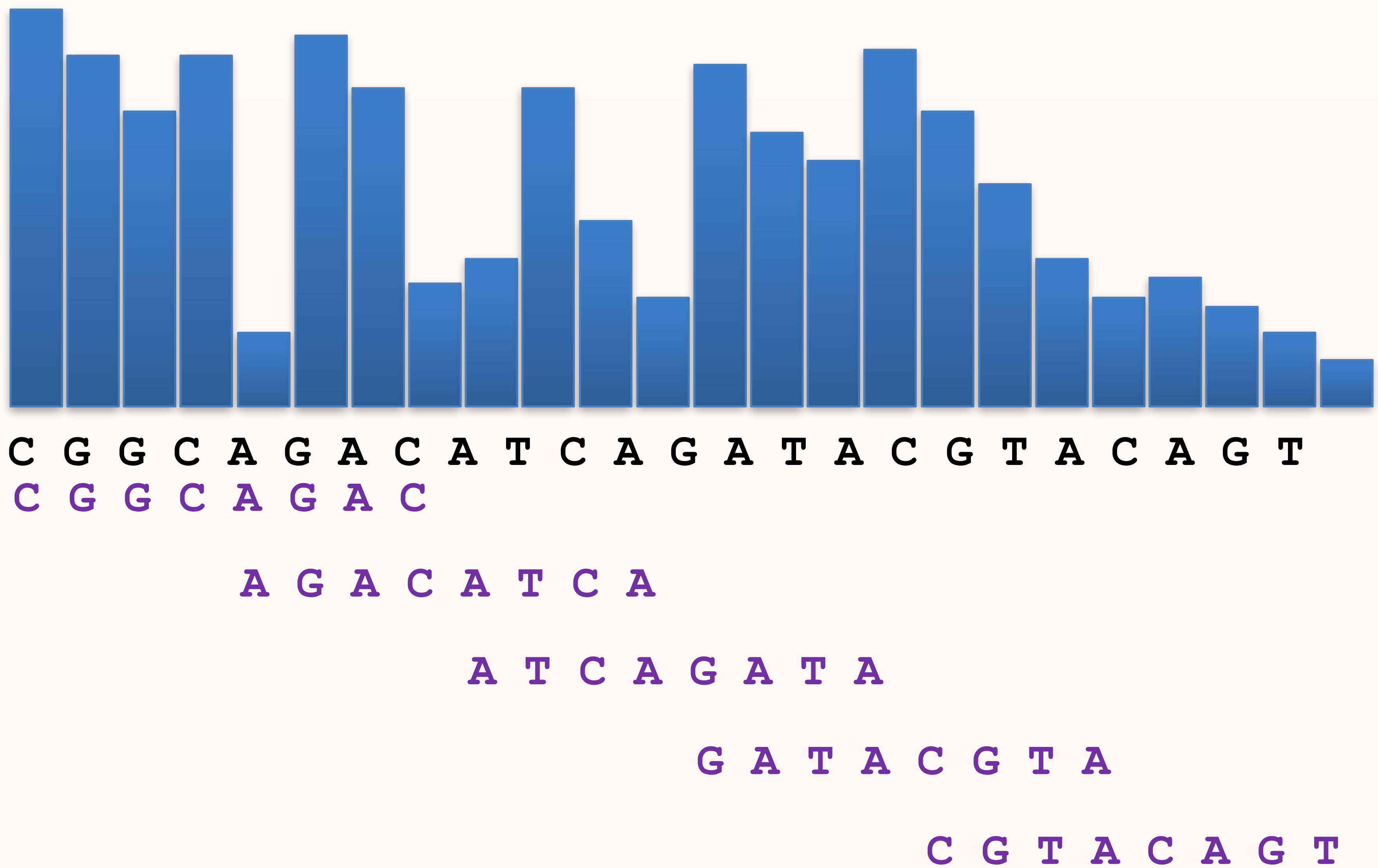
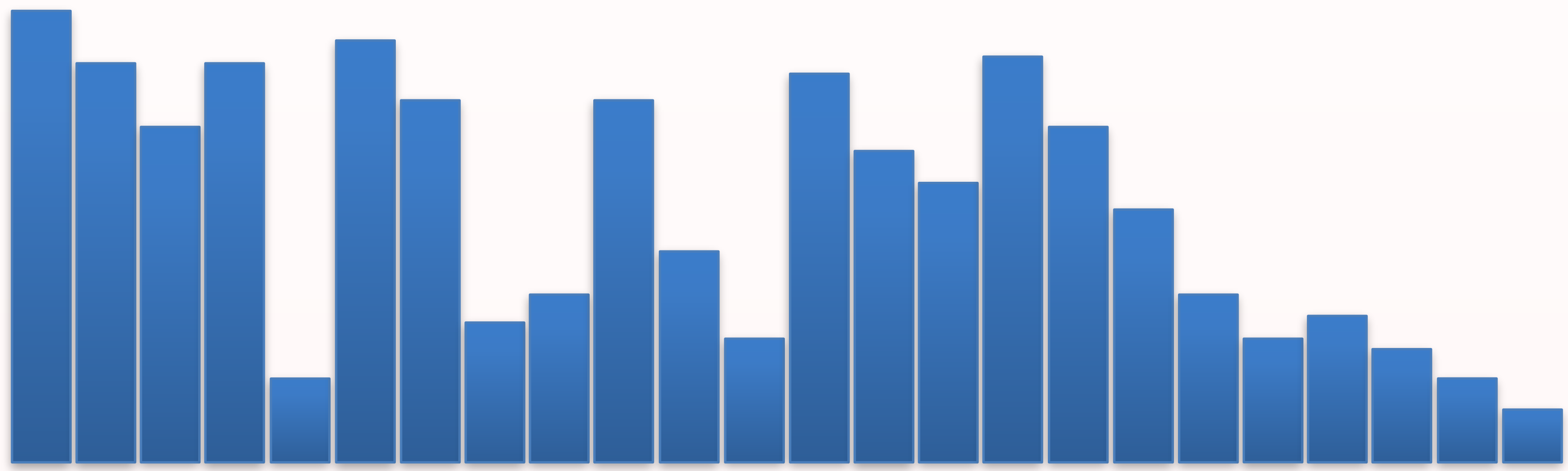


Quartz [Yu, et al. 2015]

Preprocessing

Compression



C G G C A G A C A T C A G A T A C G T A C A G T

C G G C A G A C

C G T C A G A C

A G A C A T C A

A G A A A T C A

A T C A G A T A

A T C A G A T A

G A T A C G T A

G A T A C G G A

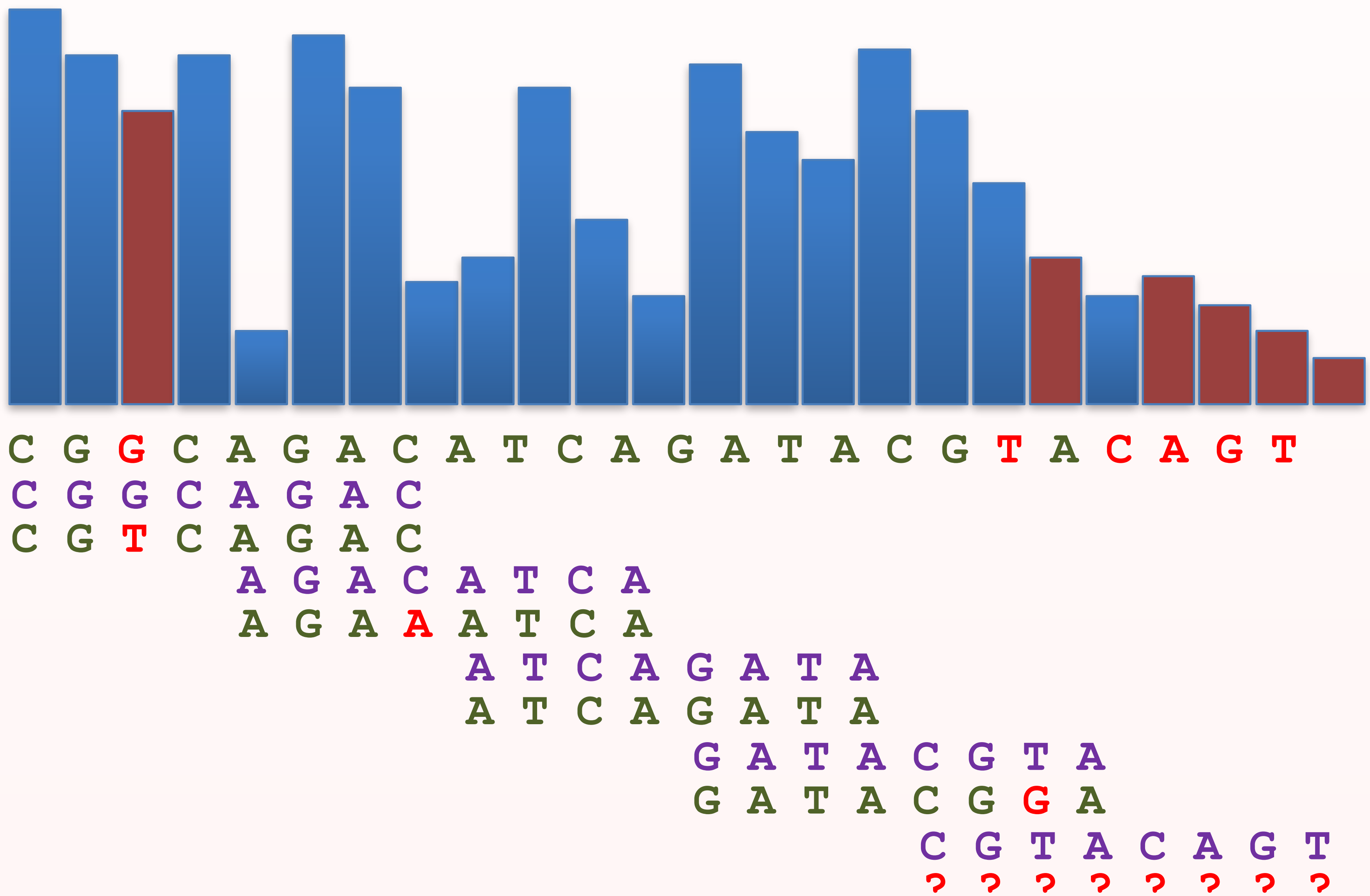
C G T A C A G T

? ? ? ? ? ? ? ?

Quartz [Yu, et al. 2015]

Preprocessing

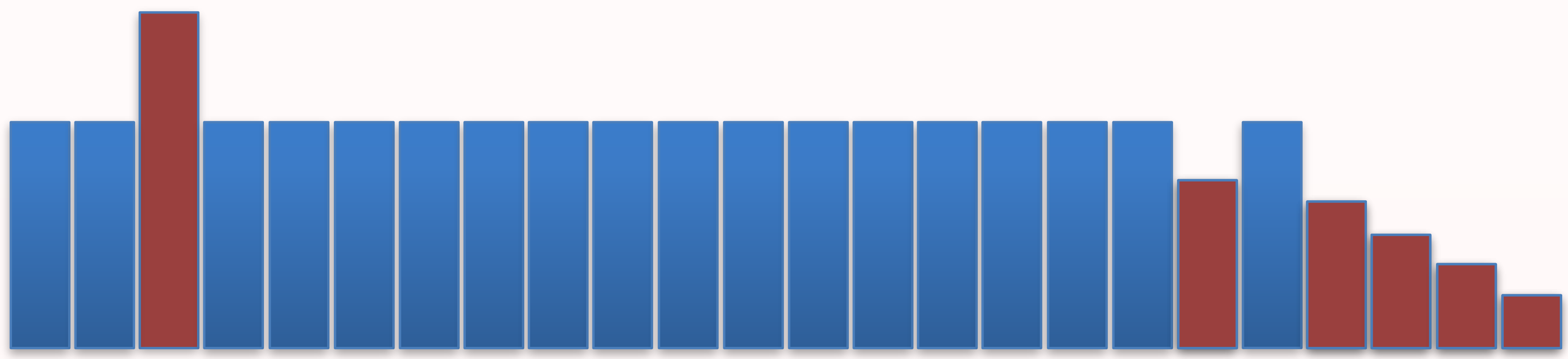
Compression



Quartz [Yu, et al. 2015]

Preprocessing

Compression



Approximate k-mer search

Naïve approaches

Approximate k-mer search
Naïve approaches

- Need to quickly find all *3k* Hamming neighbors of each k-mer from the read in the dictionary to identify mis-matched bases.

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- Naïve approaches
  - Sorted list
    - Memory efficient but binary search is CPU and cache inefficient
  - Hash tables
    - Faster CPU-wise, but memory and cache inefficient

Approximate k-mer search

Locality sensitive hashing

An (R, cR, P_1, P_2) -sensitive LSH family F of hash functions $h : M \to S$ is defined if

$\forall p, q \in M$, a uniformly random $h \in F$ satisfies:

if $||p - q|| \leq R$ then $\mathbb{P}\left(h(p) = h(q)\right) \geq P_1$

If $||p - q|| \geq cR$ then $\mathbb{P}\left(h(p) = h(q)\right) \leq P_2$

Project k-mers onto random $\frac{k}{2}$-mers, forming a $(1, c, \frac{1}{2}, 2^{c-1})$-sensitive family of hash functions under the Hamming metric

Approximate k-mer search

Double hashing for fun and profit

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- Notice that each $h : M \rightarrow S$ comes with an orthogonal projection $h' : M \rightarrow S$

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Double hashing for fun and profit

- Notice that each $h : M \to S$ comes with an orthogonal projection $h' : M \to S$
- Also, if $||p, q|| \leq 1$ then by counting, at least one of $h(p) = h(q)$ or $h'(p) = h'(q)$ must hold.

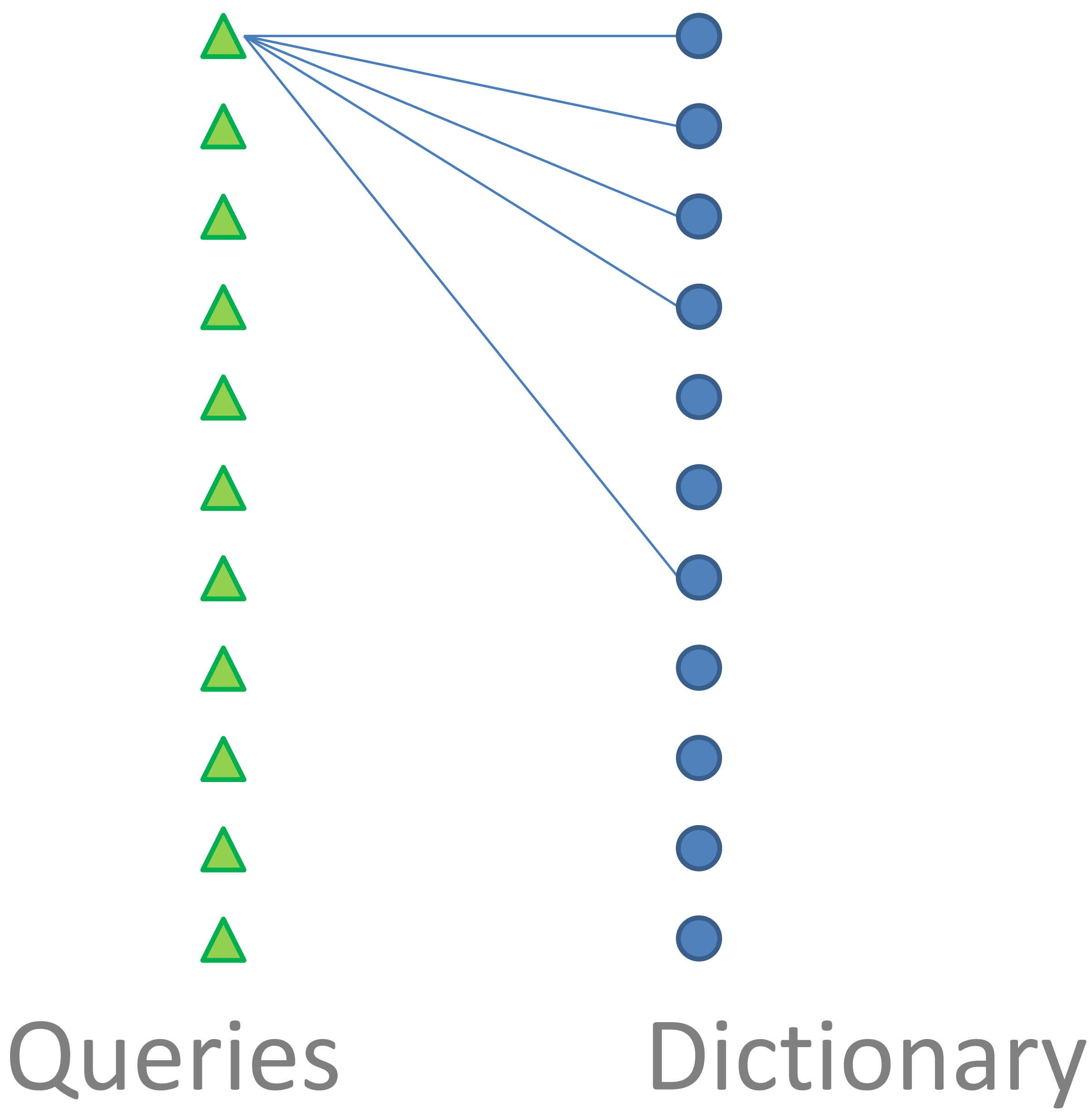
Approximate k-mer search

Double hashing for fun and profit

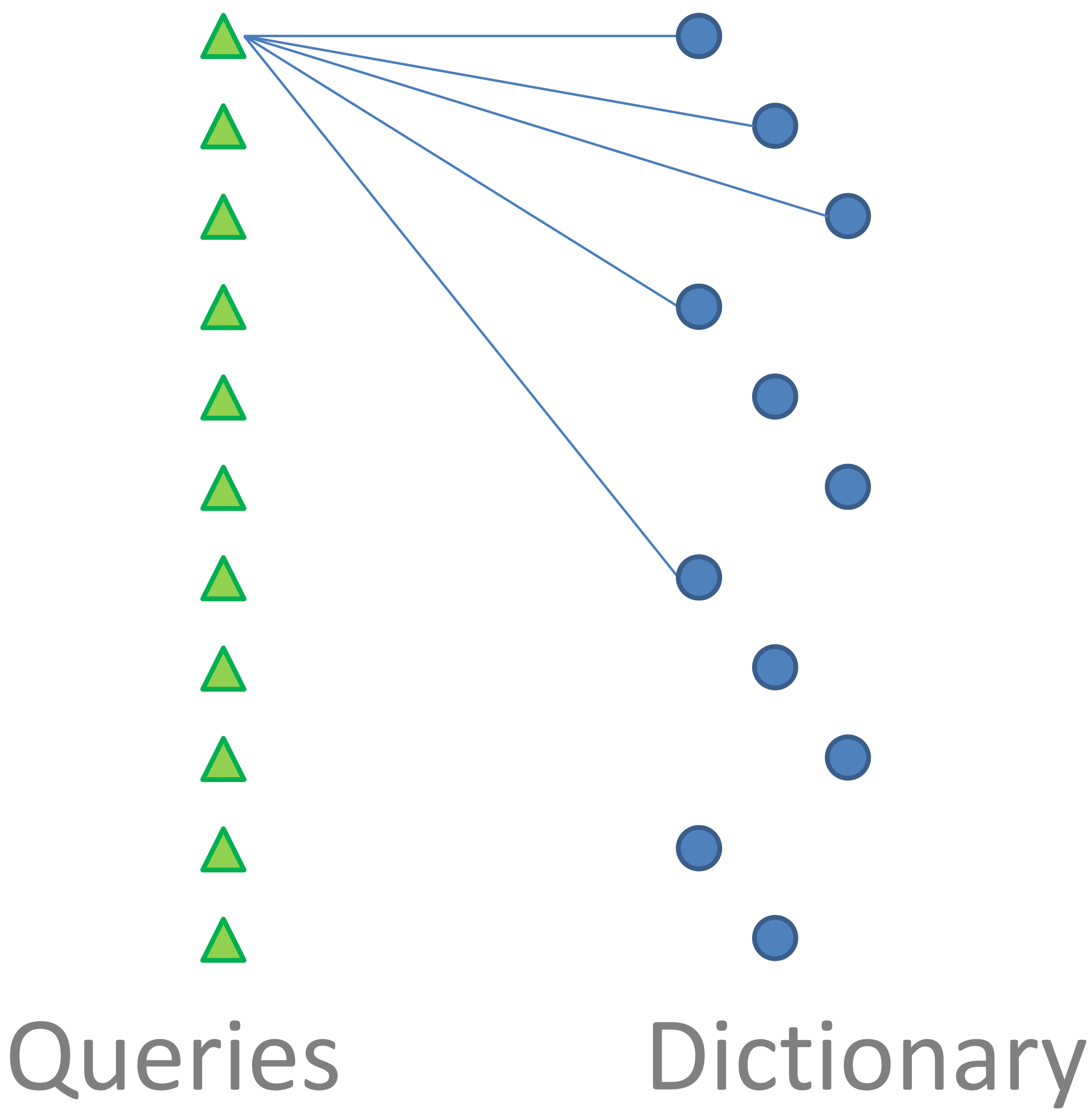
- Notice that each $h : M \to S$ comes with an orthogonal projection $h' : M \to S$
- Also, if $||p, q|| \leq 1$ then by counting, at least one of $h(p) = h(q)$ or $h'(p) = h'(q)$ must hold.
- Thus, by double hashing, all Hamming neighbors of a *k*-mer can be found by looking in just two hash buckets.
  - Better cache-efficiency
  - Cheating by carefully choosing the projection and sorting the buckets gives also processor-efficiency.

Approximate k-mer search

Fast retrieval of Hamming neighbors

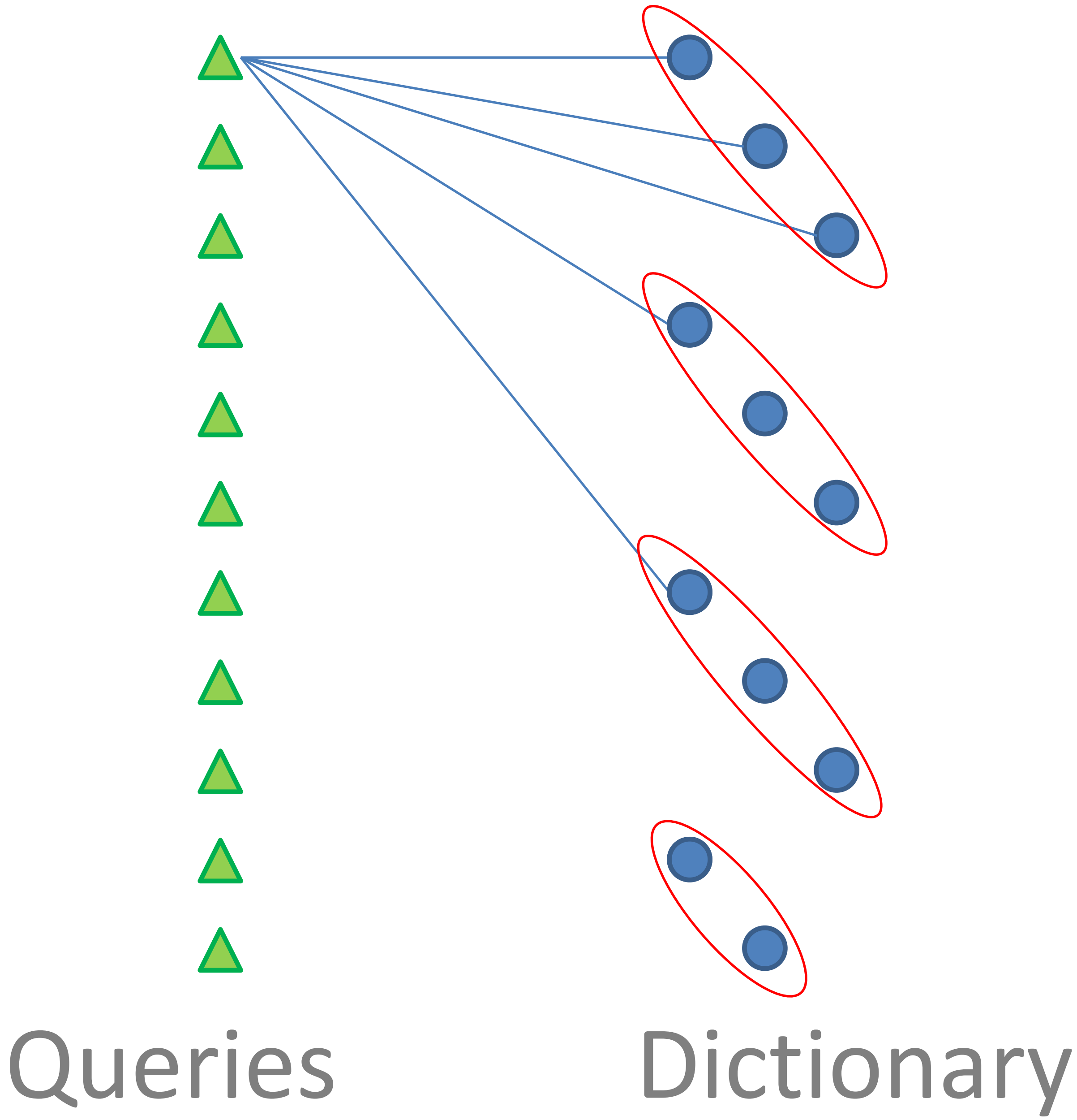


Approximate k-mer search
Fast retrieval of Hamming neighbors



Approximate k-mer search

Fast retrieval of Hamming neighbors

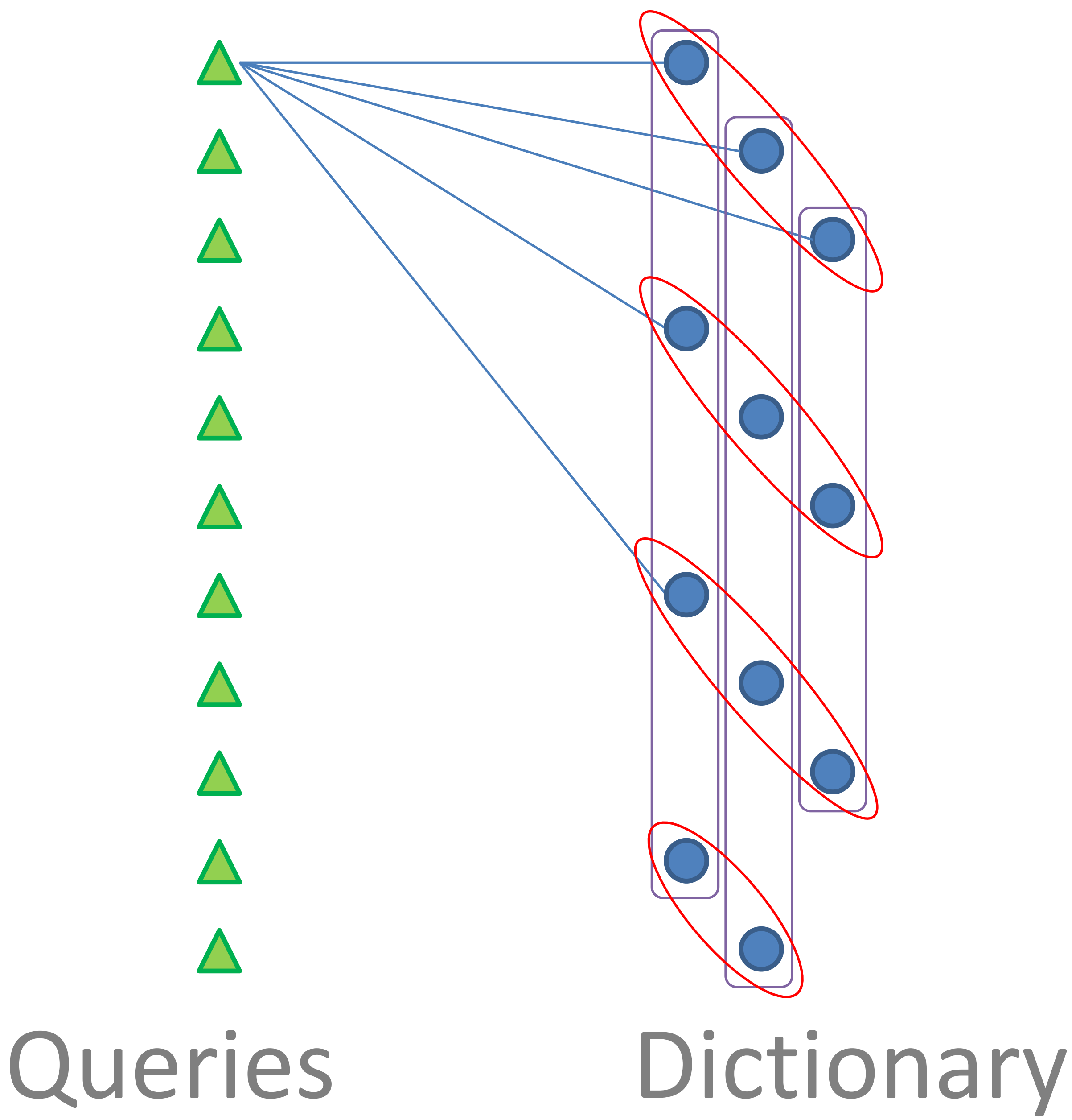


Clustered by front half of k-mer

```
C G G C A G A C
C G G C C G A C
C G G C A G T C
```

Approximate k-mer search

Fast retrieval of Hamming neighbors



Clustered by front half of k-mer

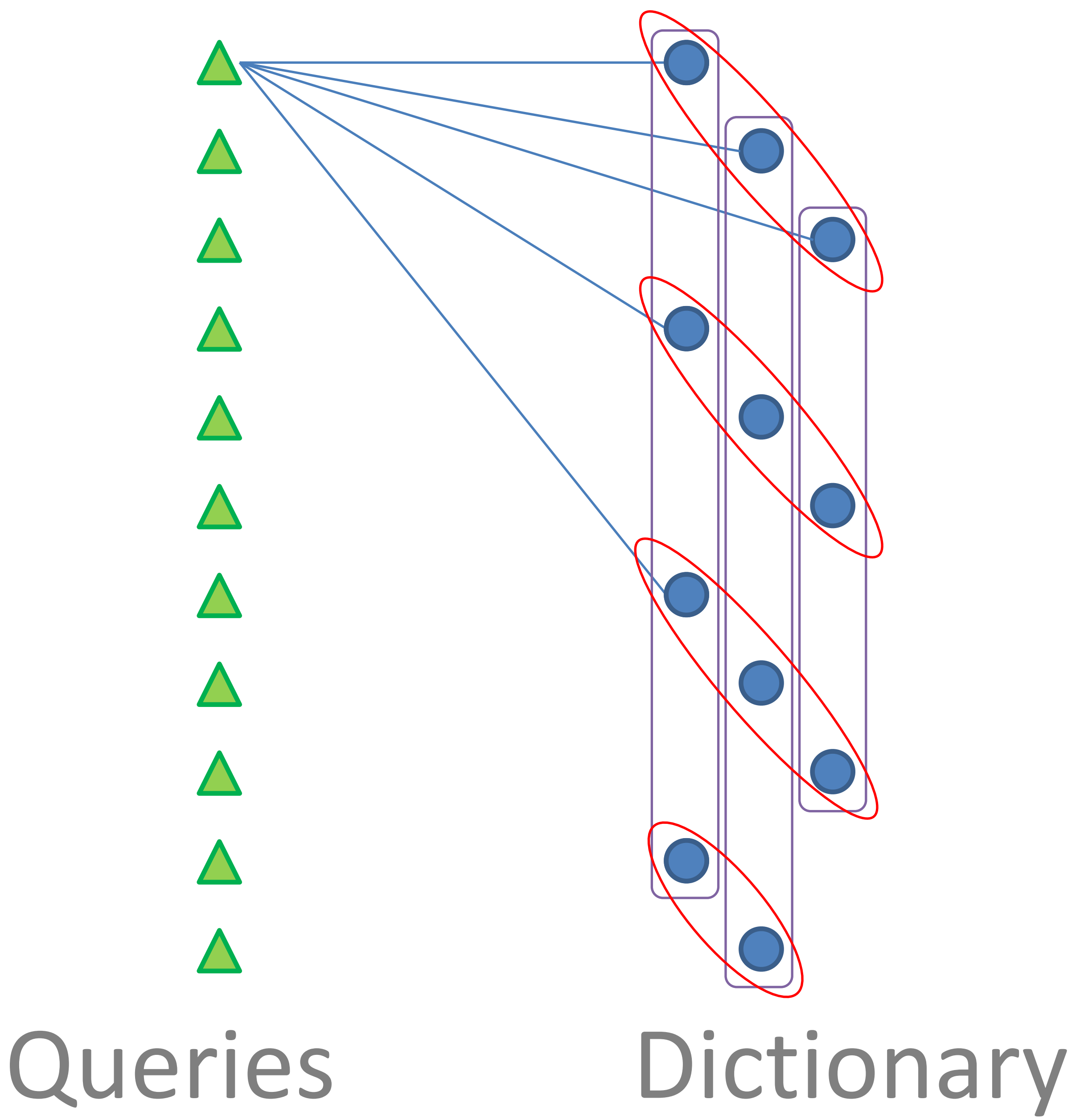
```
C G G C A G A C
C G G C C G A C
C G G C A G T C
```

Clustered by back half of k-mer

```
A G G C A G A C
G G G C A G A C
C C G C A G A C
T A T A A G A C
```

Approximate k-mer search

Fast retrieval of Hamming neighbors



Clustered by front half of k-mer

C G G C A G A C
C G G C C G A C
C G G C A G T C

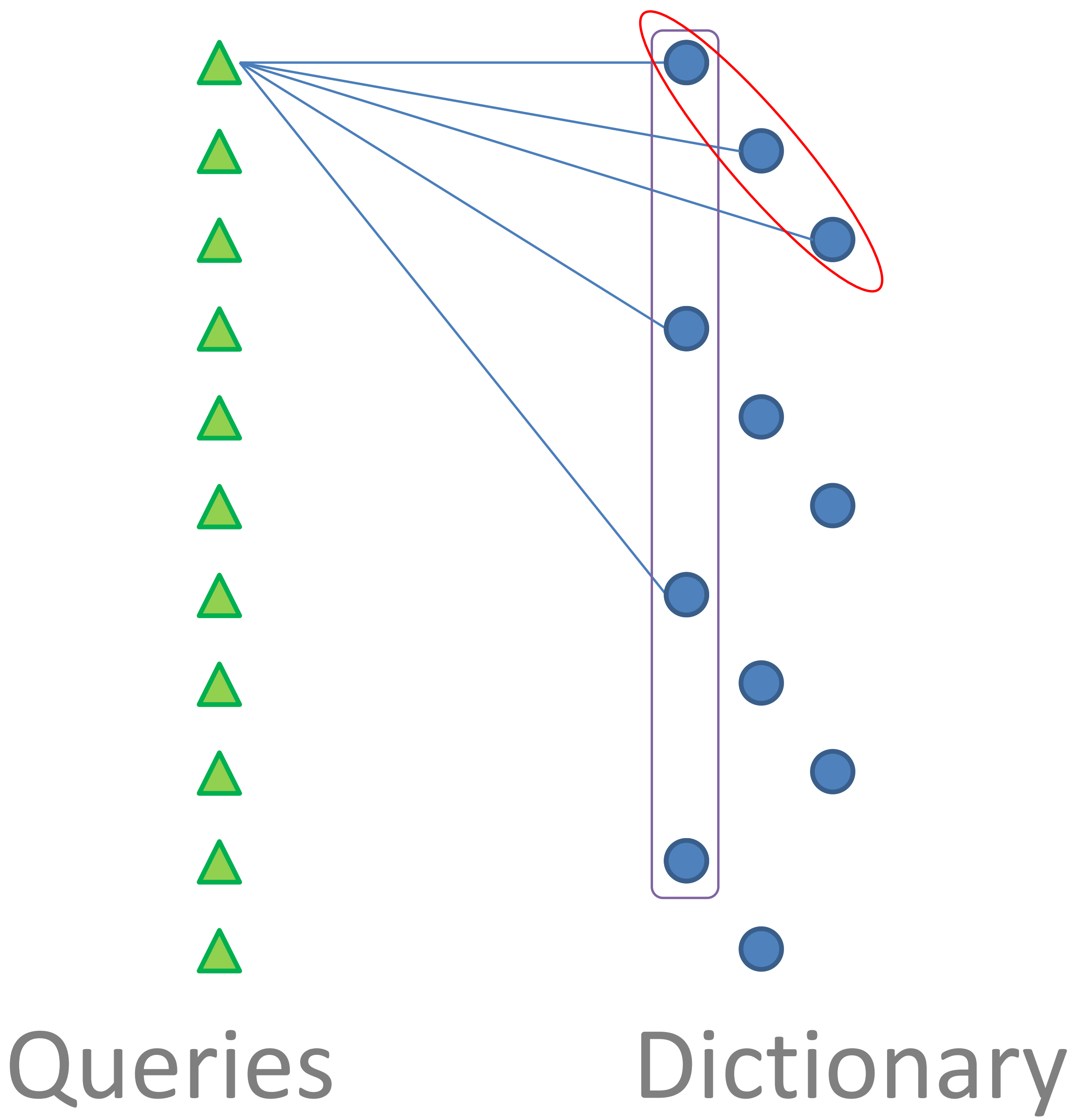
Clustered by back half of k-mer

A G G C A G A C
G G G C A G A C
C C G C A G A C
T A T A A G A C

= C G G C A G A C

Approximate k-mer search

Fast retrieval of Hamming neighbors



Clustered by front half of k-mer

C G G C A G A C
C G G C C G A C
C G G C A G T C

Clustered by back half of k-mer

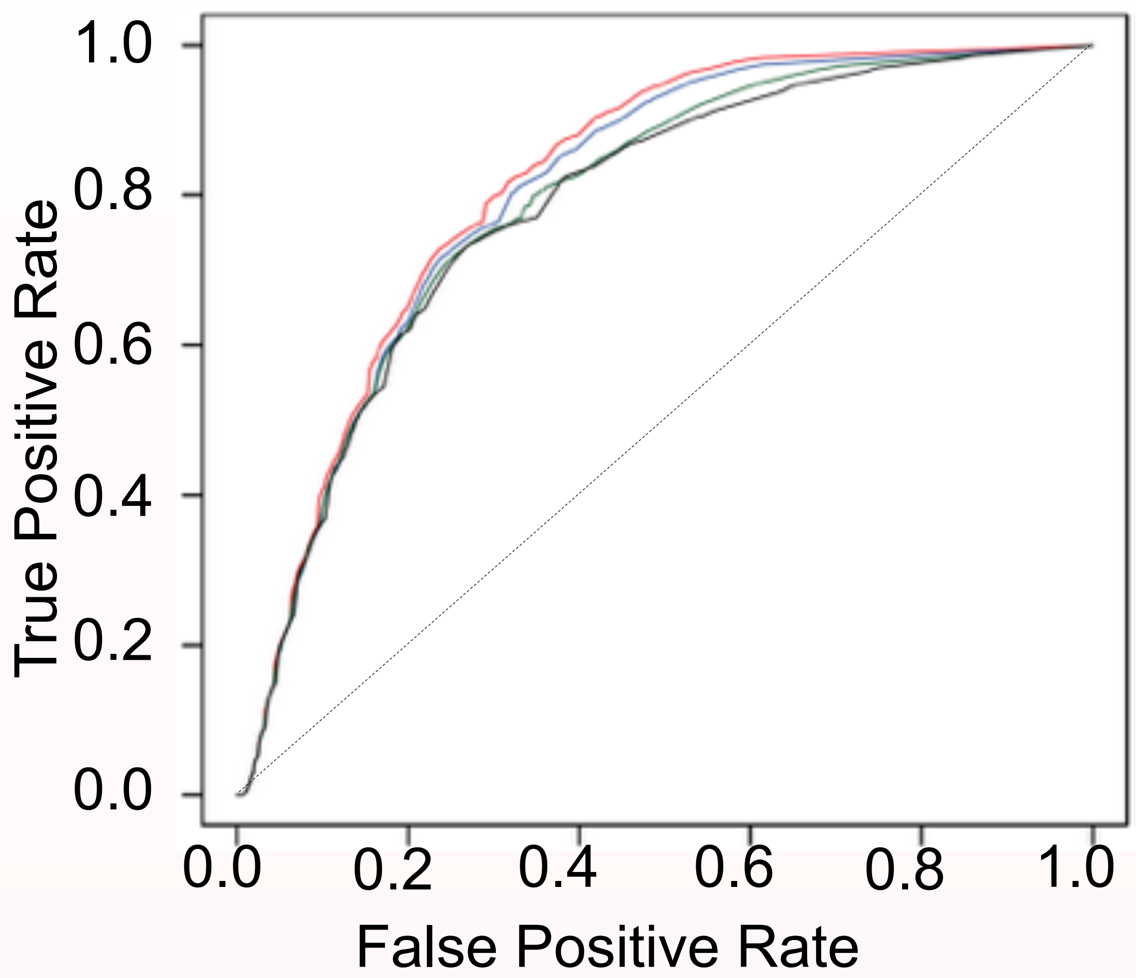
A G G C A G A C
G G G C A G A C
C C G C A G A C
T A T A A G A C

 = C G G C A G A C

Result Highlights

Comparison with other methods

Method	Bits/Q	Time (s)	Area Under ROC Curve
Uncompressed	8	N/A	0.8254
Quartz	0.3564	**2,696**	0.8288
QualComp	0.5940	33,316	0.8053
Janin et al.	0.5376	164,702	0.8019



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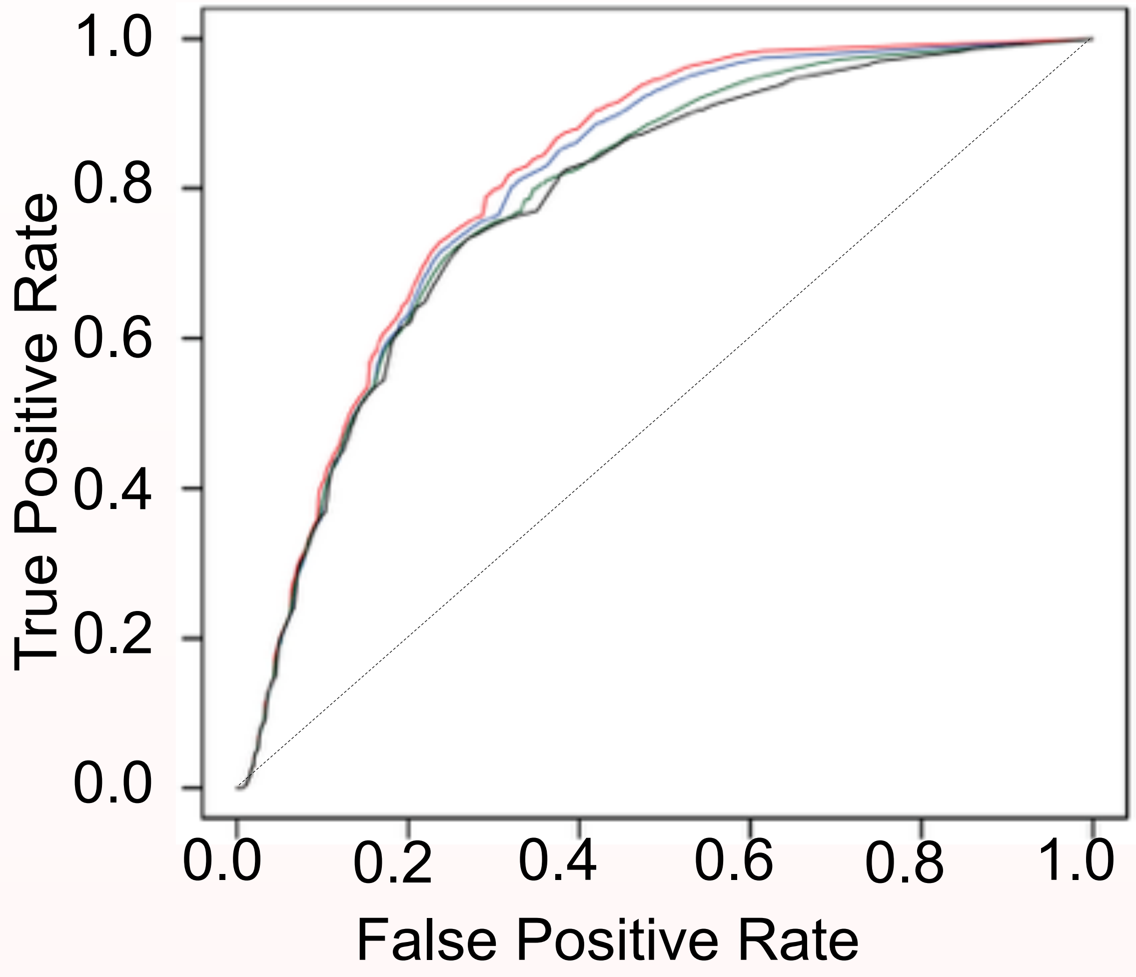


Quartz is orders of magnitude faster

A word on k-mers

MINCE: 15-mers optimal (8-mer labels!)

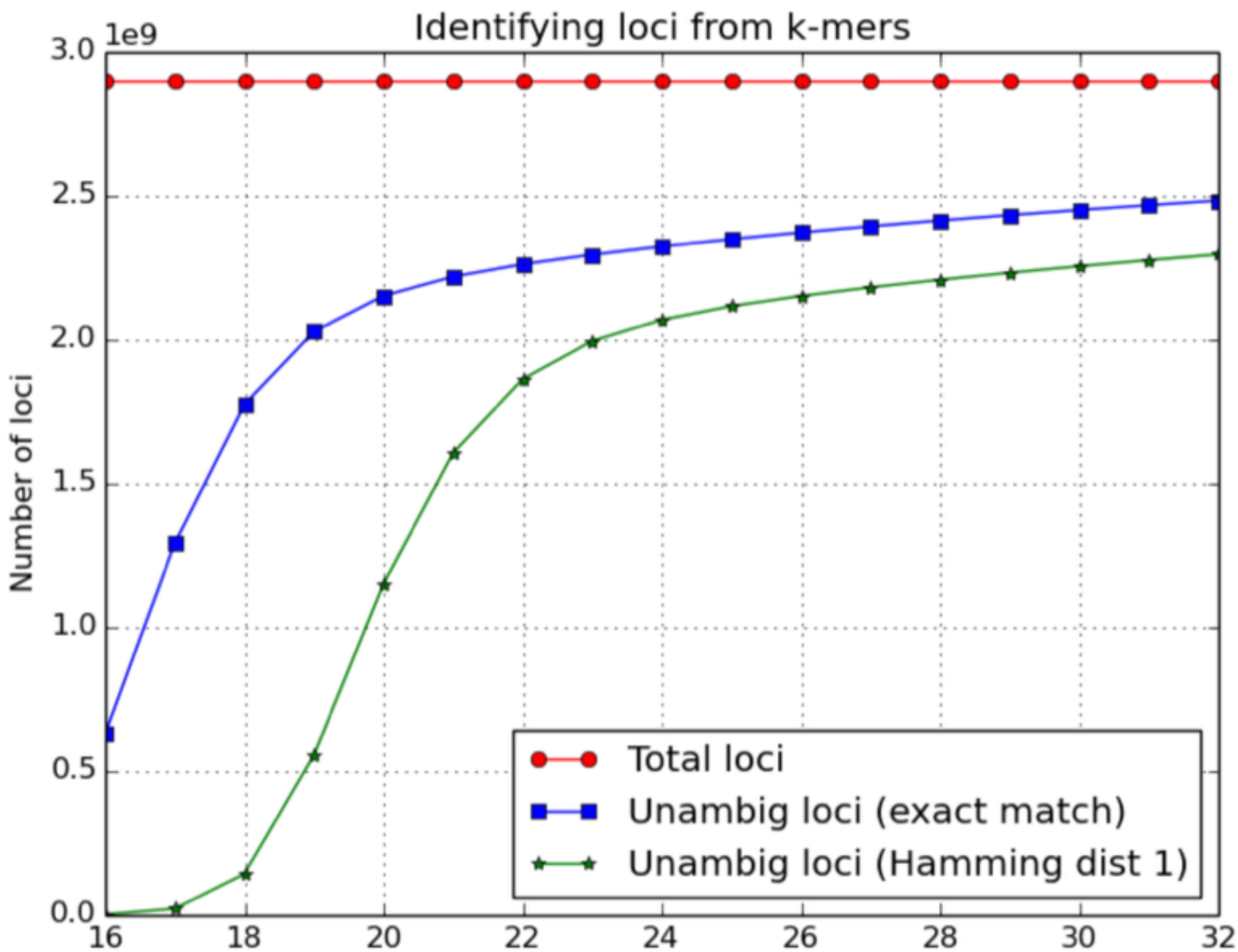
- using labels as search heuristic; don't want too many

Quartz: 32-mers optimal

- in a genome, most 8-mers may exist; most 32-mers will not
- and they tend to be unique

	k=16	k=32
unique	21.8%	85.7%
unique at Hamming 1	0.0008%	79.3%

Uniqueness of k-mers (hg19)



Why not longer k-mers?

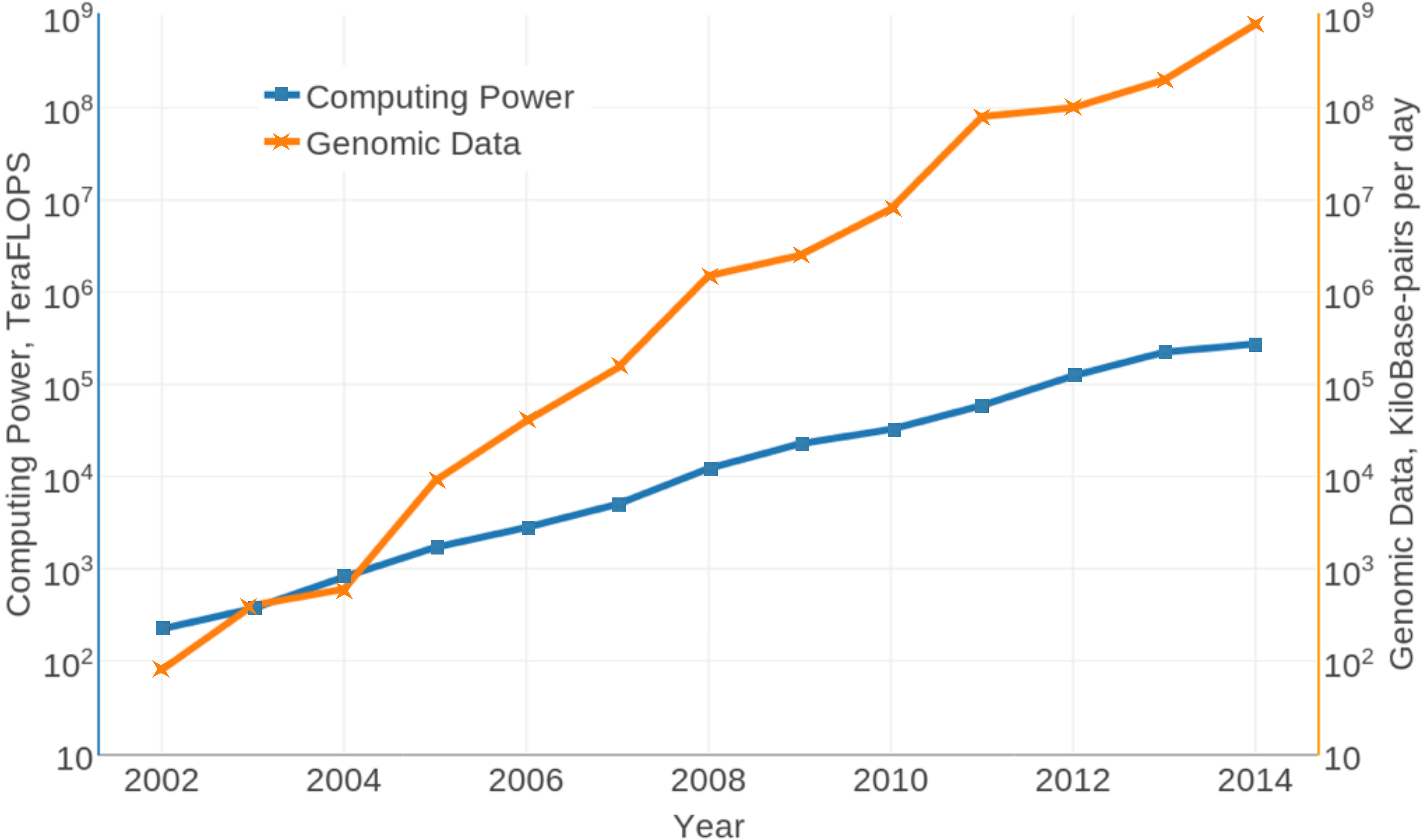
Want to ensure at most 1 sequencing error per k-mer

Assume independence of errors
Error rate of p

Likelihood of l errors $\binom{k}{l}(1-p)^{k-l}p^l$

1% error rate			2% error rate		
k=32	l≥2	2%	k=32	l≥2	13%
k=64	l≥2	13%	k=64	l≥2	36%

Compression for speed



Compressive genomics

caBLAST [Loh, et al. 2012]

caBLASTP [Daniels, et al. 2013]

BLAST uses seed-and-extend

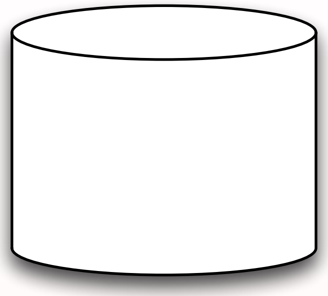
but must extend on many fruitless seeds

Use compression to reduce the search space

How does this compression work?

How does this compression work?

Coarse Database

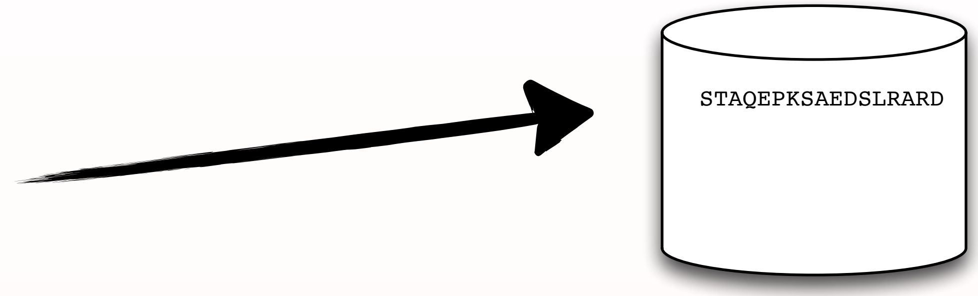


STAQEPKSAEDSLRARD

How does this compression work?

Coarse Database

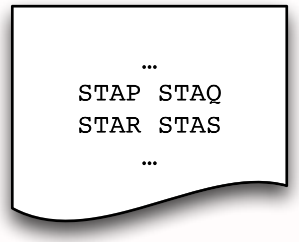
STAQEPKSAEDSLRARD



How does this compression work?

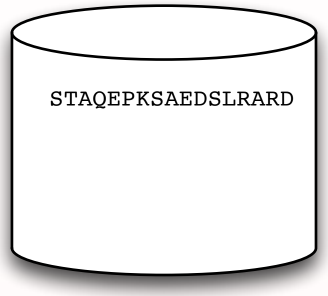
How does this compression work?

Seed Table



STAQEPKSAEDSLRARD

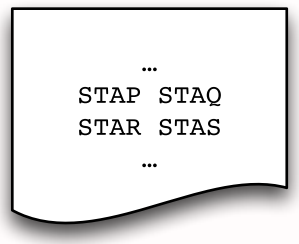
Coarse Database



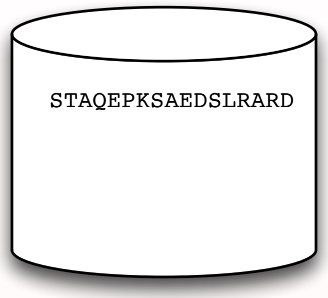
LQSTAQEPKSAEQRDSVNARDRQRNVIIAQE

How does this compression work?

Seed Table



Coarse Database



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LQSTAQEPKSAEQRDSVNARDRQRNVIIAQE

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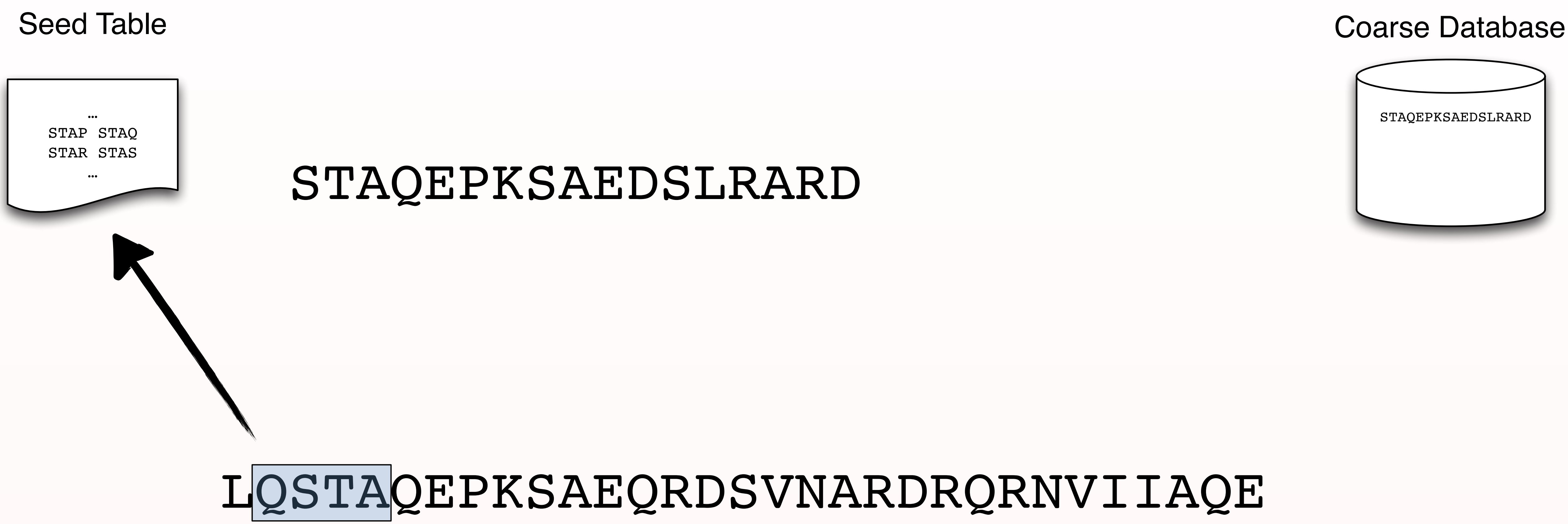

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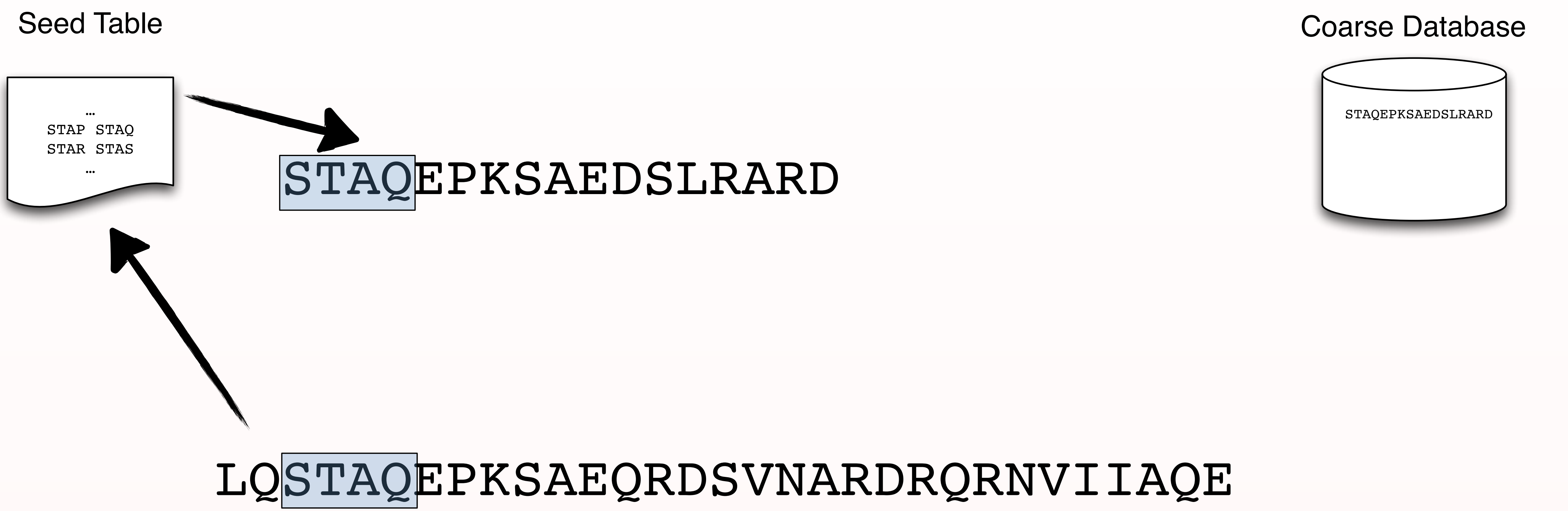


How does this compression work?

Seed Table

…
STAP STAQ
STAR STAS
…

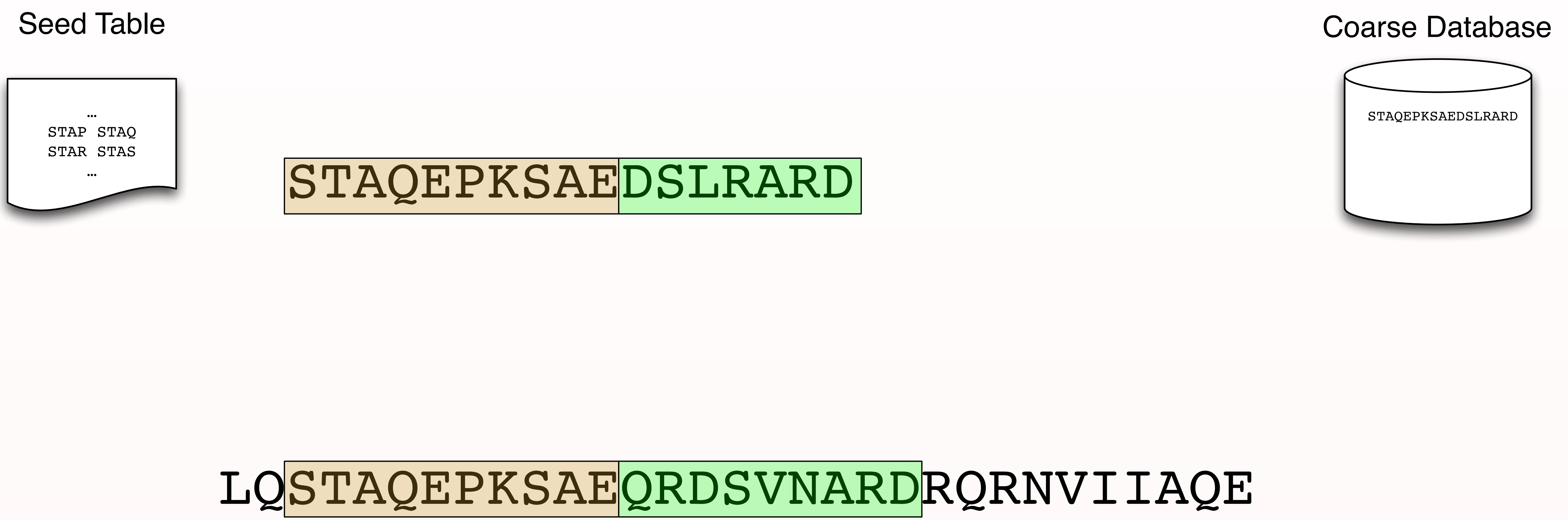
Coarse Database

STAQEPKSAEDSLRARD

$\boxed{\texttt{STAQEPKSAE}}\texttt{DSLRARD}$

$\texttt{LQ}\boxed{\texttt{STAQEPKSAE}}\texttt{QRDSVNARDRQRNVIIAQE}$

How does this compression work?



How does this compression work?

Seed Table

…
STAP STAQ
STAR STAS
…

Coarse Database

STAQEPKSAEDSLRARD

STAQEPKSAEDSLRARD

--DSLRARD

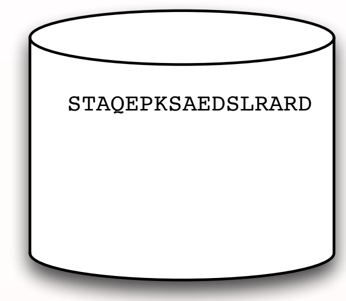
QRDSVNARD

LQSTAQEPKSAEQRDSVNARDRQRNVIIAQE

How does this compression work?

Seed Table

Coarse Database



STAQEPKSAEDSLRARD

--DSLRARD

QRDSVNARD

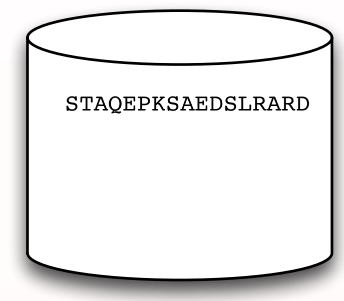
LQSTAQEPKSAEQRDSVNARDRQRNVIIAQE

LQ QR VN

How does this compression work?

Seed Table

Coarse Database



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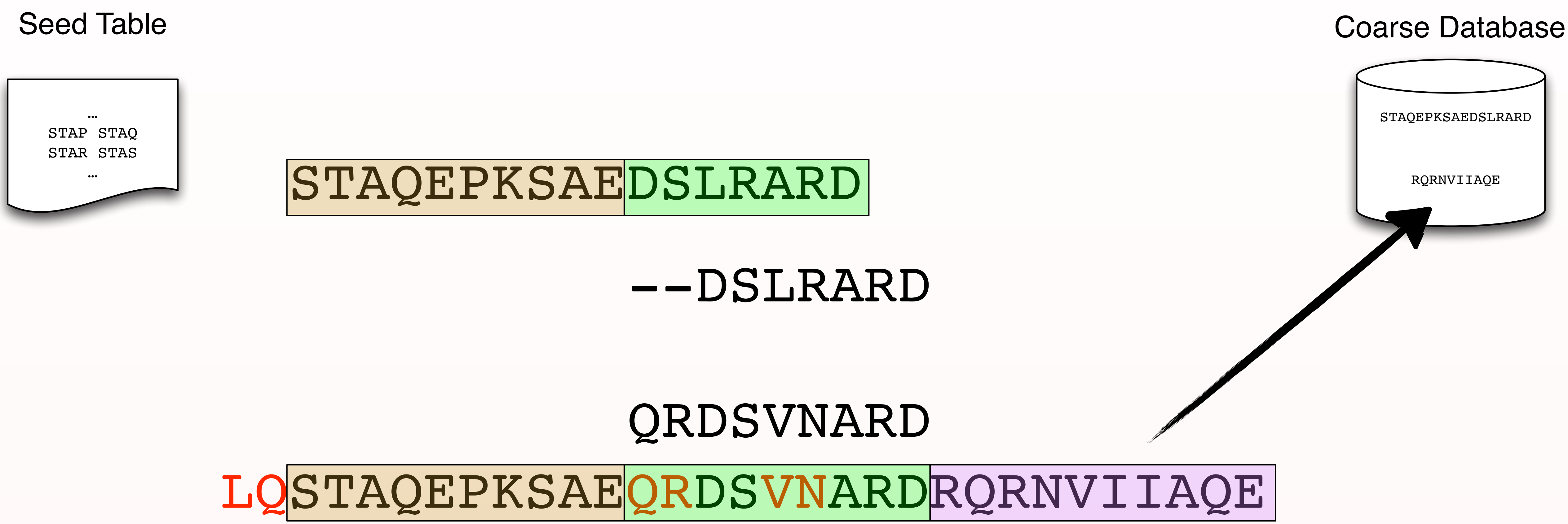

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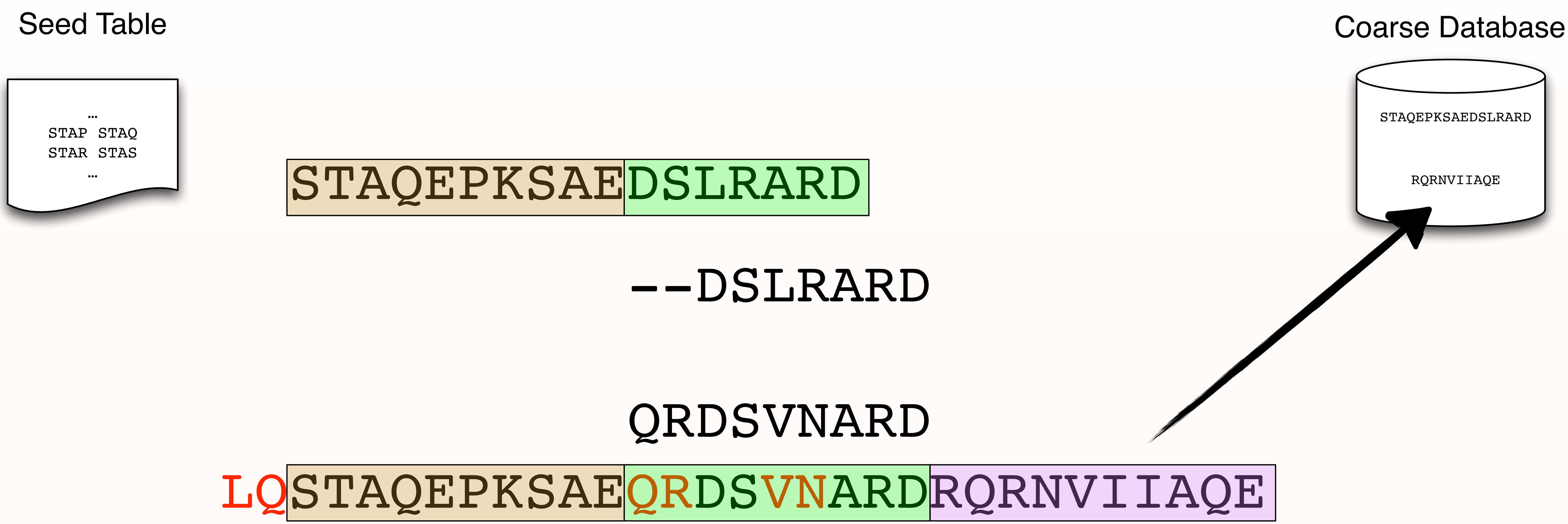


Lossless compression!

How does compressed search work?

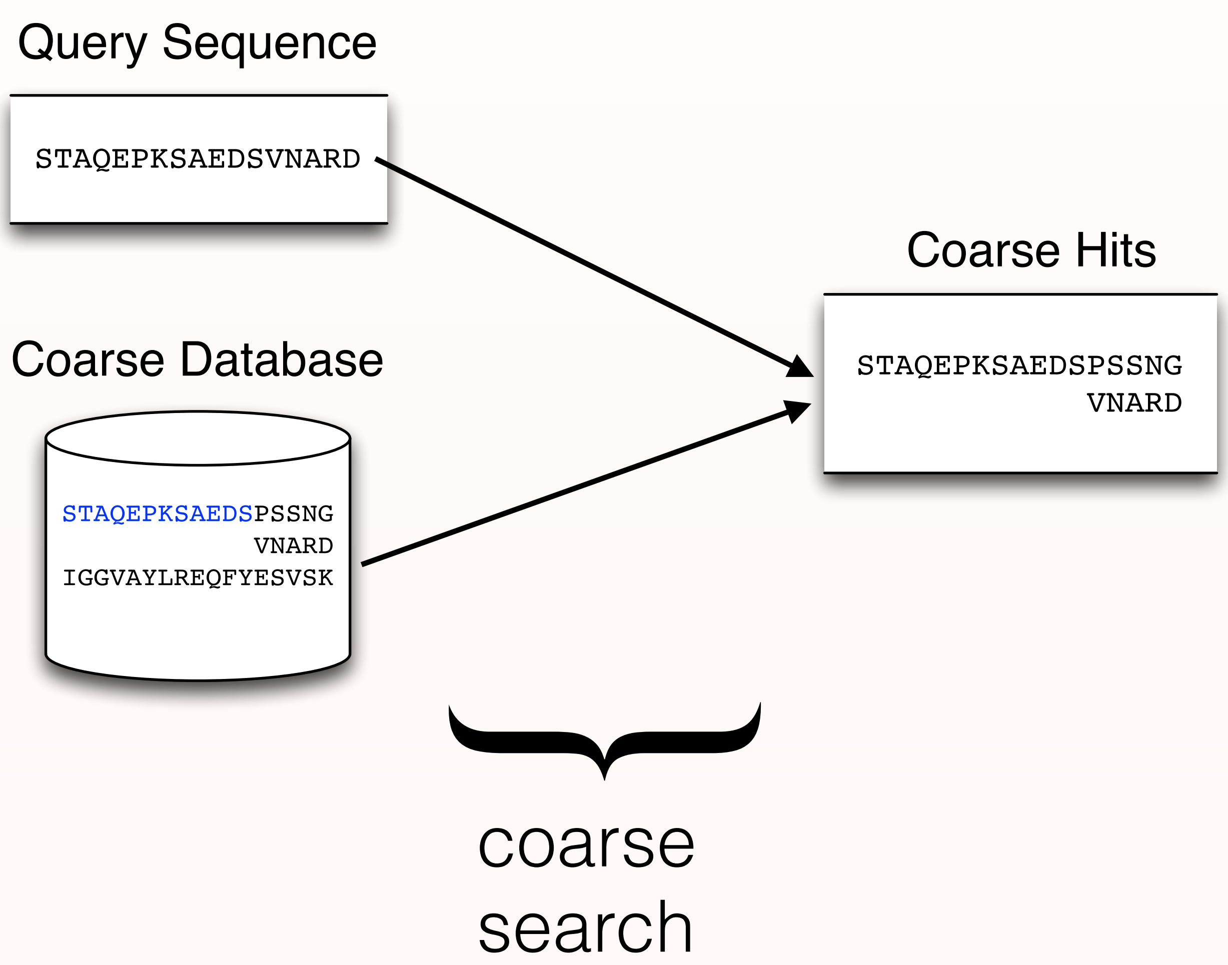
How does compressed search work?

Query Sequence

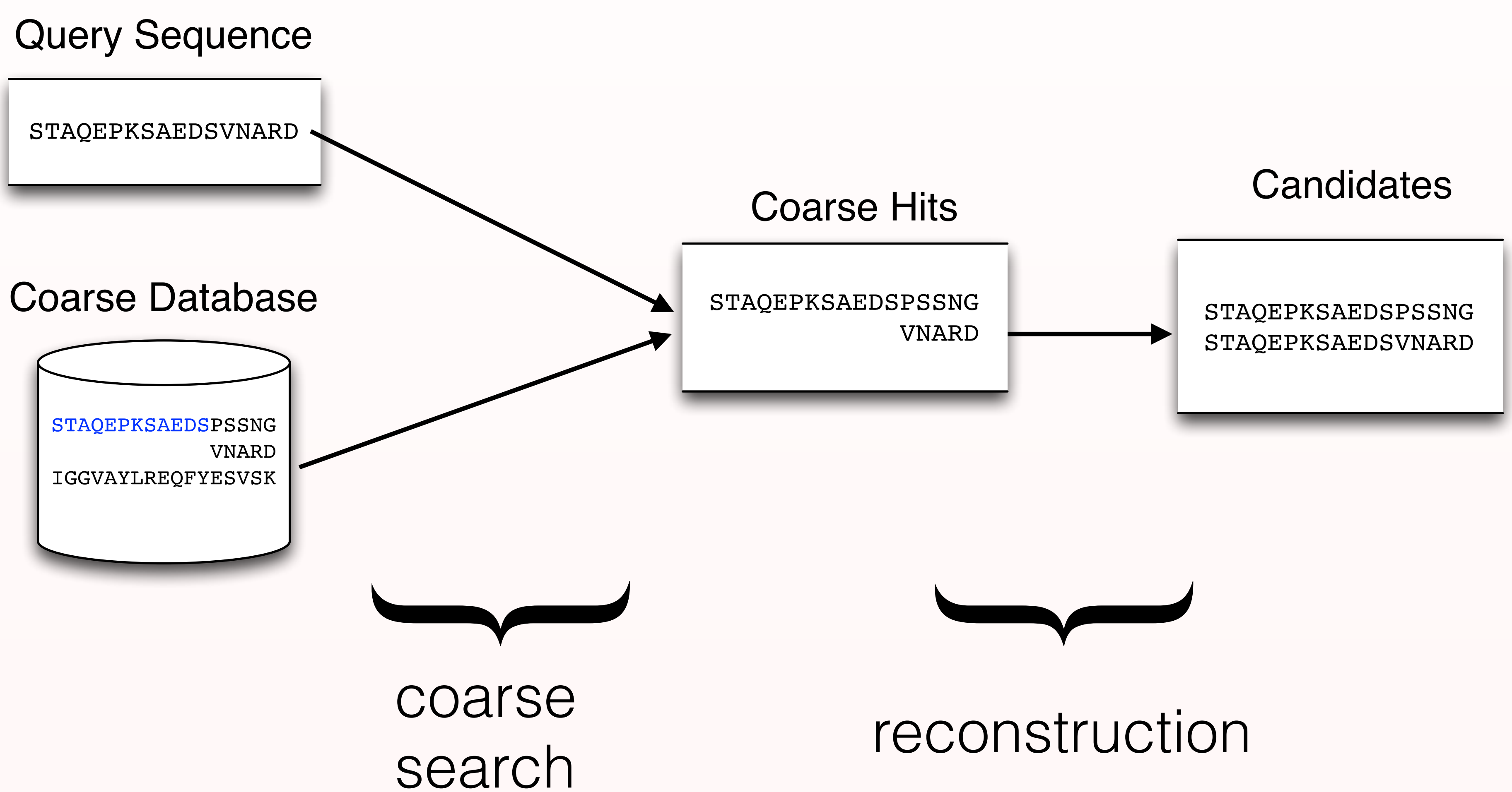
STAQEPKSAEDSVNARD

Coarse Database

How does compressed search work?



How does compressed search work?



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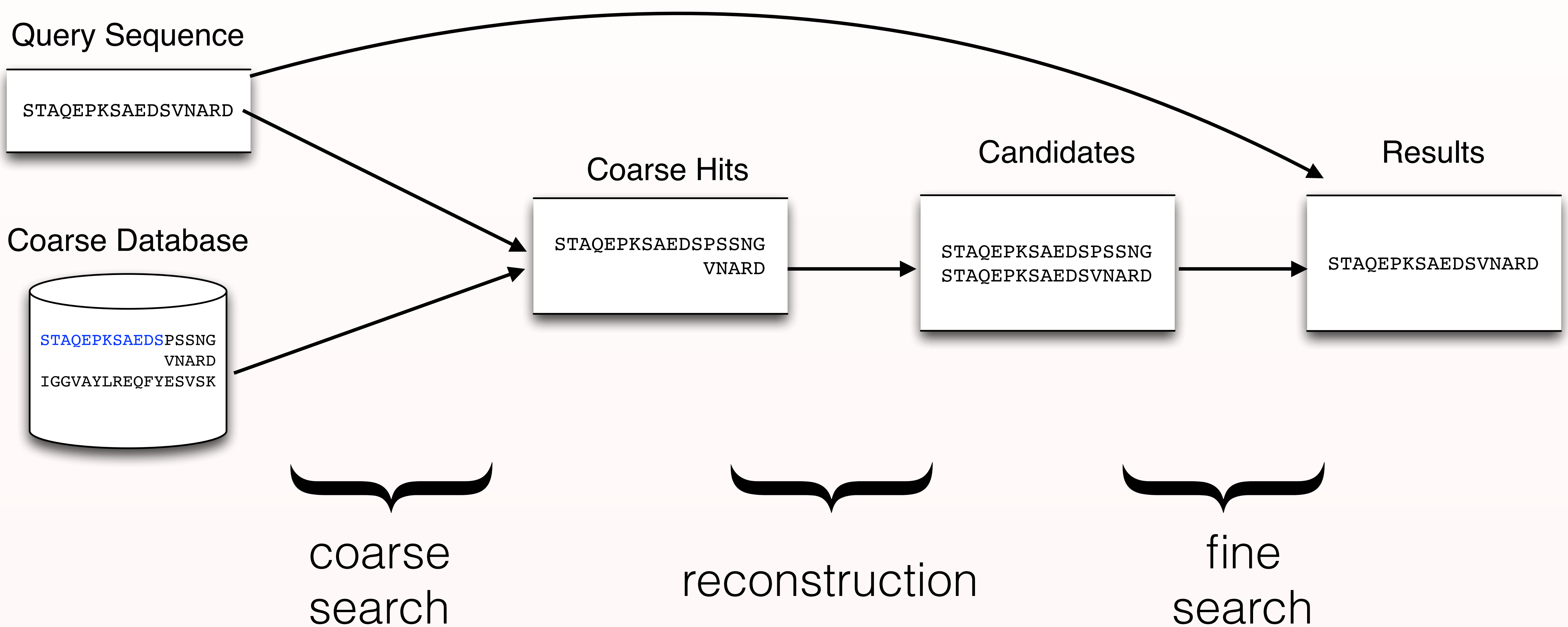
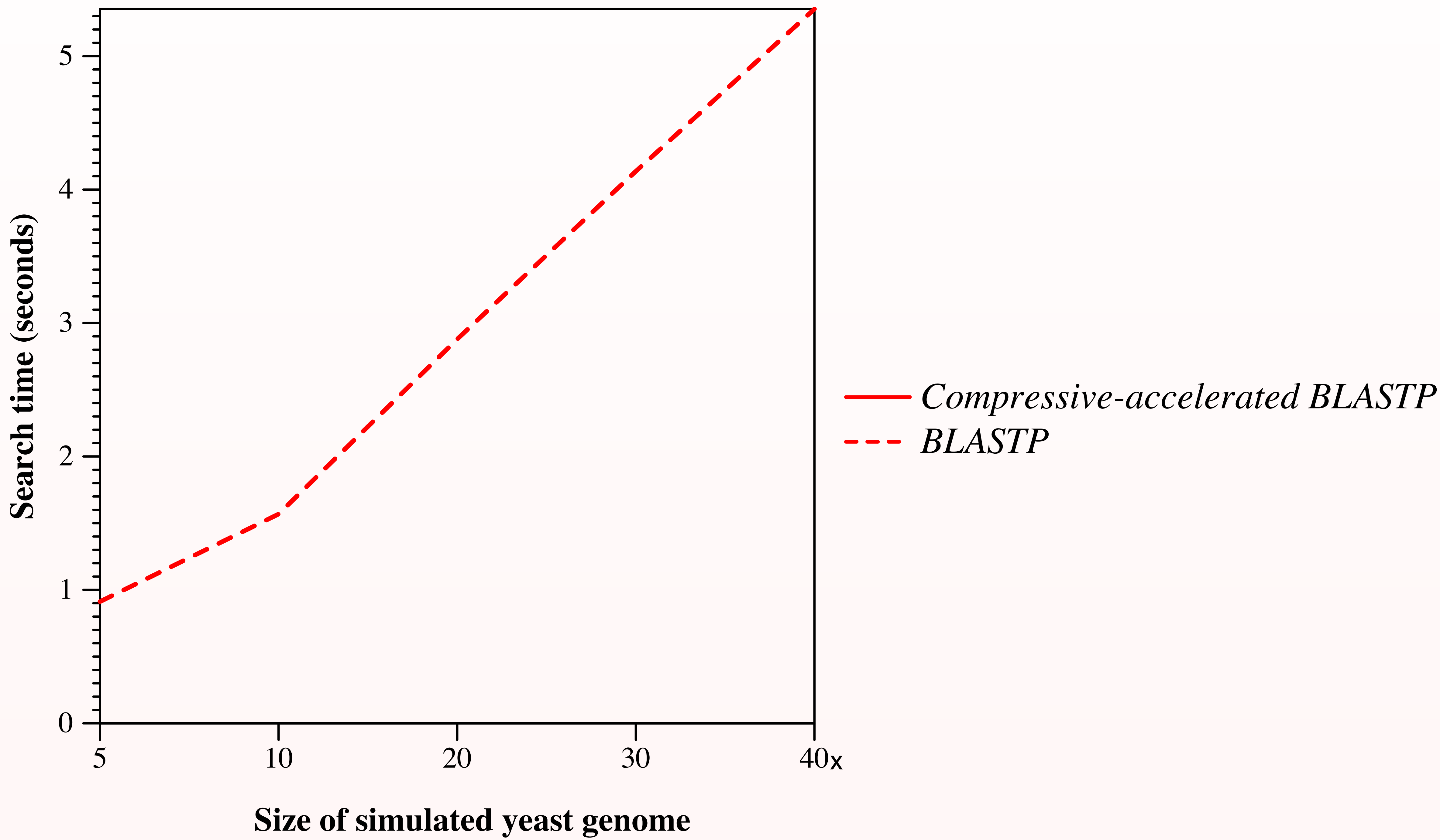
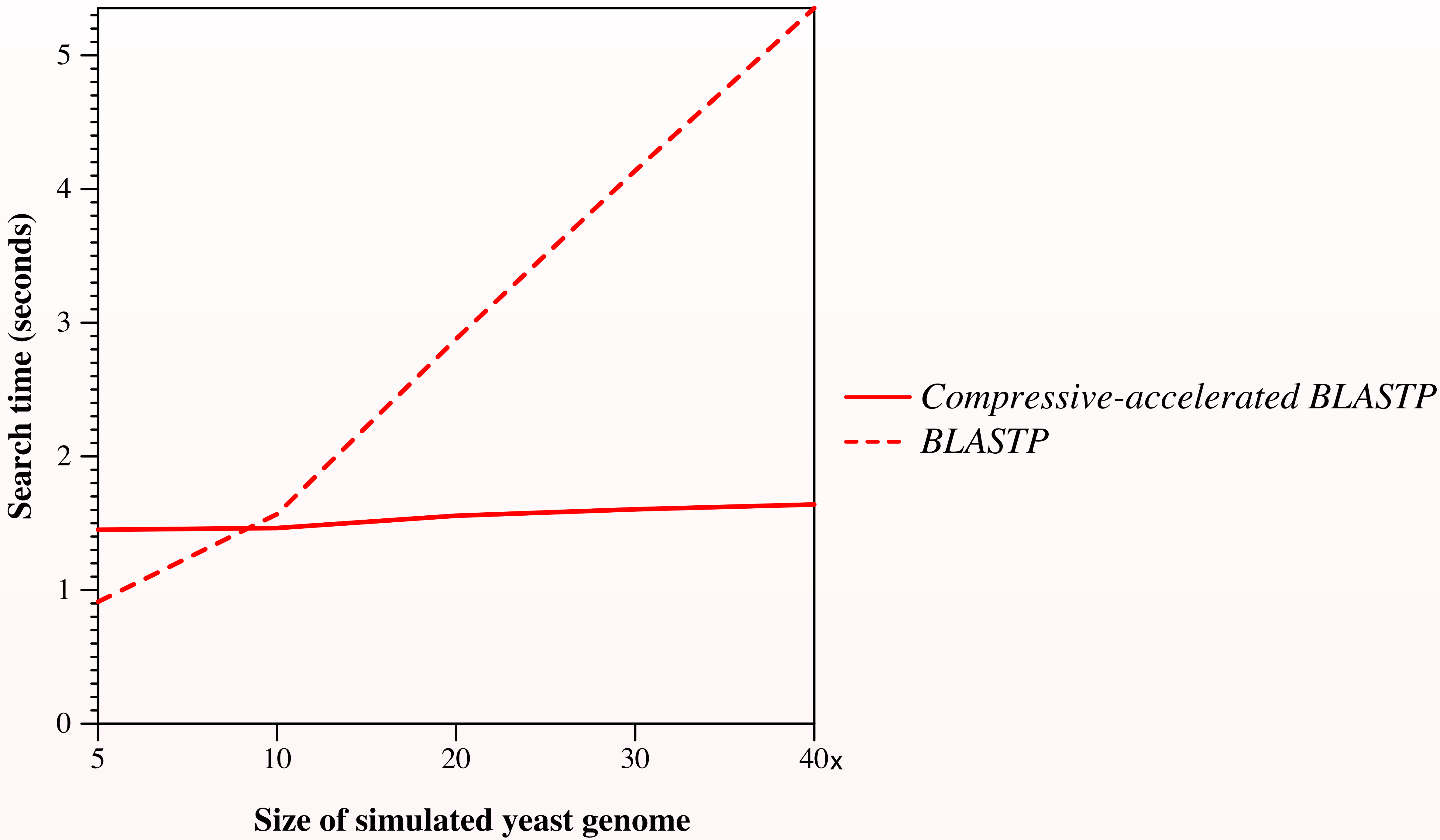


Simulated data growth



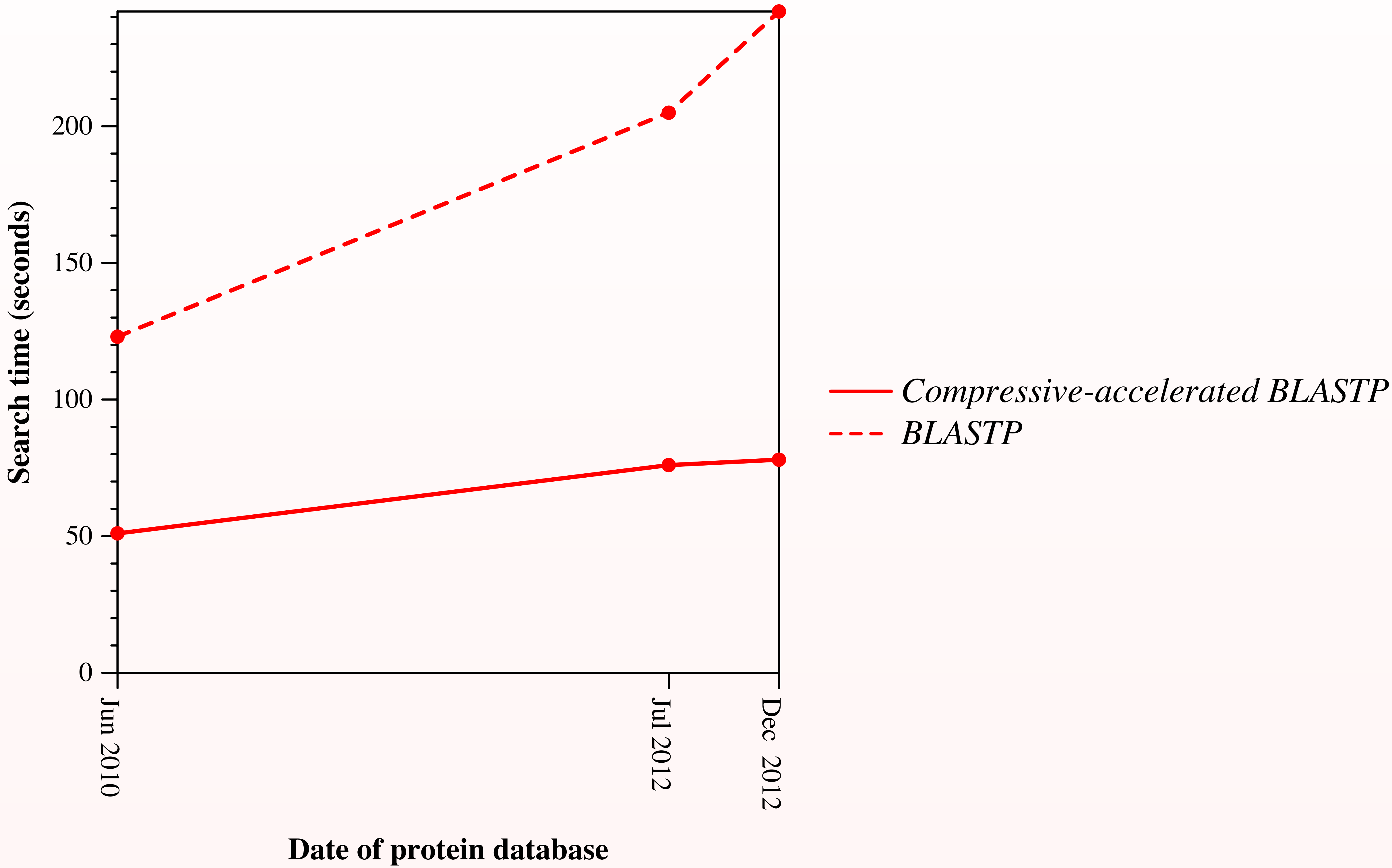
Daniels, Gallant, Peng, Baym, Cowen, Berger 2013

Simulated data growth

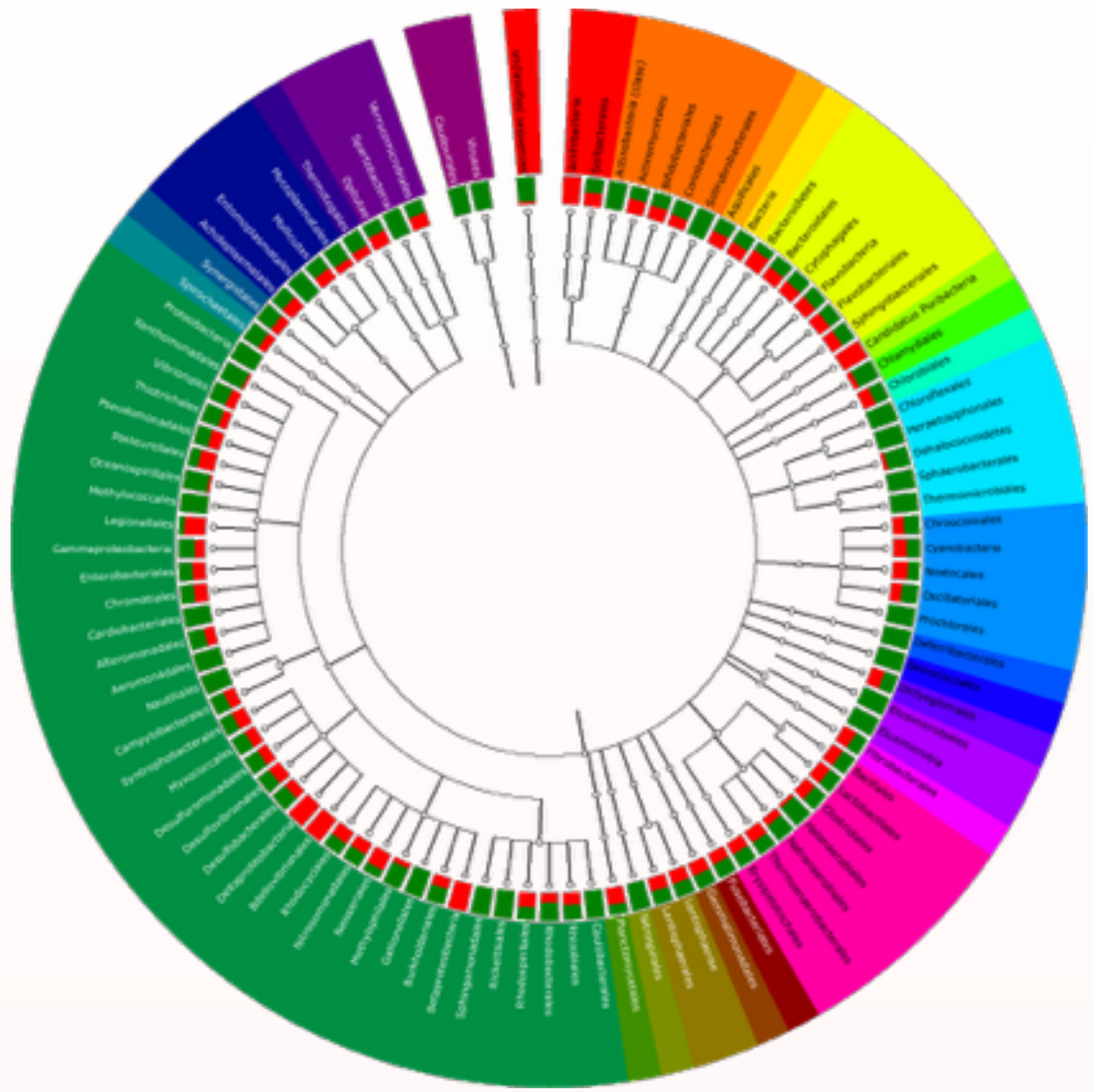


Daniels, Gallant, Peng, Baym, Cowen, Berger 2013

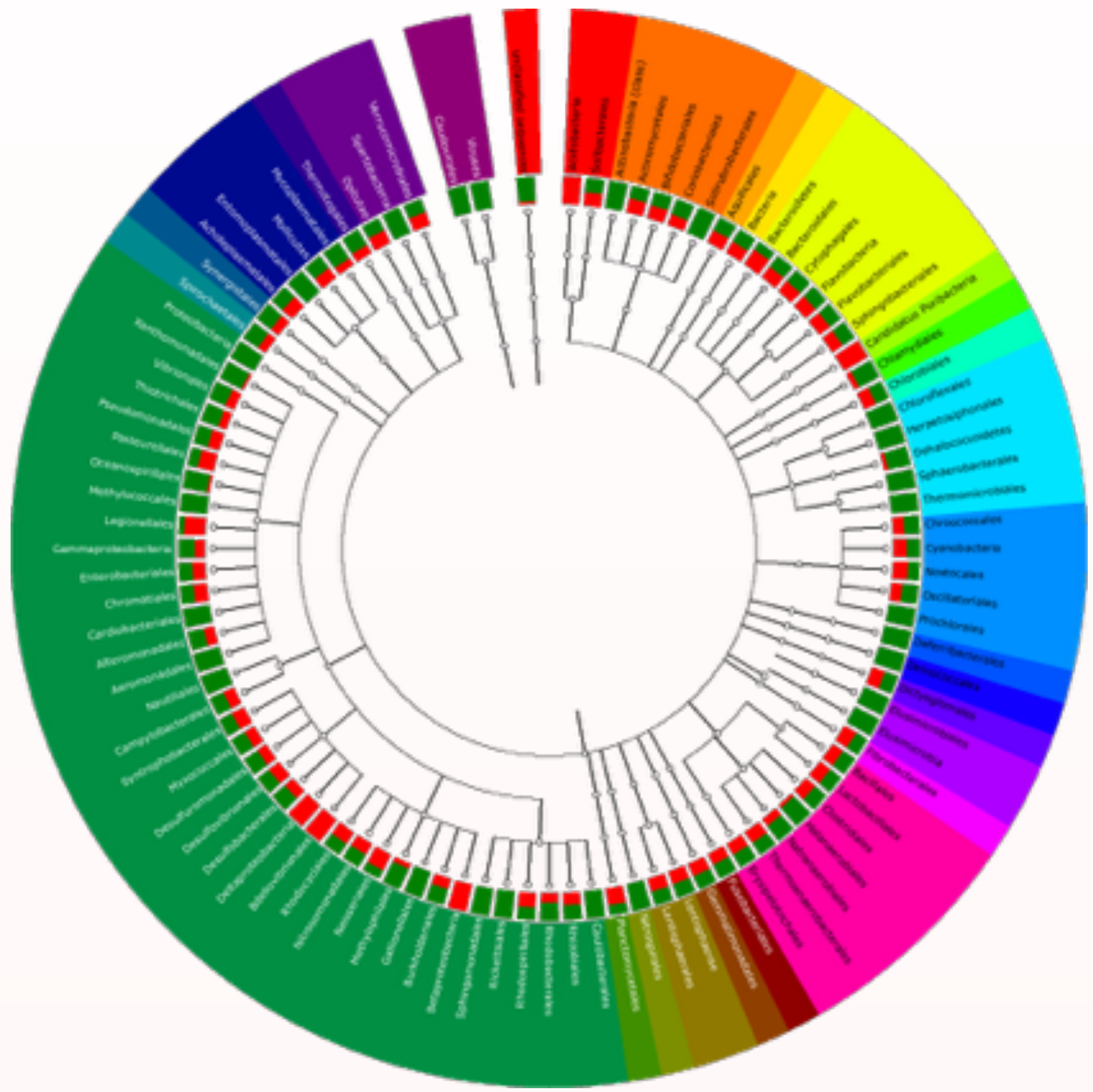
Real data growth on a protein database



Metagenomics



Metagenomics



Problem: Given reads from a microbiome, match each read with similar proteins.

BLASTX [Altschul, et al. 1990]
RapSearch2 [Zhao, et al. 2012]
DIAMOND [Buchfink, et al. 2015]

Metagenomics

BLASTX [Altschul, et al. 1990]
RapSearch2 [Zhao, et al. 2012]
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Metagenomics

Metagenomic Reads

```
>read1
ACGTGGCTATCAACTCGCTAACTAA
>read2
ACGTGGCTATCAACTCGCTAACTAA
>read3
ACGTGGCTATCAACTCGCTAACTAT

...

>readk
TCGTCGAACTACATTACATTTACAG
>readk+1
TCGTCGAACTACATTACAAATACAG

...

>readm
GCTCGGACTATATATAGGCCTAGAA
...
```

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Metagenomics

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...

>readk
TCGTCGAACTACATTACATTTACAG
>readk+1
TCGTCGAACTACATTACAAATACAG

...

>readm
GCTCGGACTATATATAGGCCTAGAA
...
```

Translated ORFs

```
>read1-1
TWLSTR
>read1-2
RGYQLAN
>read1-3
VAINSLT
>read1-r1
LVSELIAT
>read1-r2
LAS
>read1-r3
RVDSH
>read2-1
SSNYITFT
>read2-2
RRTTLHLQ
>read2-3
VELHYIY
>read2-r1
CSST
>read2-r2
CKCNVVRR
>read2-r3
VNV
...
```

BLASTX [Altschul, et al. 1990]
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Metagenomics

Metagenomic Reads

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>read2-2
RRTTLHLQ
>read2-3
VELHYIY
>read2-r1
CSST
>read2-r2
CKCNVVRR
>read2-r3
VNV
...
```
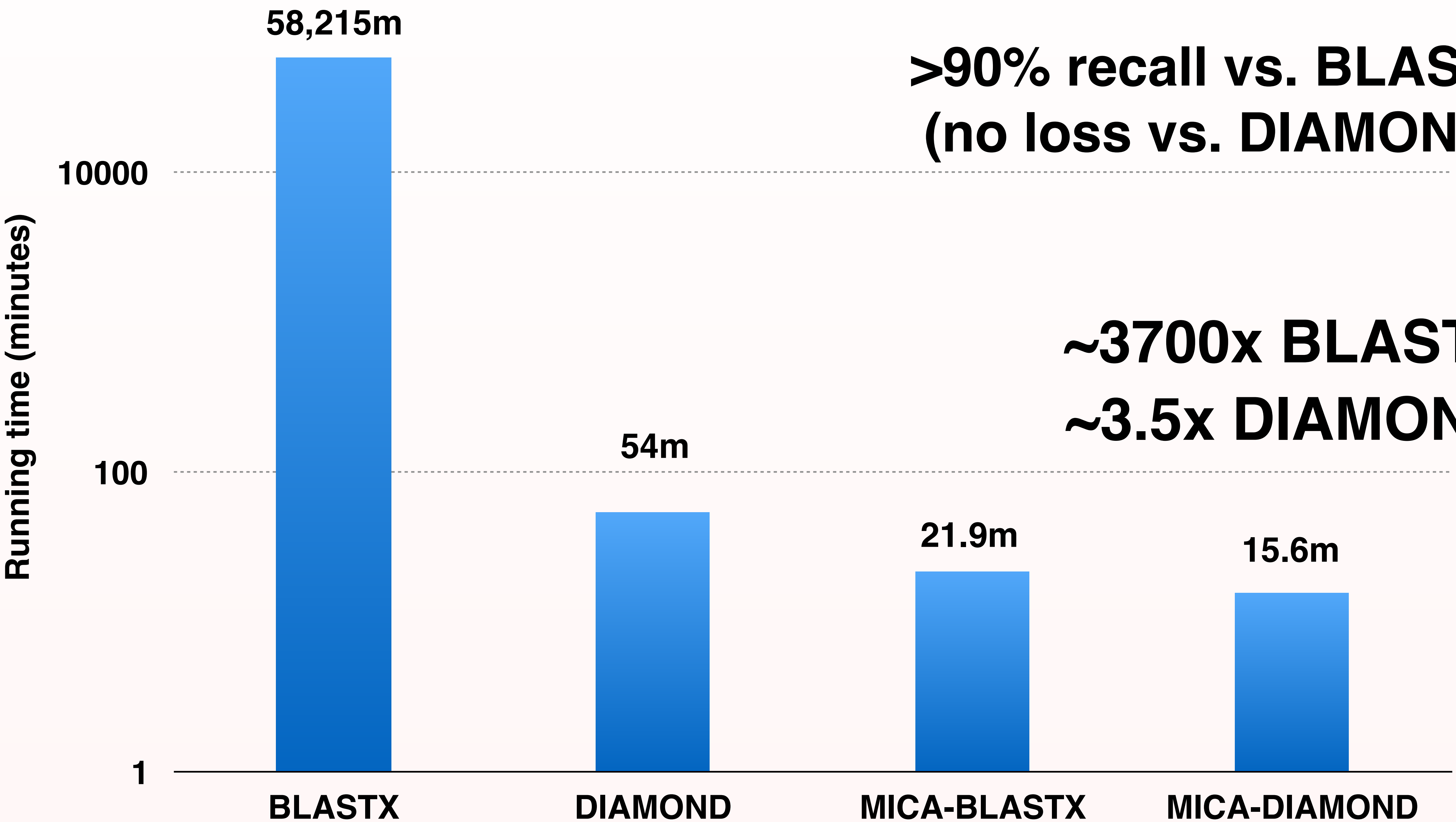

Protein Database (NR)

```
>protein 1
MRVLVINSGSSSIKYQLIEM
>protein 2
EILGKKLEELKIITCHIGNGASVAAVKY
>protein 3
LKKLLESSGCRLVRYGNILIG
...
```

BLASTX [Altschul, et al. 1990]
RapSearch2 [Zhao, et al. 2012]
DIAMOND [Buchfink, et al. 2015]

MICA [Yu, Daniels, et al. 2015]



>90% recall vs. BLASTX (no loss vs. DIAMOND)

~3700x BLASTX
~3.5x DIAMOND

American gut microbiome project NGS reads, searching NCBI NR database

Compression = clustering

Compression = clustering

Cluster similar entities

Compression = clustering

Cluster similar entities

or sub-entities

Compression = clustering

Cluster similar entities

or sub-entities

Only store the common parts once

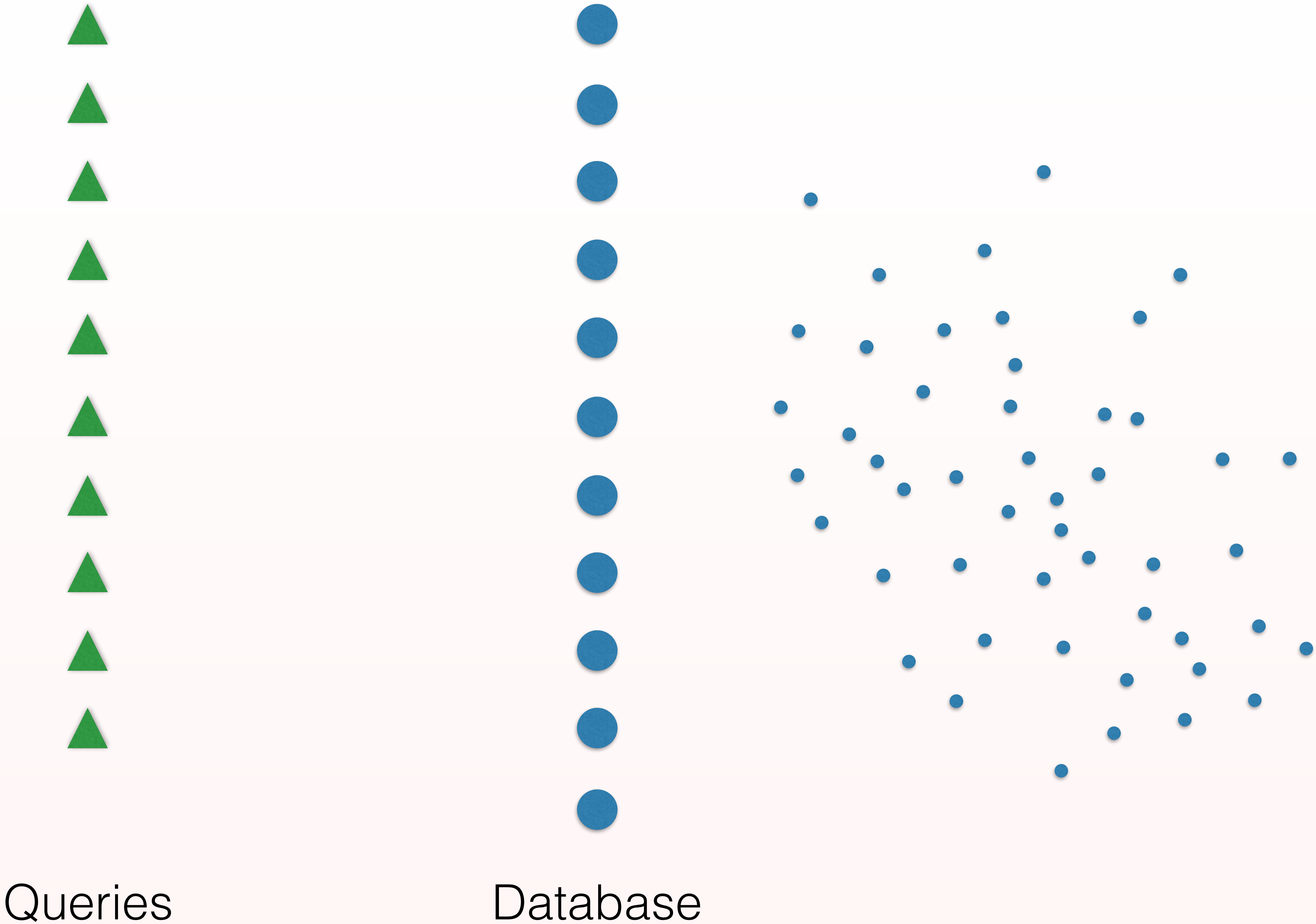
Compression = clustering

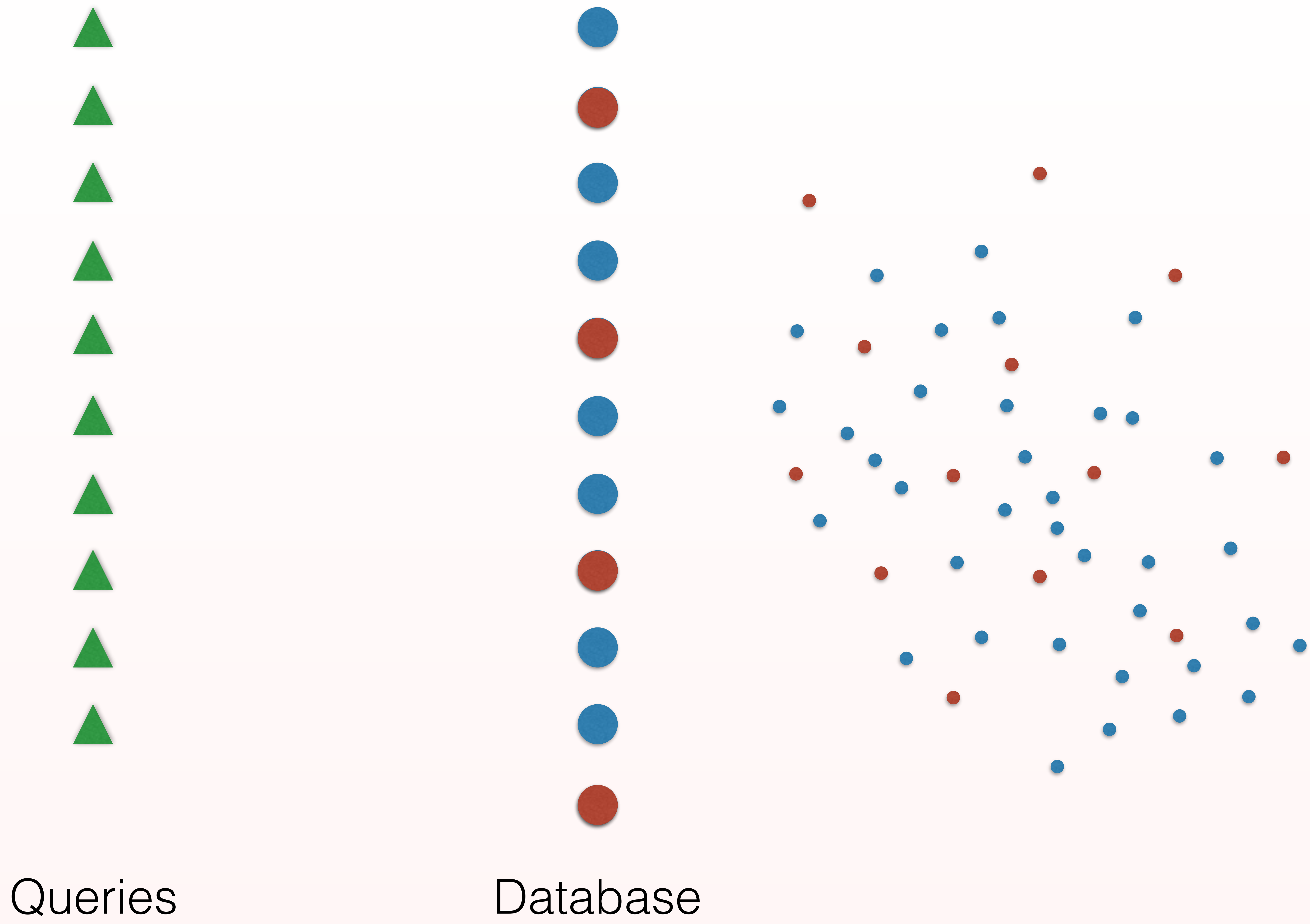
Cluster similar entities

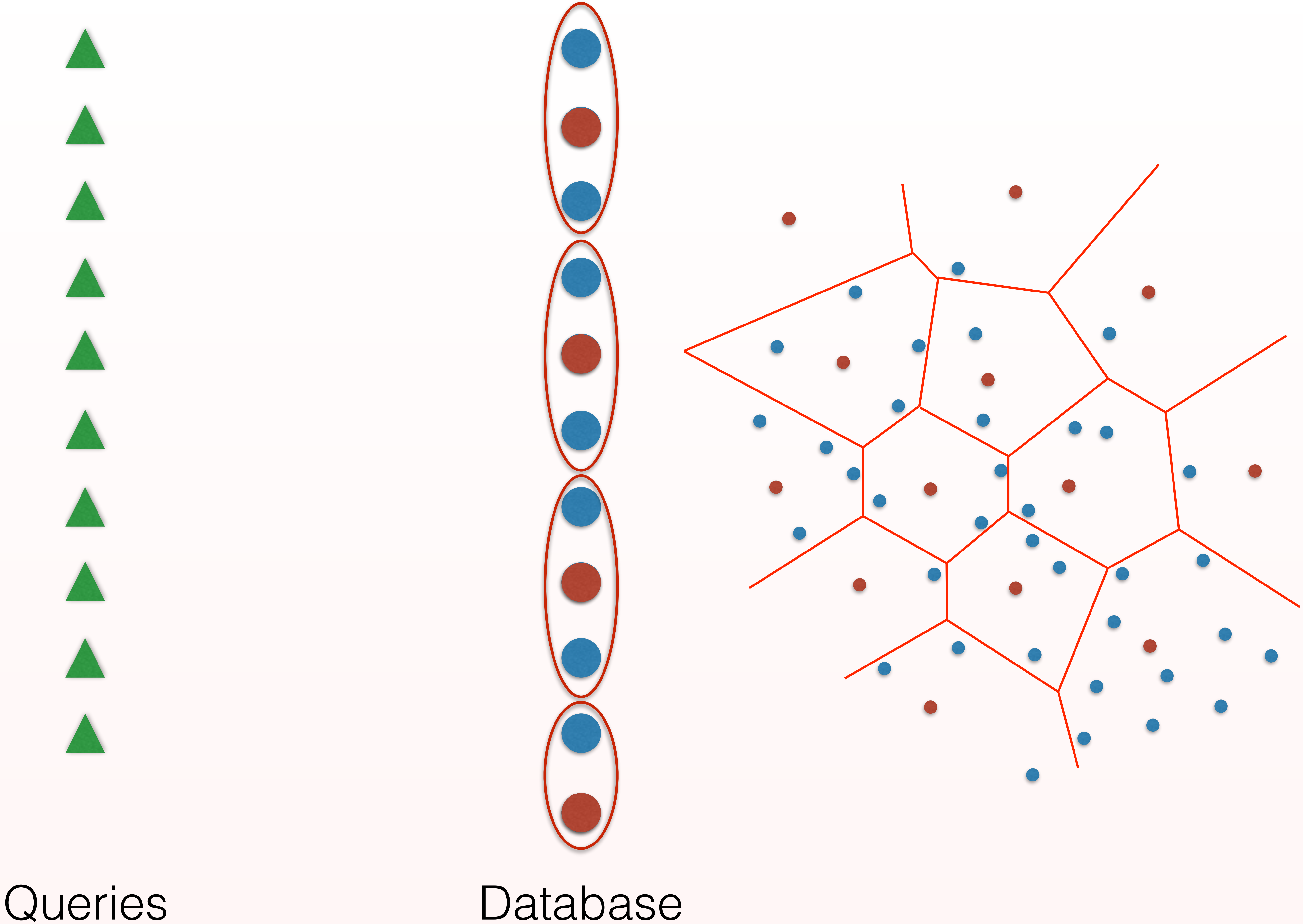
or sub-entities

Only store the common parts once

Only analyze the common parts once


Queries
Database


Queries
Database


Queries
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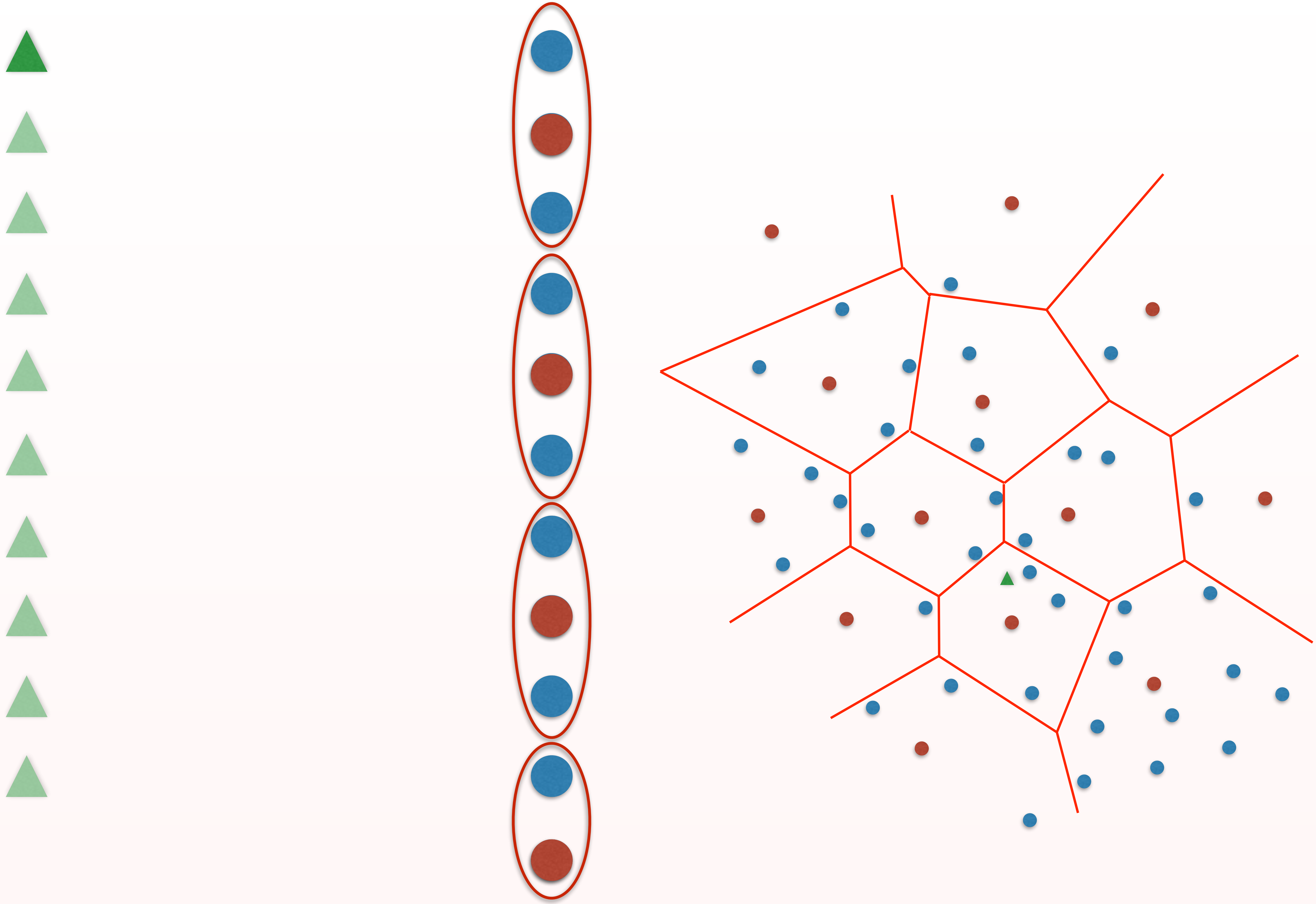
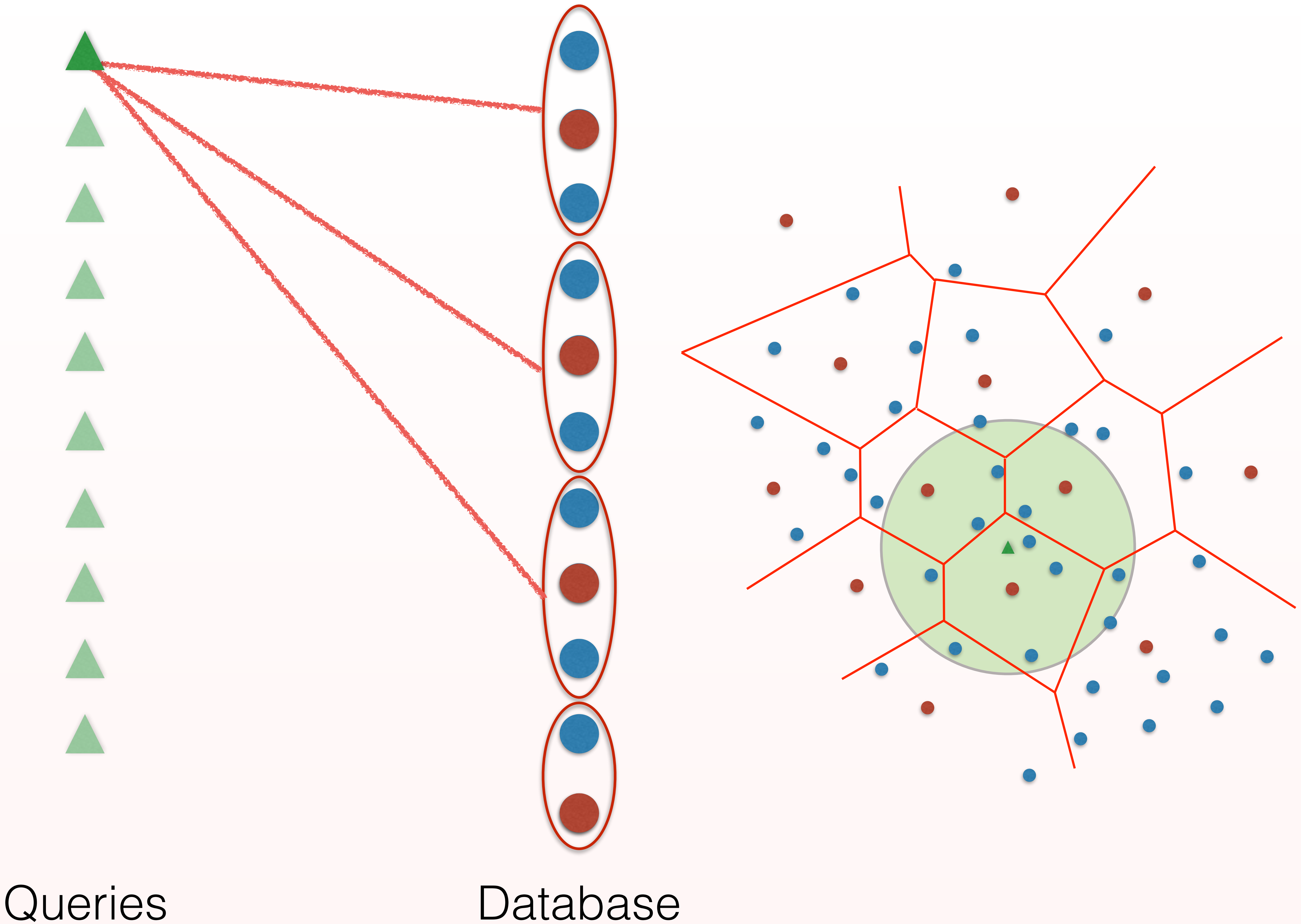
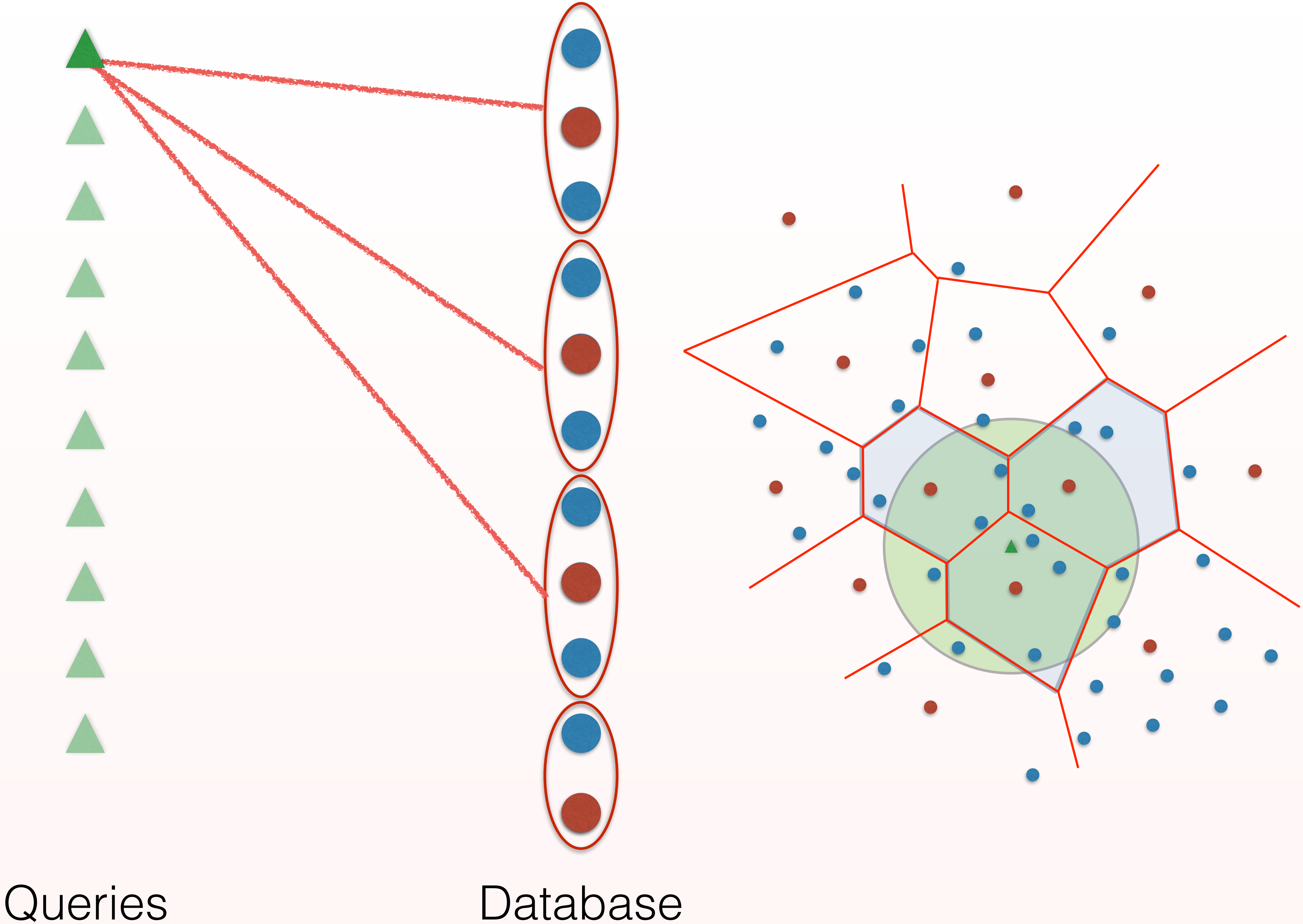


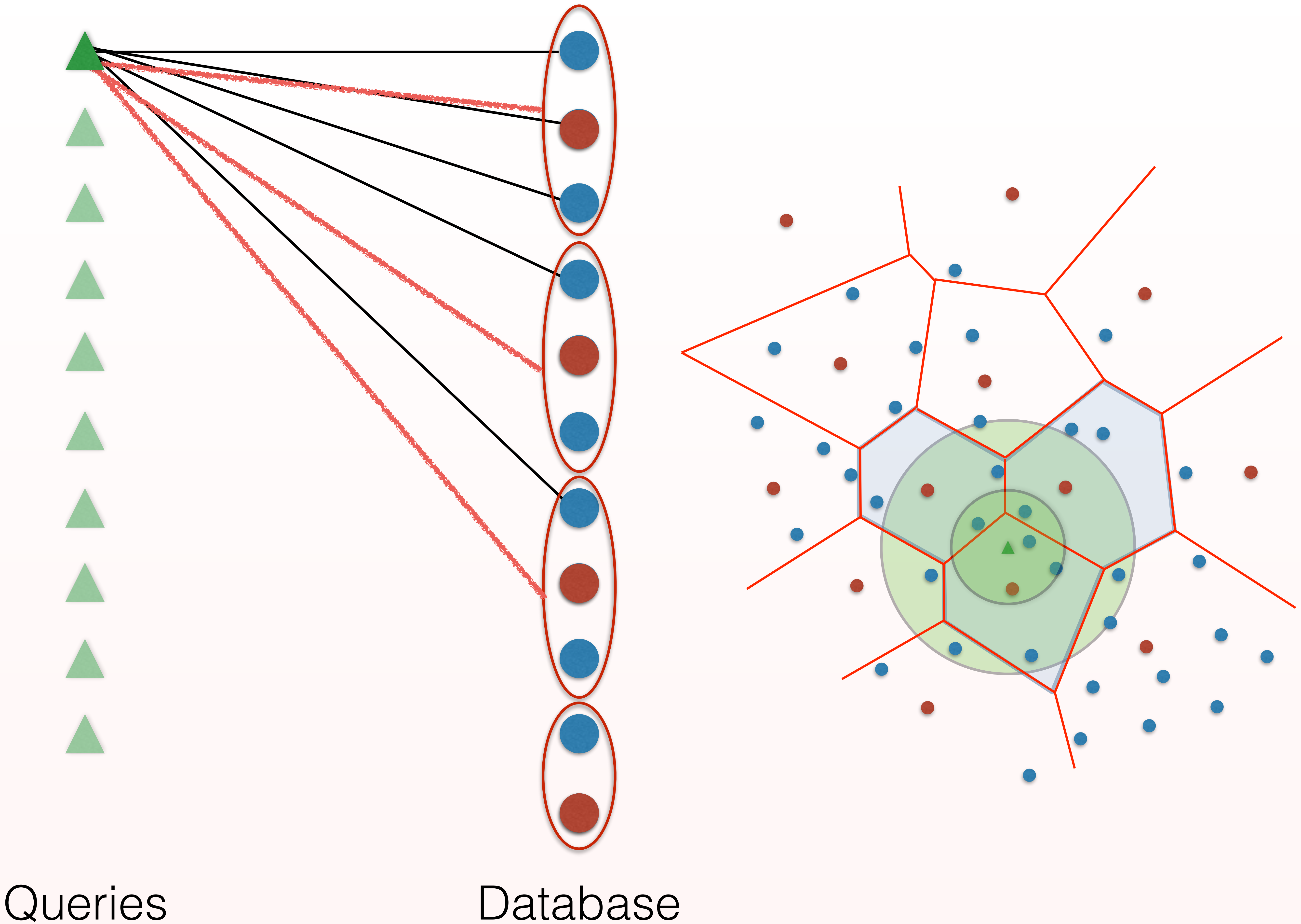
Queries

Database

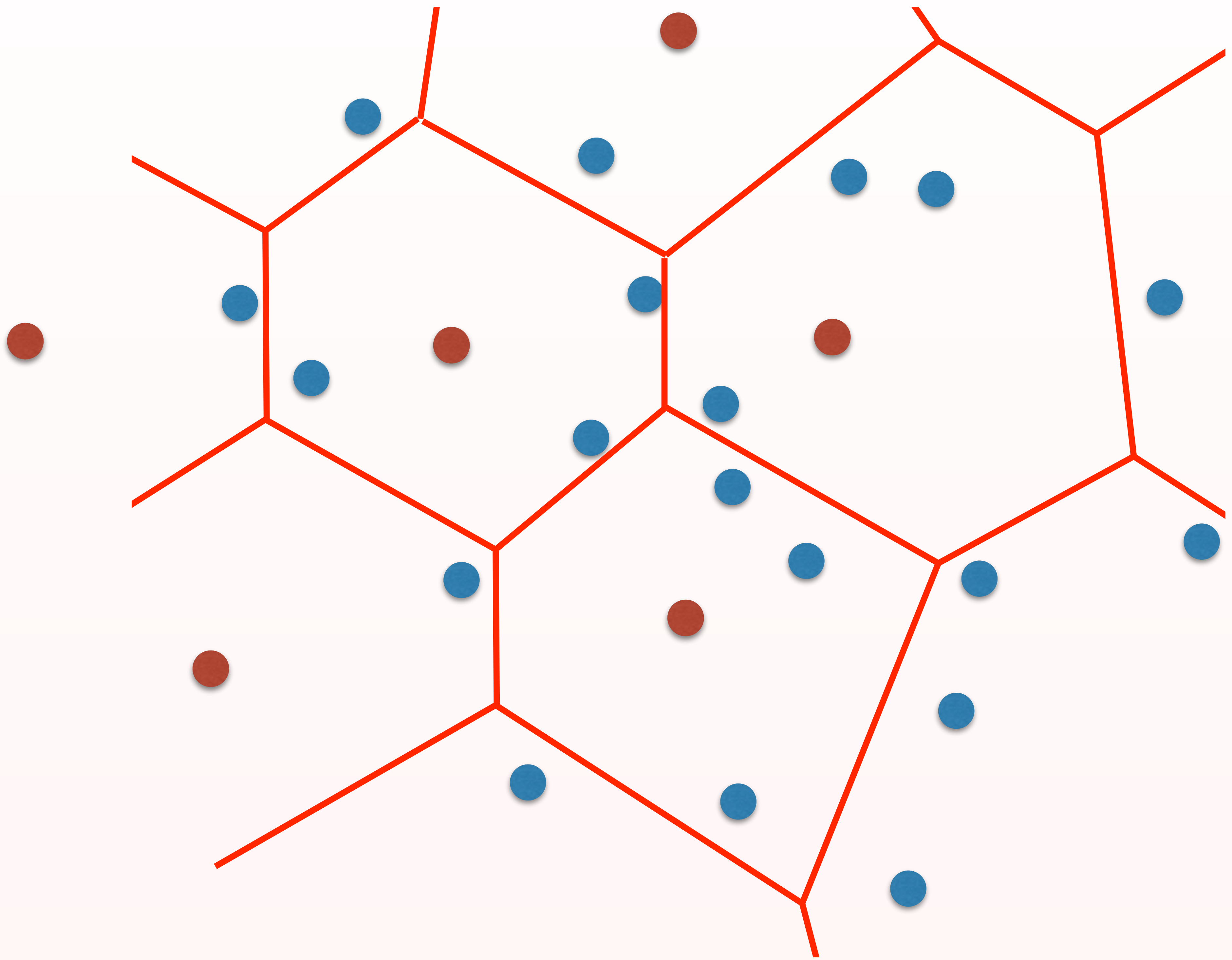

Queries
Database



Queries
Database

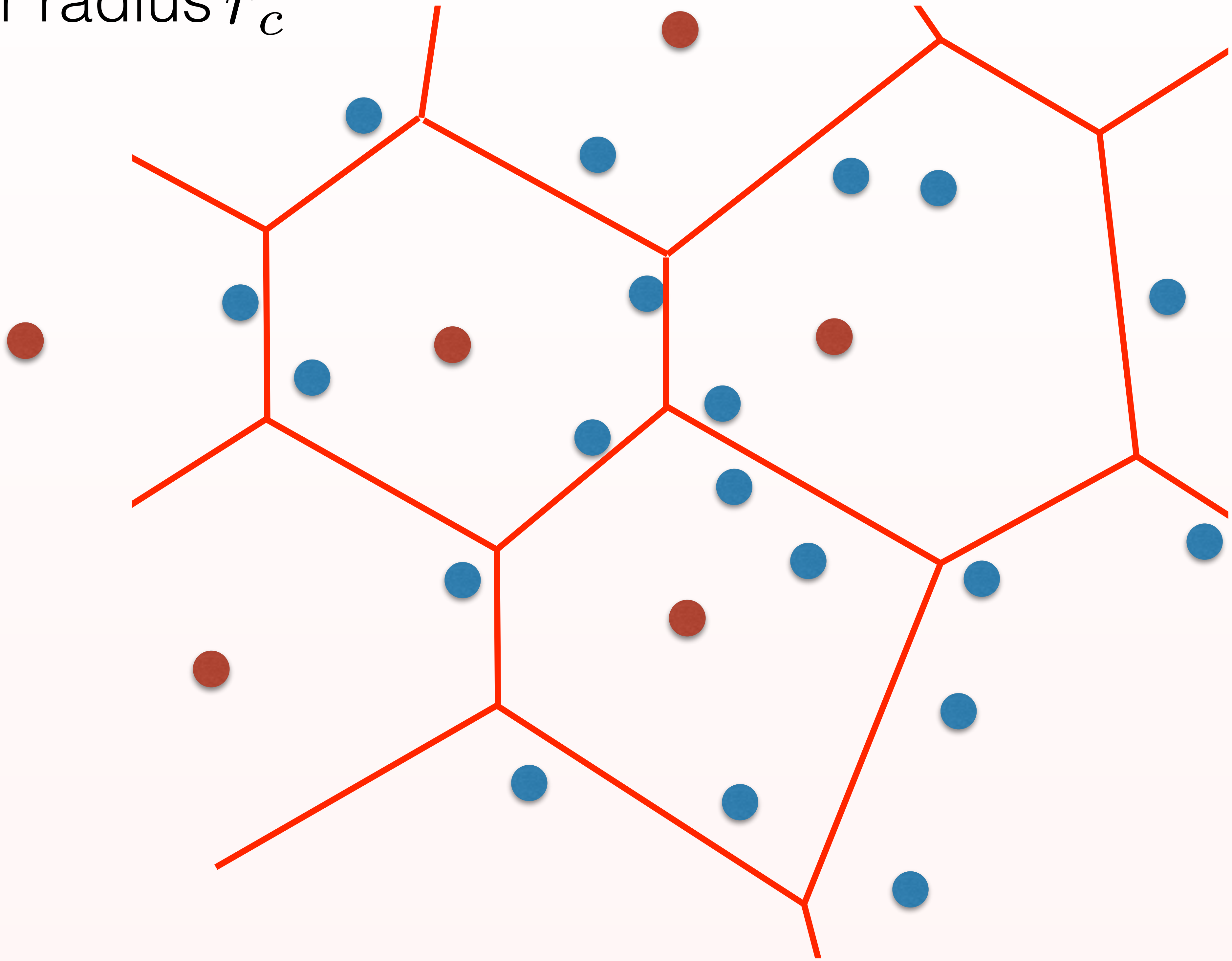

Queries
Database

Triangle inequality allows this



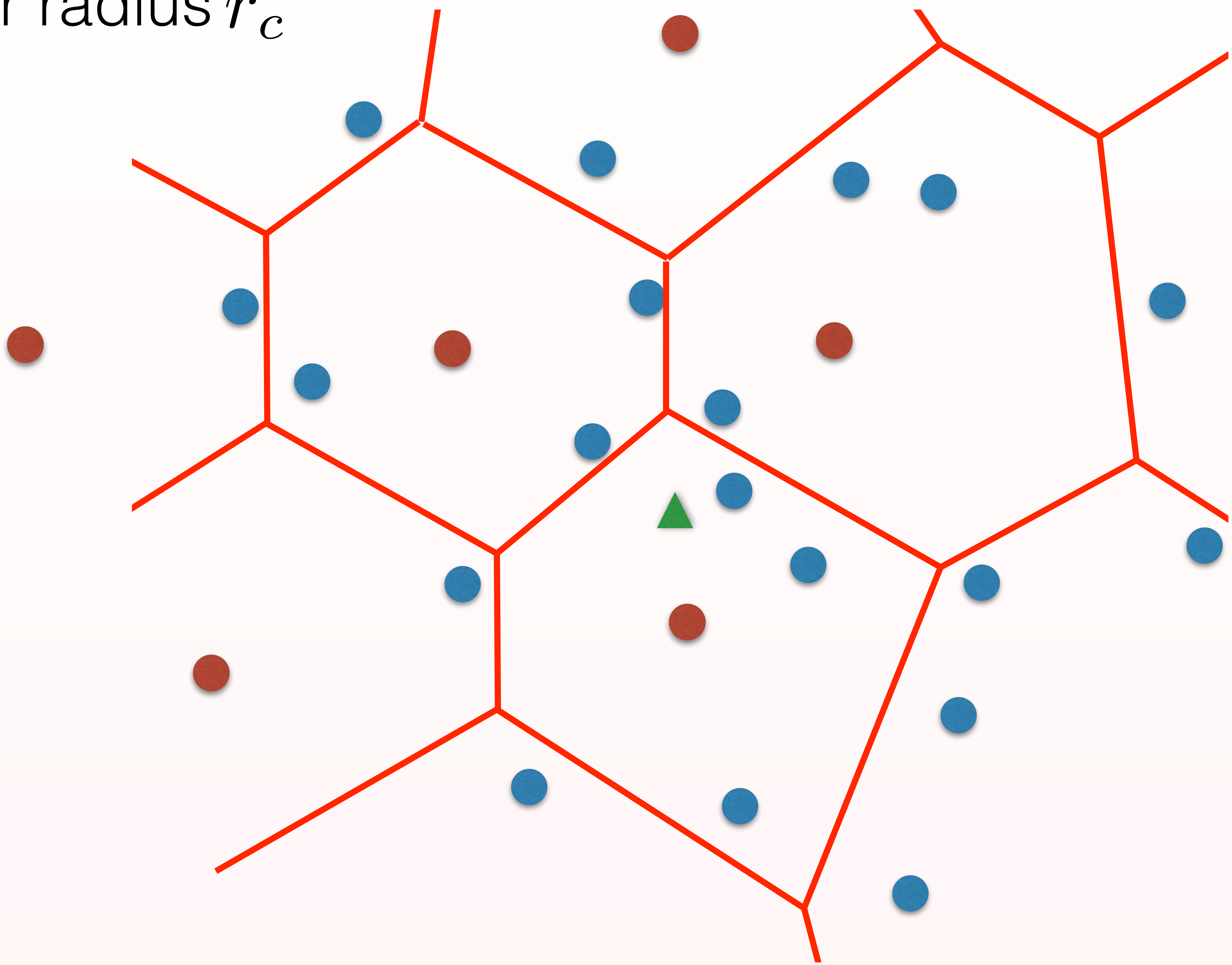
Triangle inequality allows this

cluster radius r_c



Triangle inequality allows this

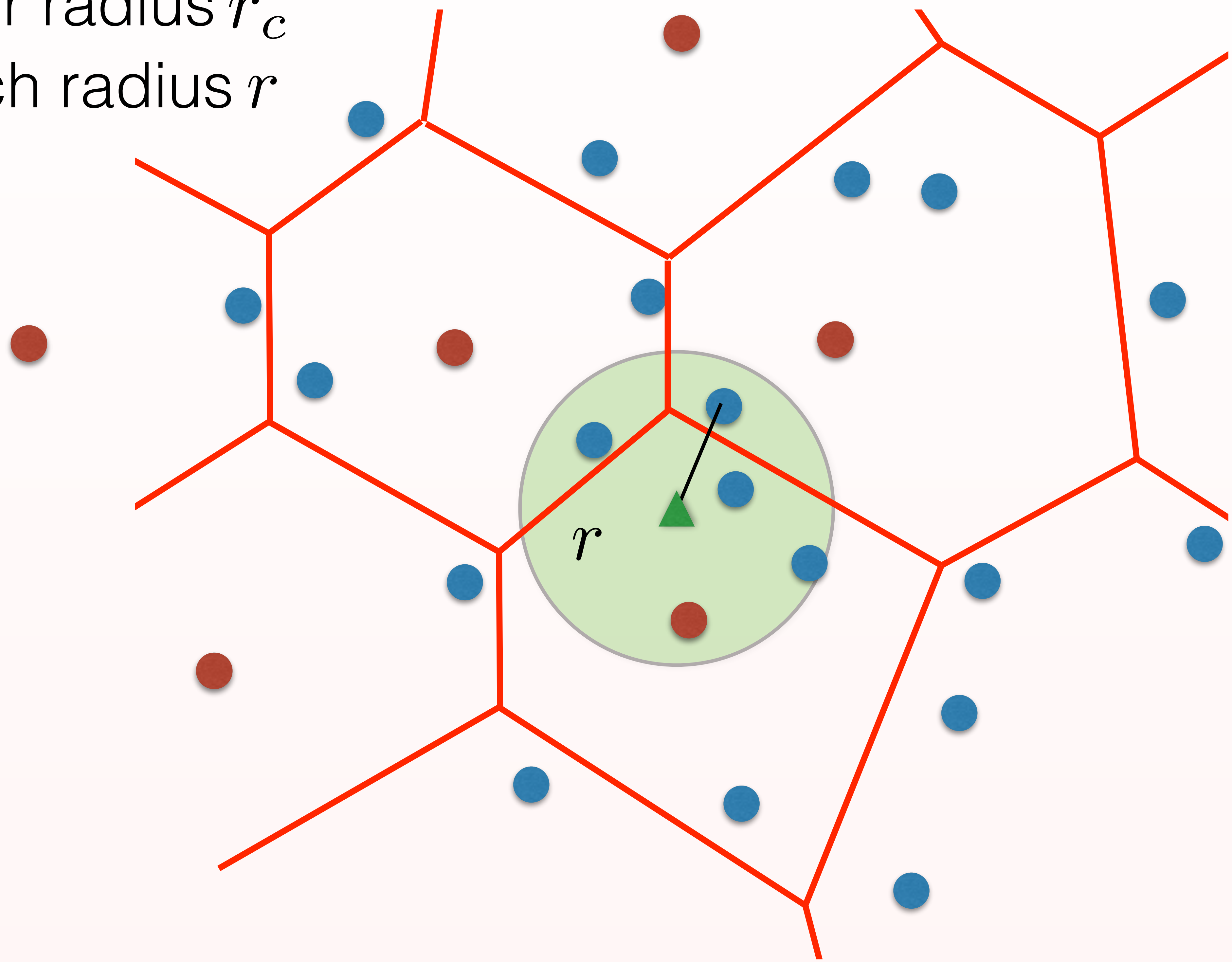
cluster radius r_c



Triangle inequality allows this

cluster radius r_c

search radius r



Triangle inequality allows this

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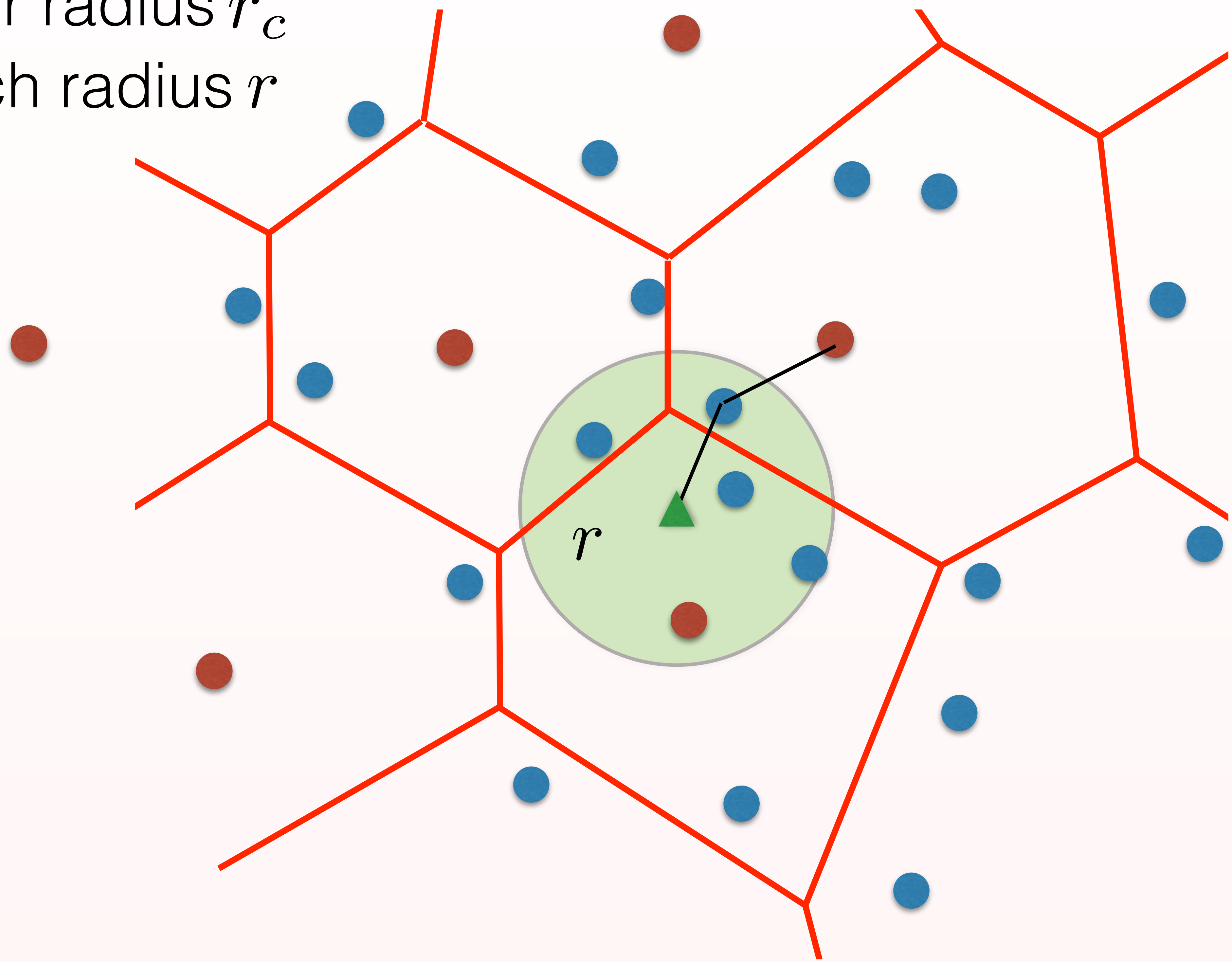

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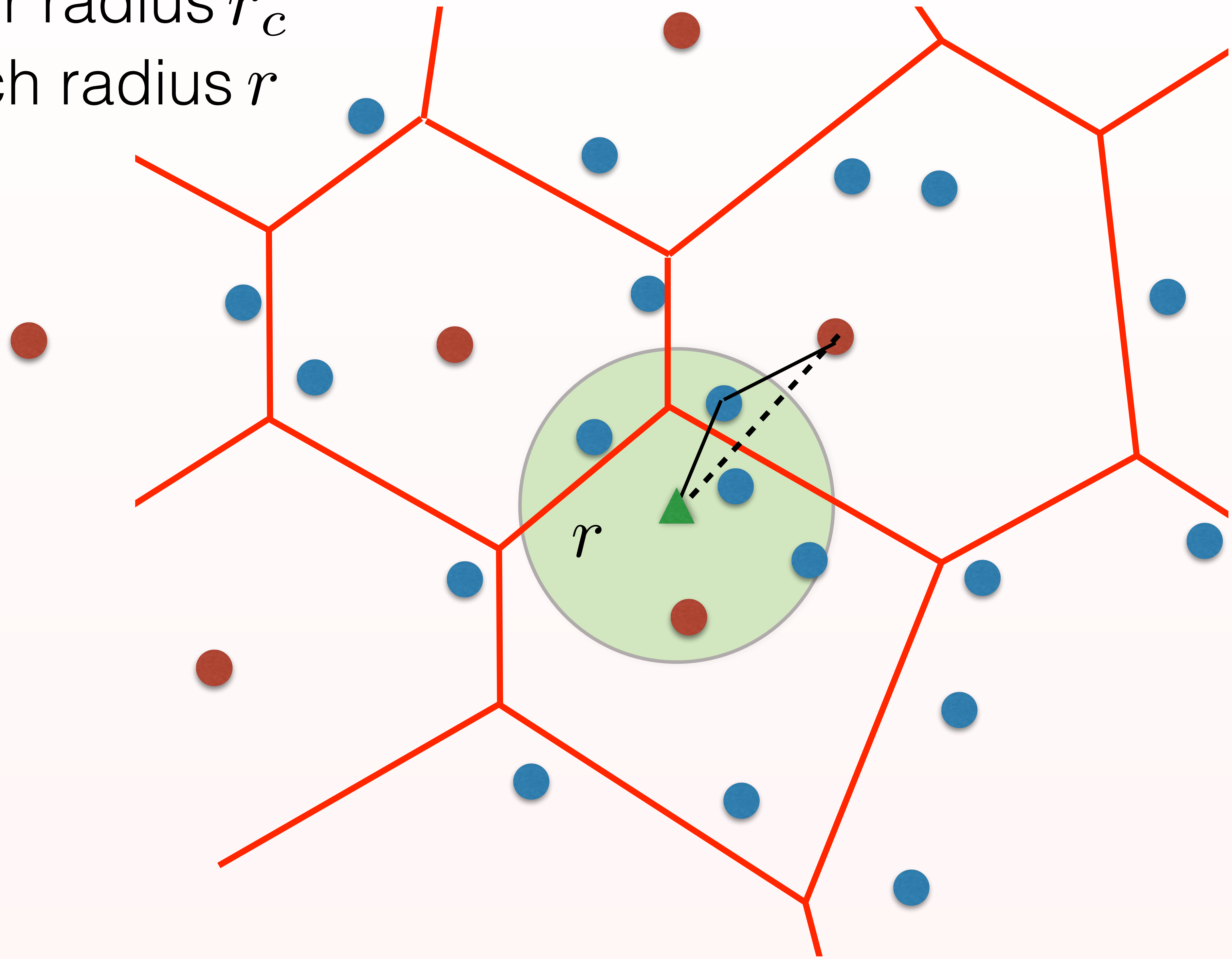

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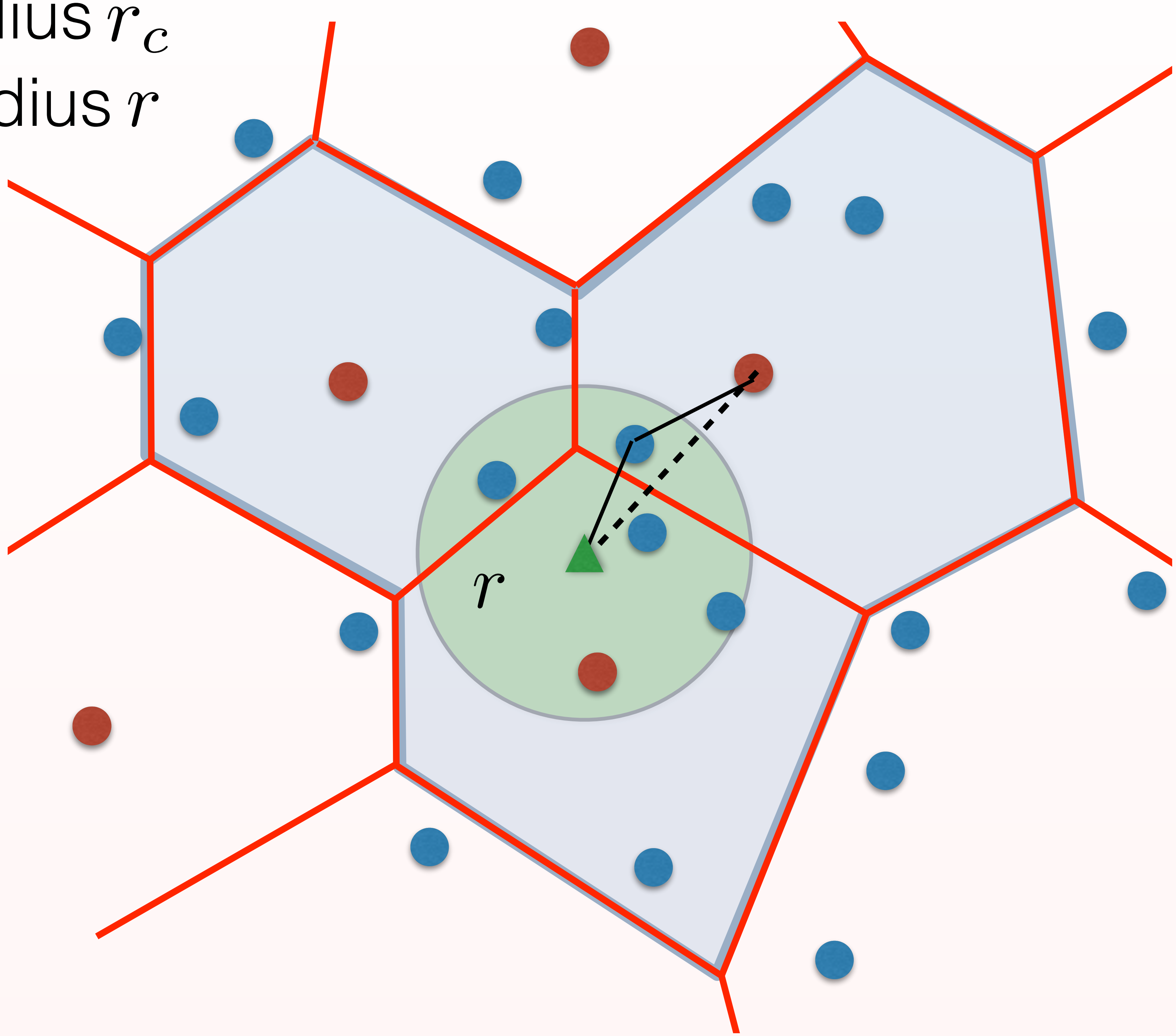

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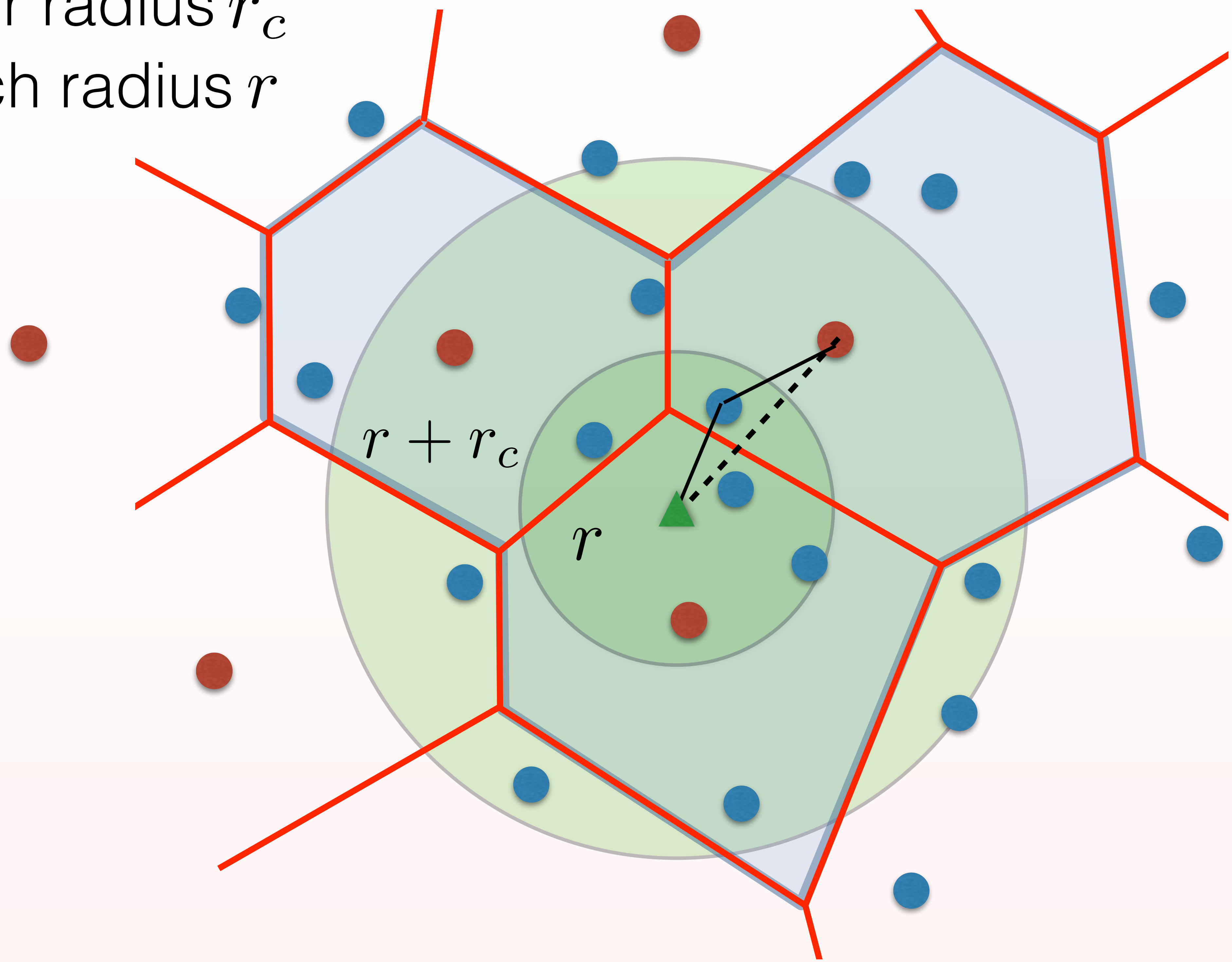

Large-scale NGS Analysis

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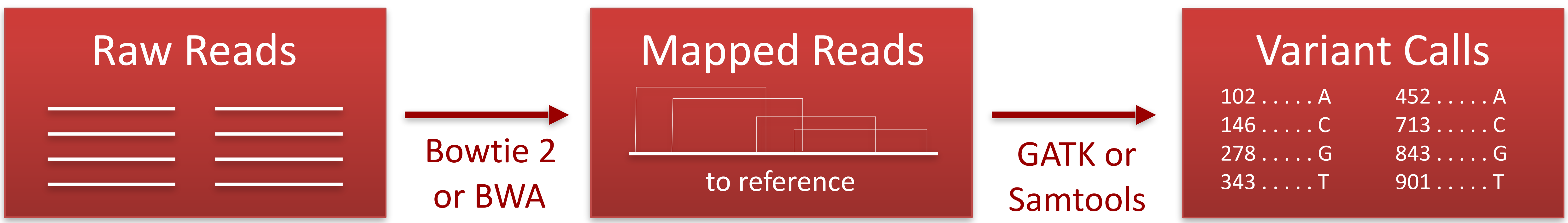
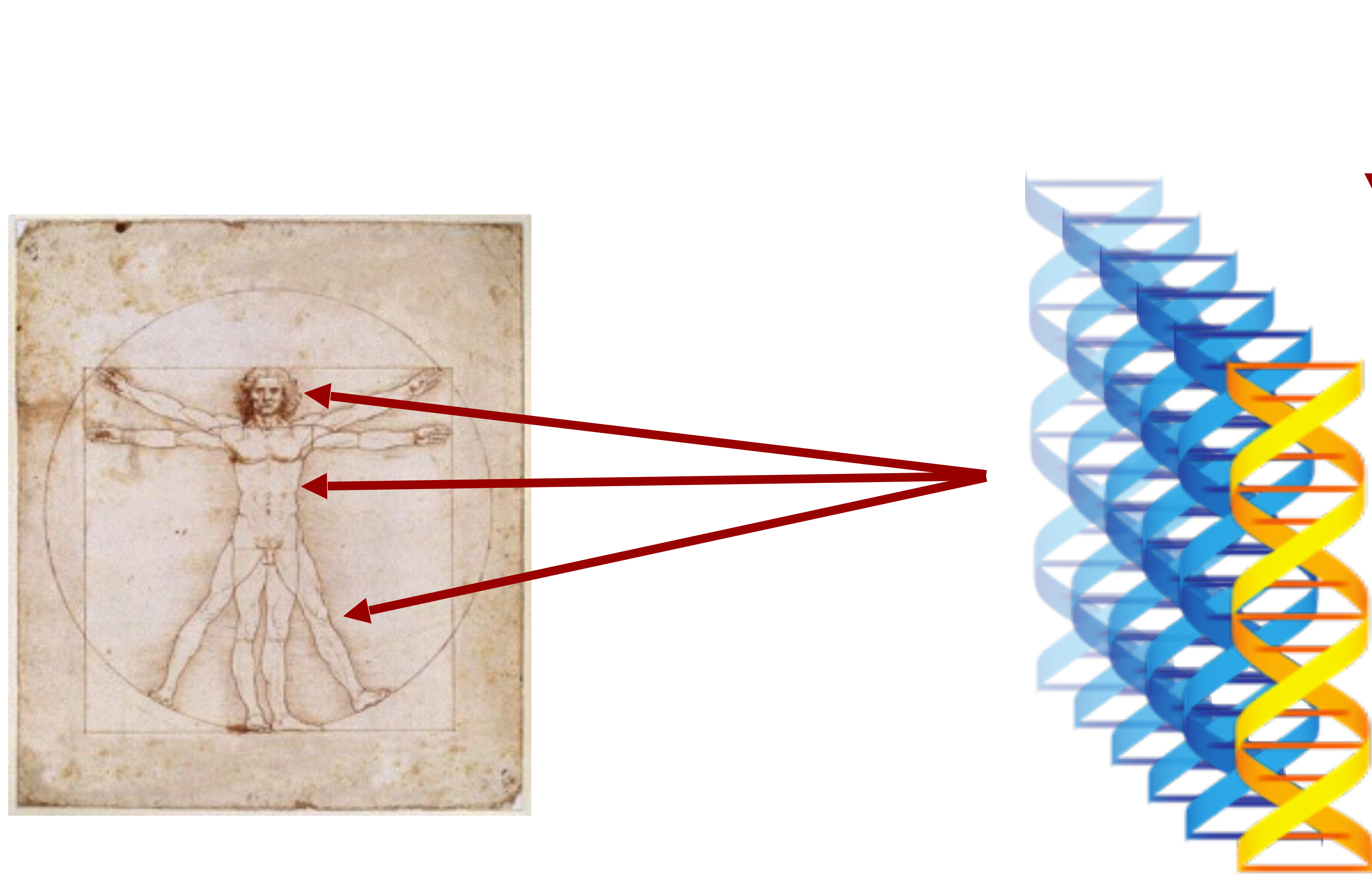


Large-scale NGS Analysis

Raw Reads → Bowtie 2 or BWA → **Mapped Reads** (to reference) → GATK or Samtools → **Variant Calls**

102 . . . . . A	452 . . . . . A
146 C	713 C
278 . . . . . G	843 . . . . . G
343 . . . . . T	901 . . . . . T



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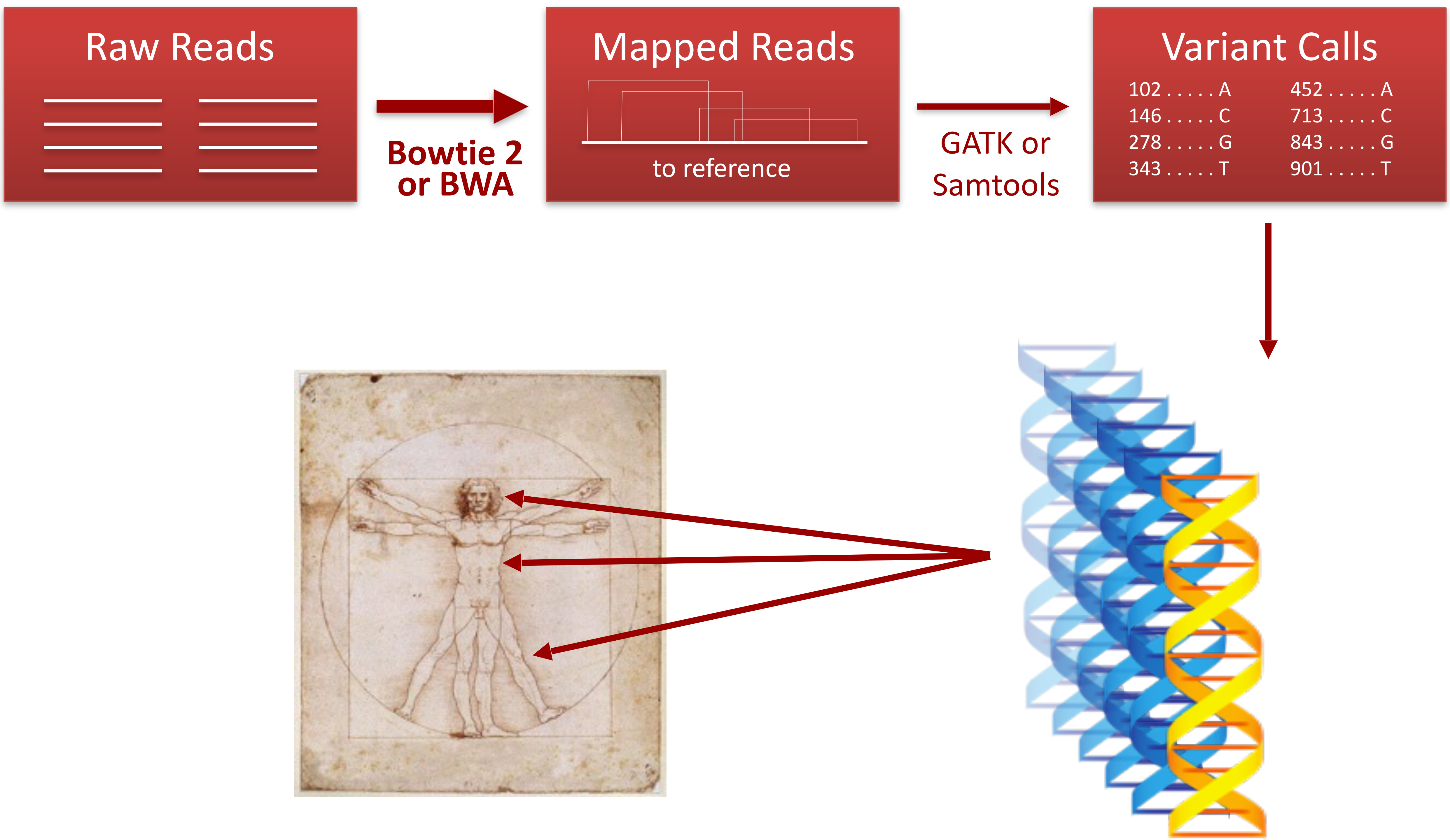
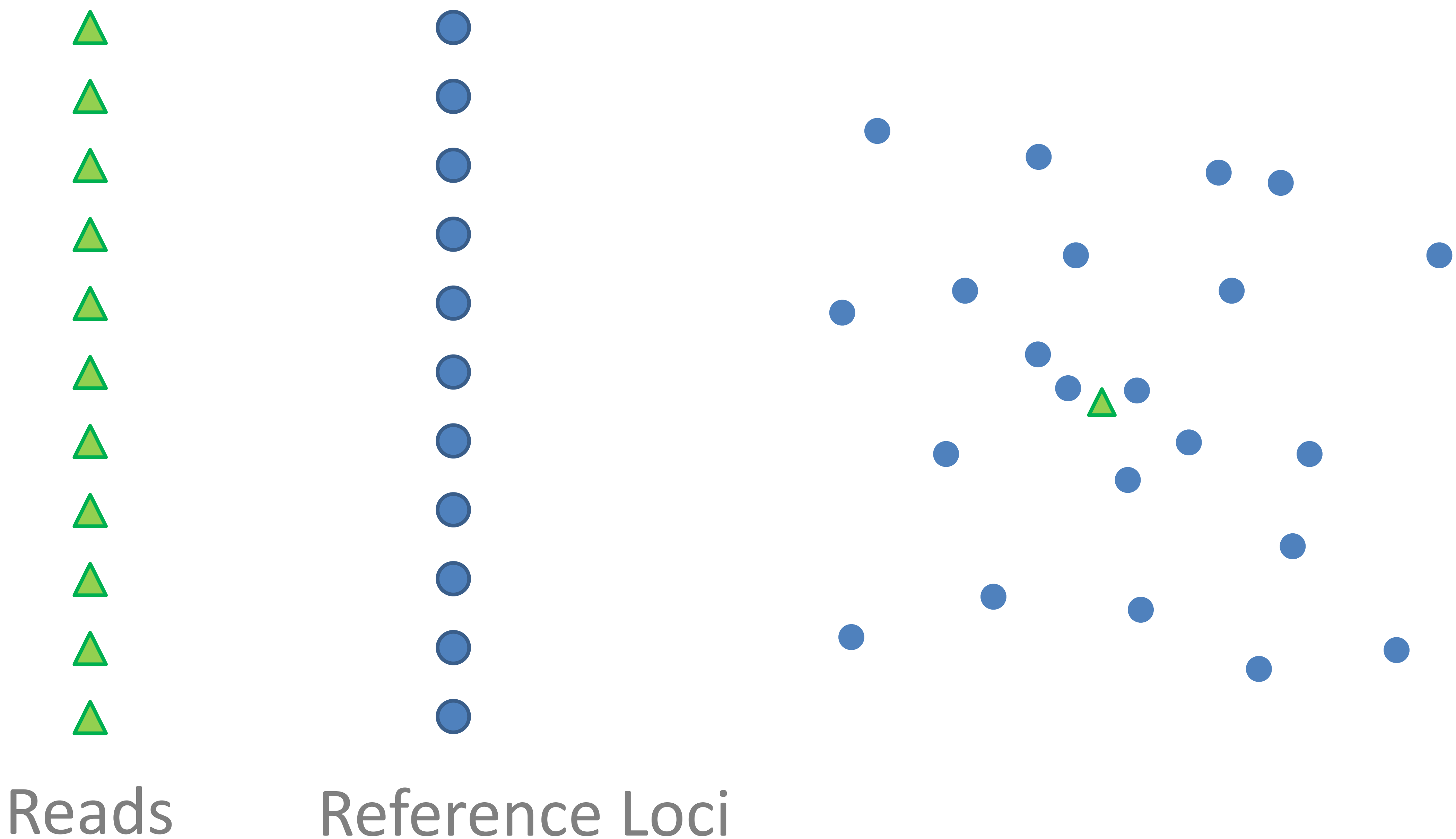


NGS-Mapping in Personal Genomics Era



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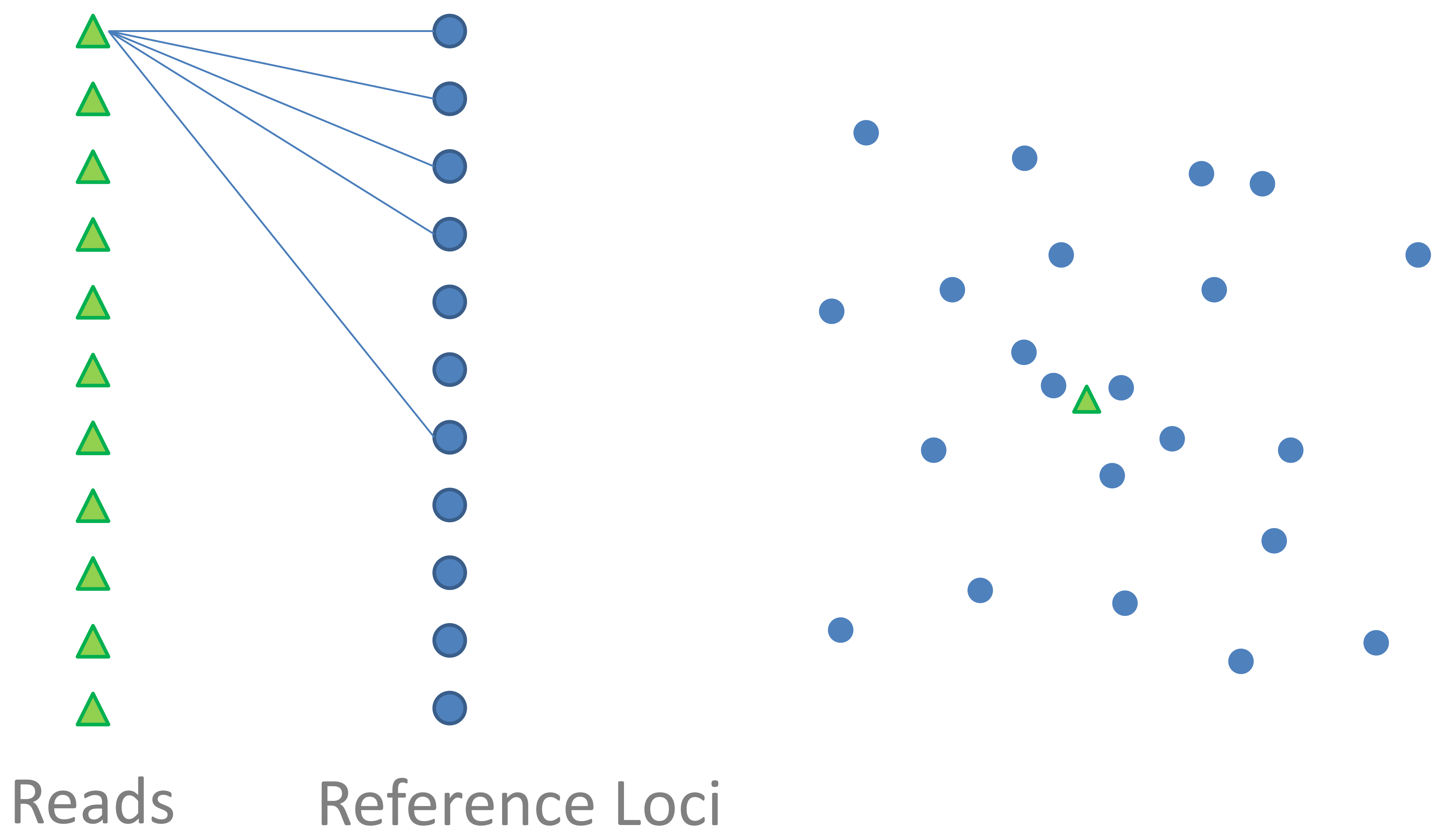

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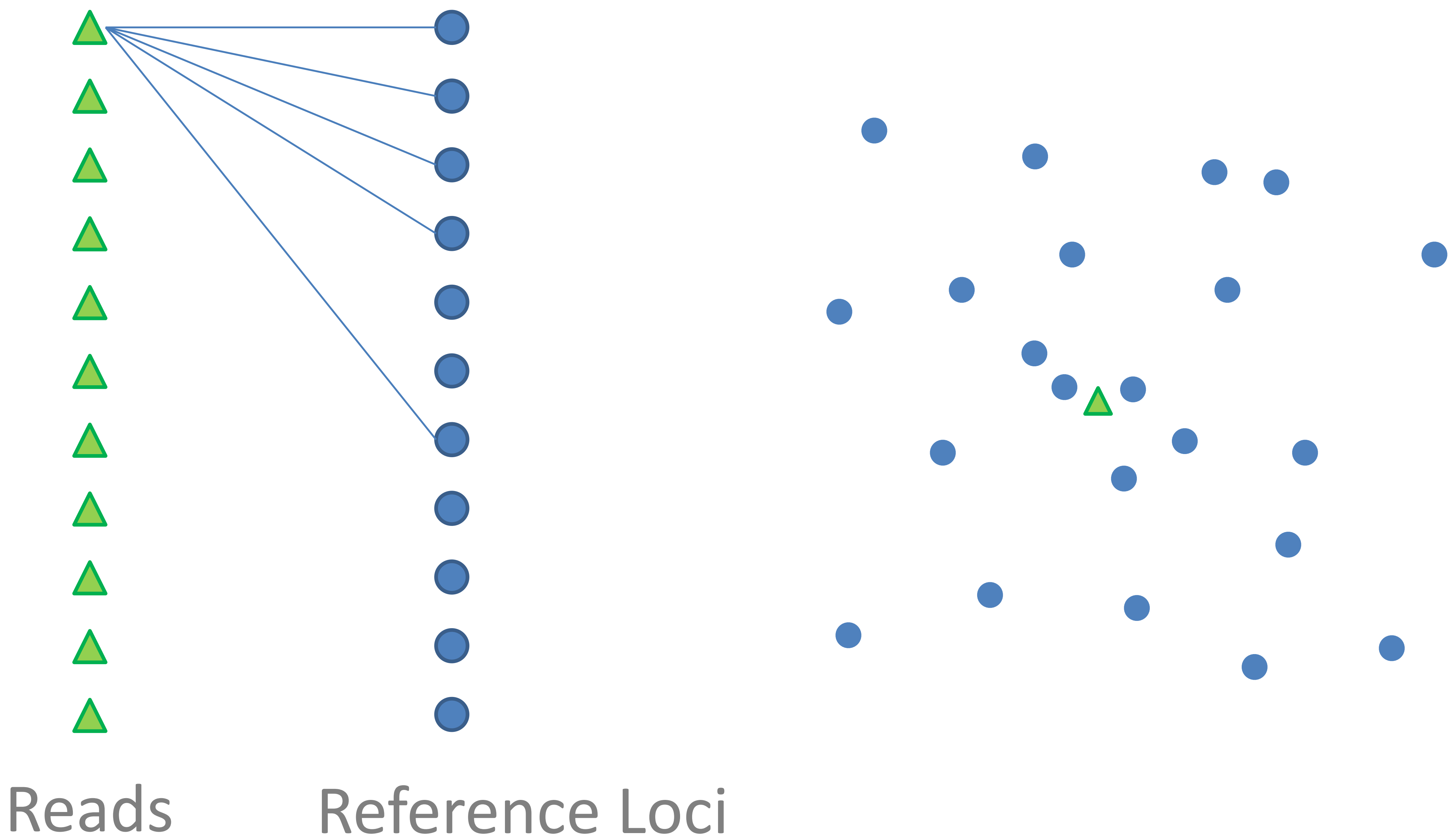
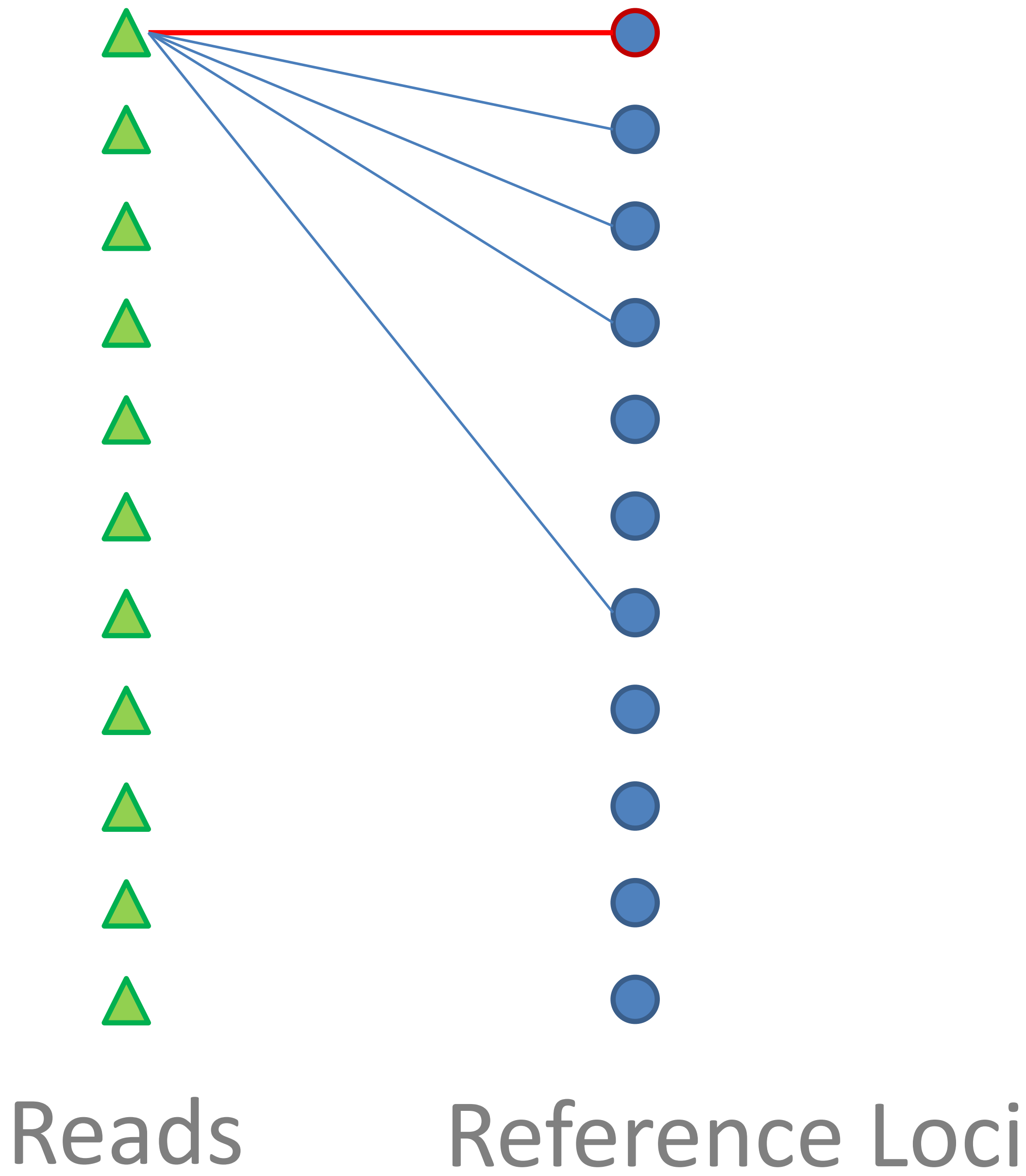
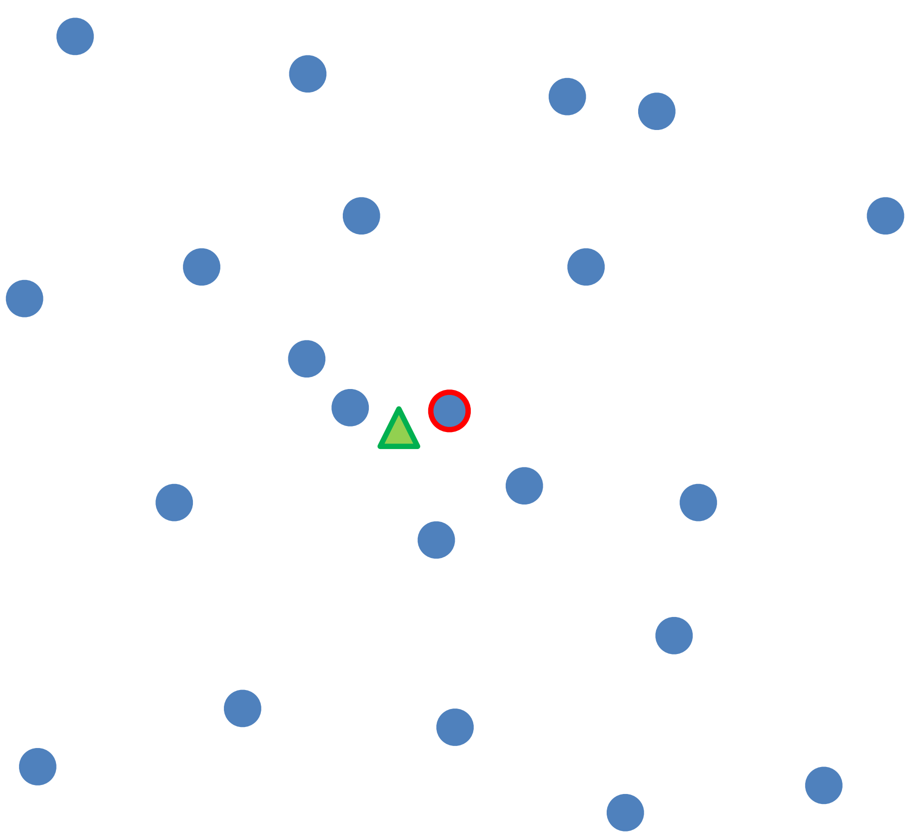


Key Intuition: Reads have lots of redundancy!

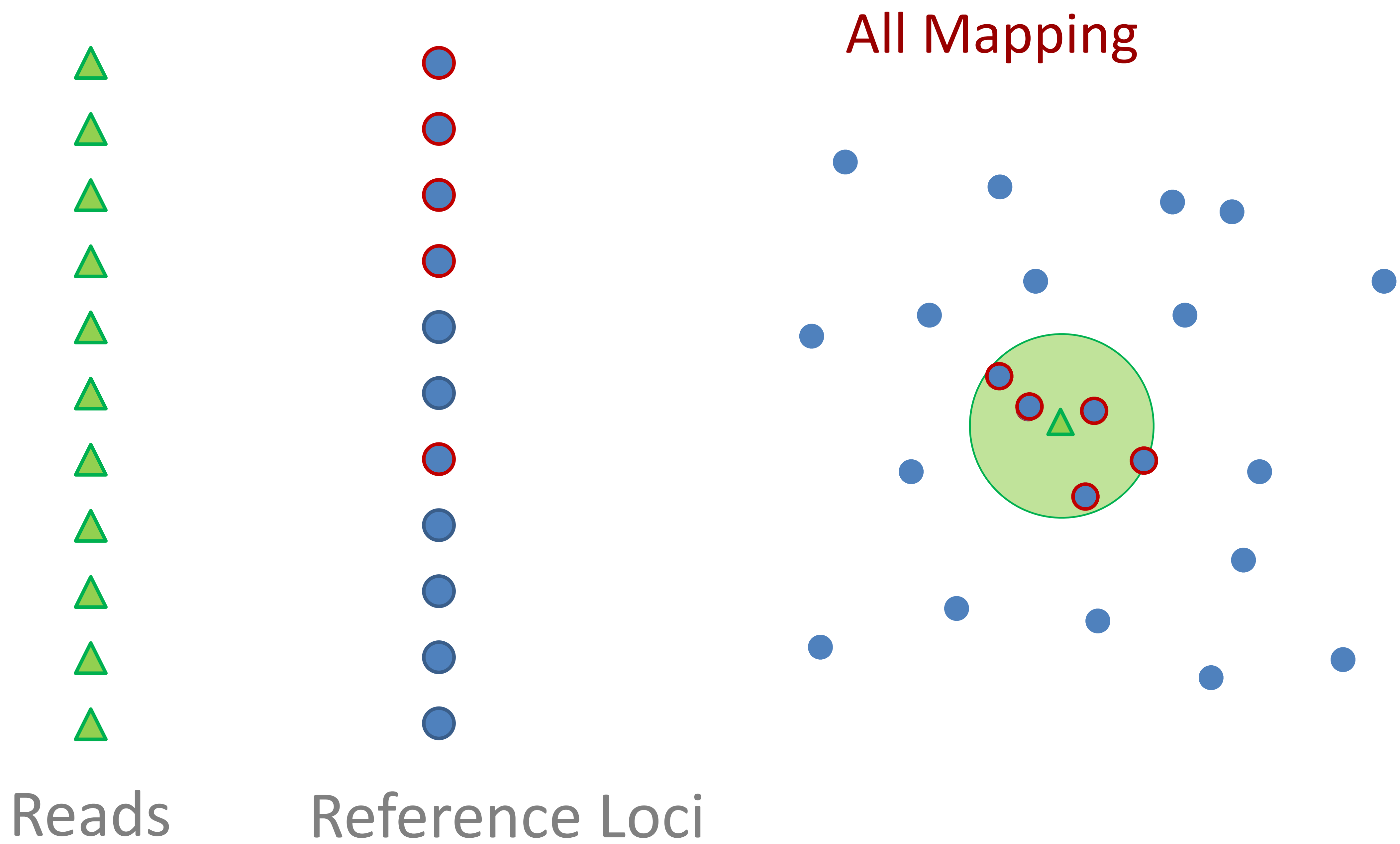
NGS-Mapping in Personal Genomics Era



Best Mapping



NGS-Mapping in Personal Genomics Era



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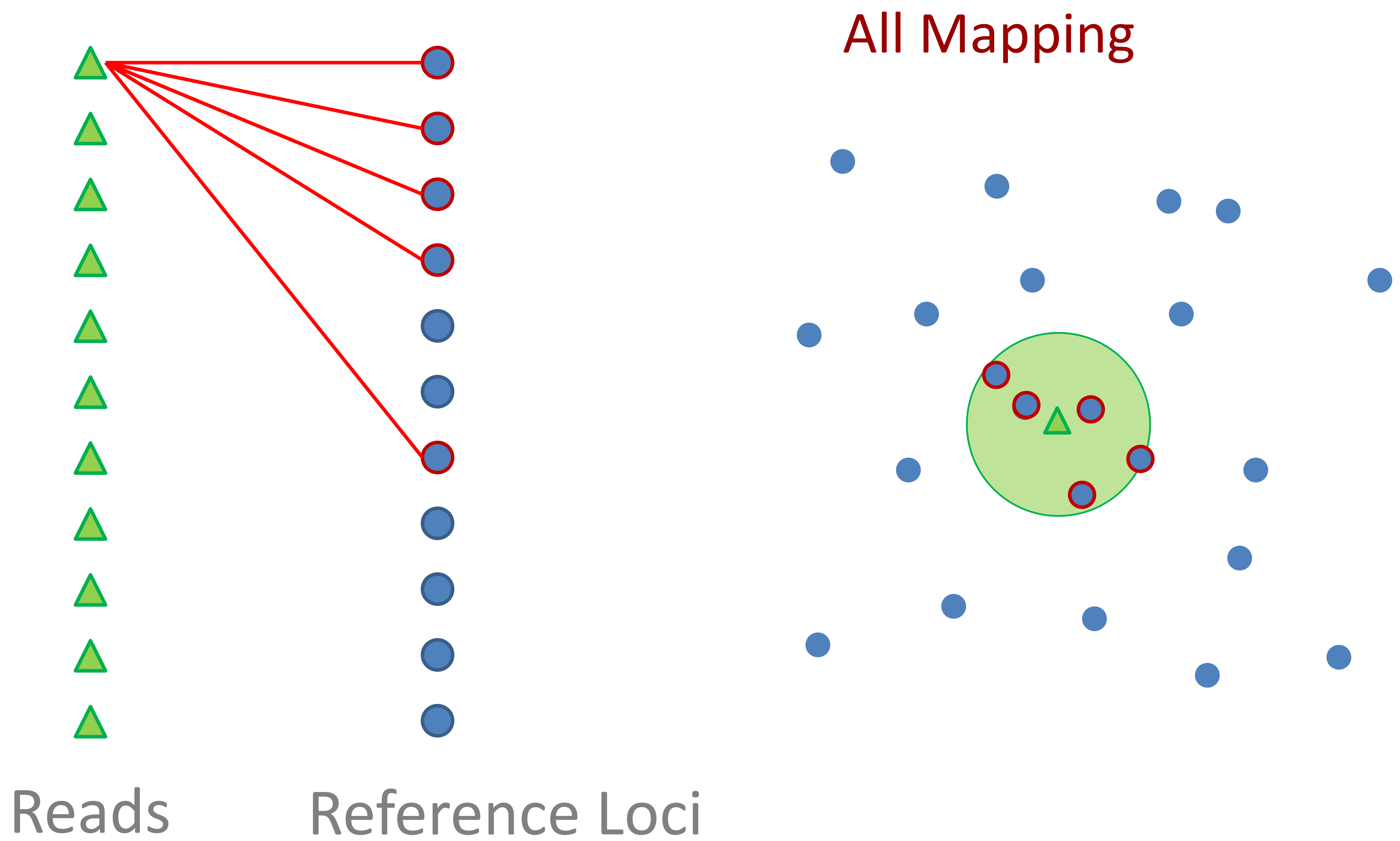
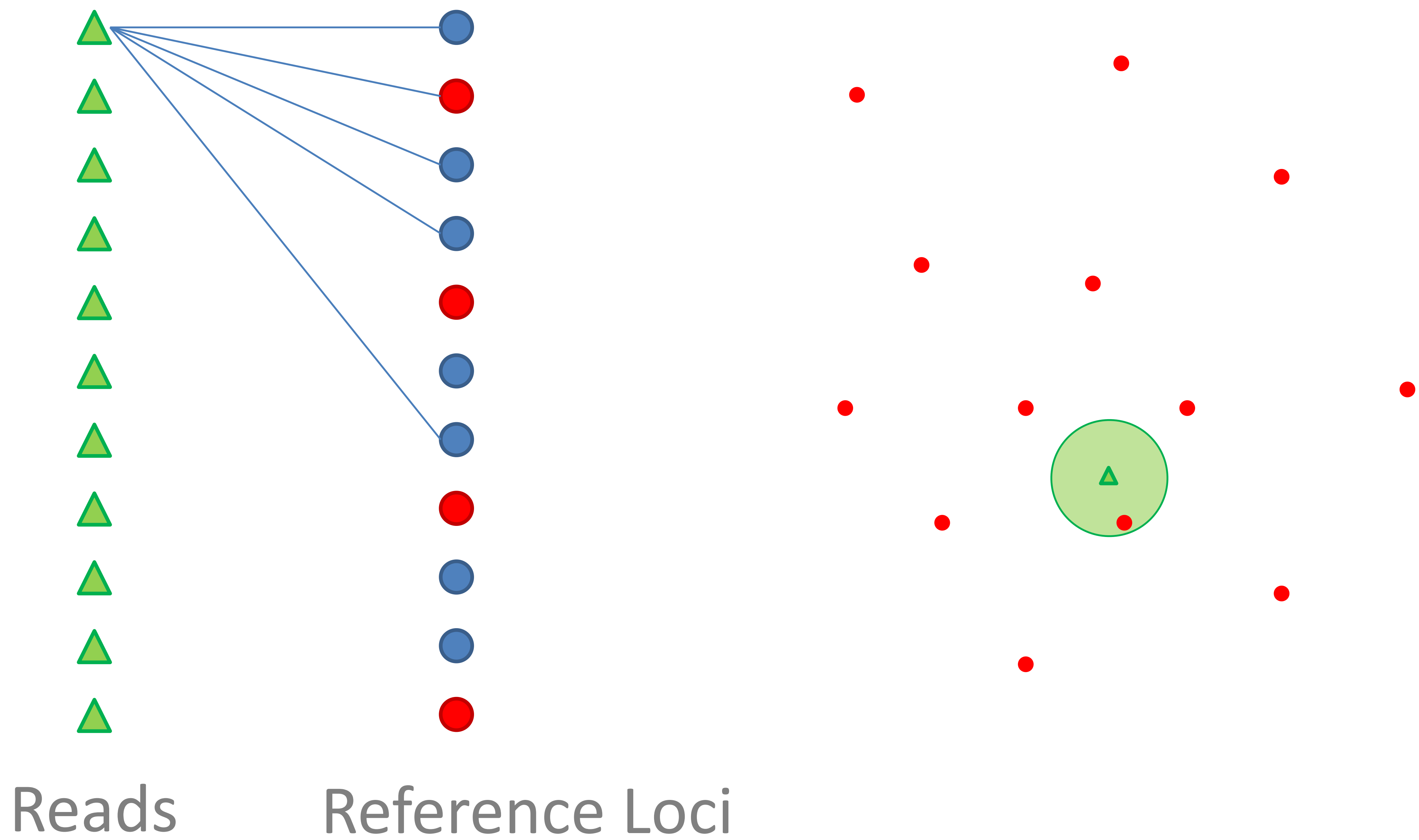


CORA [Yorukoglu, et al. accepted for publication]



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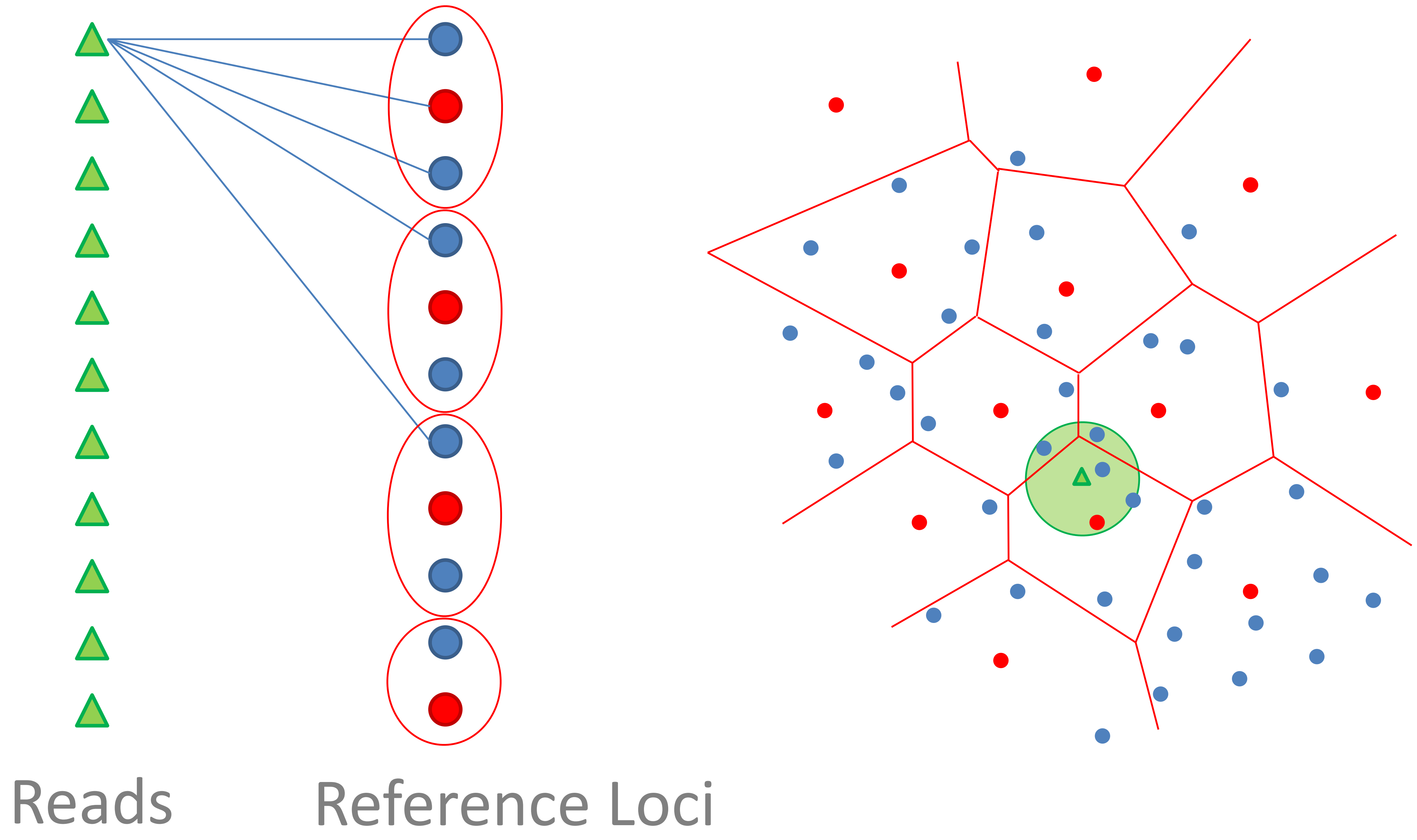

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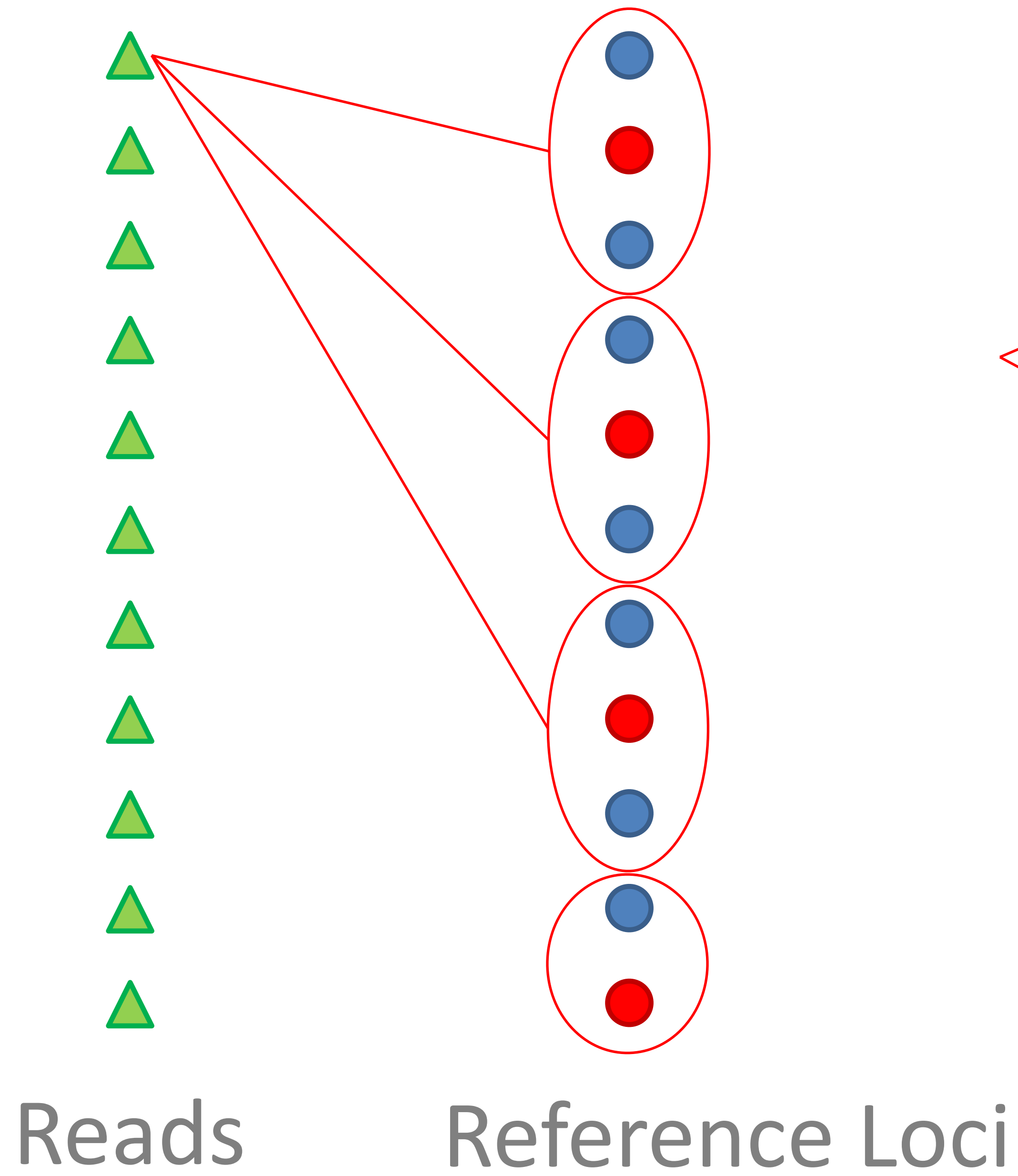

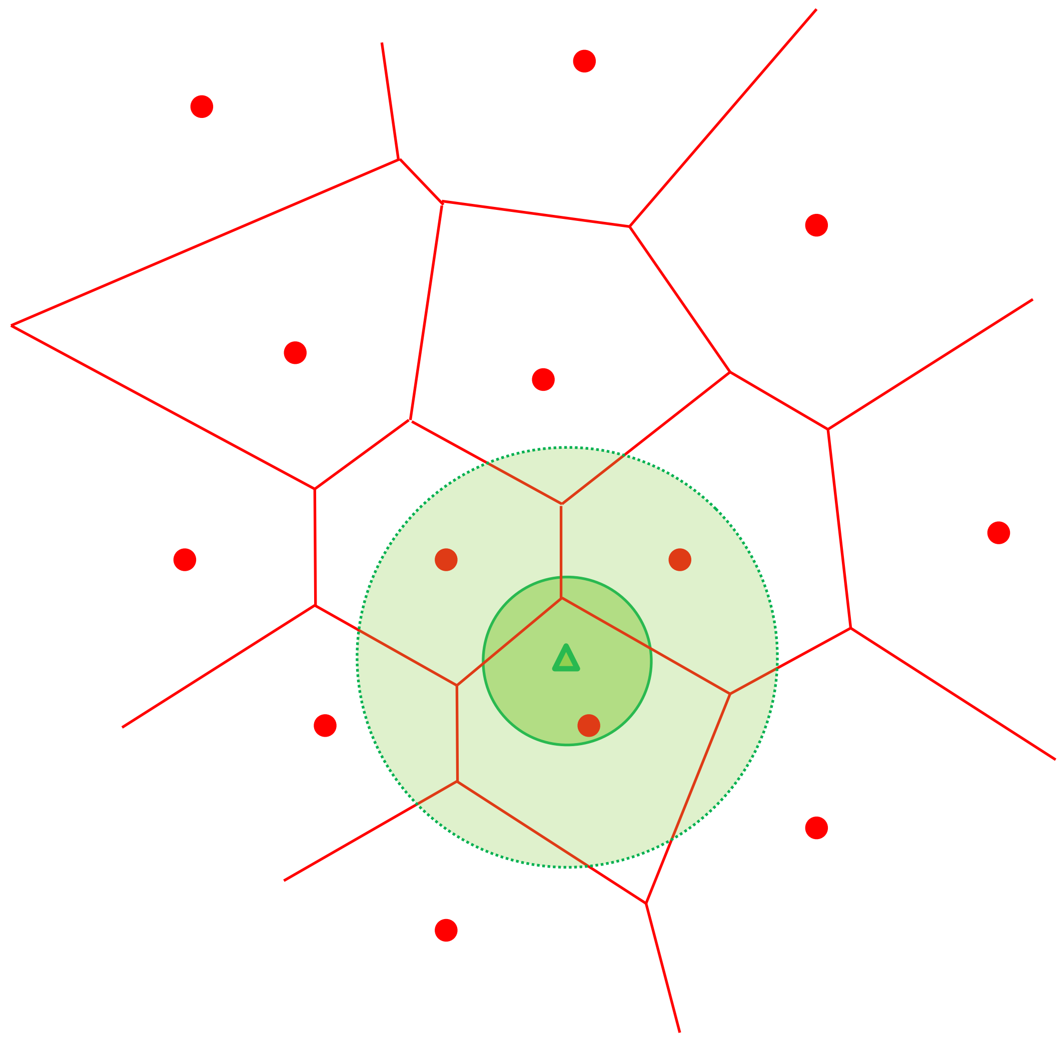

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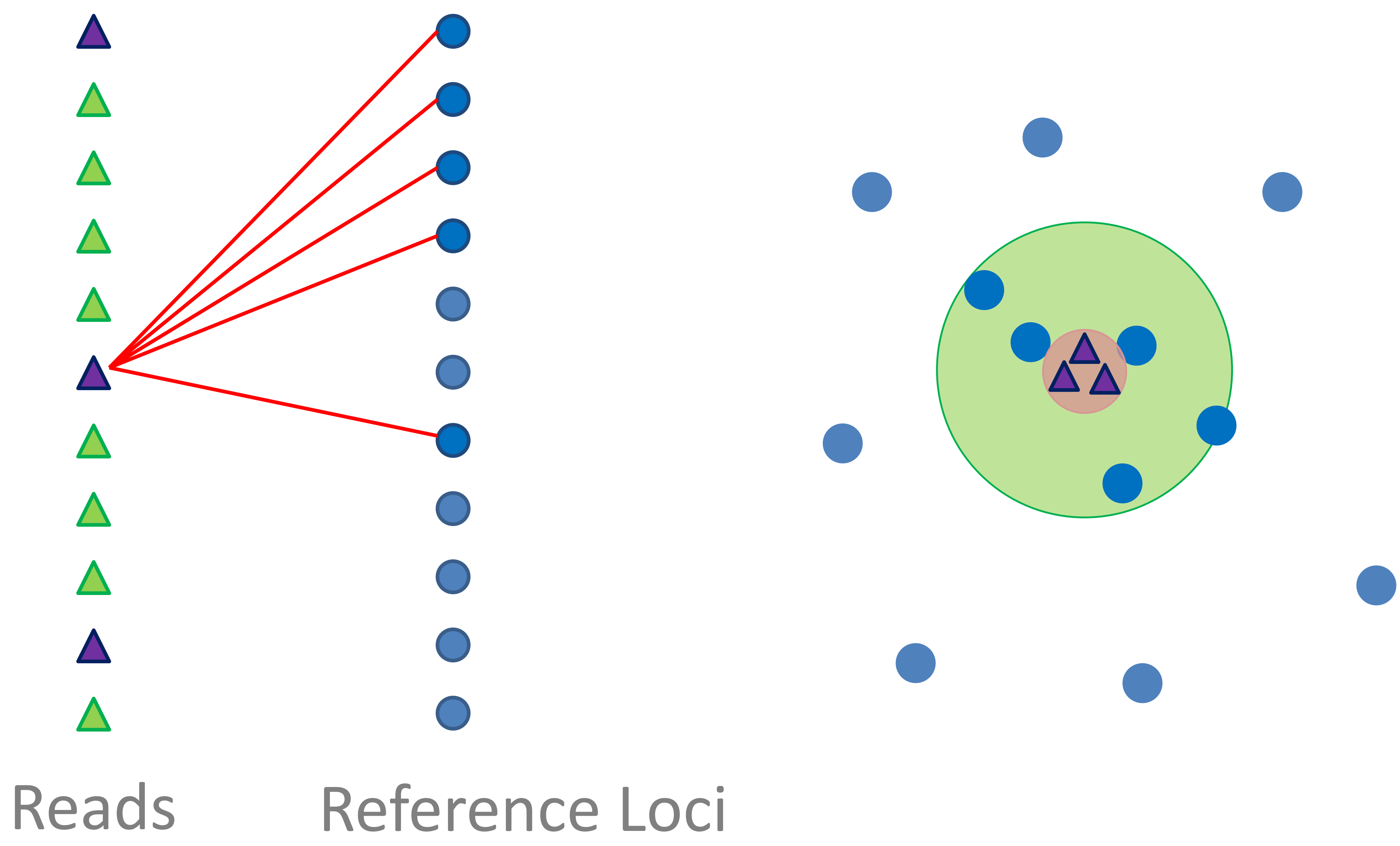

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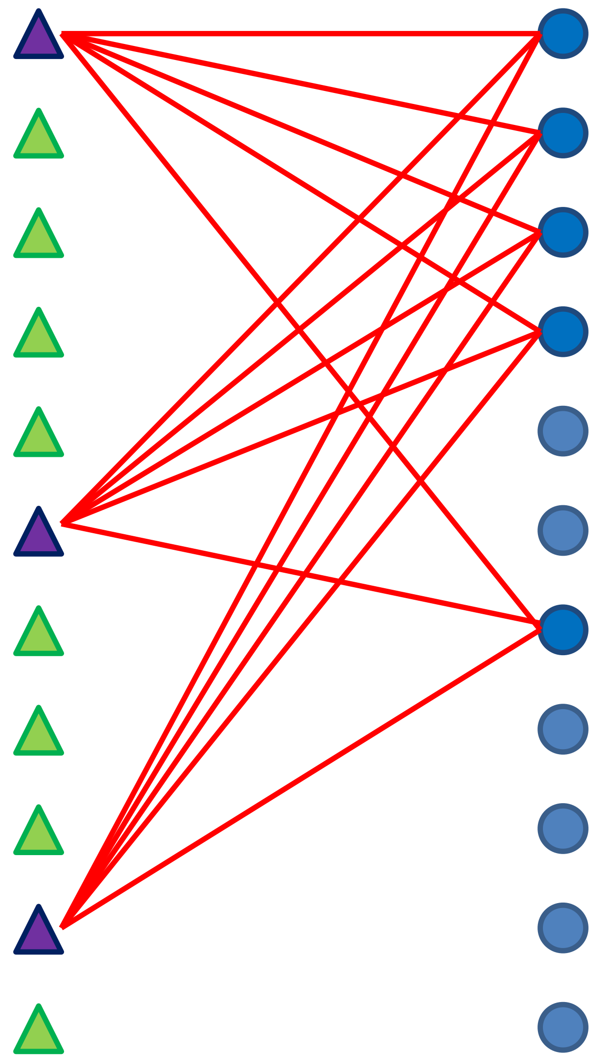
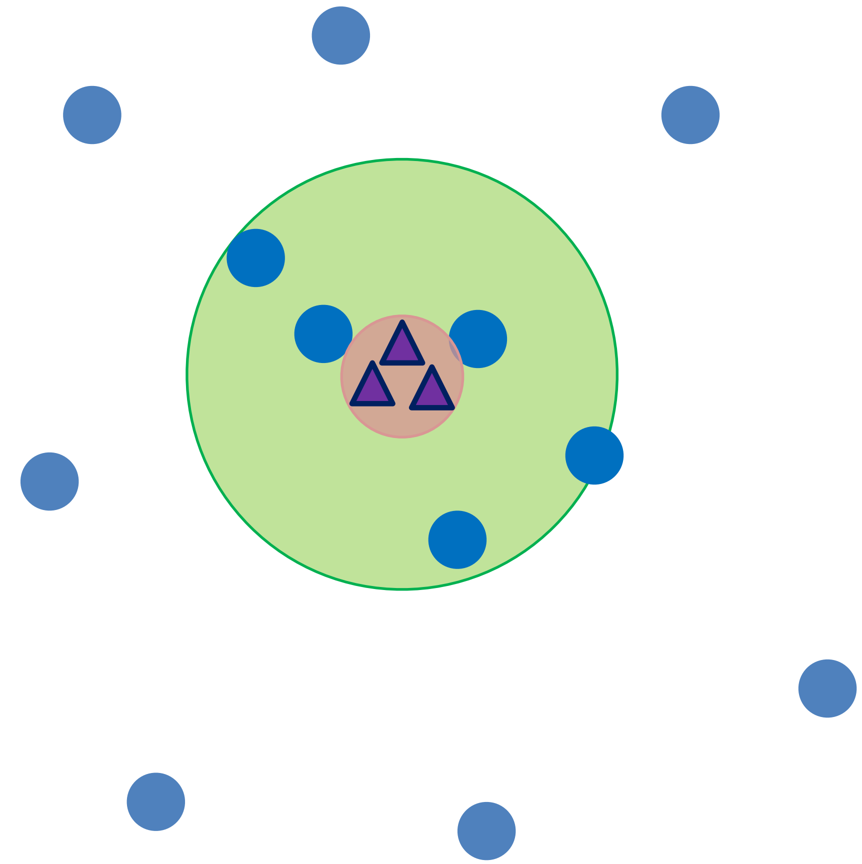


Reads Reference Loci



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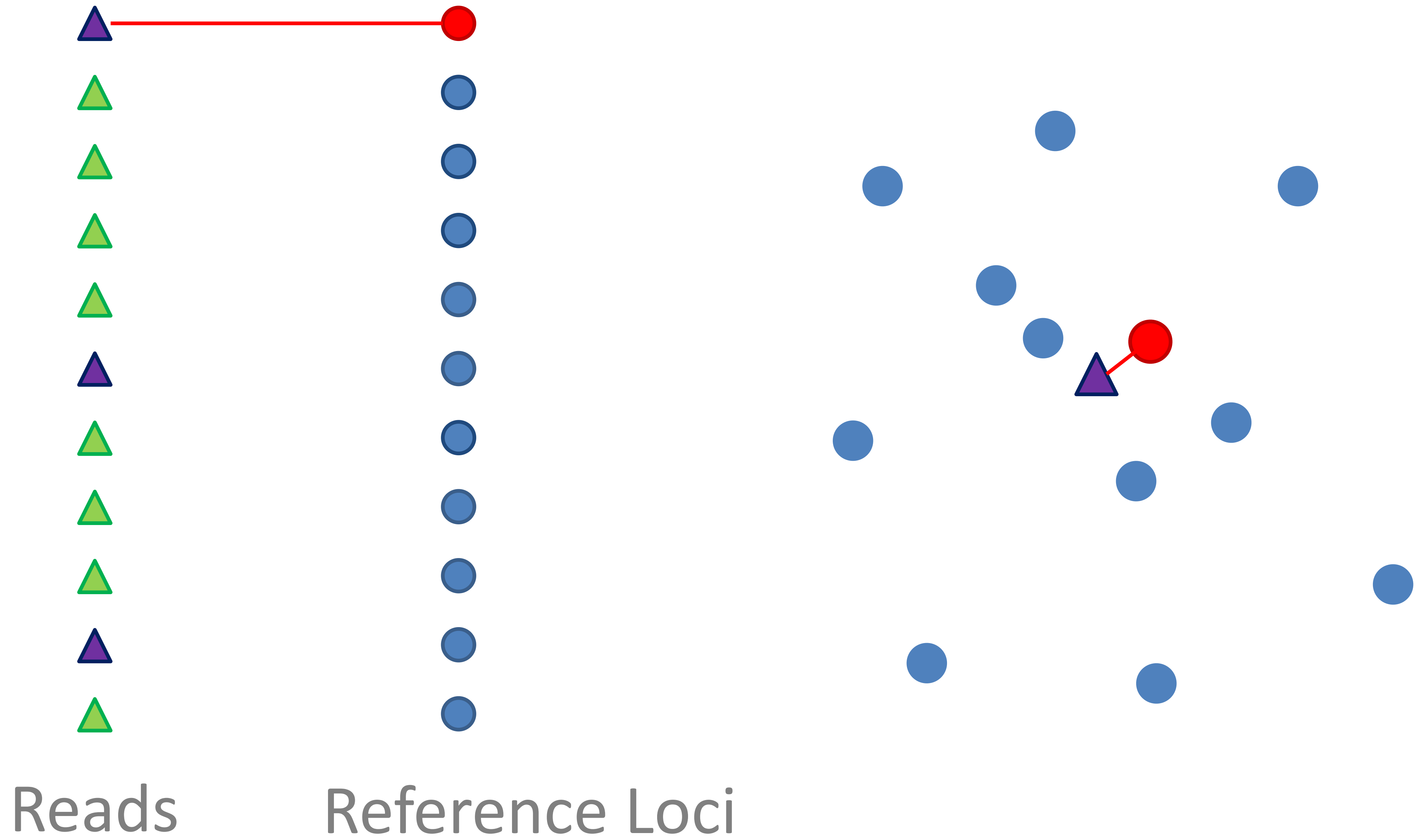

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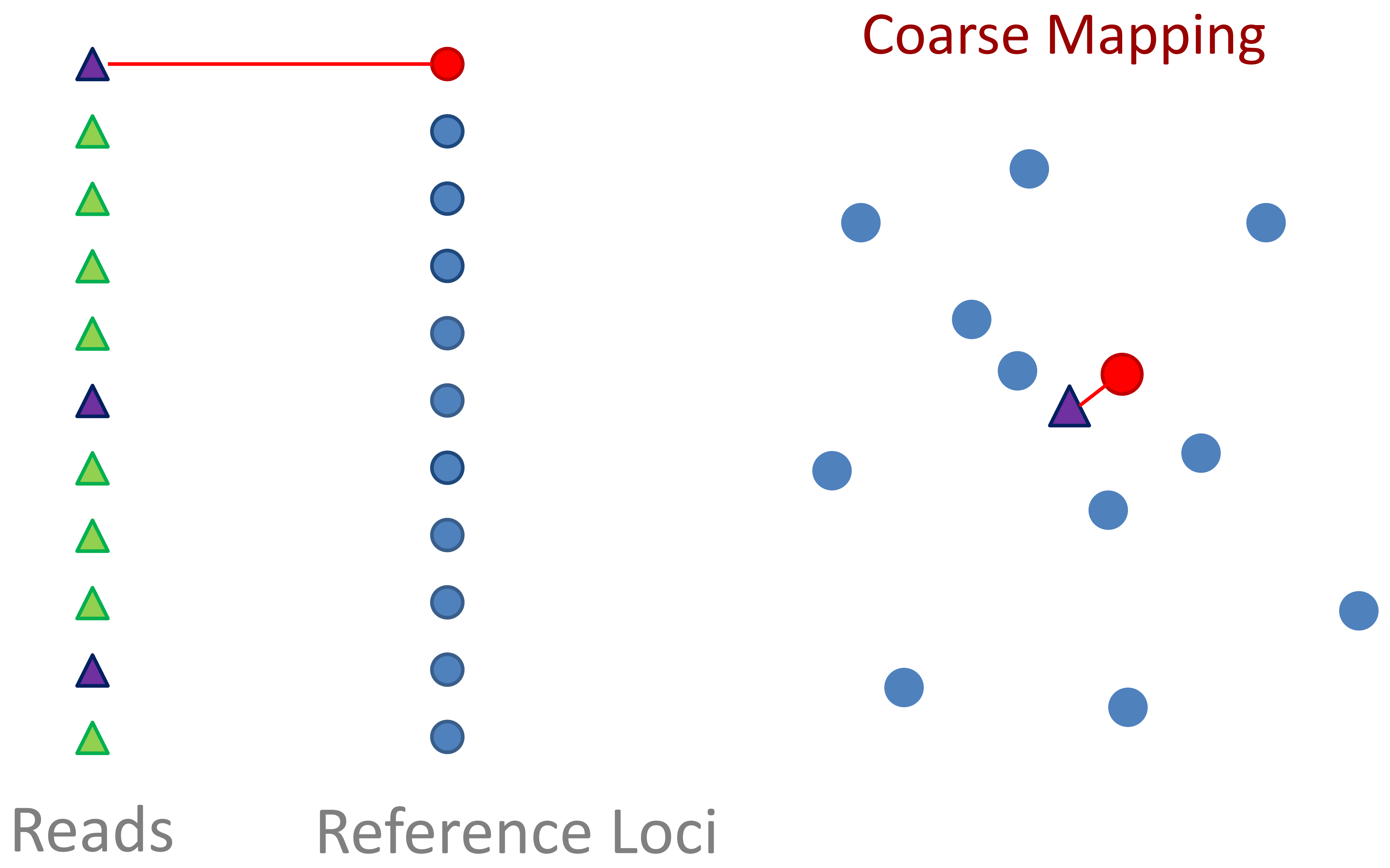

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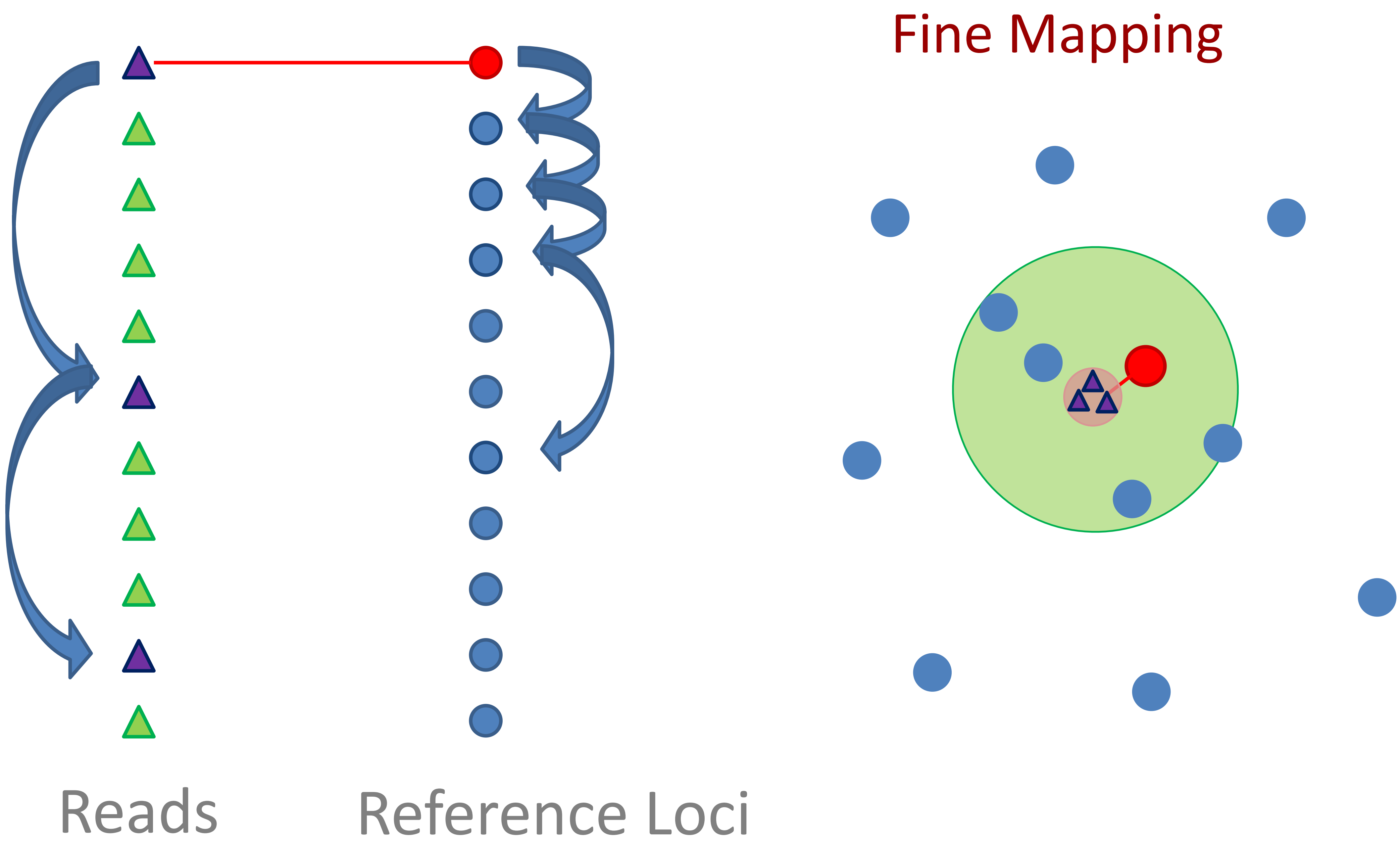
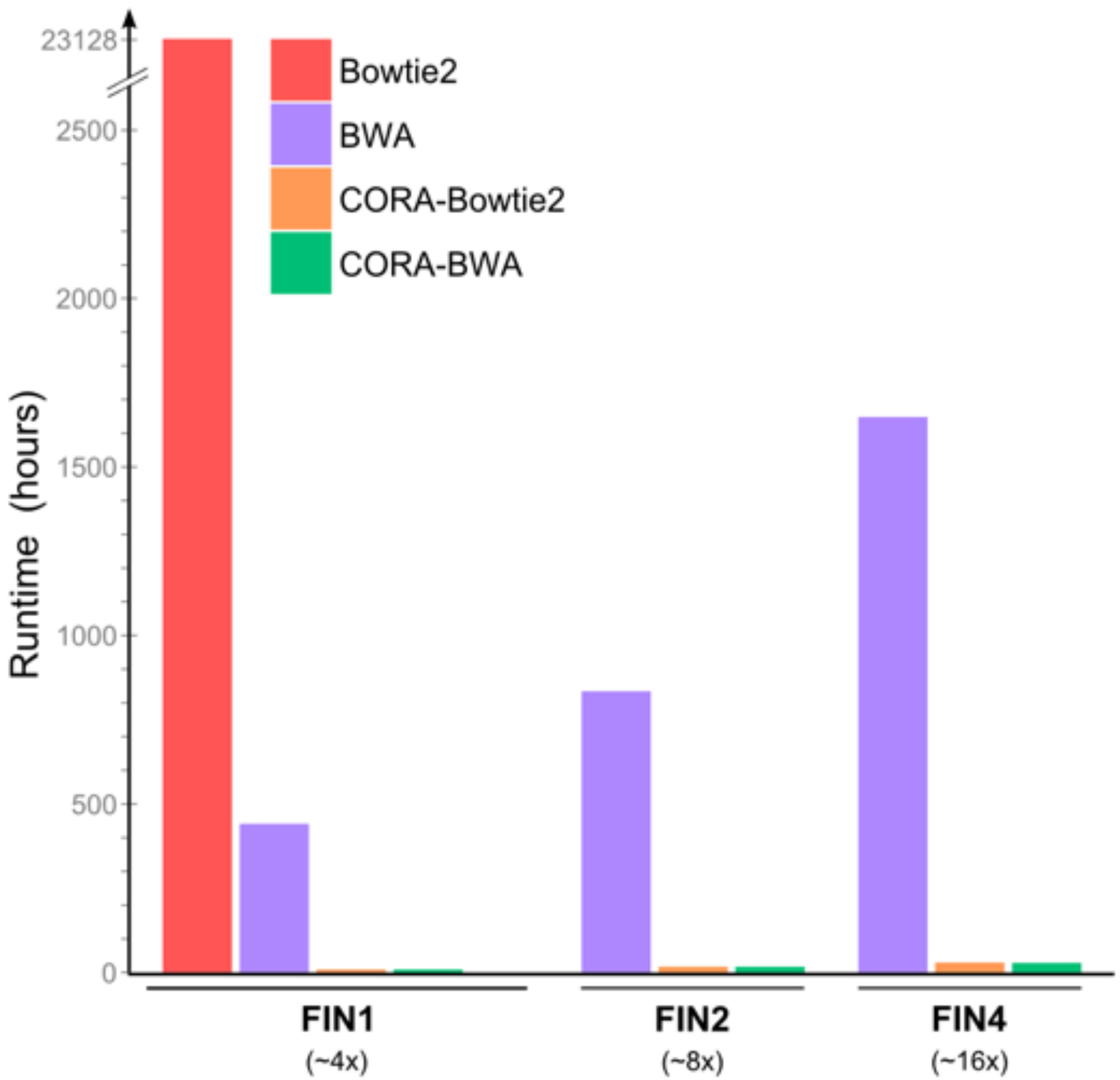


Result Highlights

CORA: 1000 Genomes Project



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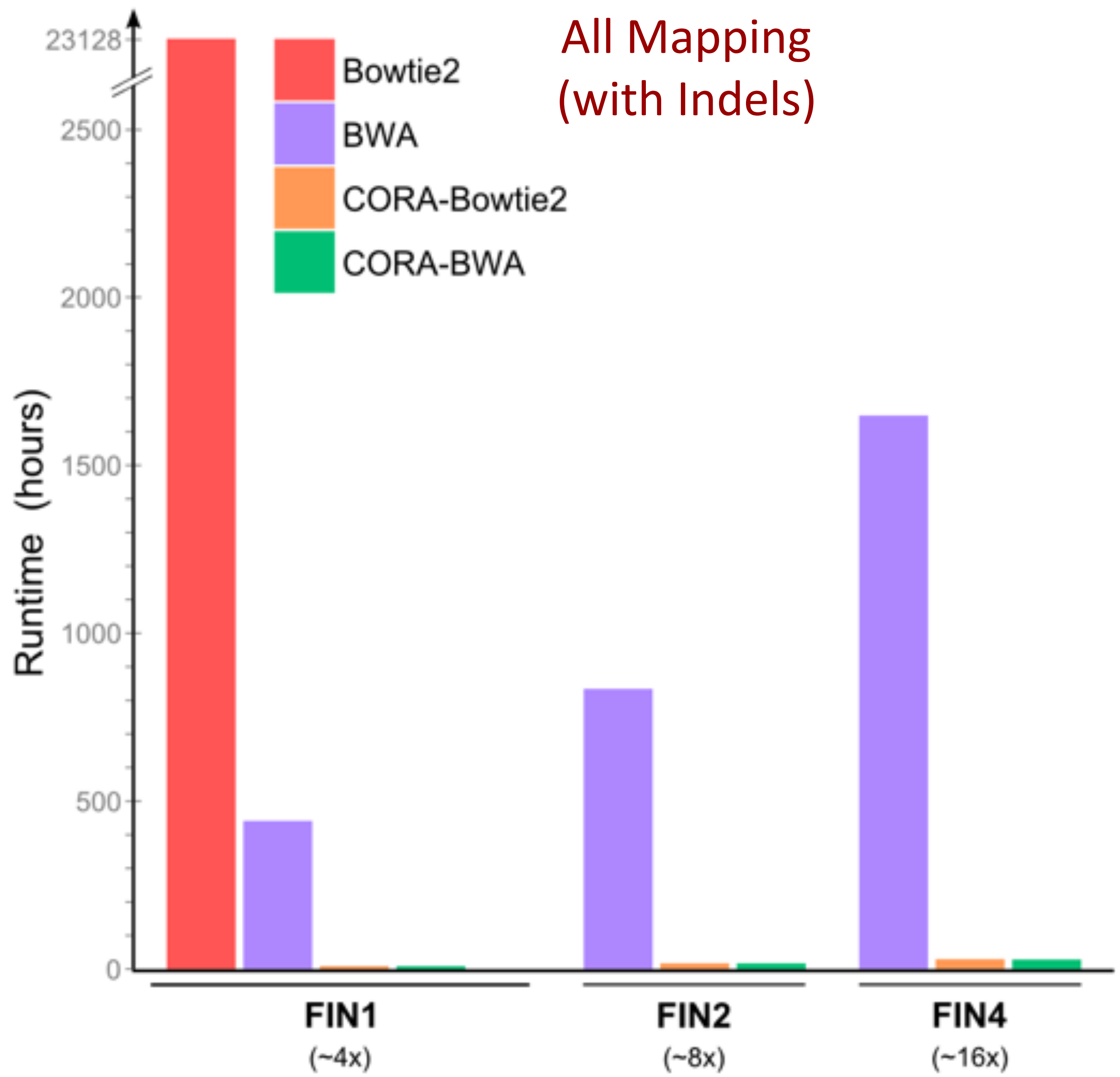

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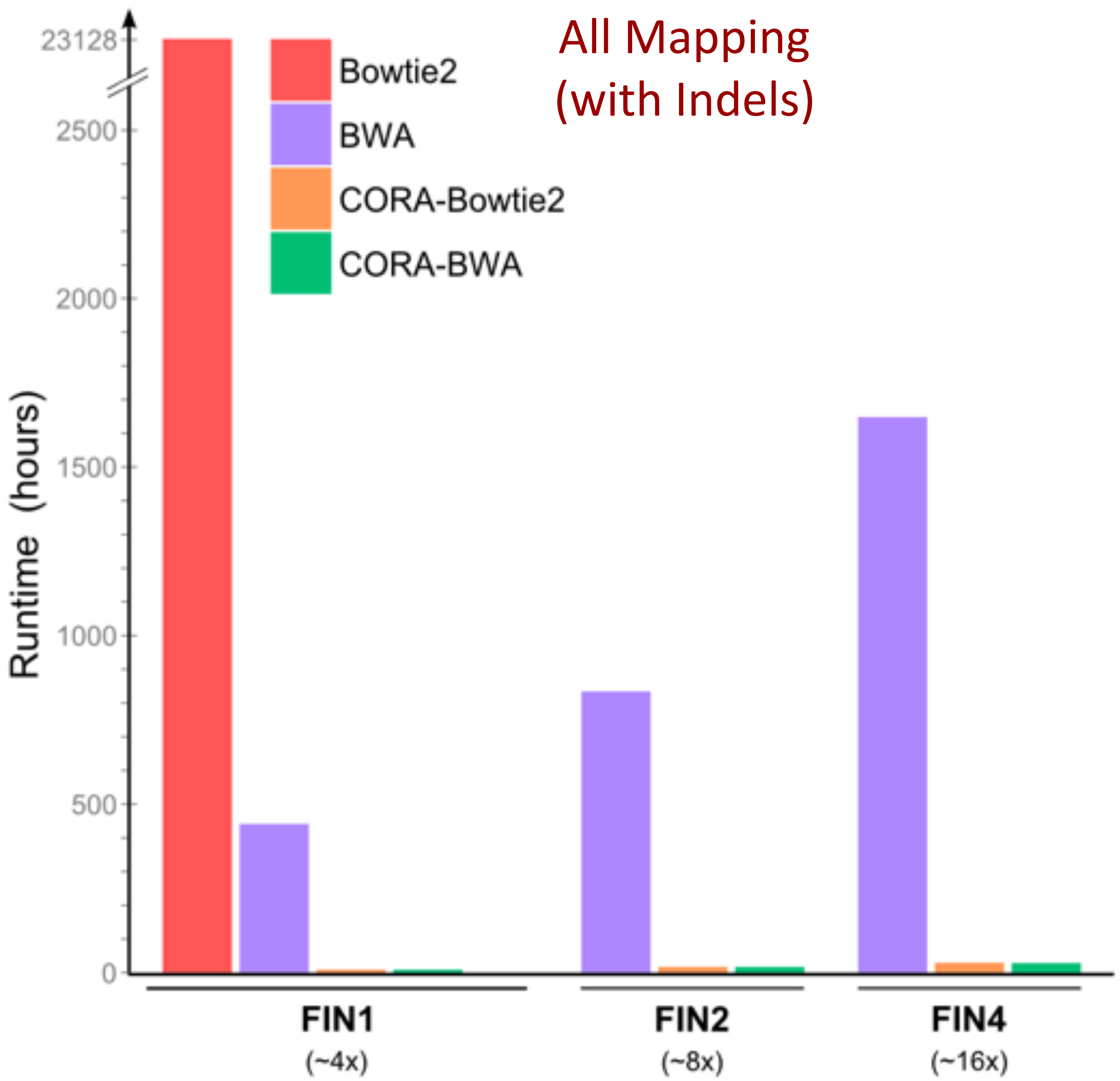

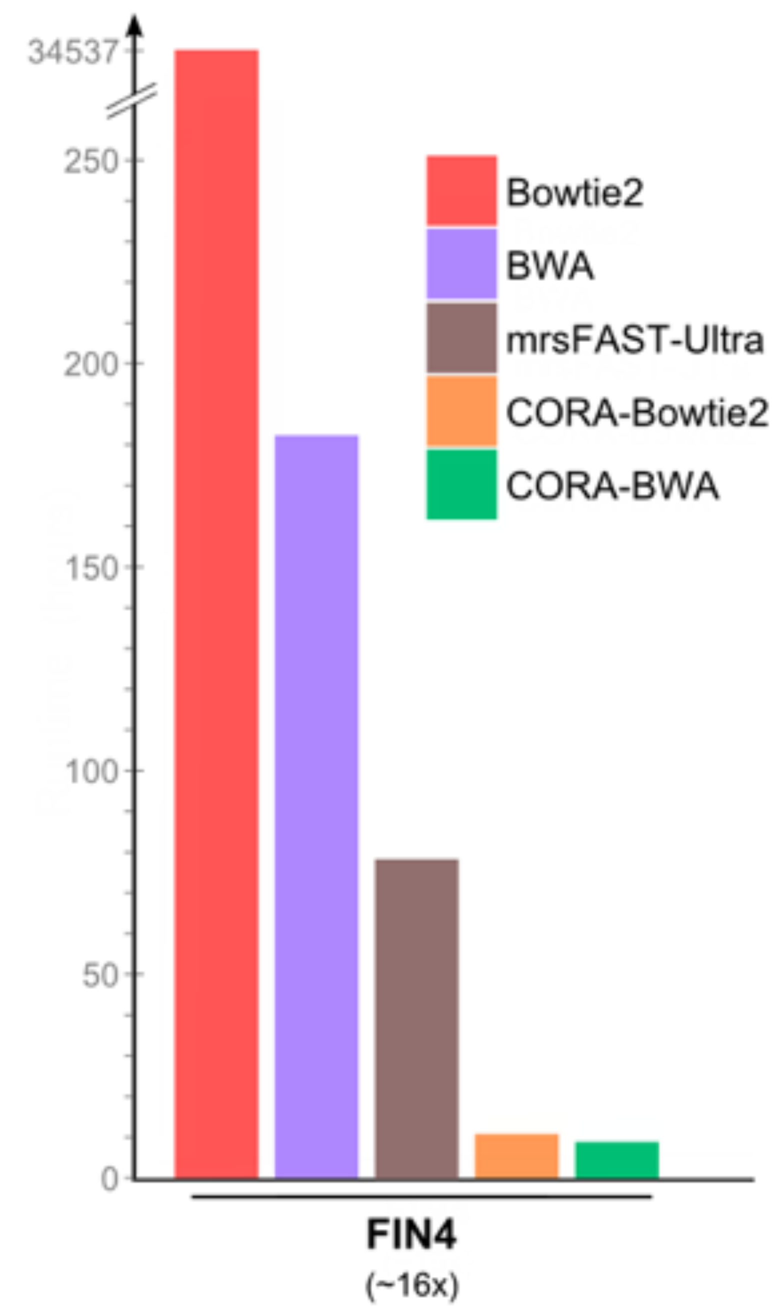

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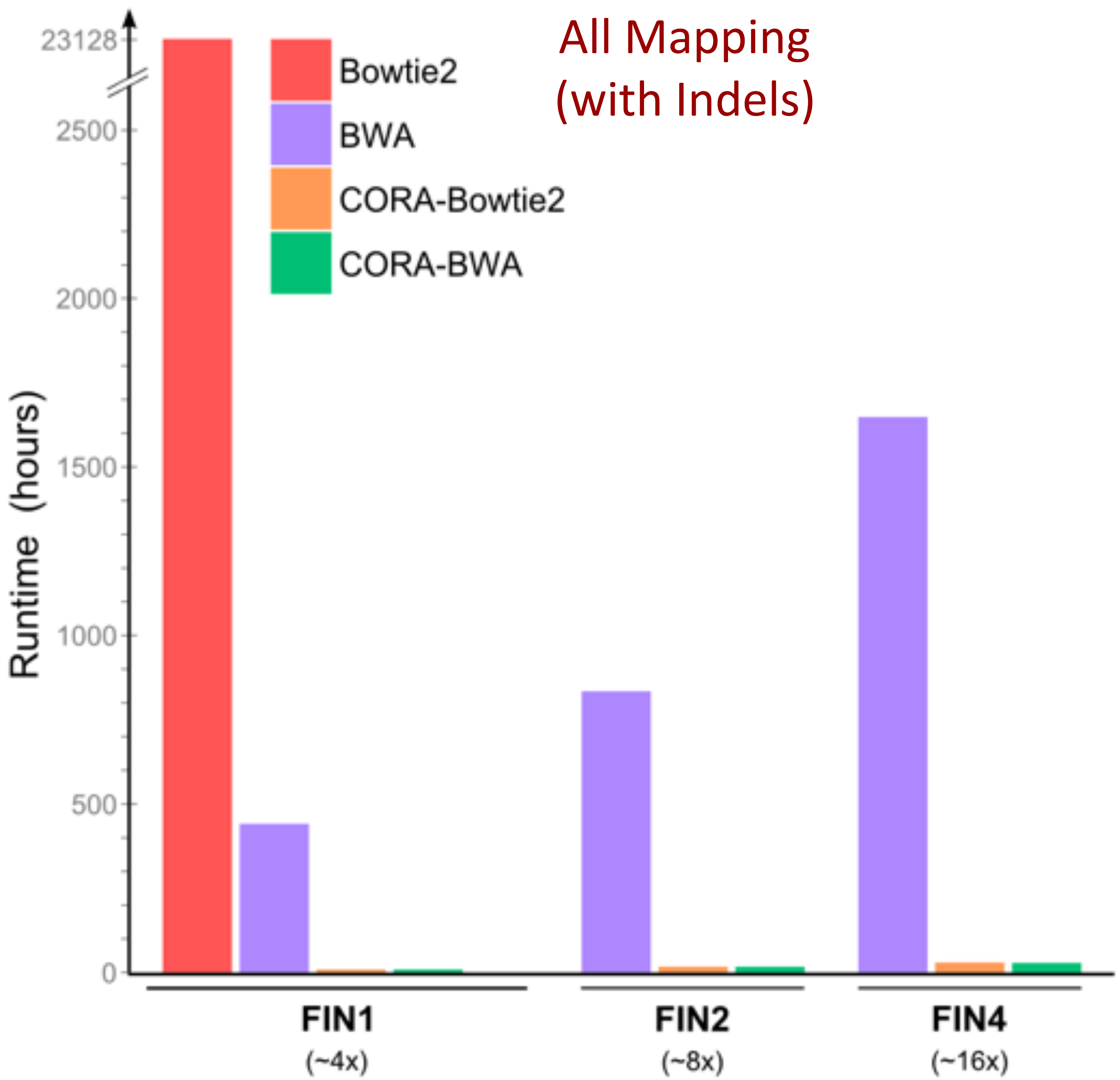

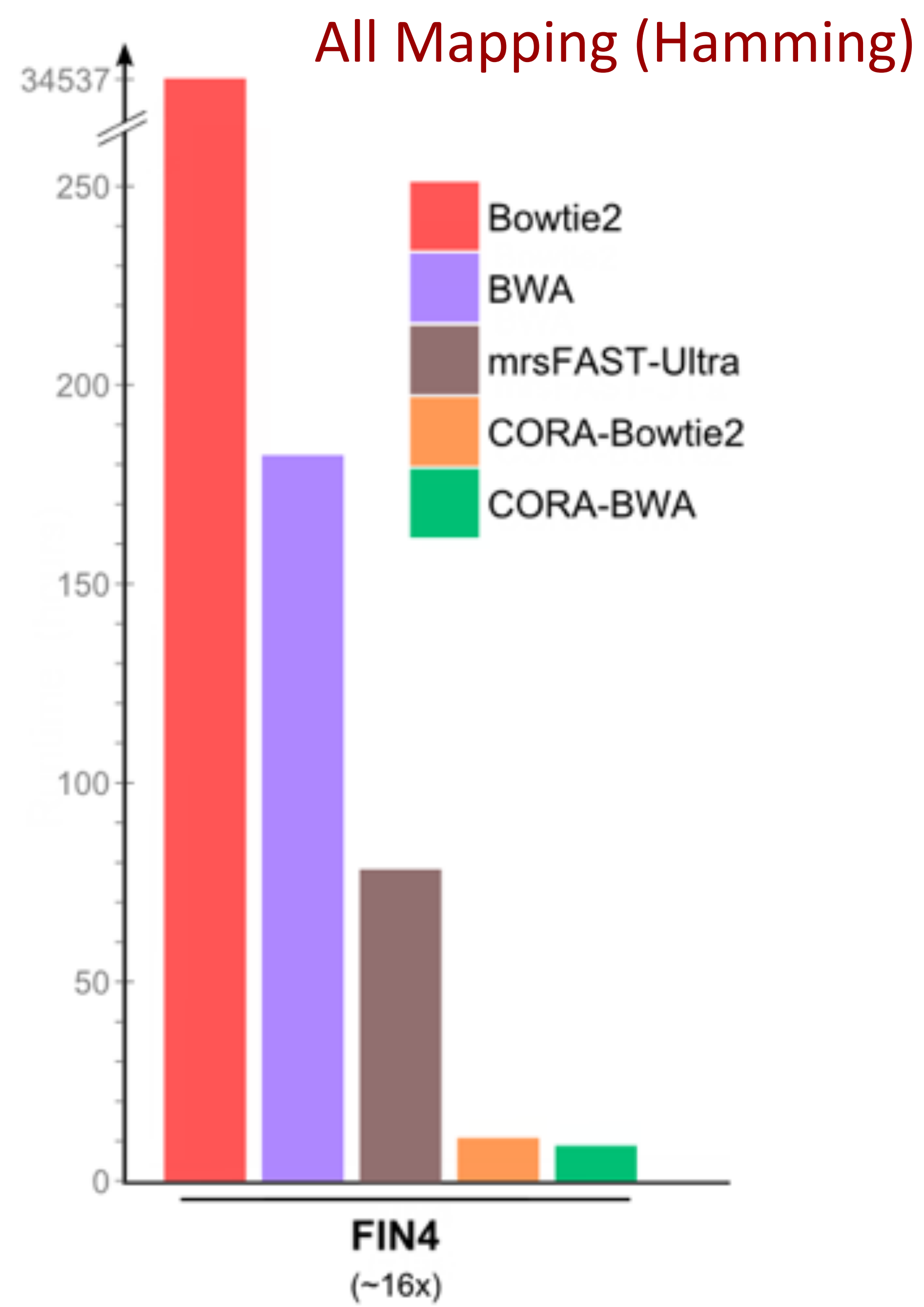

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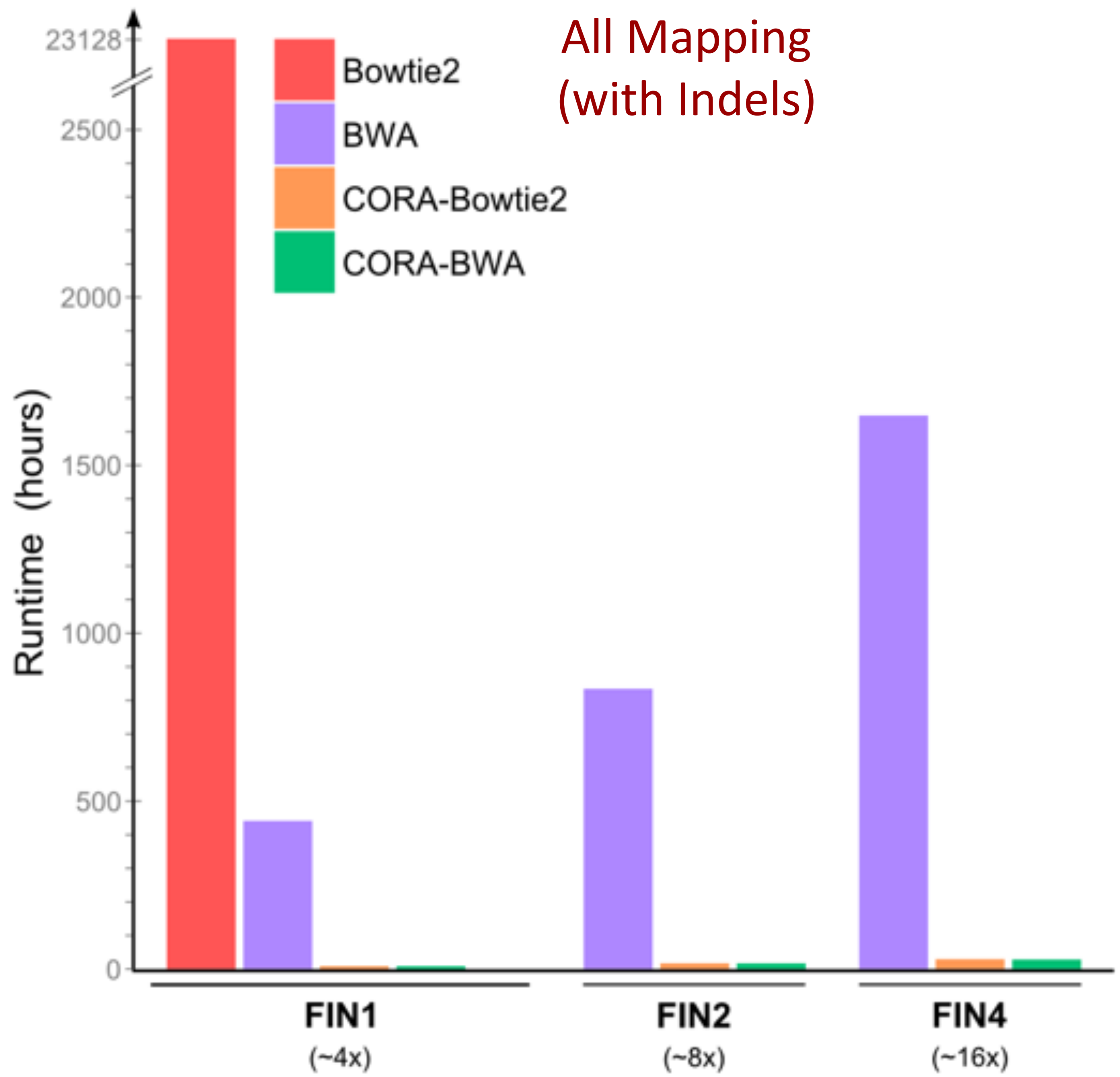

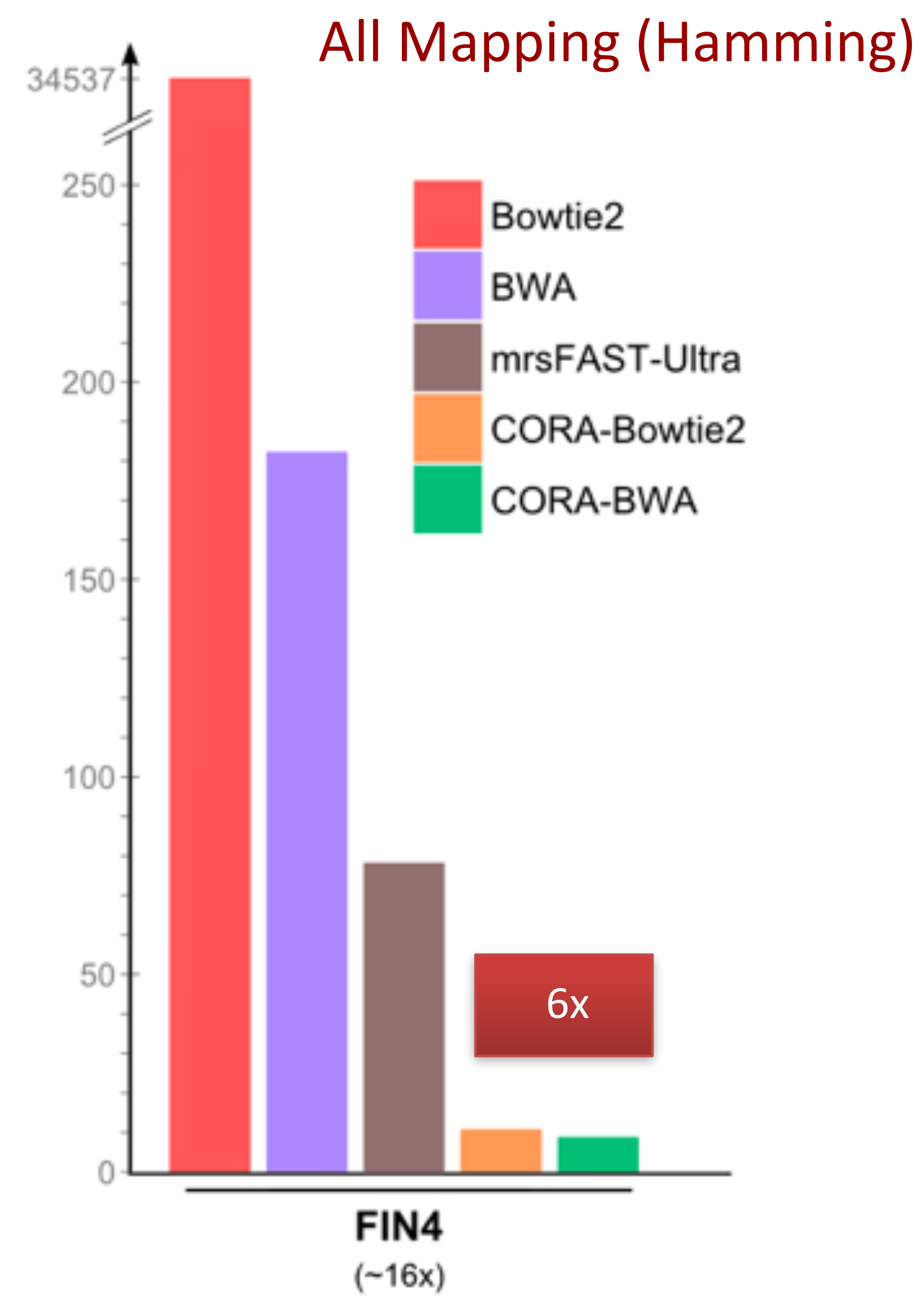

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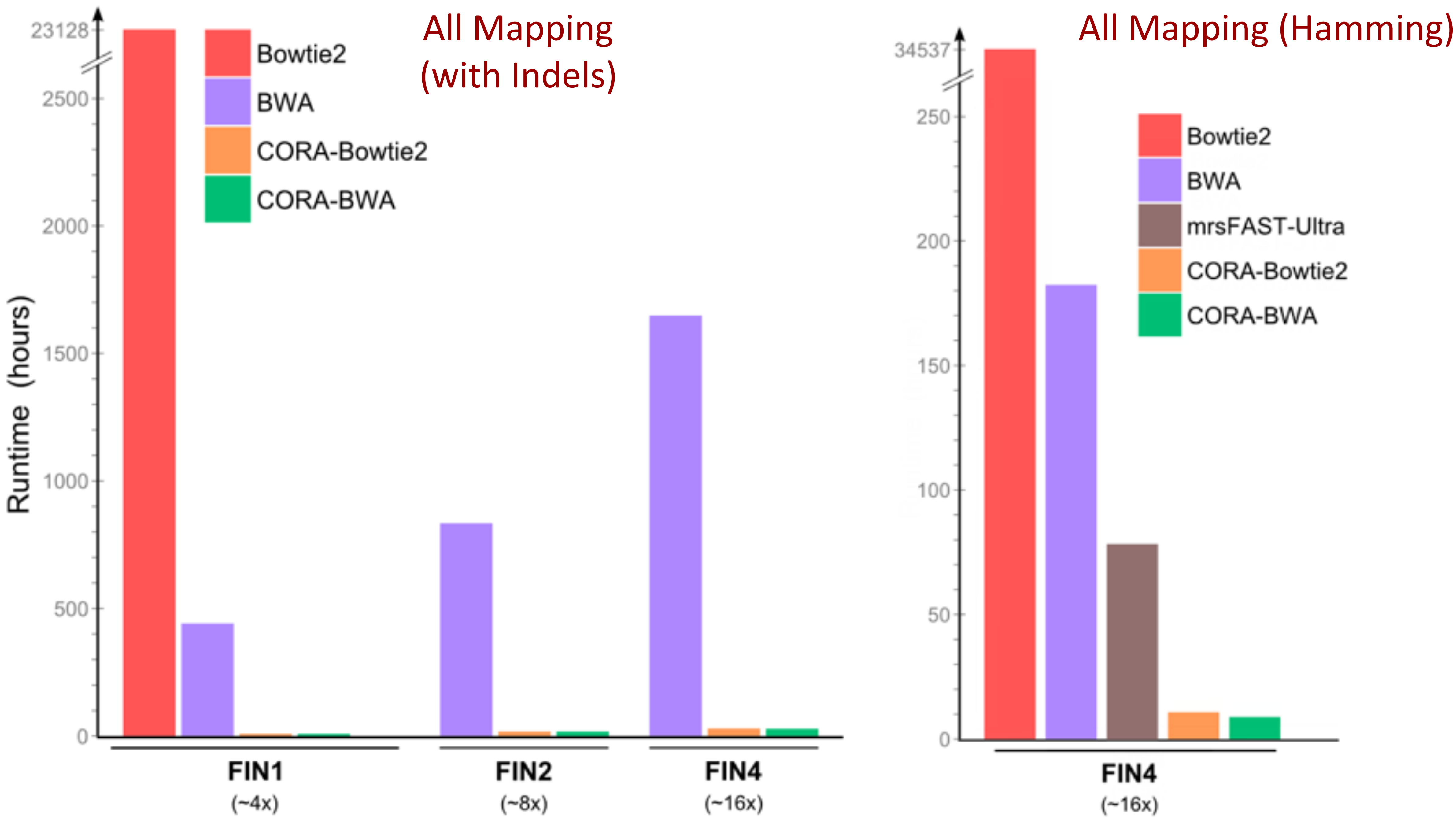
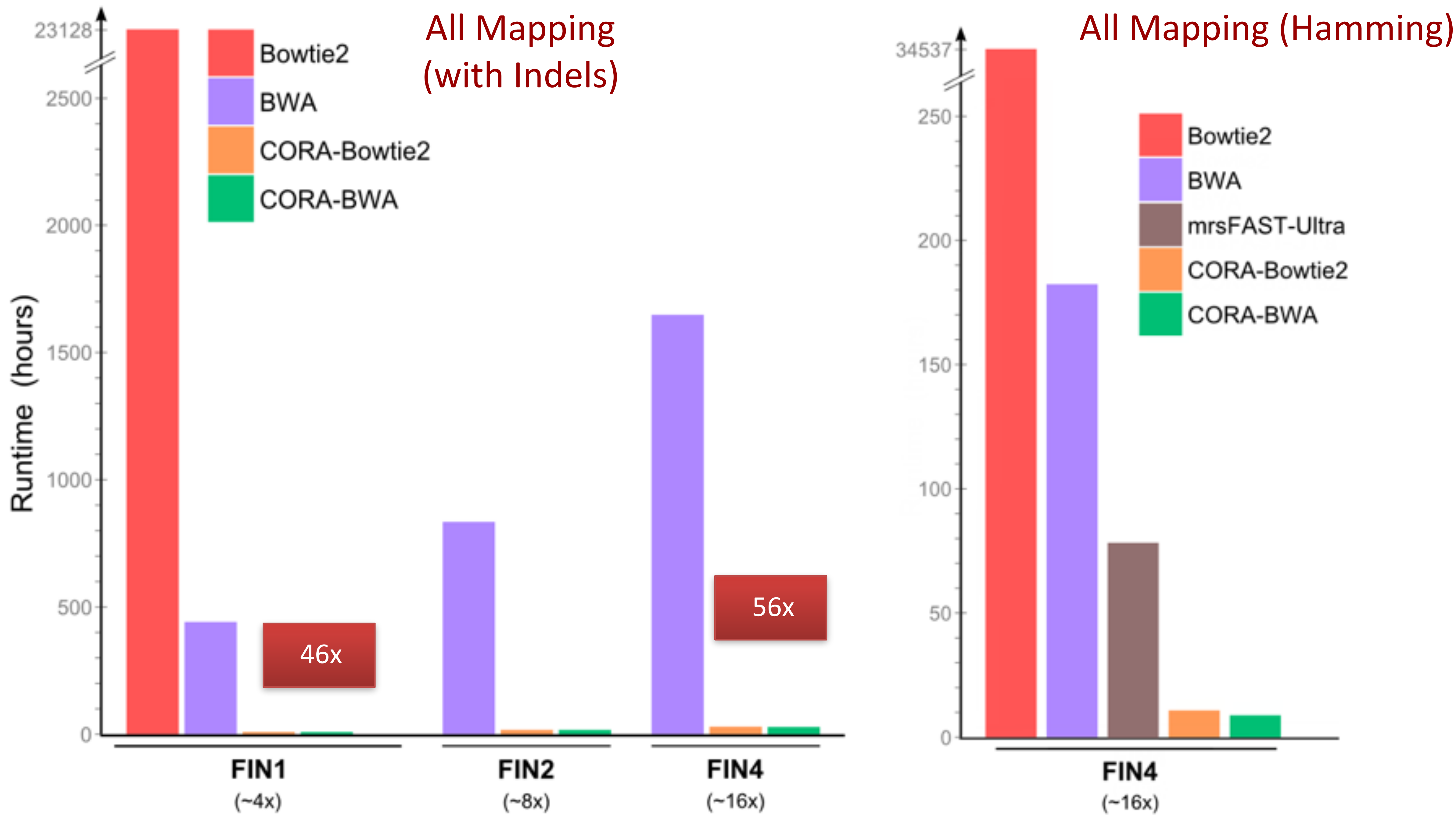


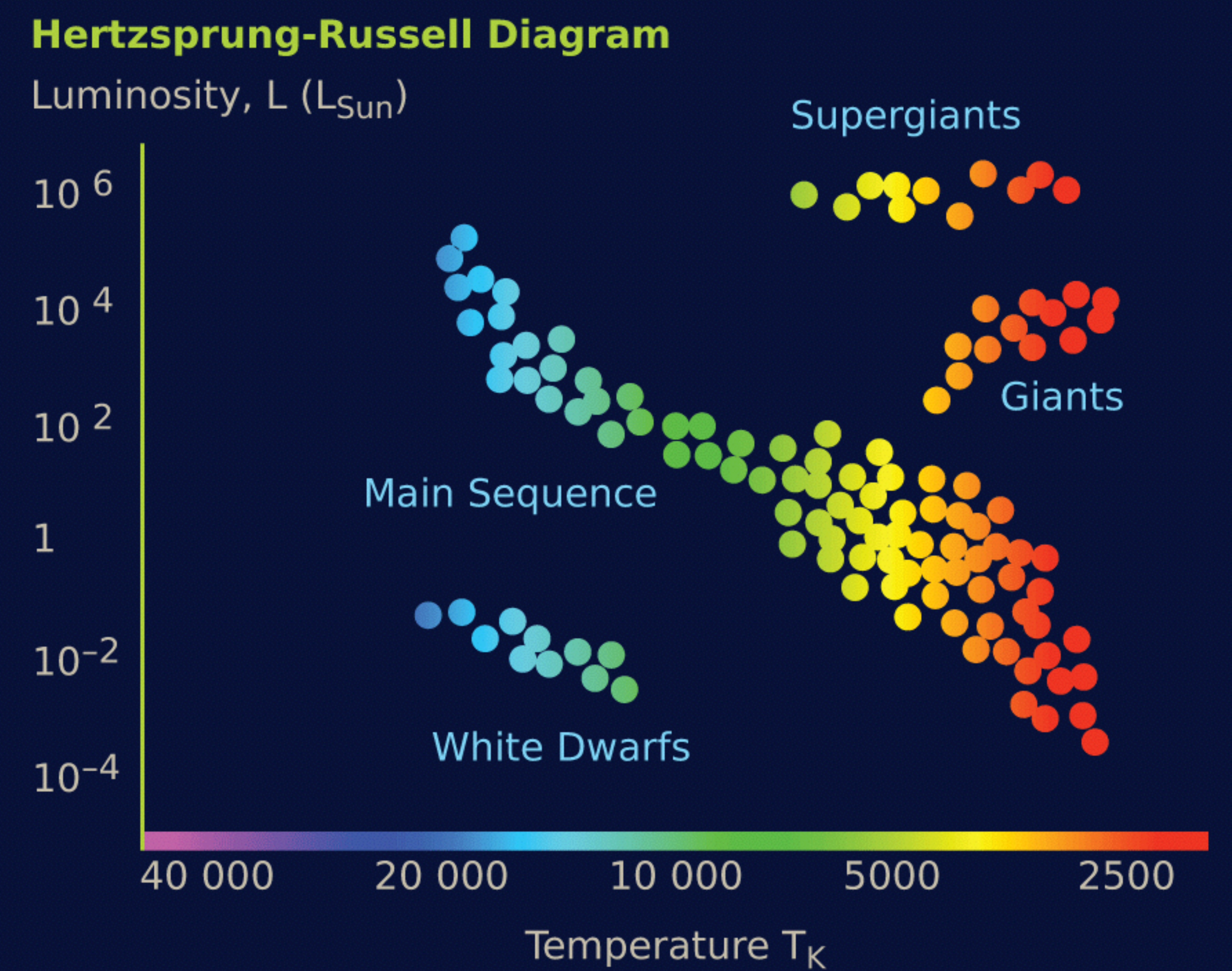
Result Highlights

CORA: 1000 Genomes Project



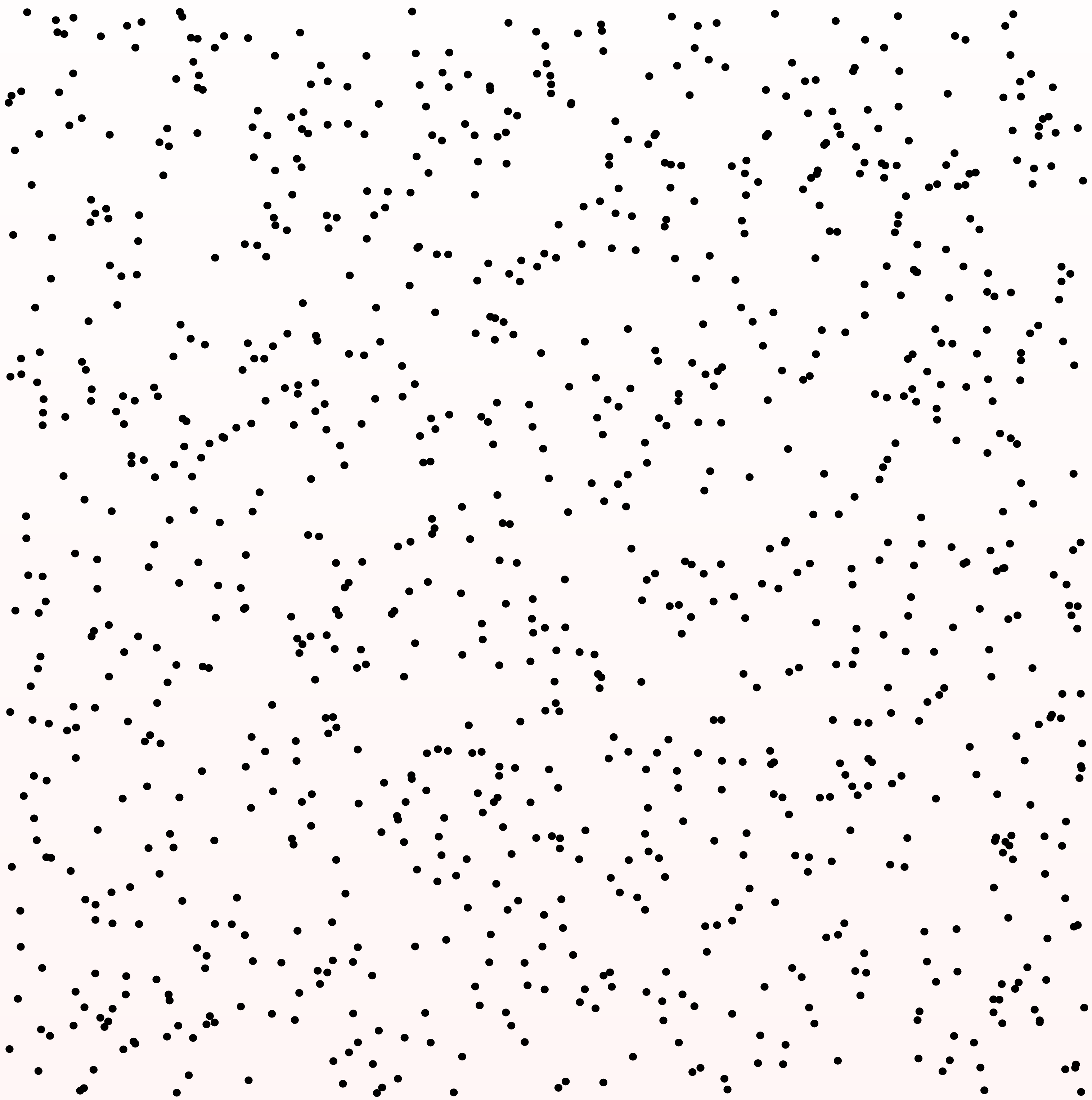
Scales sublinearly with very high sensitivity on real genomic data

Data constrained by physical process

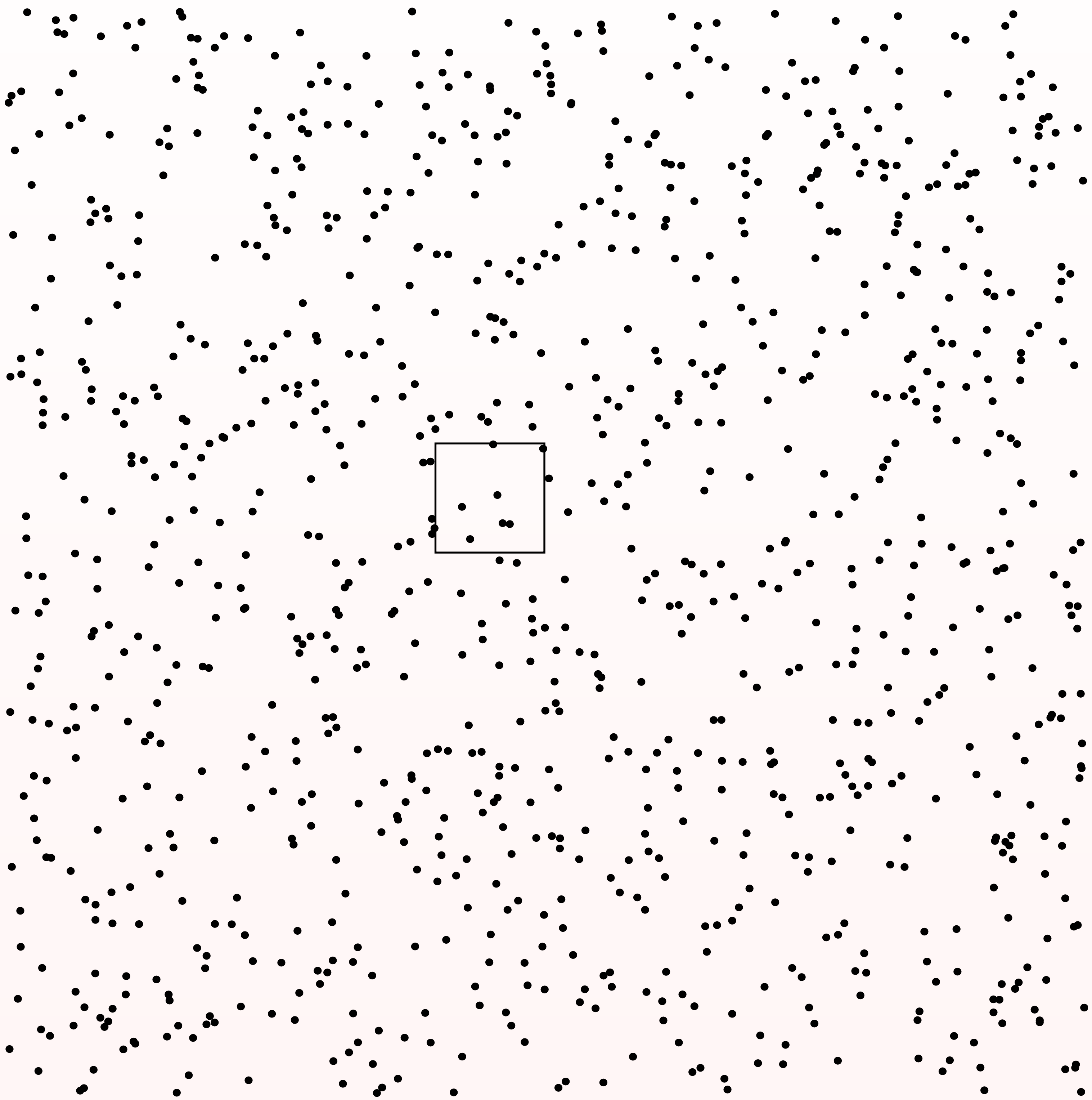


Hertzsprung-Russell Diagram
Luminosity, L (L_{Sun})
Supergiants
Giants
Main Sequence
White Dwarfs
10^6
10^4
10^2
1
10^{-2}
10^{-4}
40 000
20 000
10 000
5000
2500
Temperature T_K

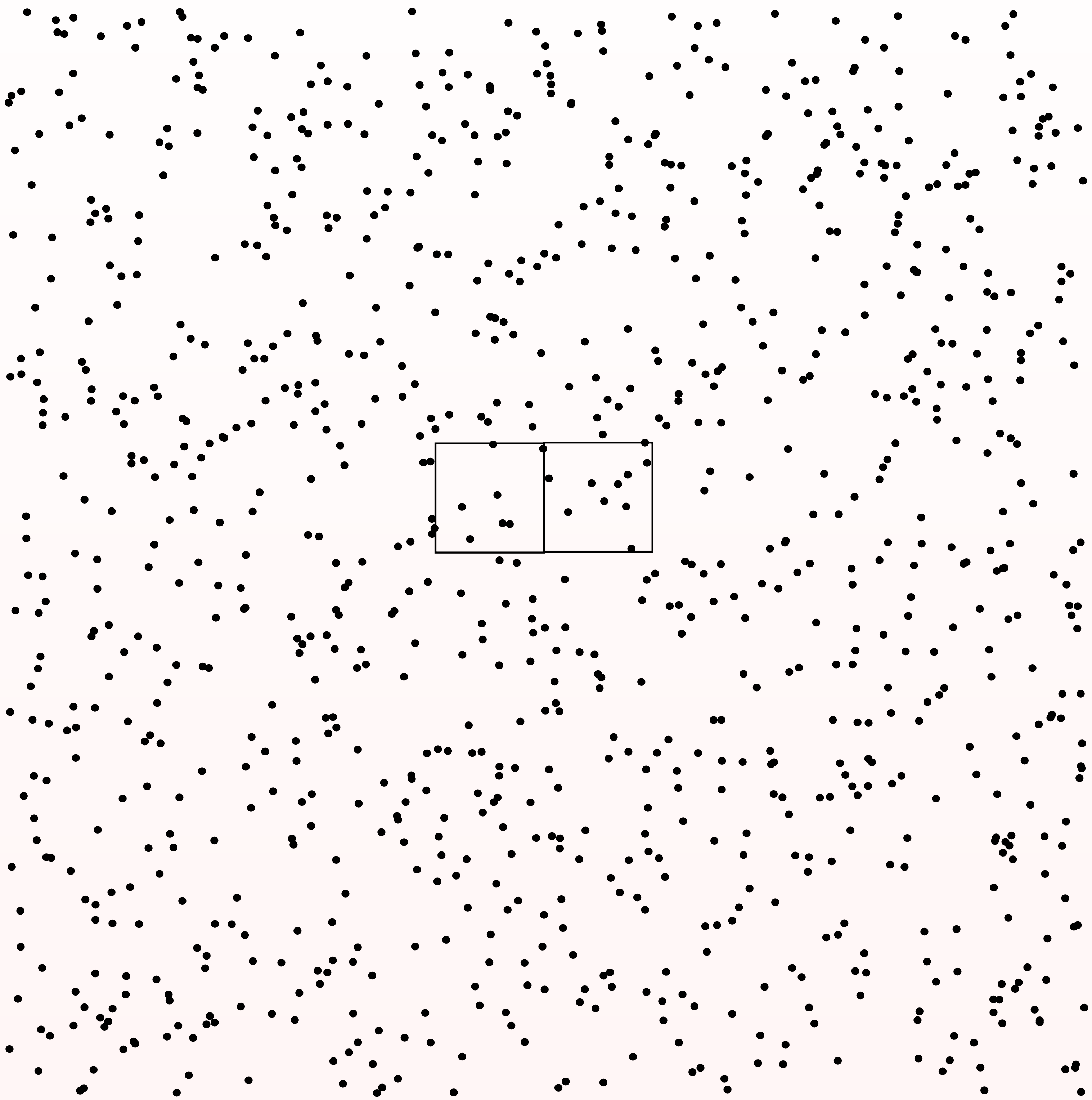
Grid search



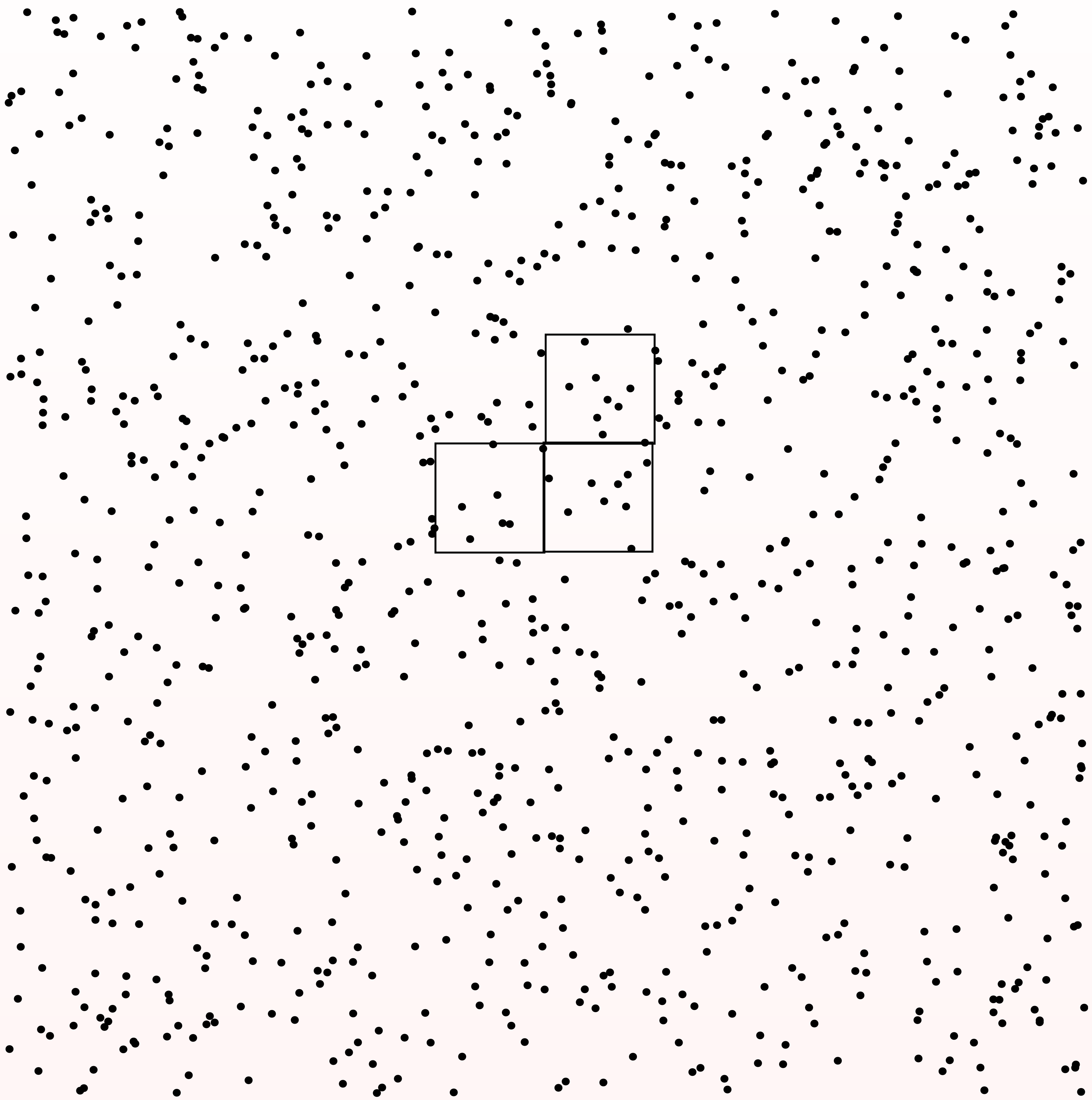
Grid search



Grid search



Grid search



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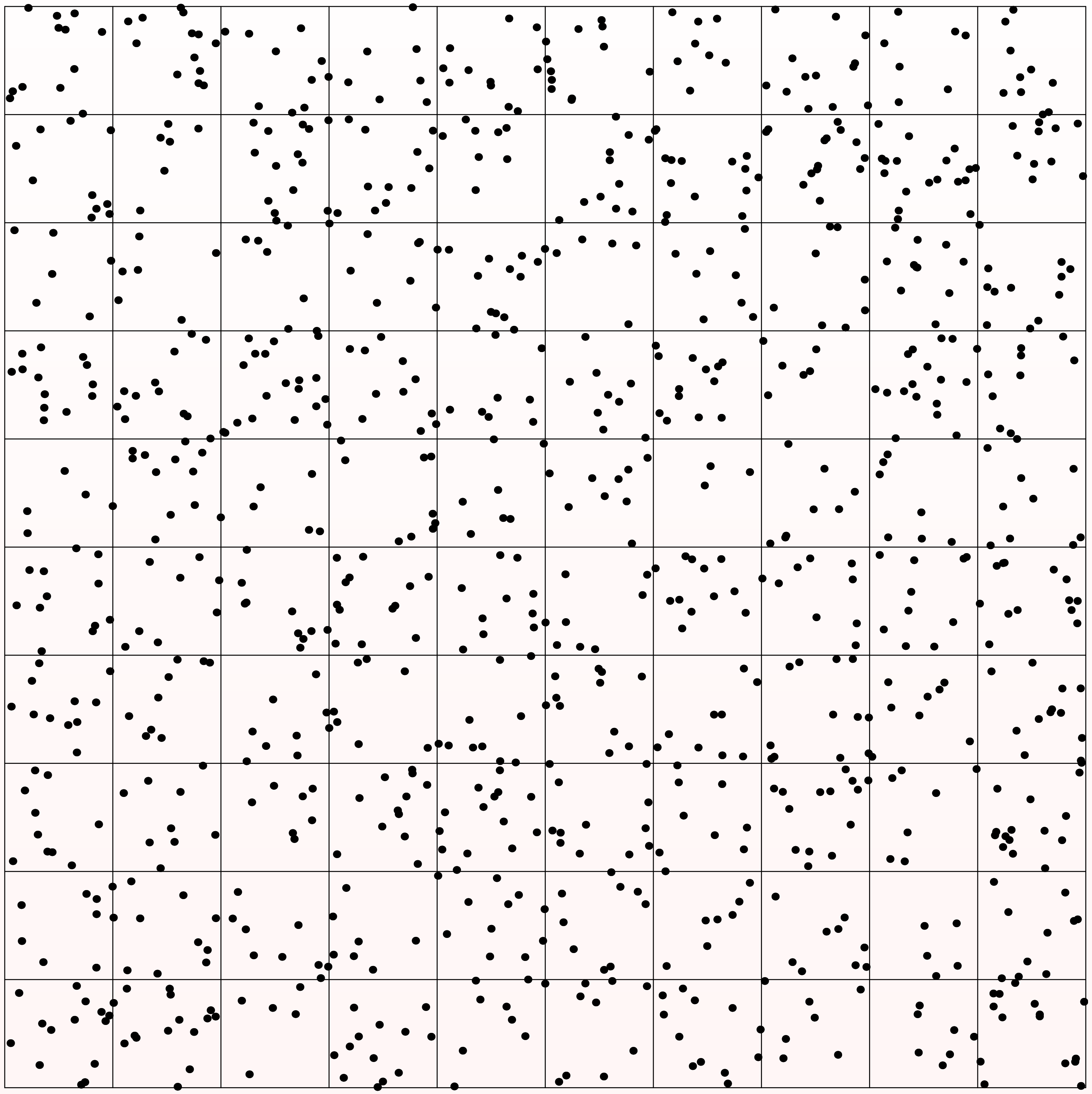
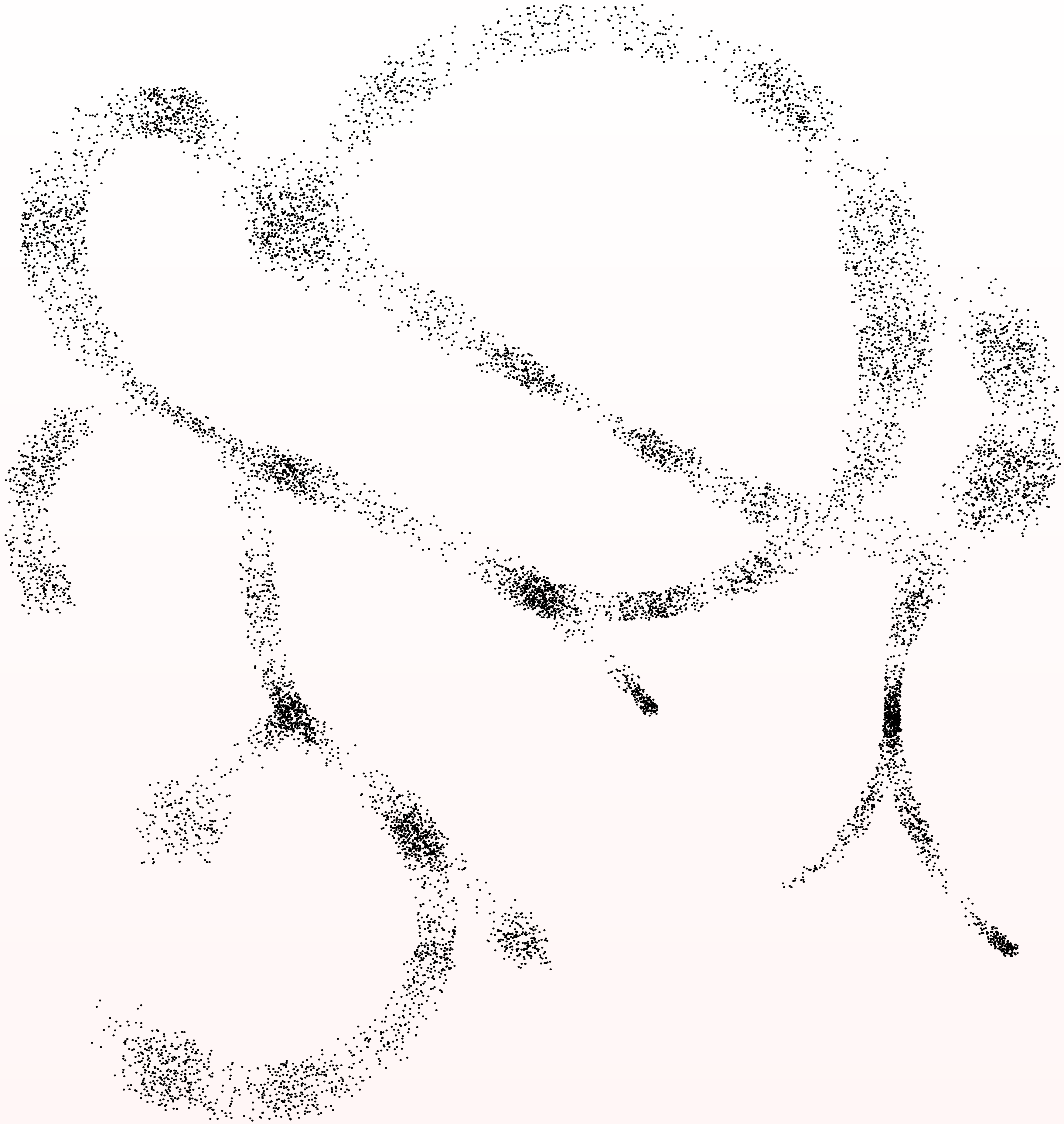
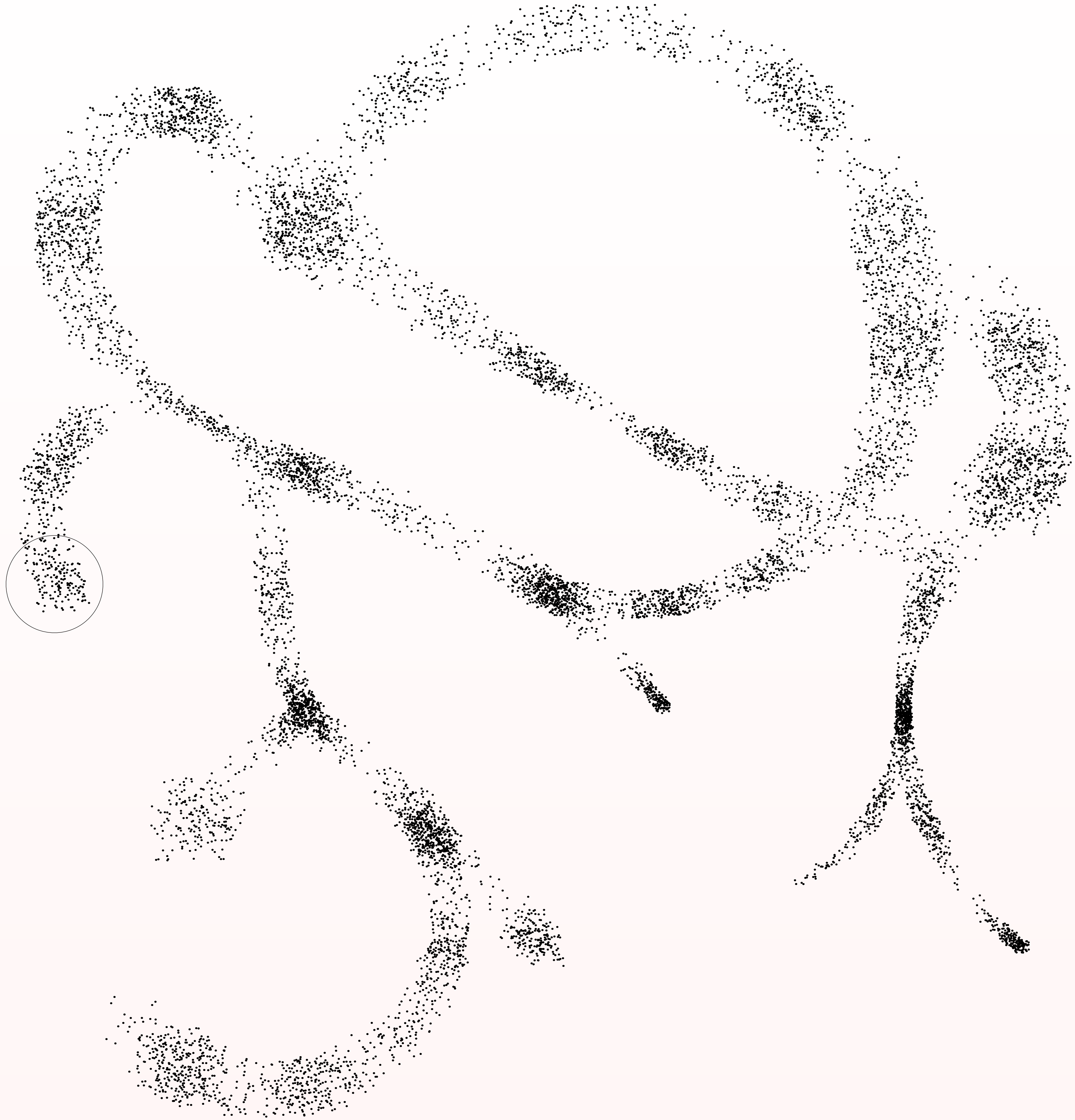
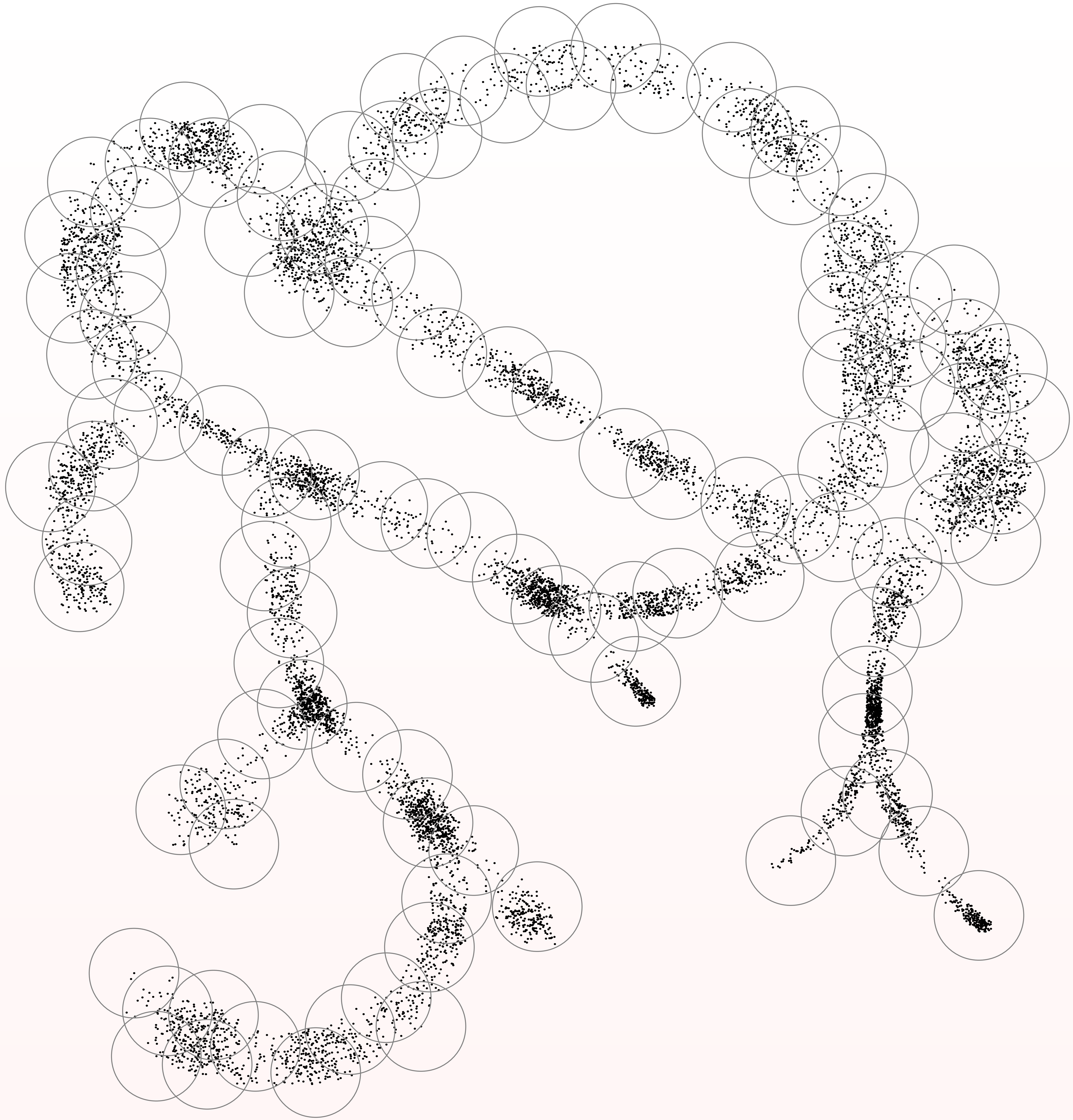
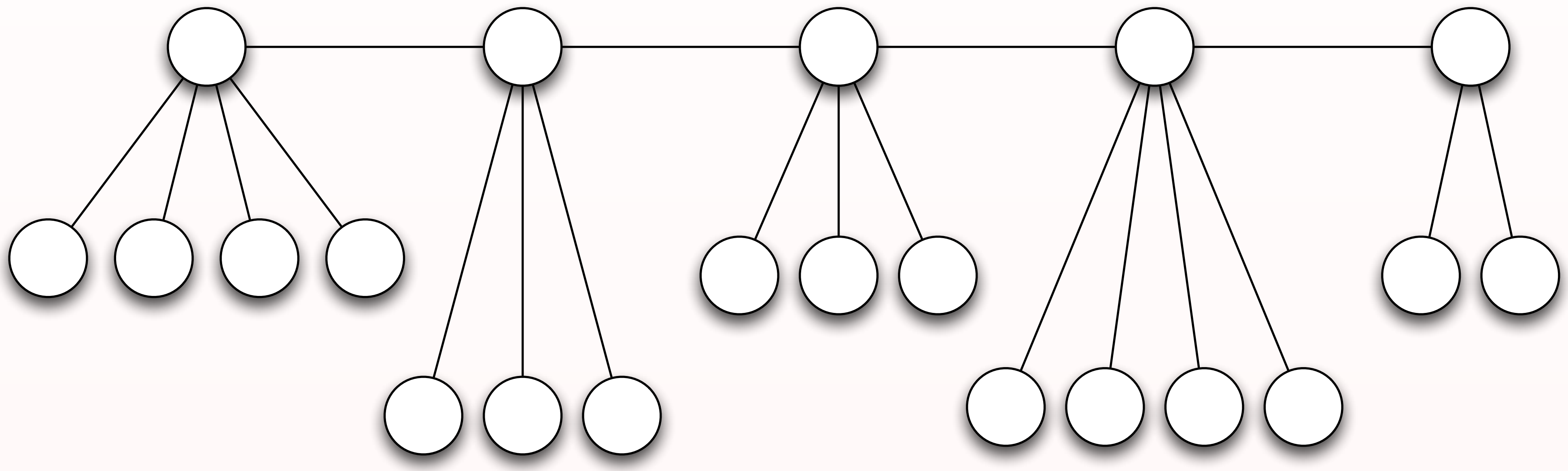








The search tree



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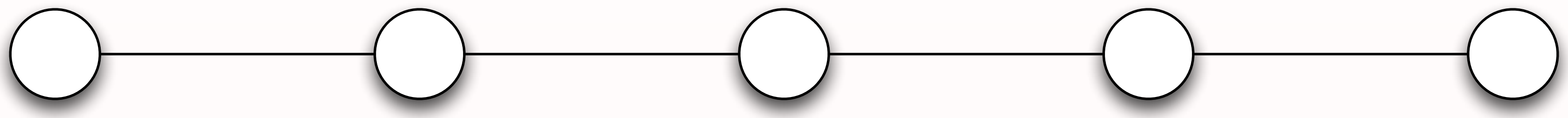
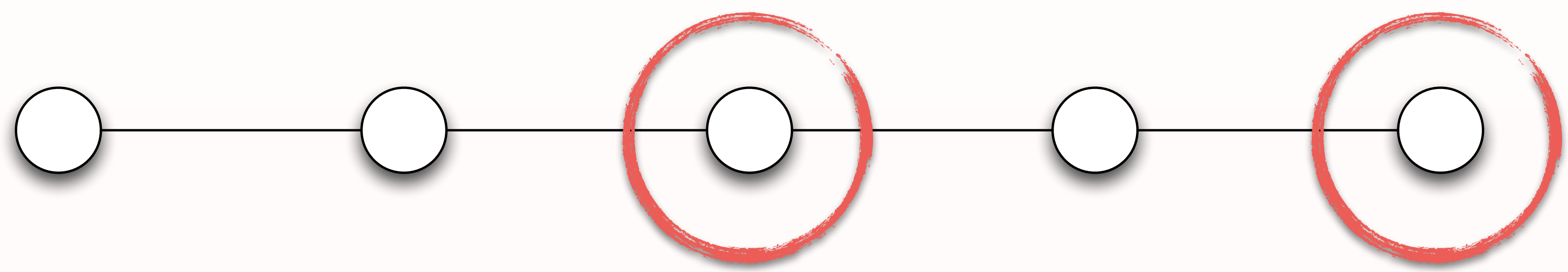


coarse search

The search tree

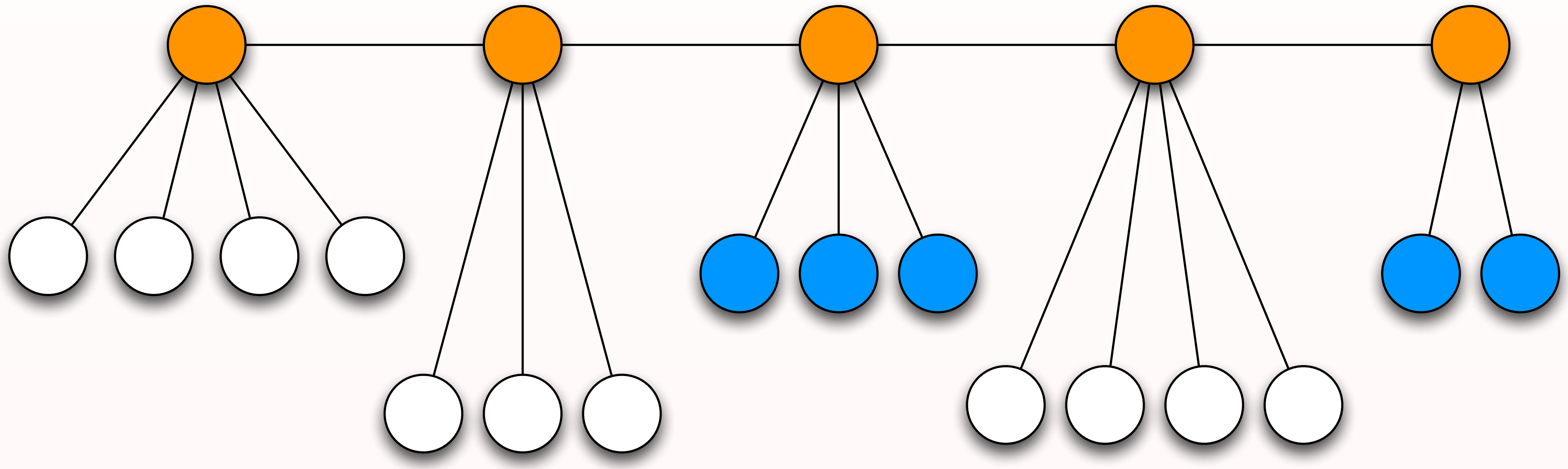


coarse search

The search tree

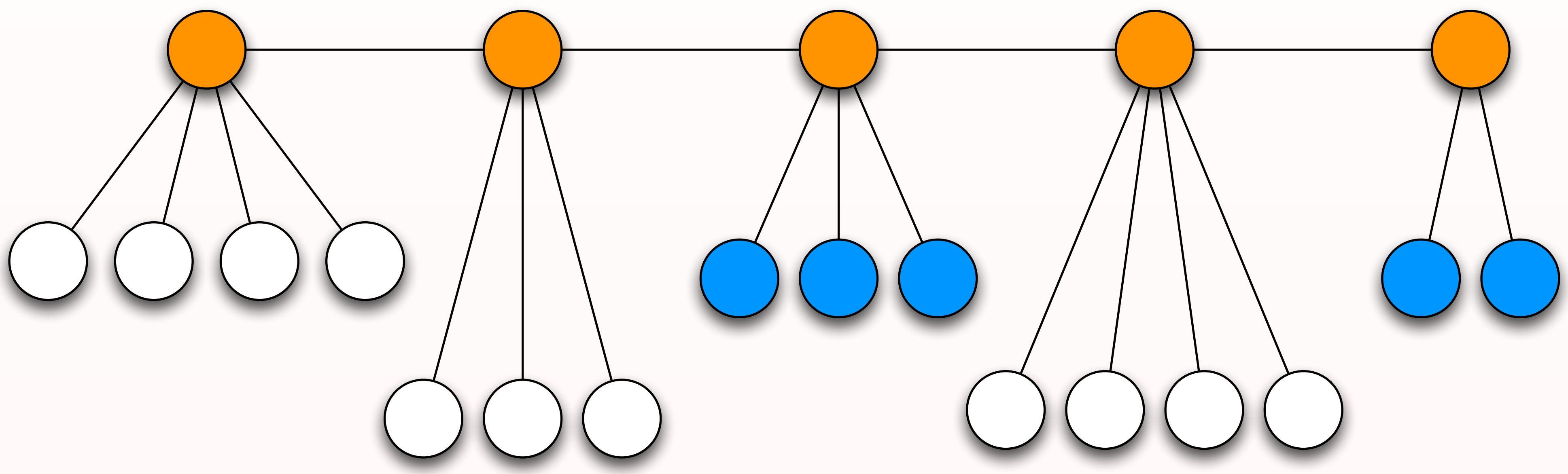
fine search

The search tree



$$O(\textit{coarse} + \textit{fine})$$

The search tree



$$O(\quad k \quad + fine)$$

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$$\dim_{\text{Minkowski}}(D) := \lim_{\rho \to 0} \frac{\log N_\rho(D)}{\log 1/\rho}$$

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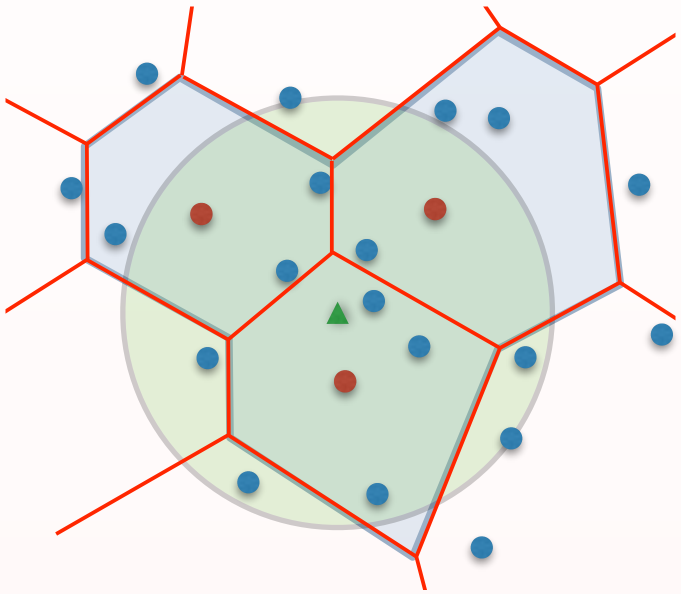

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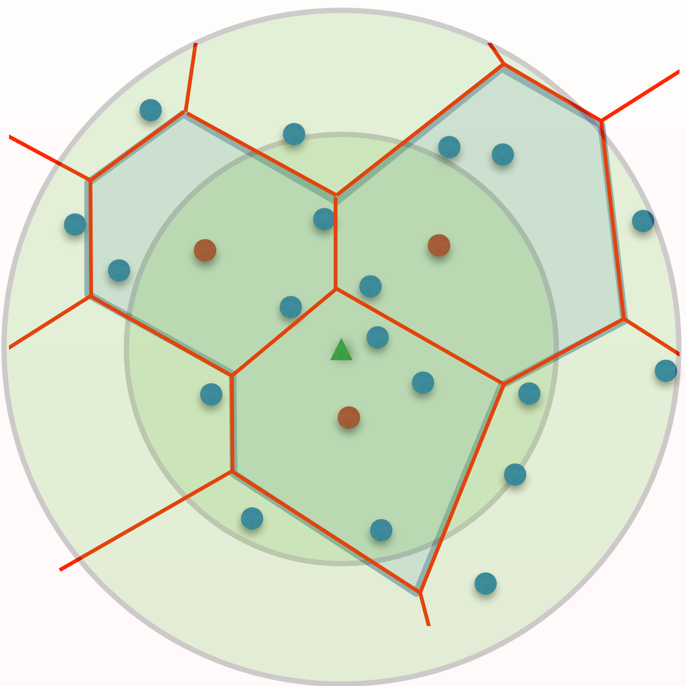

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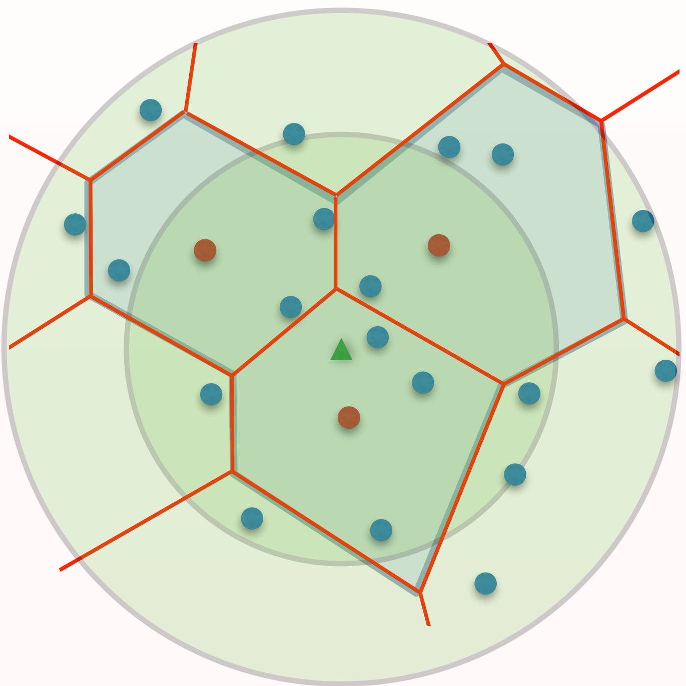

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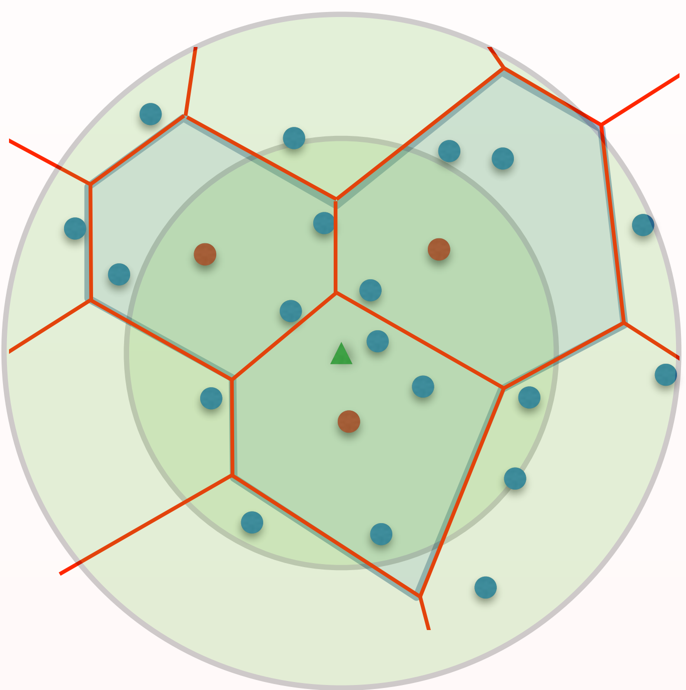

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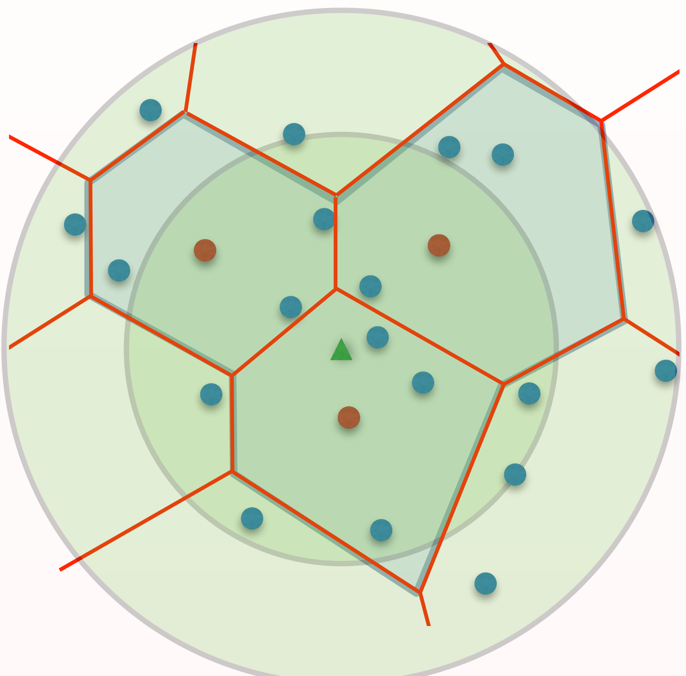

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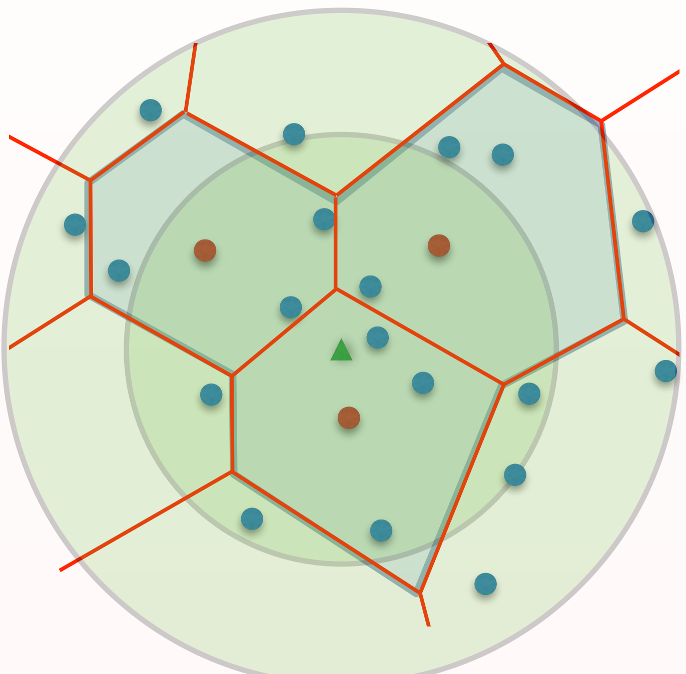

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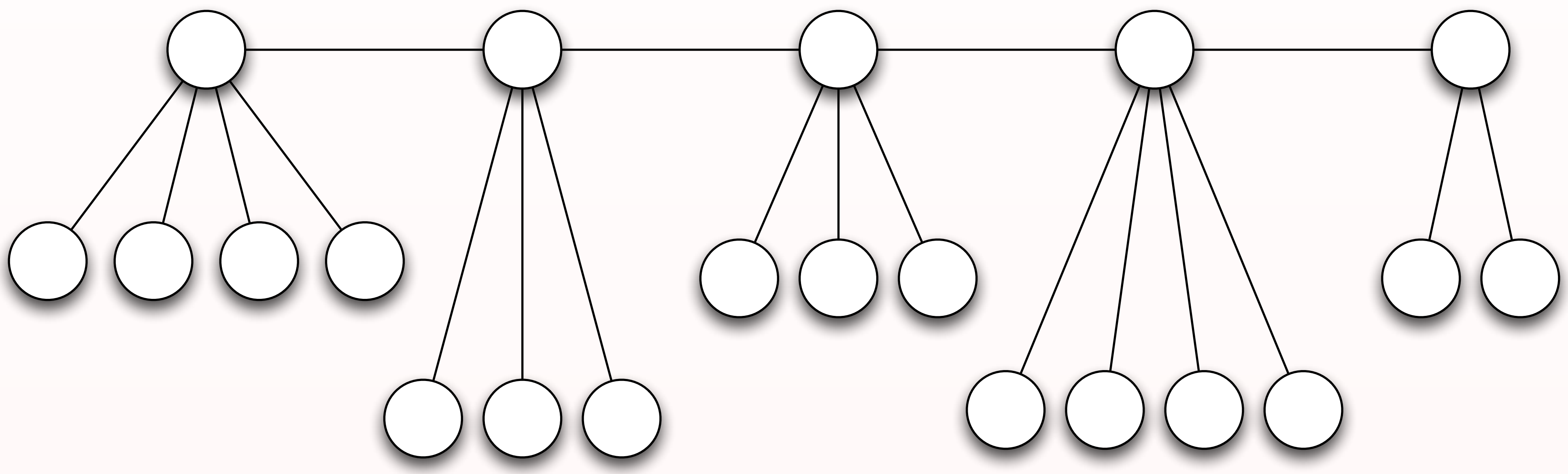
Entropy-scaling data structure



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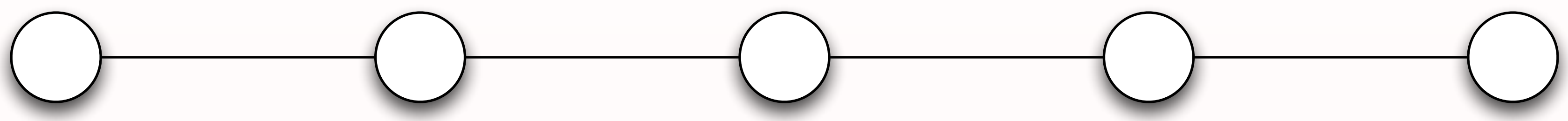

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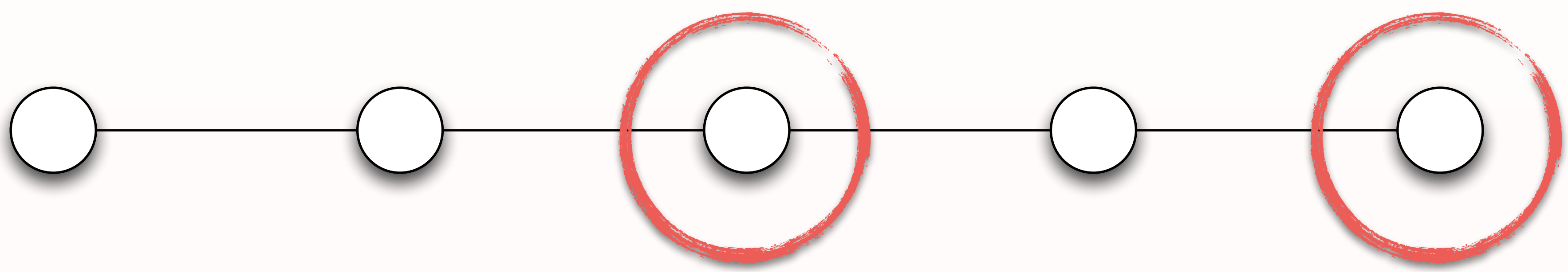

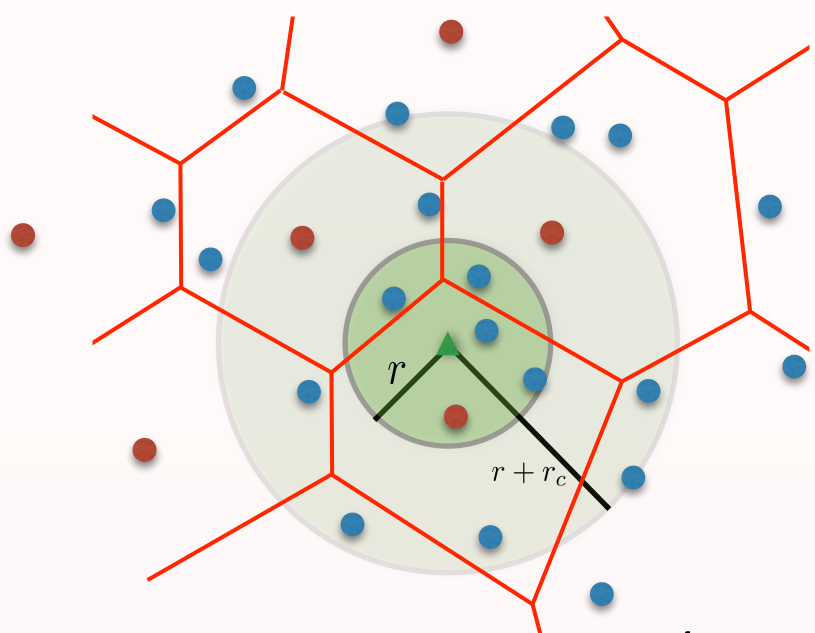

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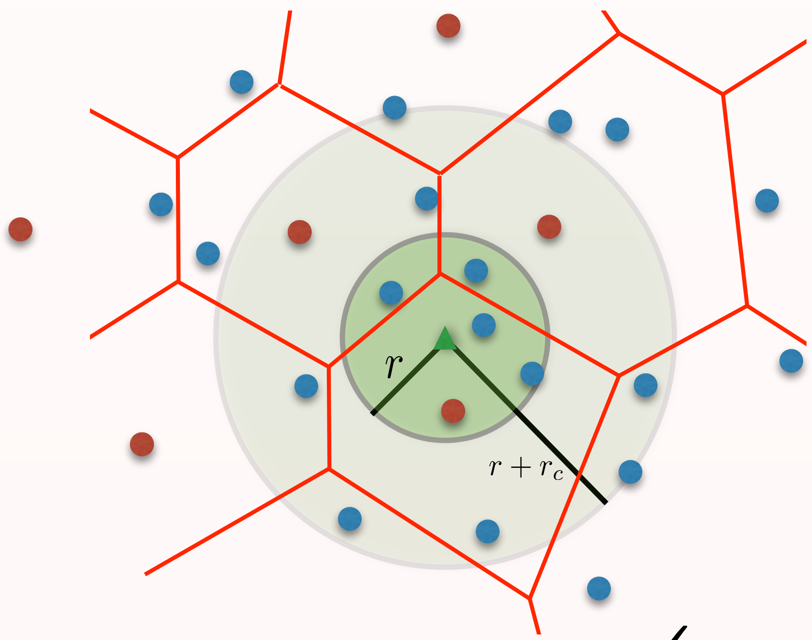

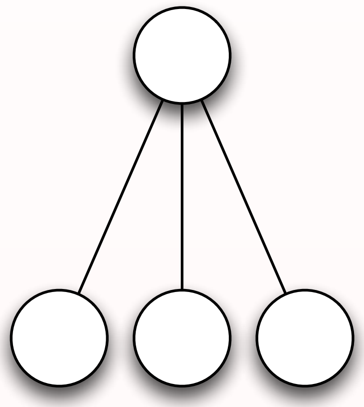

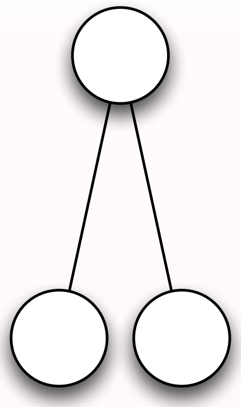

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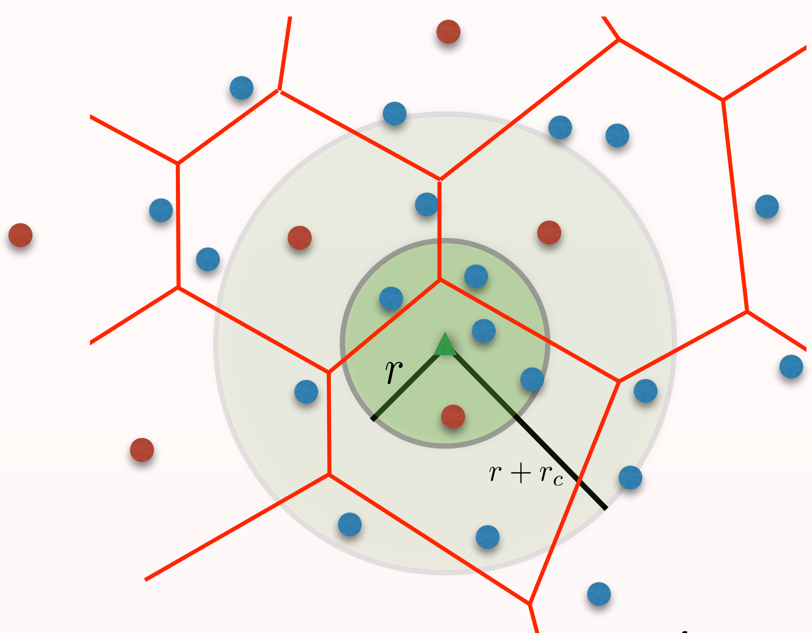

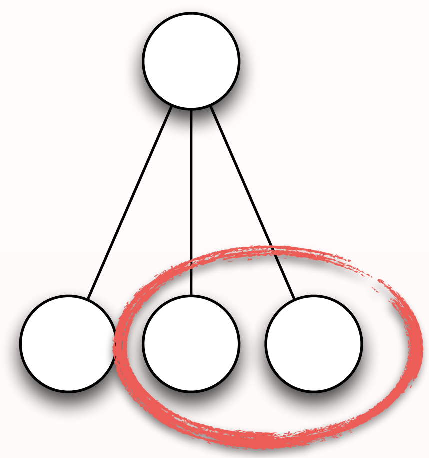

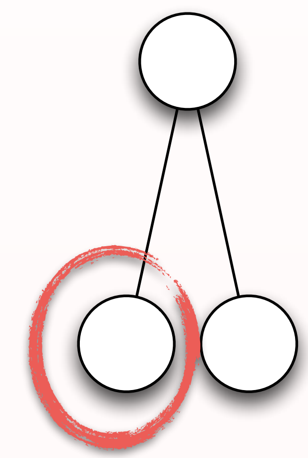

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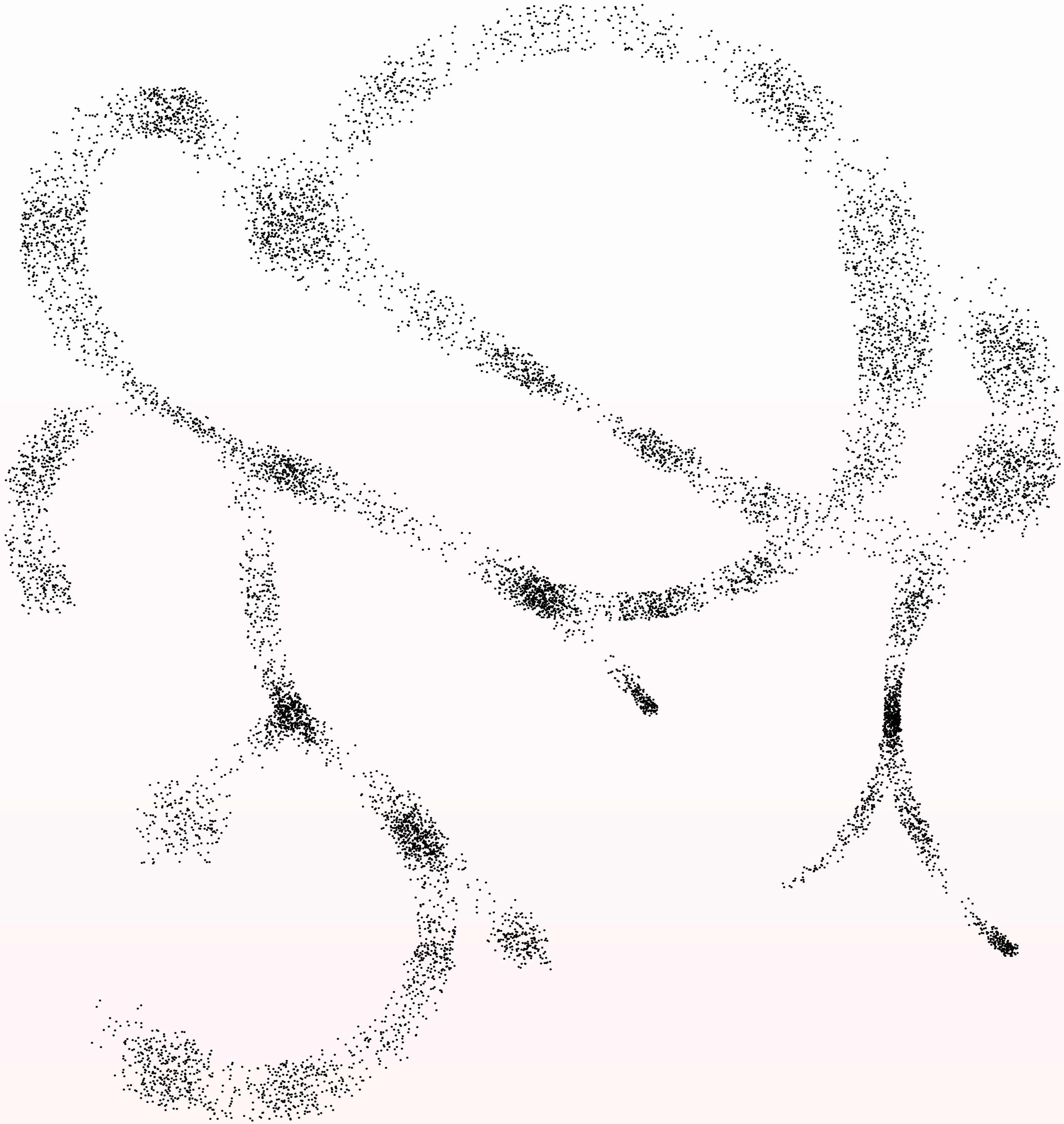

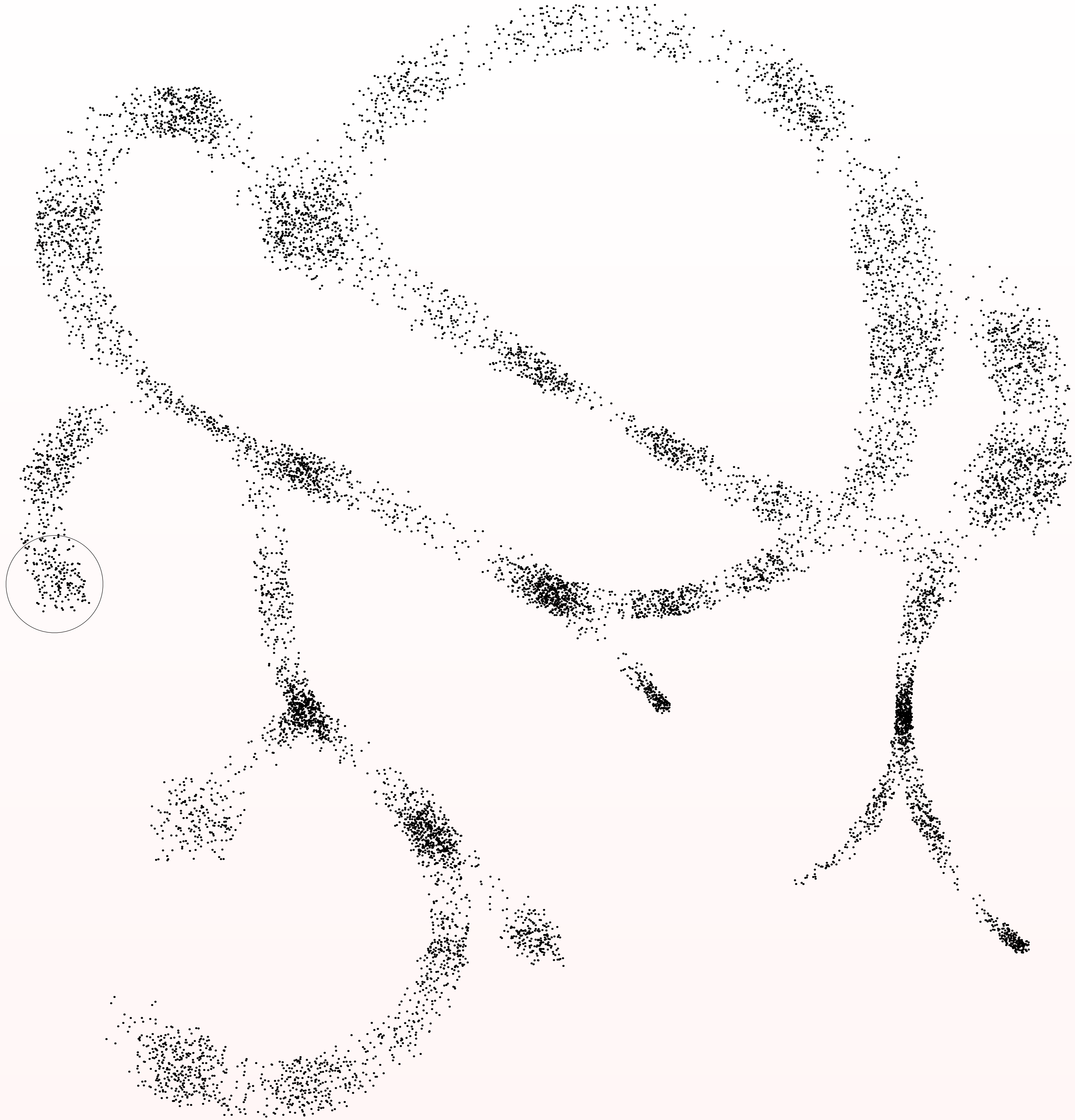

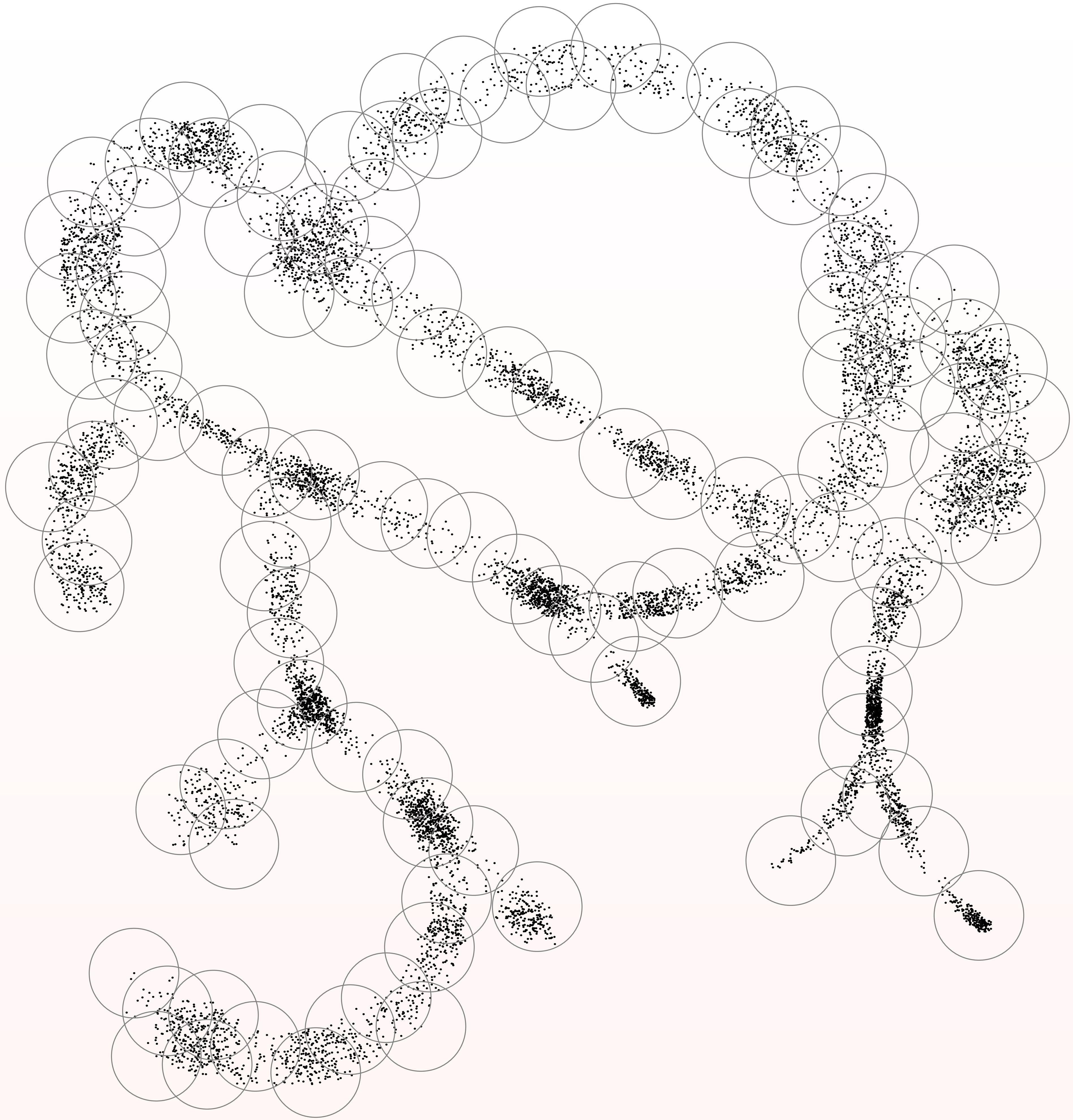

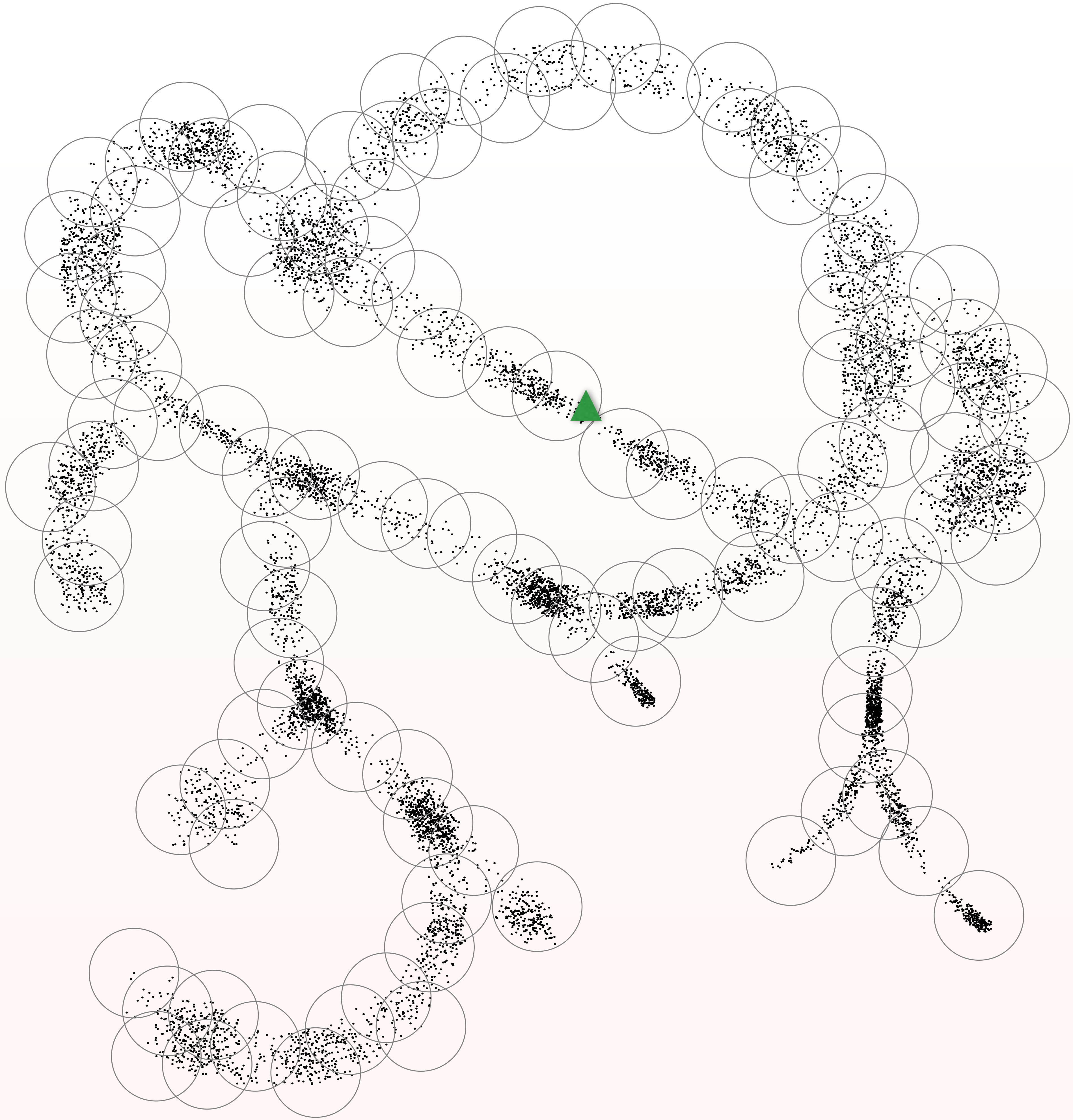

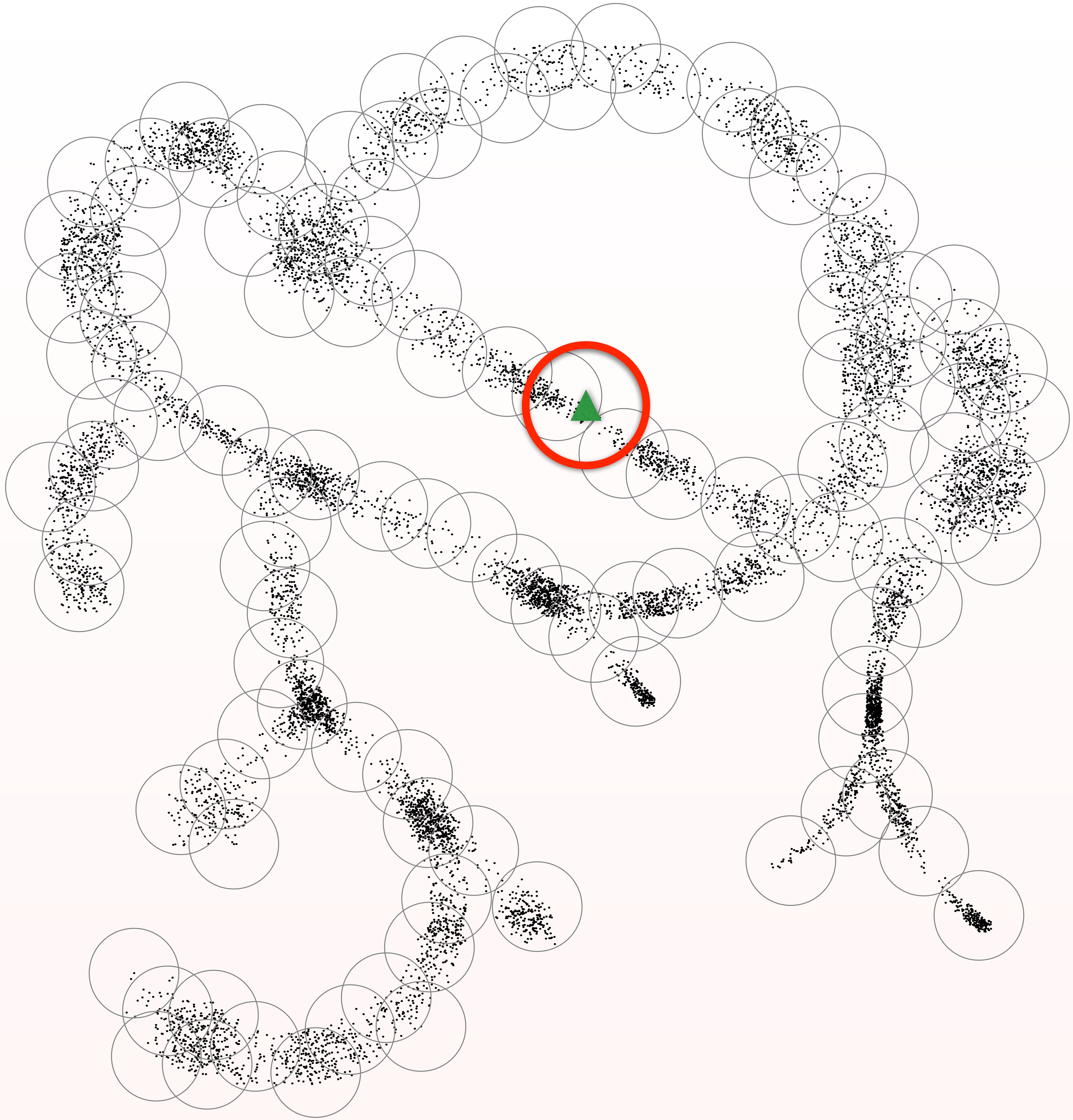

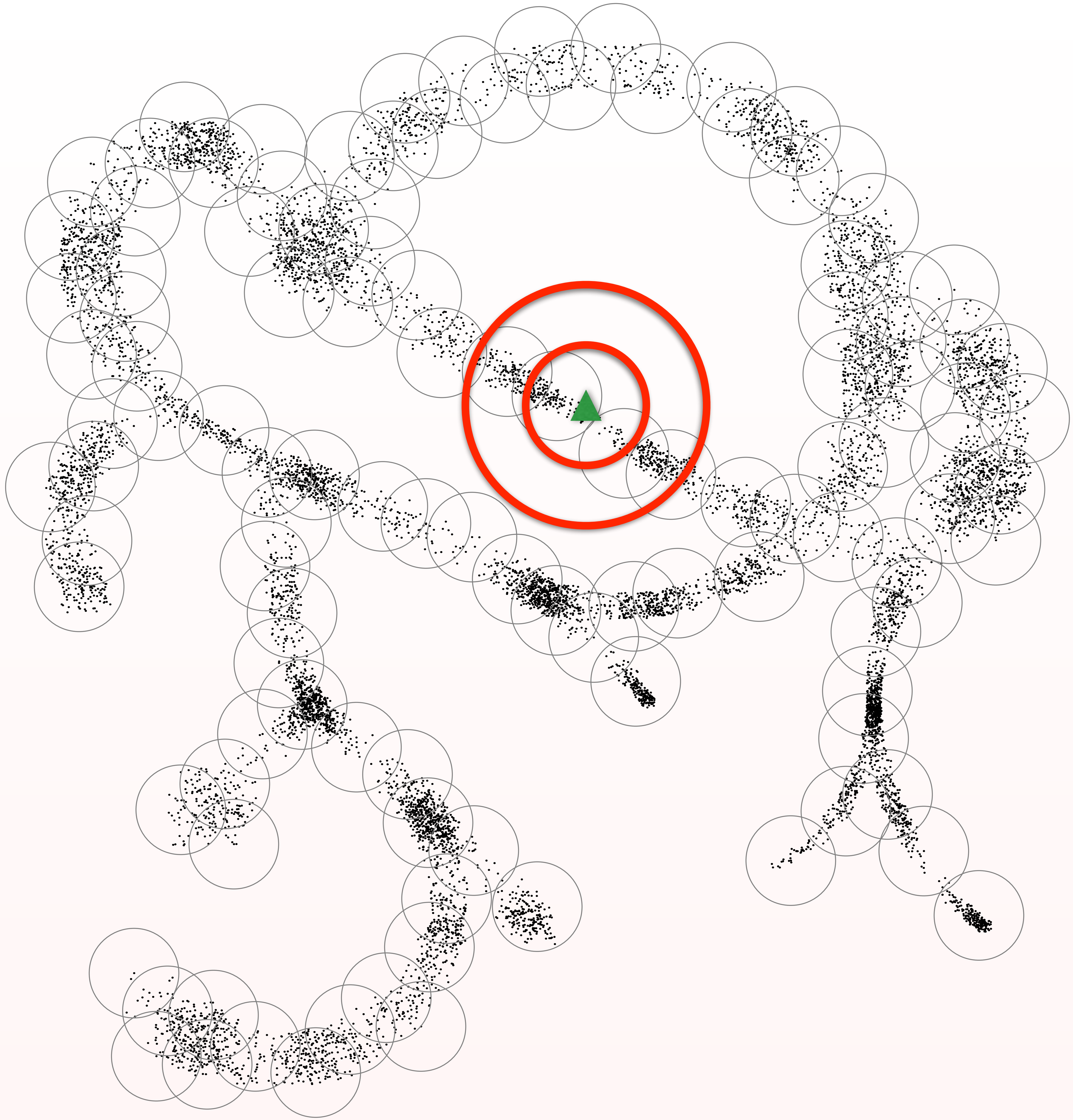

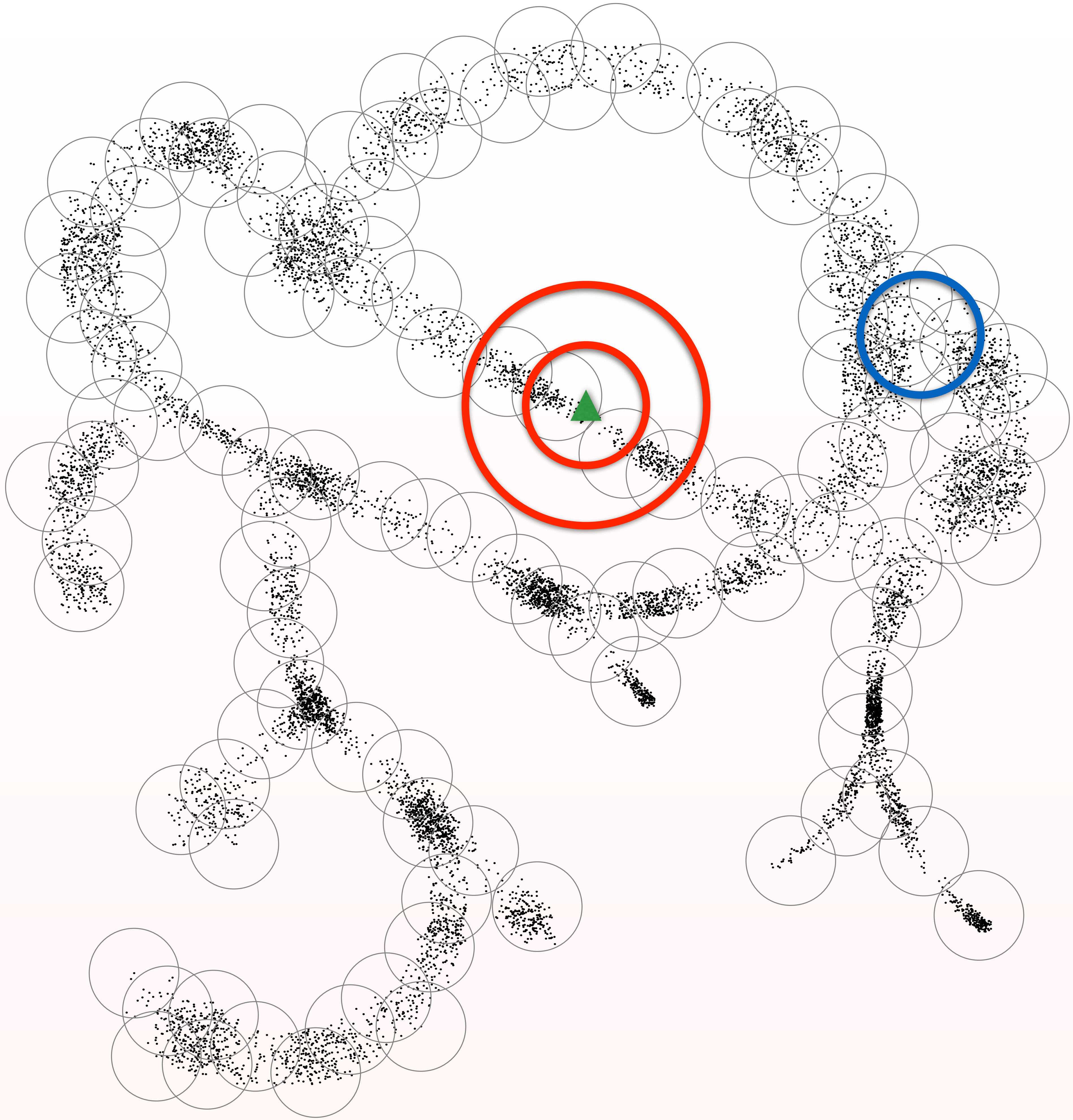

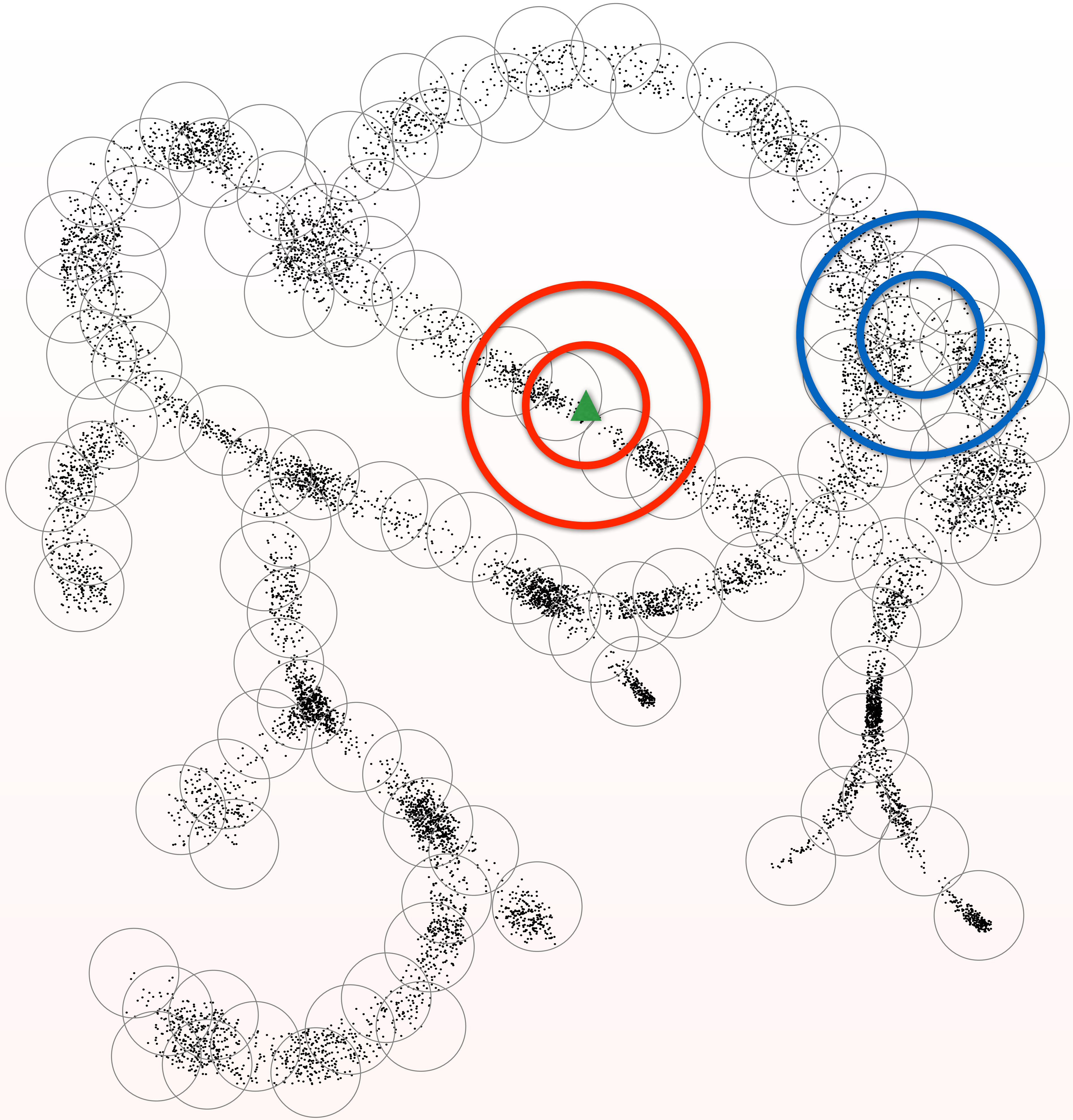

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