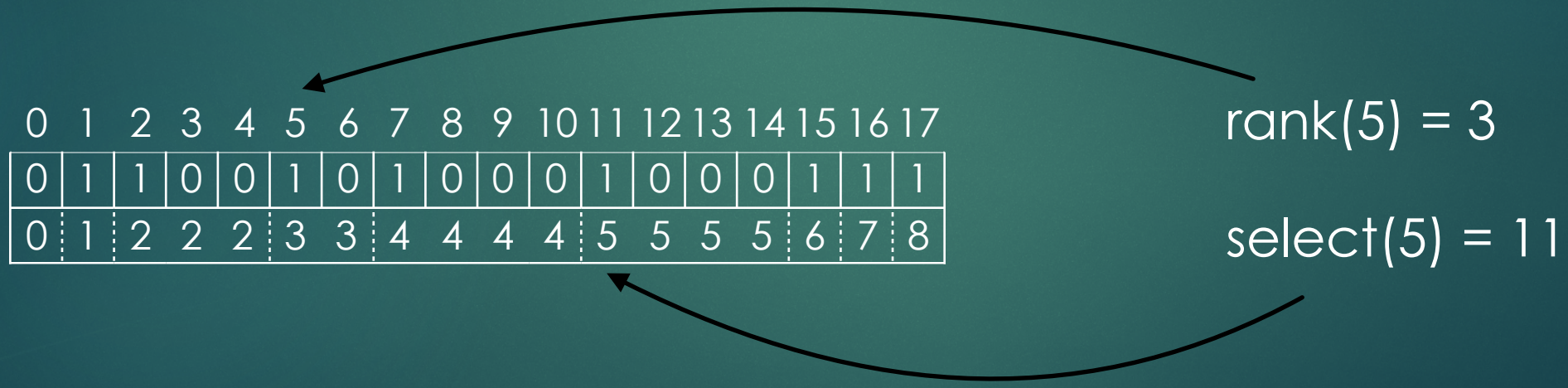
The colored de Bruijn Graph as a Sequence Index

Unless otherwise noted, slides courtesy of Fatemeh Almodaresi

Succinct Data Structures & Operations[8]

- Represent an object in a space close to the theoretic lower bound
- Provide specific constant time operations



Main Topics

- Rainbowfish
  - Succinct colored de Bruijn graph representation
- Pufferfish
  - Efficient Compacted de Bruijn graph indexing representation
  - Dense and Sparse

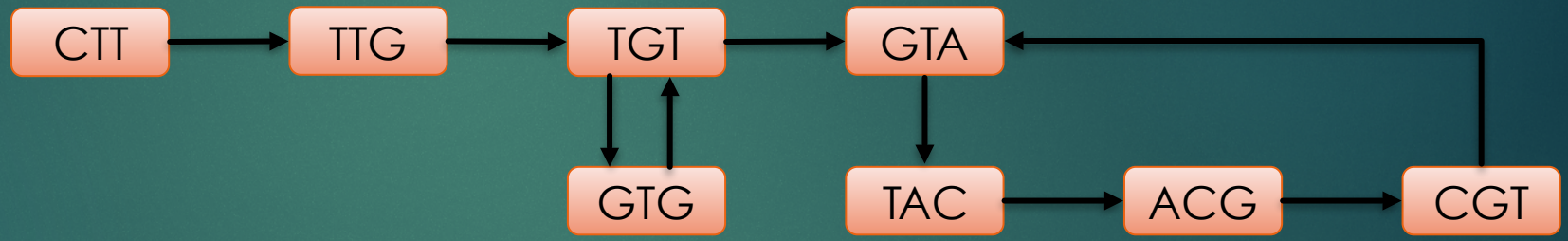
de Bruijn Graph[1-3]

Edge-centric Variant

K = 4

Sample:

CTTGTGTACGTA



A directed graph to represent a (set of) sequence(s) in terms of their k-mer components.

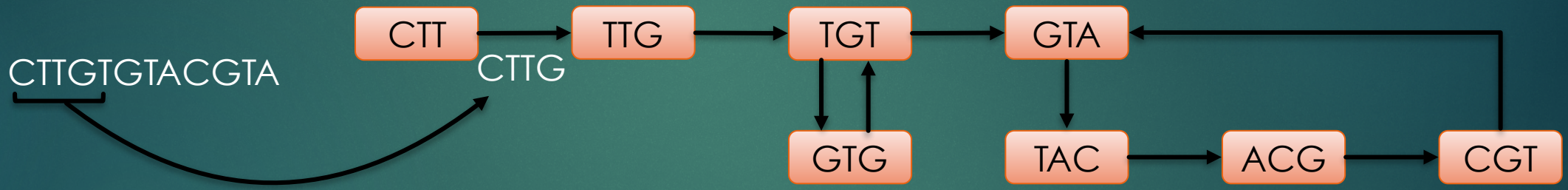
K-mer : unique substring of size k

de Bruijn Graph[1-3]

Edge-centric Variant

K = 4

Sample:

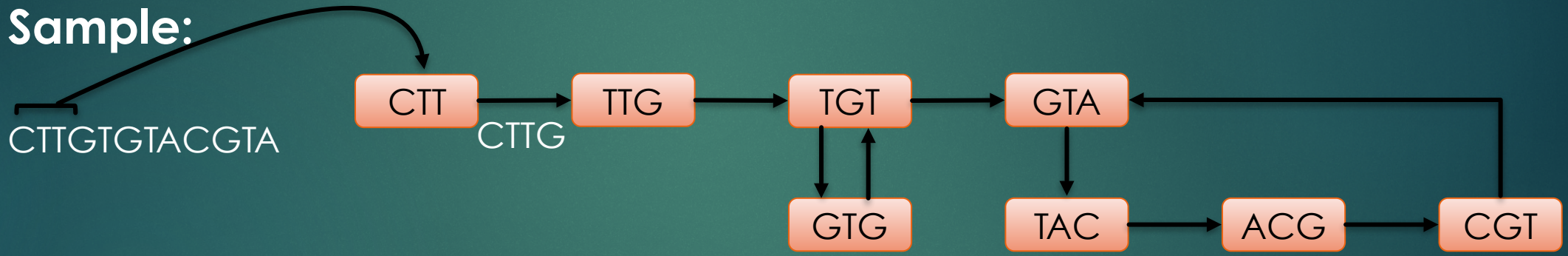


de Bruijn Graph[1-3]

Edge-centric Variant

K = 4

Sample:



de Bruijn Graph[1-3]

Edge-centric Variant

K = 4

Sample:

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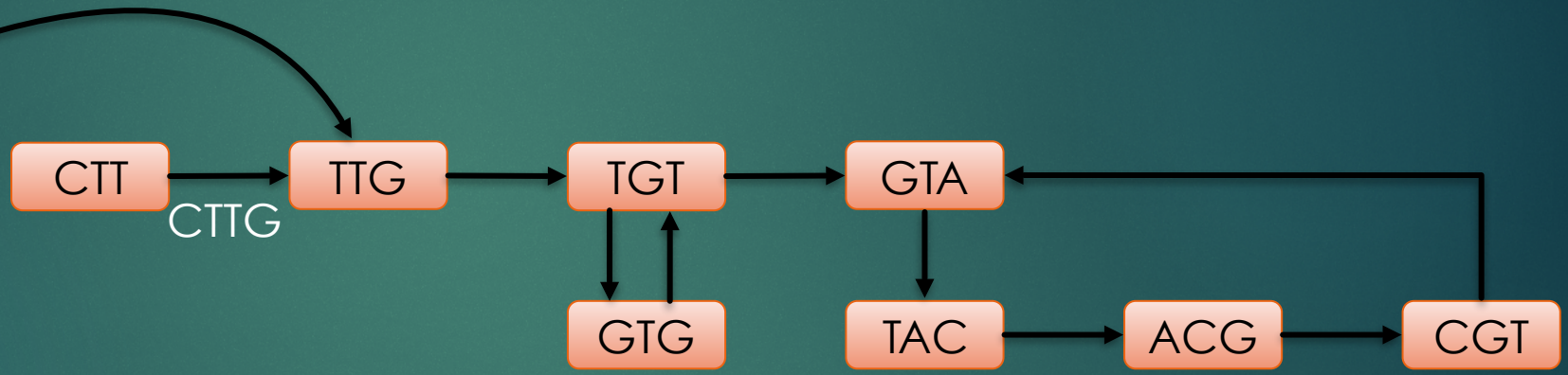

de Bruijn Graph[1-3]

Edge-centric Variant

K = 4

Sample:

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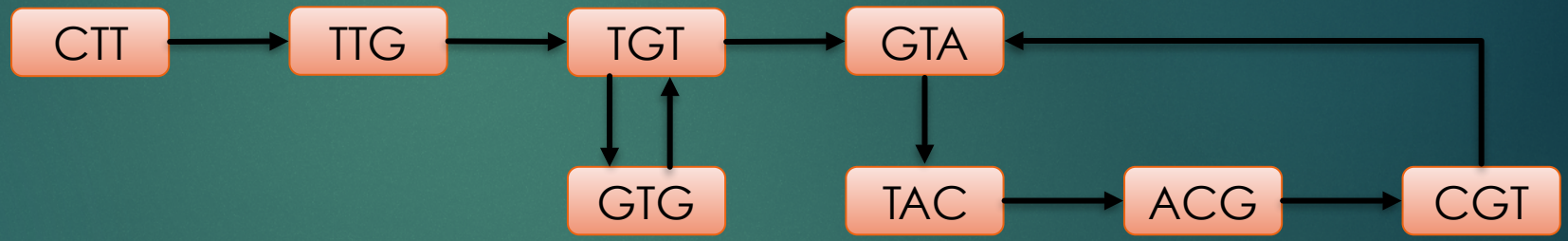

- Genome/Transcriptome Assembly
- Sequence Indexing

Rainbowfish

Rainbowfish: A Succinct Colored de Bruijn Graph Representation*

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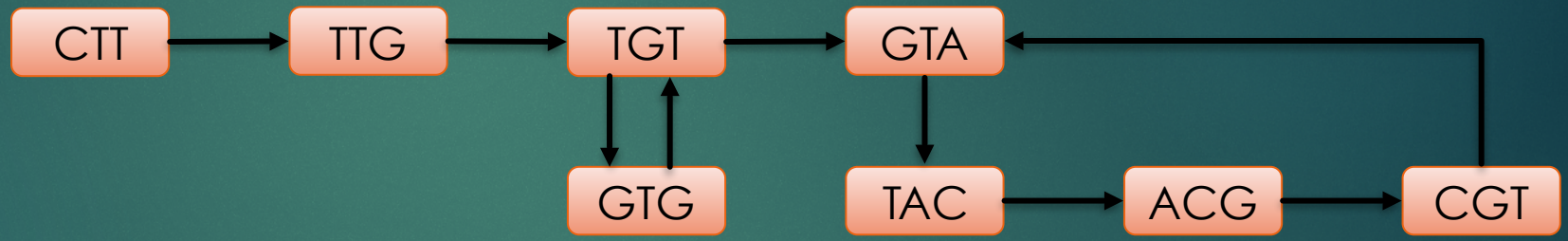
WABI 2017

Colored de Bruijn Graph

K = 4

Sample:

CTTGTGTACGTA

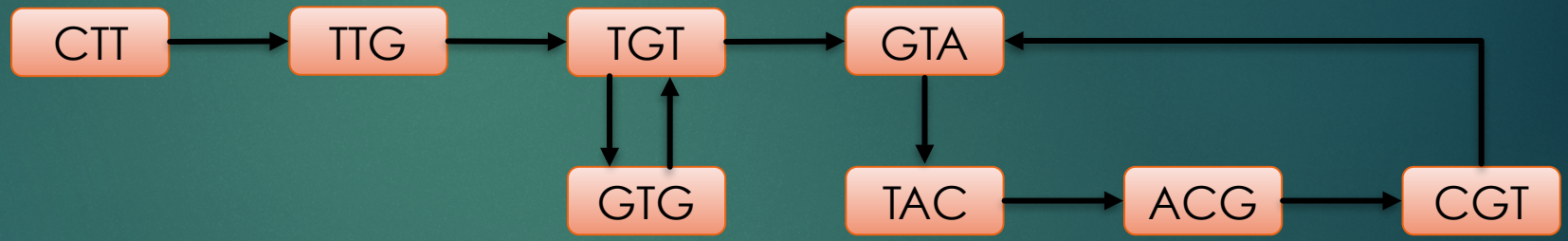


Colored de Bruijn Graph

K = 4

Sample:

- CTTGTGTACGTA

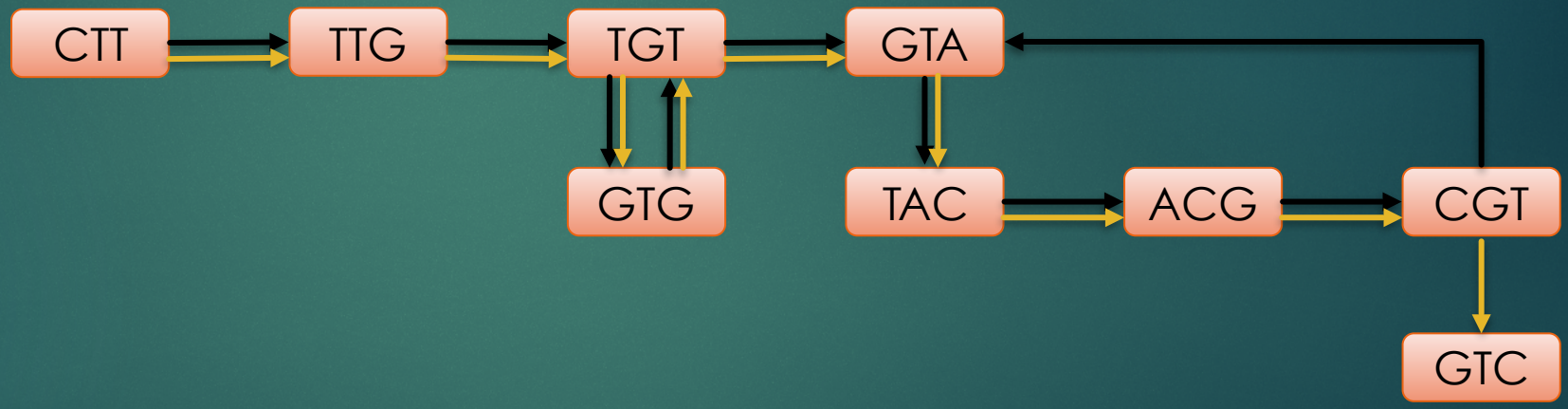


Colored de Bruijn Graph

K = 4

Samples:

- CTTGTGTACGTA
- CTTGTGTACGTC

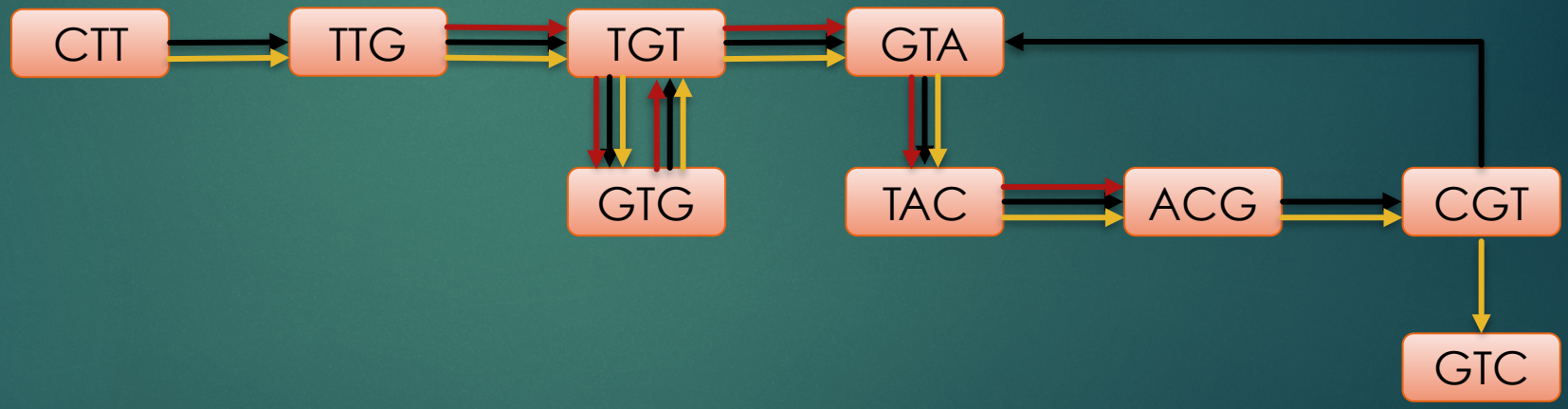


Colored de Bruijn Graph

K = 4

Samples:

- CTTGTGTACGTA
- CTTGTGTACGTC
- TTGTGTACG



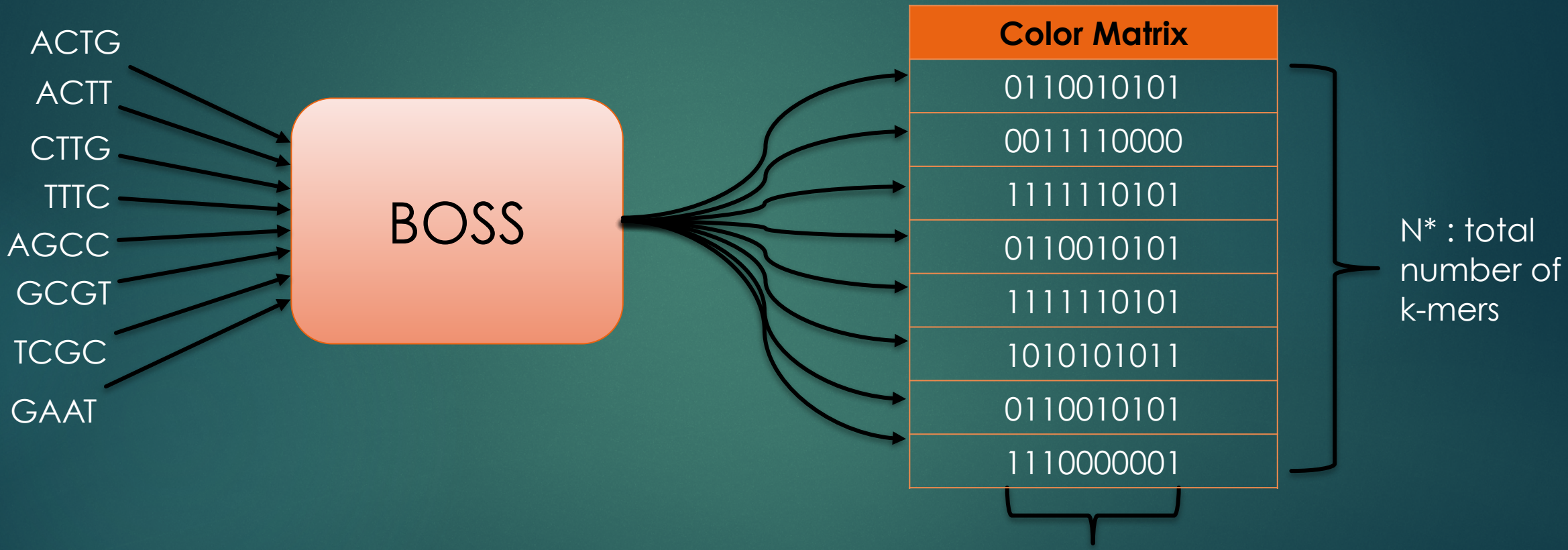
Colored de Bruijn Graphs (cdBg)

- Cortex[4]
  - Introduces cdBgs
  - Hash-table based representation for dBg
  - K-mer frequency for each color
  - 5 bytes per <color,k-mer>
  - Optimized for speed
  - Considerably large in space

Colored de Bruijn Graphs

- VARI[7]
  - In conjunction with BOSS[5]. BOSS is:
    - an efficient representation of dBgs
    - uses succinct data structures and rank and select operations to navigate through dBg
    - Returns an index for each k-mer
  - Represent Colors in a Color Matrix
  - Compress Color Matrix using bit-encoding schemes (Elias-fano)

BOSS → VARI



* Details of the BOSS representation require additional dummy k-mers

VARI

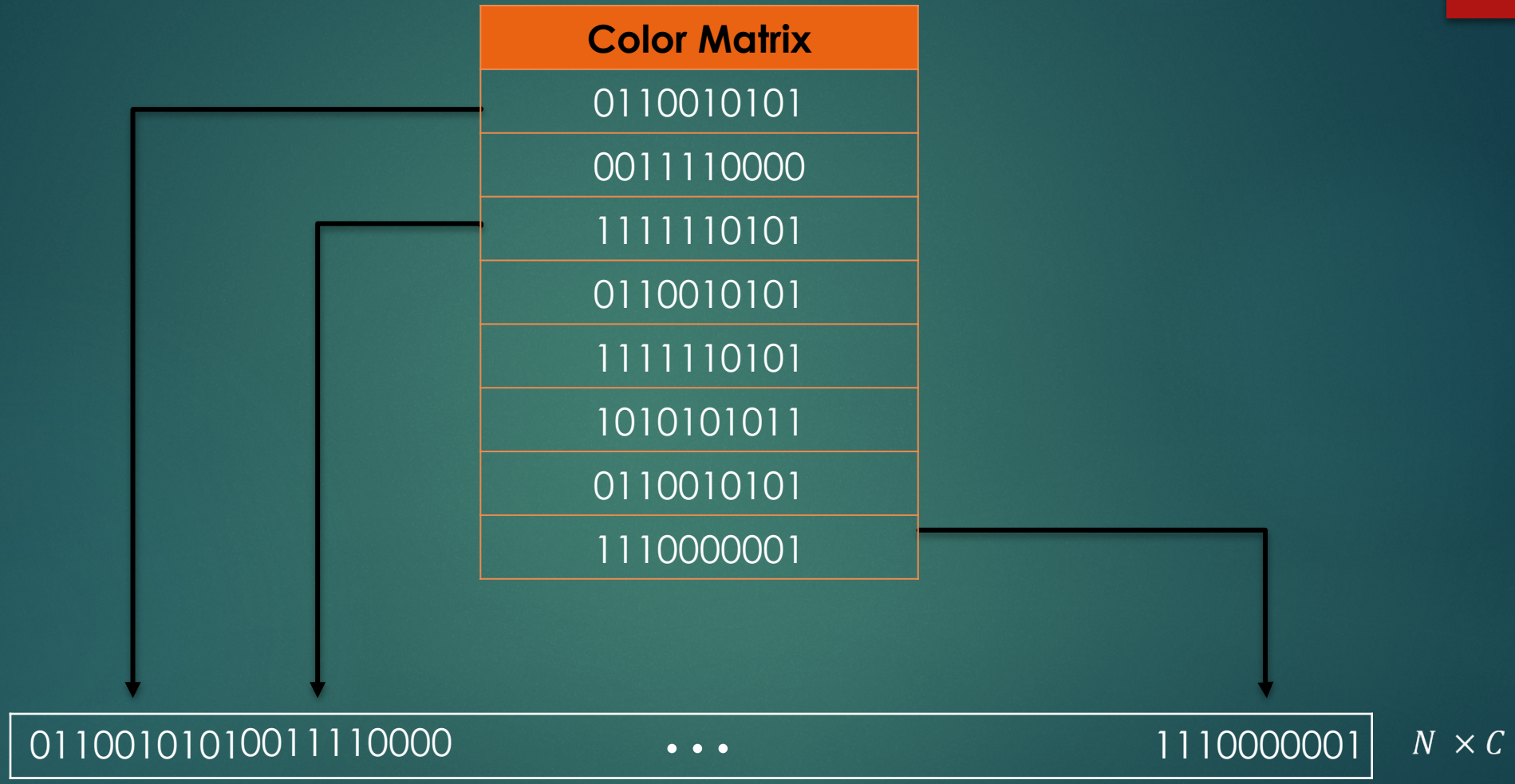
Color Matrix
0110010101
0011110000
1111110101
0110010101
1111110101
1010101011
0110010101
1110000001

VARI

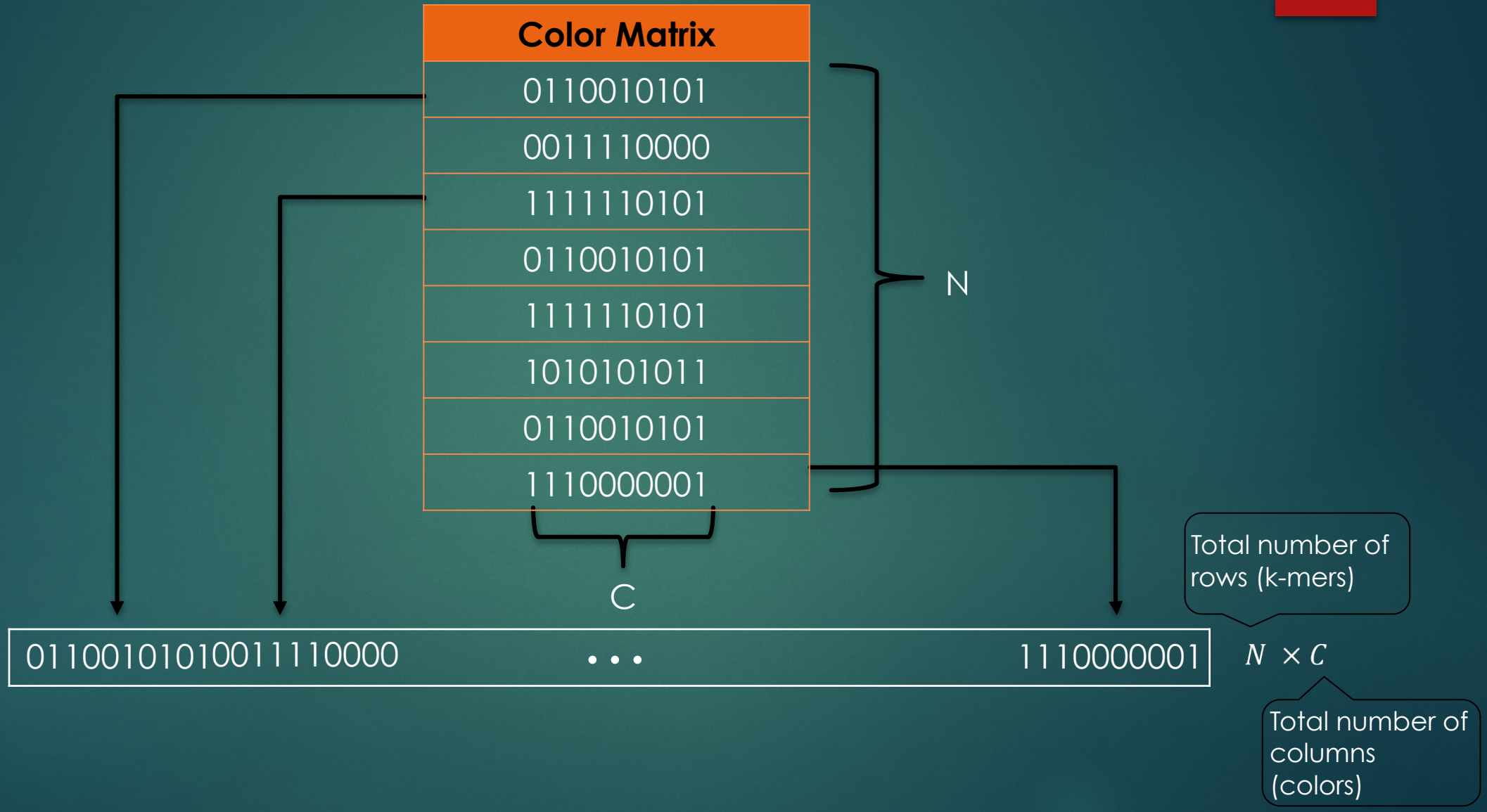
Color Matrix
0110010101
0011110000
1111110101
0110010101
1111110101
1010101011
0110010101
1110000001

0110010101 0011110000 • • • 1110000001

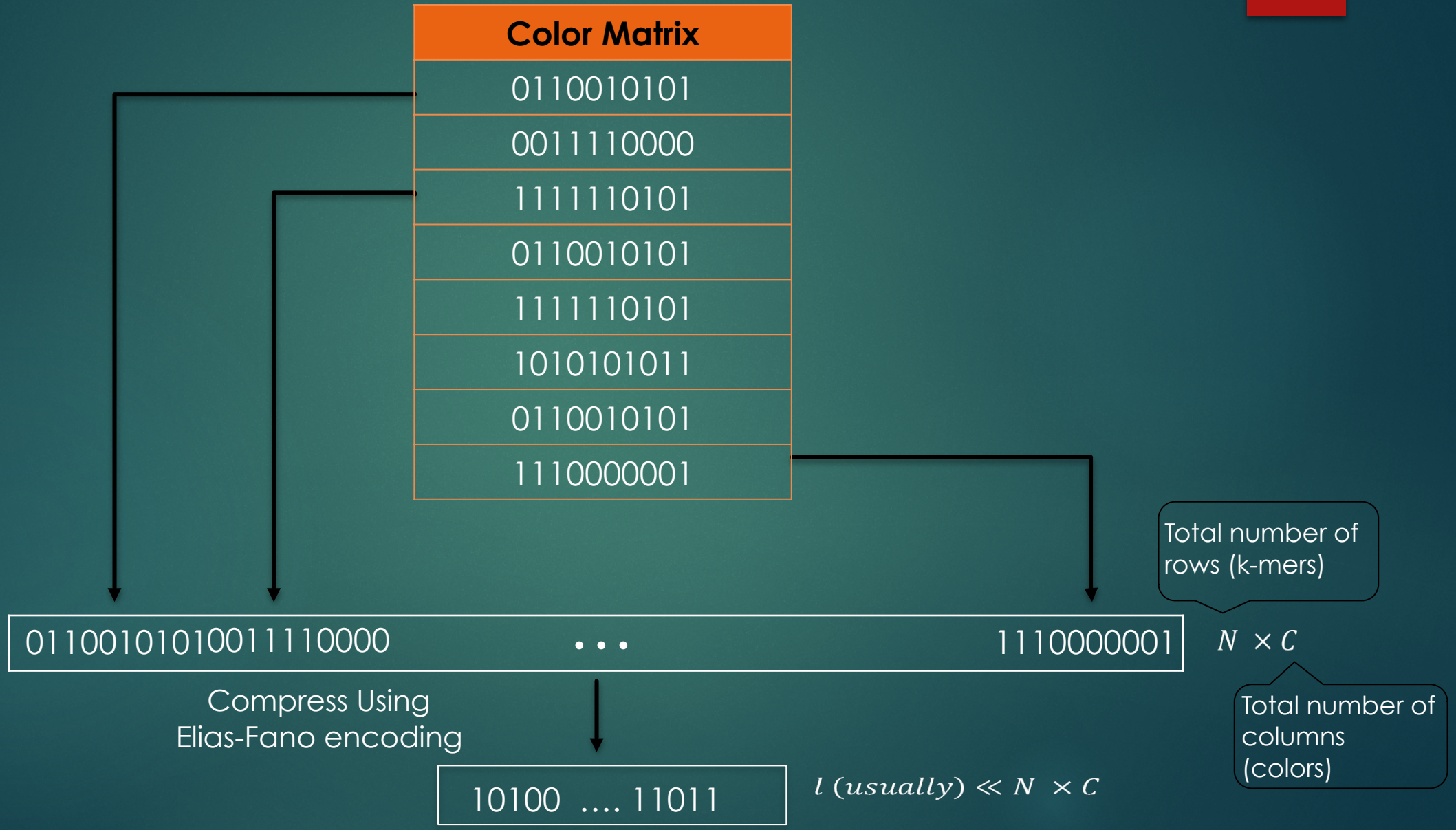
VARI


Color Matrix
0110010101
0011110000
1111110101
0110010101
1111110101
1010101011
0110010101
1110000001
0110010101001111000 0
• • •
1110000001
N × C

VARI


Color Matrix
0110010101
0011110000
1111110101
0110010101
1111110101
1010101011
0110010101
1110000001
N
C
Total number of rows (k-mers)
0110010101001111000 • • • 1110000001
$N \times C$
Total number of columns (colors)

VARI


Color Matrix
0110010101
0011110000
1111110101
0110010101
1111110101
1010101011
0110010101
1110000001
Total number of rows (k-mers)
01100101010011110000
• • •
1110000001
$N \times C$
Total number of columns (colors)
Compress Using Elias-Fano encoding
10100 11011
$l\ (usually) \ll N \times C$

VARI results compared to Cortex

Datasets	No. of k-mers	Colors	Cortex	VARI
Plant (k=32)	1,709,427,823	4	100.93 GB	3.53 GB (sdBG=0.89 GB, sC=1.95 GB)
E. Coli (k=32)	158,501,209	3,765	NA	42.17 GB (sdBG=0.09 GB, sC=38.35 GB)
Beef Safety (k=32)	40,995,794,366	88	NA	245.54 GB (sdBG=27.08 GB, sC=200.34 GB)

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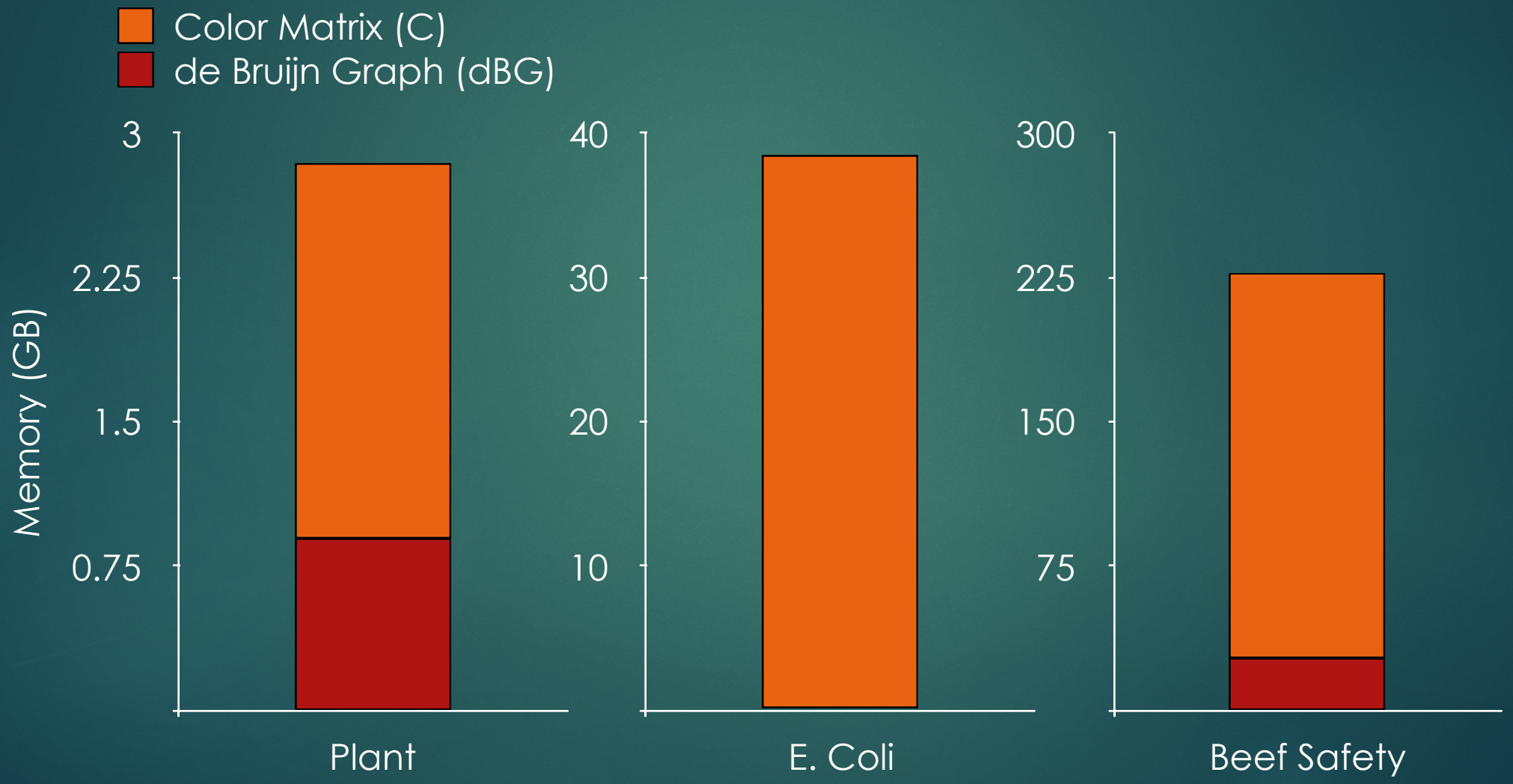
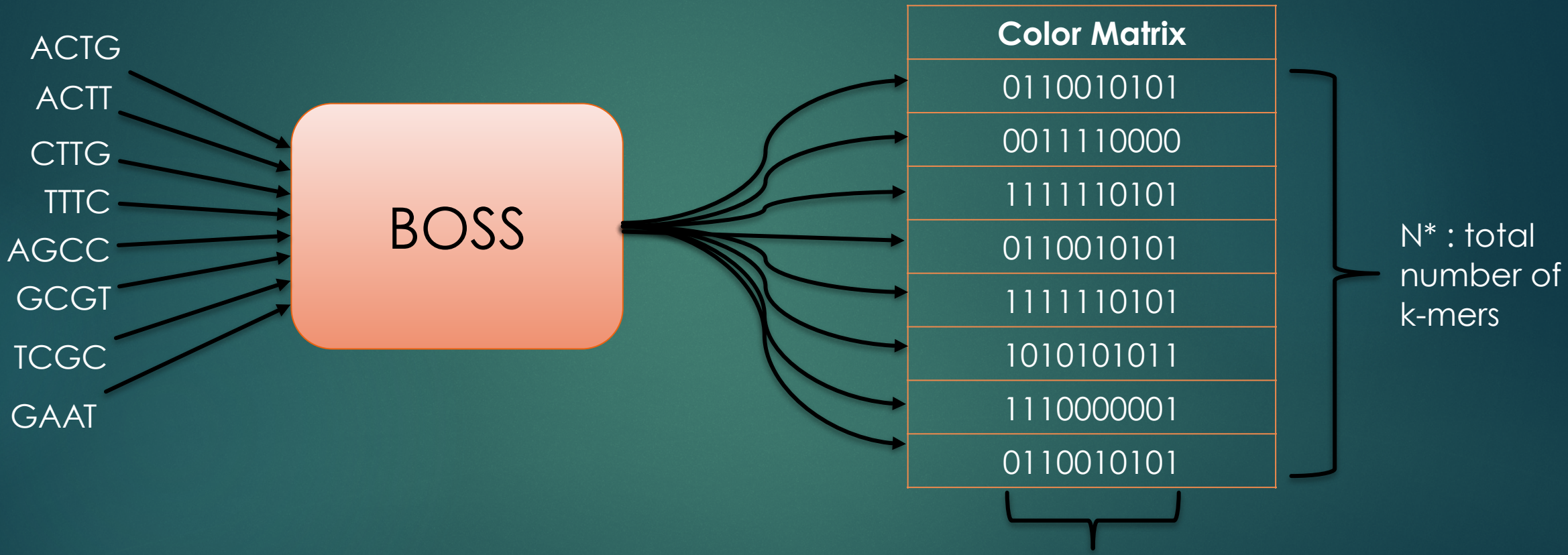
VARI results compared to Cortex

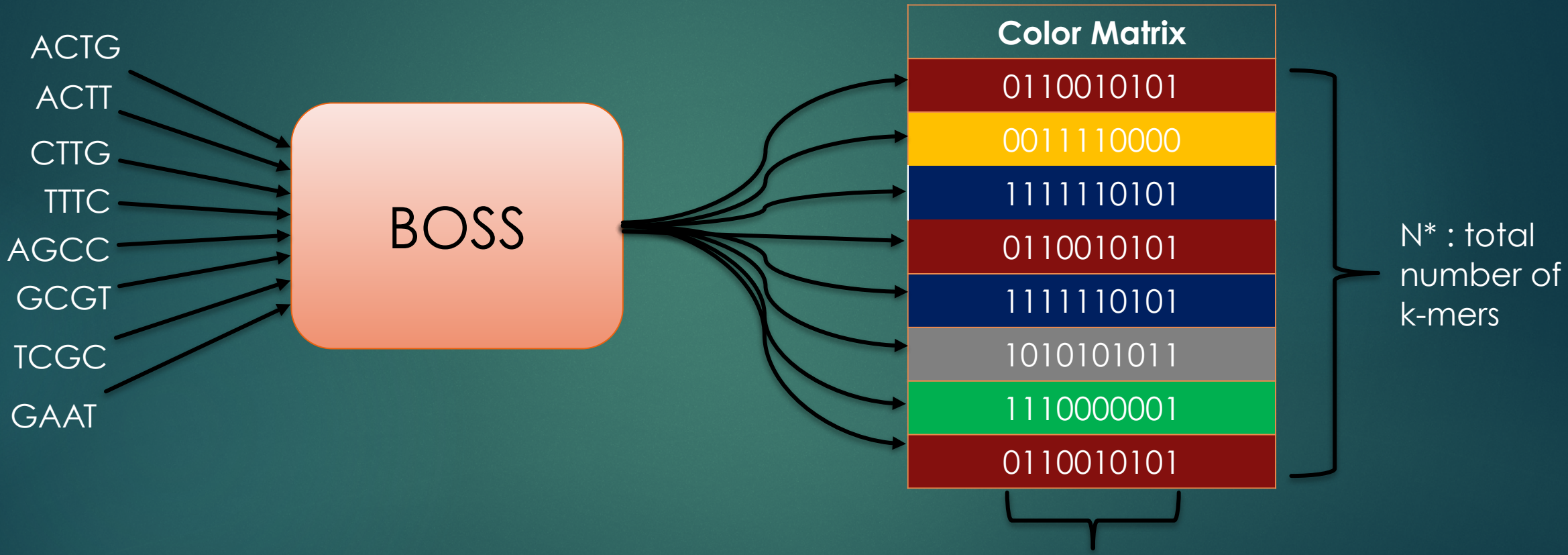


BOSS + VARI



* Details of the BOSS representation require additional dummy k-mers

BOSS + VARI

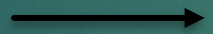


* Details of the BOSS representation require additional dummy k-mers

VARI to Rainbowfish

Equivalence Table

Color Matrix
0110010101
0011110000
1111110101
0110010101
1111110101
1010101011
1110000001
0110010101



Color Matrix
0
1
2
0
2
3
4
0

*

Label	Equivalence Class
0	0110010101
1	0011110000
2	1111110101
3	1010101011
4	1110000001

* This idea was briefly discussed in BFT[6] paper

Rainbowfish

Equivalence Table

Label	Equivalence Class
0	0110010101
1	0011110000
2	1111110101
3	1010101011
4	1110000001

+

Color Matrix
0
1
2
0
2
3
4
0

Rainbowfish

Equivalence Table

Label	Equivalence Class
0	0110010101
1	0011110000
2	1111110101
3	1010101011
4	1110000001

Color Matrix
0
1
2
0
2
3
4
0

Equivalence Bitvector

Label Bitvector

Rainbowfish

Equivalence Table

Label	Equivalence Class
0	0110010101
1	0011110000
2	1111110101
3	1010101011
4	1110000001

E = 5

C : total number of colors

Color Matrix
0
1
2
0
2
3
4
0

N : total number of k-mers

$l = E \times C$

0110010101	0011110000	1111110101	1010101011	1110000001

Equivalence Bitvector

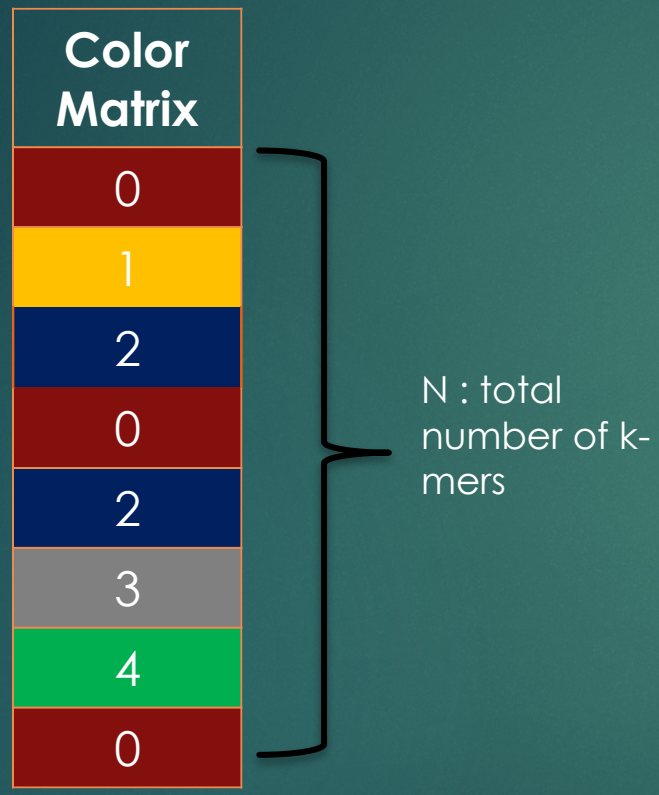
$l = N \times \log_2 E \leq N \times C$

000	001	010	000	010	011	100	000

Label Bitvector

Majority of the space

Rainbowfish
Equivalence Table



Datasets	$\frac{l}{N \times C}$
E. Coli (10)	0.9
E. Coli (1000)	0.02
E. Coli (5598)	0.004
Plant (4)	1
Beef Safety (88)	< 0.34
Human Txme (95,146)	< 0.0002

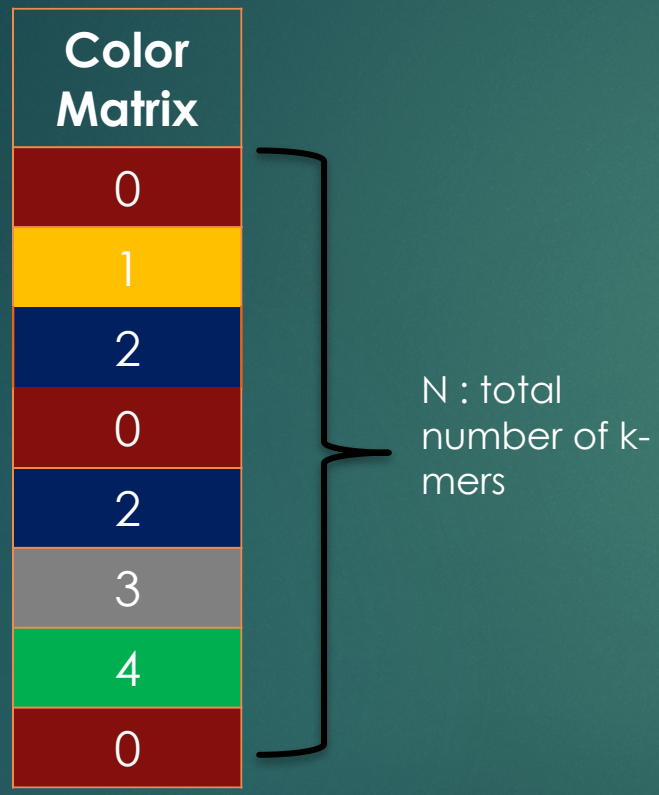
000 001 010 000 010 011 100 000

Label Bitvector

$$l = N \times \log_2 E \leq N \times C$$

Rainbowfish

Equivalence Table



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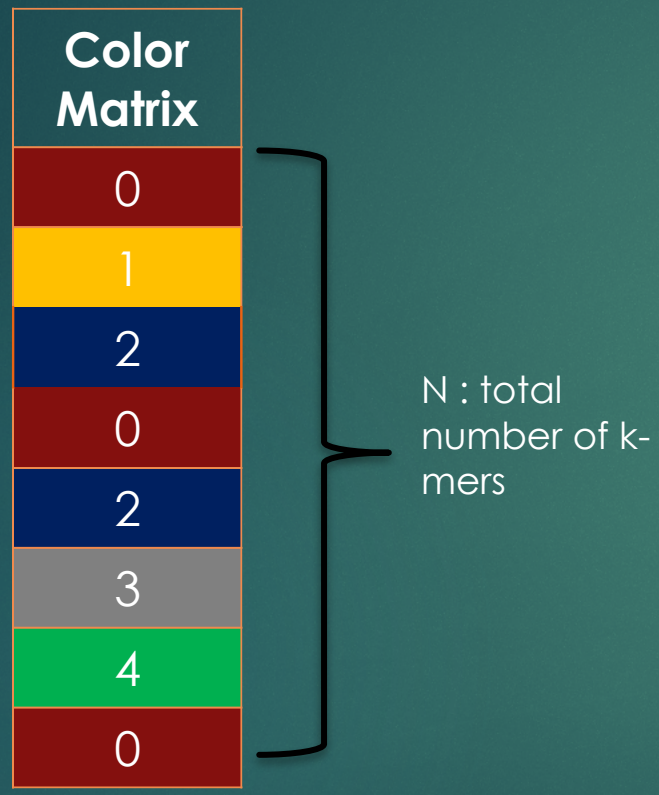
000 001 010 000 010 011 100 000

Label Bitvector

$$l = N \times \log_2 E \leq N \times C$$

Rainbowfish
Equivalence Table



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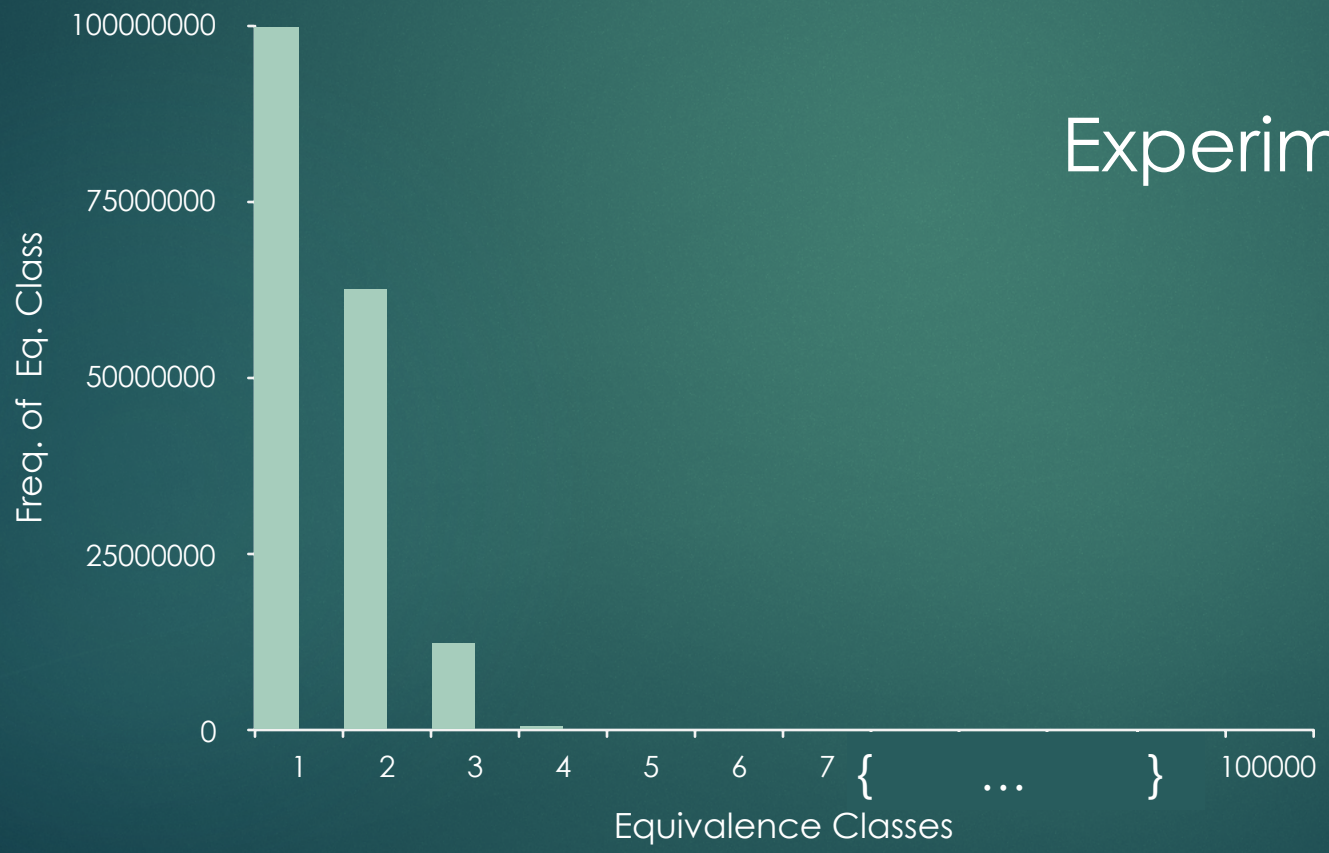
000 001 010 000 010 011 100 000

Label Bitvector

$$l = N \times \log_2 E \leq N \times C$$

Rainbowfish

Label & Boundary Bitvectors



Experimental Observation

Rainbowfish

Label & Boundary Bitvectors

Label	Equivalence Class	Freq.
0	0110010101	3
1	0011110000	1
2	1111110101	2
3	1010101011	1
4	1110000001	1

*

Equivalence Bitvector

Color Matrix
0
1
2
0
2
3
4
0

Label Bitvector

* This idea is briefly discussed in BFT paper

Rainbowfish

Label & Boundary Bitvectors

Label	Equivalence Class	Freq. *
0	0110010101	3
1	1111110101	2
2	0011110000	1
3	1010101011	1
4	1110000001	1

Equivalence Bitvector

Color Matrix
0
2
1
0
1
3
4
0

Label Bitvector

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Rainbowfish

Label & Boundary Bitvectors

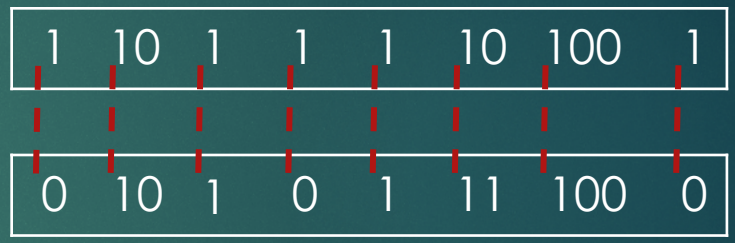
Label	Equivalence Class
0	0110010101
1	1111110101
2	0011110000
3	1010101011
4	1110000001

*

Equivalence Bitvector

Color Matrix
0
2
1
0
1
3
4
0

Boundary Bitvector



Label Bitvector

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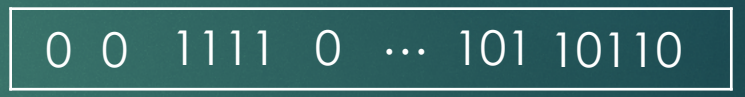
Rainbowfish

Label & Boundary Bitvectors

Label Bitvector

Boundary Bitvector



Label Bitvector

$$N \times \log_2(E) \quad vs \quad 2\sum_{i=1}^{E} \log_2(i) \times freq_{ec_i}$$

Why is Rainbowfish Succinct

- Uses amount of space close to information-theoretic optimum
  - Z: Information-theoretic Optimal
  - $Z + o(Z)$: Space by data structure
- Common Operations for navigation:
  - Rank
  - Select

Why Is Rainbowfish Succinct

- ***Lemma 1:***

  The size of each color class label is bounded by $\log_2 M$ bits, where M is the total number of distinct color classes. For a dataset with N distinct k-mers coming from C input samples (i.e., colors), we have that $M \leq \min(N, 2^C)$.

- ***Theorem 1:***

  Given an ordering of edges (or k-mers) in a de Bruijn Graph, the space needed by rainbowfish to represent a set of colors attached to each edge is bounded by $O(MC + NH(X_e))$.

  - M: Number of distinct color classes
  - C : Number of colors
  - N : Number of distinct k-mers
  - $H(X_e) : -\sum_{i=1}^{M} P(X_i) \log_2 P(X_i)$ is the entropy over random variable X_i which shows the frequency distribution of the color classes

Why Is Rainbowfish Succinct

- ***Theorem 2***

  The lower bound to represent a mapping from an ordered list of k-mers in a de Bruijn graph to a set of color classes is $log_2(MN - M.M!)$ bits, where M is the number of distinct color classes, N is the number of edges, and for a dataset with N distinct k-mers coming from C input samples (i.e., colors), we have that $M \leq \min(N, 2^C)$.

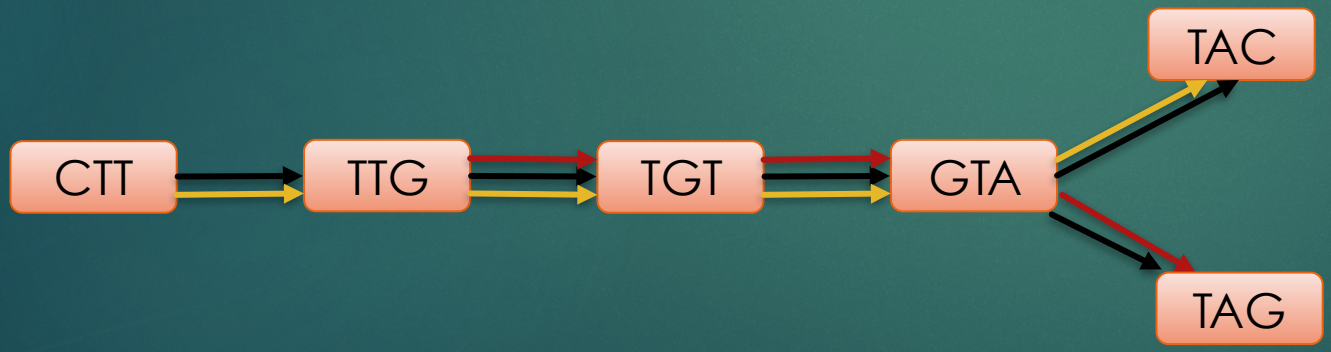
- Counting argument (Lower bound)
  - Count number of ways to map M distinct color class to N set of edges
  - Assign set of M edges a distinct color class : $M!$
  - Assign colors to $N - M$ in any possible manner : $M^{N-M}.M!$
  - To represent any of these we need at least $\log_2(M^{N-M}.M!)$
  - $= (N - M)\, log_2\, M + Mlog_2(M) - 0.44M + O(\log_2 M) \geq Nlog_2 M - 0.44M$
  - Given $1 \leq M \leq N$, $Nlog_2 M$ dominates lower bound

Why Is Rainbowfish Succinct

- Succinct Definition + Lemma 1 + Theorem 1 + Theorem 2
- $\mathrm{S} = Z + o(Z)$
- $Z \geq N log_2 M$
- $\mathrm{s} = O\big(MC + NH(X_e)\big) \leq 2N log_2 M$
- $\mathrm{S} = \mathrm{s} + \mathrm{o}(\mathrm{N})$ for overhead of the metadata to perform select
- $\mathrm{S} = Z + o(Z)$

Rainbowfish Query

- Basic Query: search(k-mer, color)
  - Returns true if the **k-mer** is assigned to the **color** in dbg or false otherwise
- Use search(k-mer, color) in "Bubble Calling"[4]



Navigation Through de Bruijn Graph

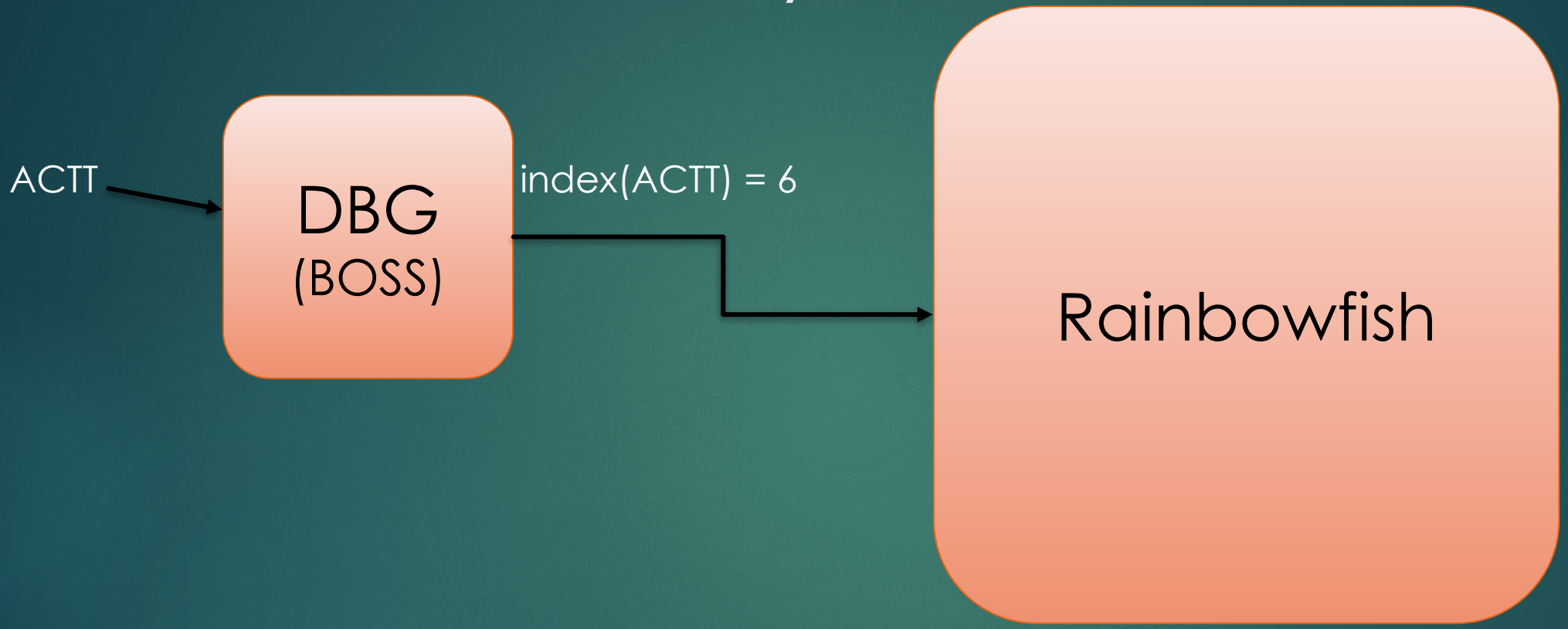
For each k-mer

search(k-mer, color1)

search(k-mer, color2)

Until one of these are false

Rainbowfish Query



Rainbowfish Query

Boundary Bitvector

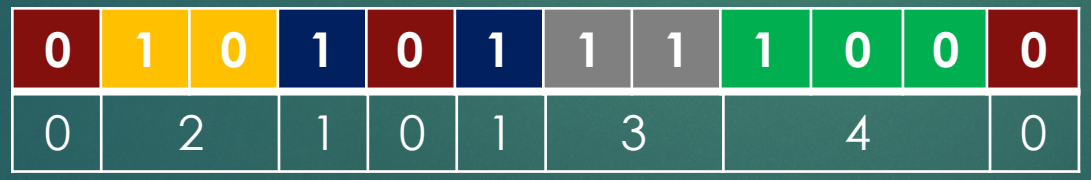
Label Bitvector

Equivalence Bitvector

Rainbowfish Query

index(ACTT) = 6

Boundary Bitvector



Label Bitvector

Equivalence Bitvector

Rainbowfish Query

index(ACTT) = 6

Select(i=6)=8

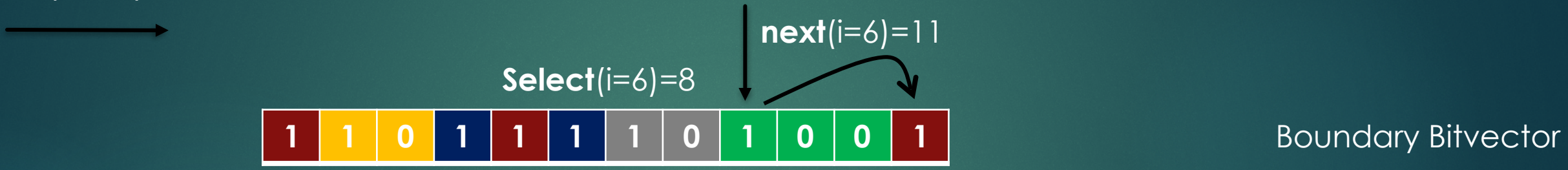
Boundary Bitvector

Label Bitvector

Equivalence Bitvector

Rainbowfish Query

index(ACTT) = 6



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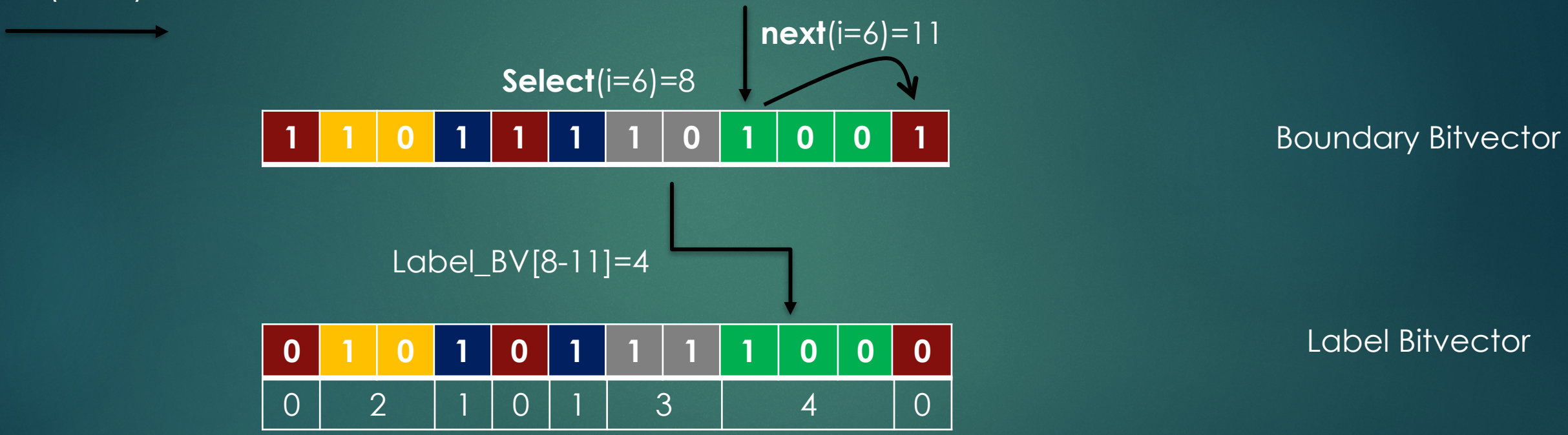

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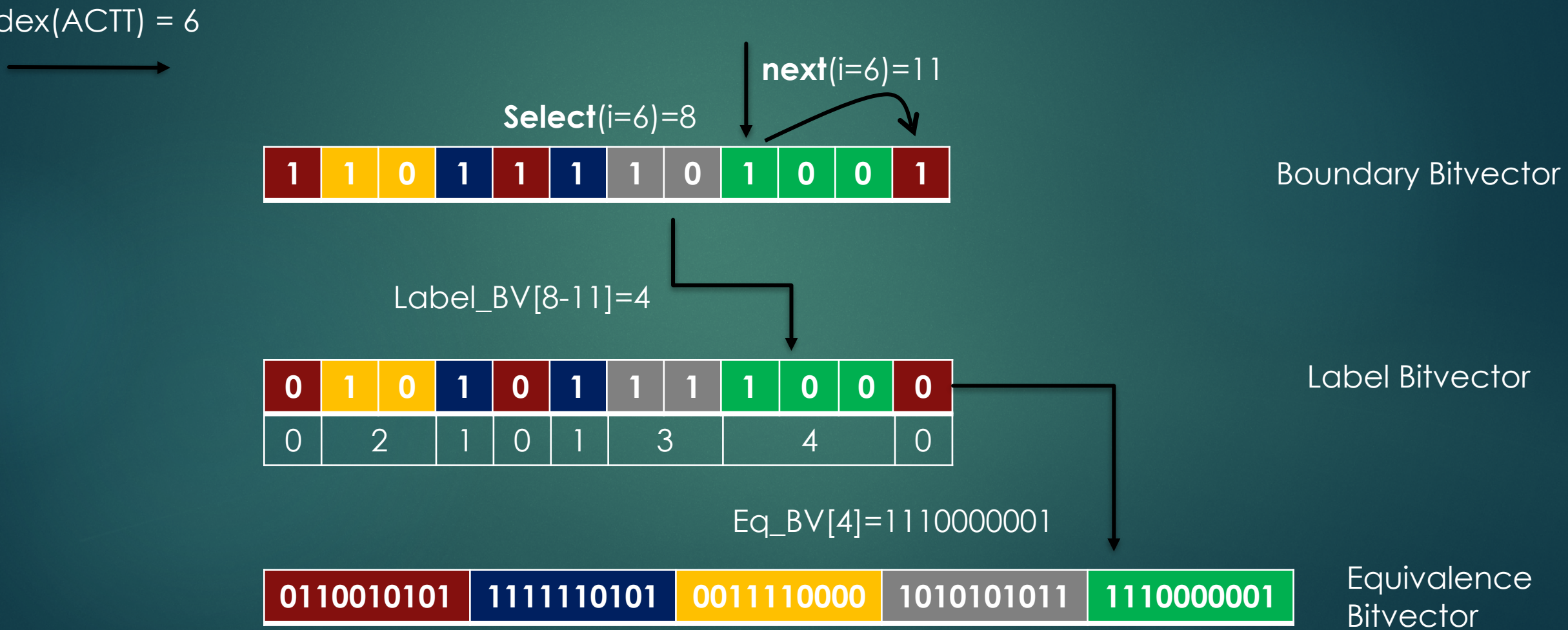

Characteristics of Datasets

Datasets	# of Colors (C)	# k-mers (N)	# Color Eq. Cls (E)
E. Coli 10	10	28,273,951	479
E. Coli 1000	1000	157,737,064	2,669,157
E. Coli 5598	5598	435,705,390	7,000,715
Plant	4	2,520,140,426	16
Beef Safety	88	> 97,096,576,010	623,022,532
Human Txme	95,146	> 159,441,804	340,762

Disk Space*(MB)

Datasets	Uncompressed Color Matrix	VARI	Rainbowfish
E. Coli 10	34	58	20
E. Coli 1000	18,804	8,848	475
E. Coli 5598	290,761	58,718	2,938
E. Coli 1000 (k=63)	185,669	8,872	637
Plant (4)	1,202	1,603	497
Beef Safety (88)	1,007,009	210,998	144,564
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* For rainbowfish Memory and disk space is almost the same

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Construction & Query Time

	Construction Time (secs)		Bubble Calling Time (secs)	
Datasets	VARI	Rainbowfish	VARI	Rainbowfish
E. Coli 10	44	31	344	366
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Beef Safety	15,375	30,478	NA	NA
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Pufferfish

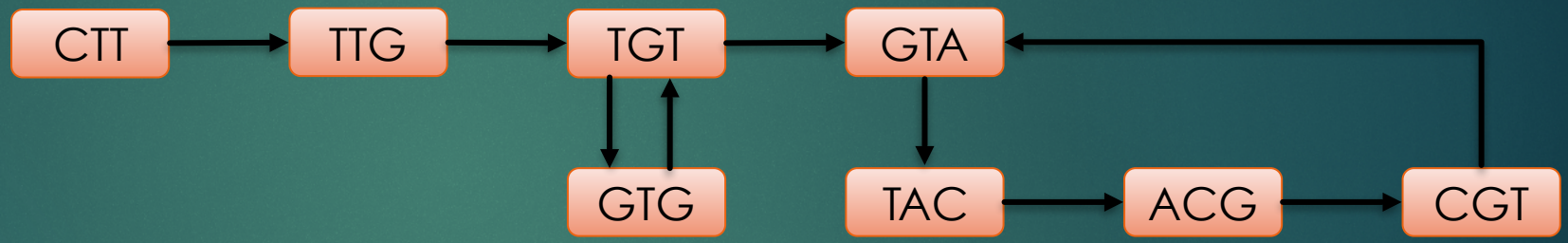

New Results
Previous
A space and time-efficient index for the compacted colored de Bruijn graph
Posted September 21, 2017.
Fatemeh Almodaresi, Hirak Sarkar, Rob Patro
Download PDF
doi: https://doi.org/10.1101/191874
Email
This article is a preprint and has not been peer-reviewed [what does this mean?].

Indexing de Bruijn Graph

K = 4

Samples:

CTTGTGTACGTA



Indexing de Bruijn Graph

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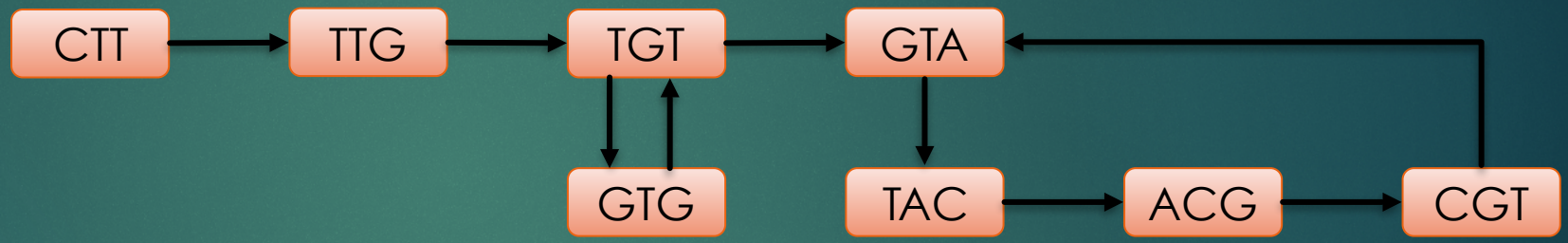

Reference: known genome or transcriptome

Indexing de Bruijn Graph

K = 4

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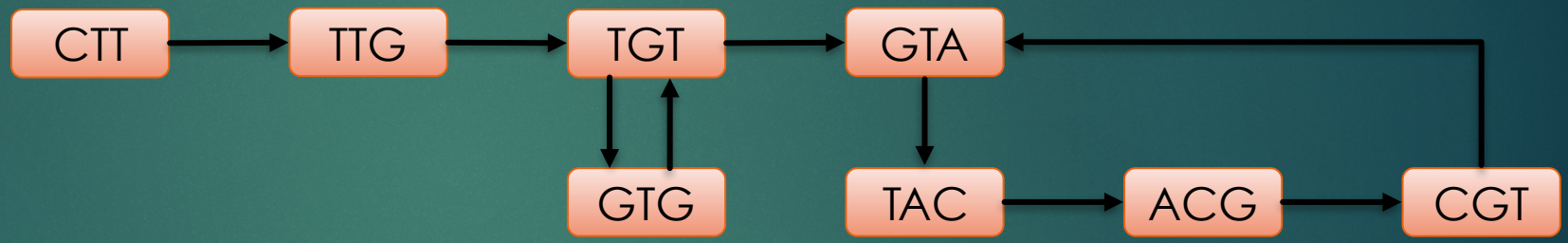

K-mer Info Table

k-mer ID	K-mer Info
0	{ref_y, p_2^y, o_2^y}, {ref_r, p_2^r, o_2^r}, {ref_r, p_2^r, o_2^r}
1	{ref_r, p_3^r, o_3^r}, {ref_g, p_3^g, o_3^g}
⋮	⋮

Reference Indexing

- Mapping and Alignment of reads to a (set of) reference
  - starting point for downstream analysis on genes and transcripts
    - Transcript and gene quantification
    - Metagenomic abundance estimation
    - …
- Time and space bottleneck
- Indexing the reference sequences
  - Efficiency in time and space

Reference Indexing

Existing indexing data structures

- linear self-indexing
  - Indexes all substrings of the text
- Hash-based indexing
  - Inverted index from words to reference positions

Reference Indexing

- **linear self-indexing**
  - Space-efficient
  - Slower search
  - variable length pattern
  - BWT and FM-index

- Bowtie2[9]
- BWA-MEM[10]

- **Hash-based indexing**
  - Take more space than linear but still Space-efficient
  - Fast search
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  - Recently used with the de bruin graph

- Genome Mapper[11]
- BGreat[12]
- deBGA[13]
- Kallisto[14]

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→ Compacted de Bruijn Graph

Compacted de Bruijn Graph

K = 4

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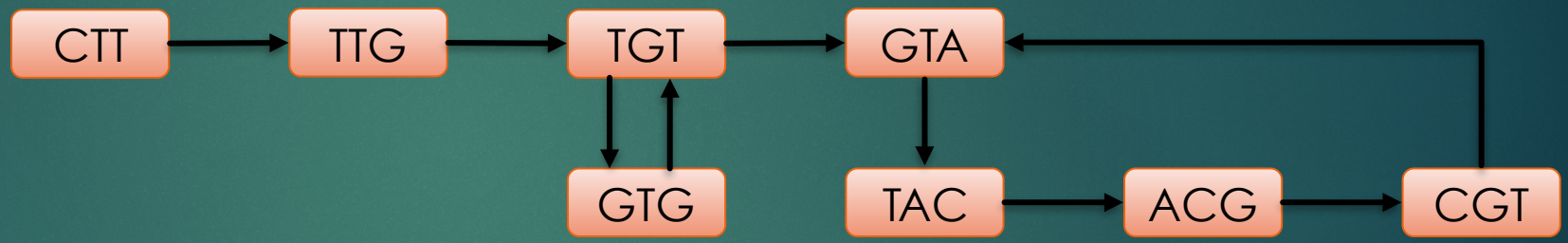

Compacted de Bruijn Graph

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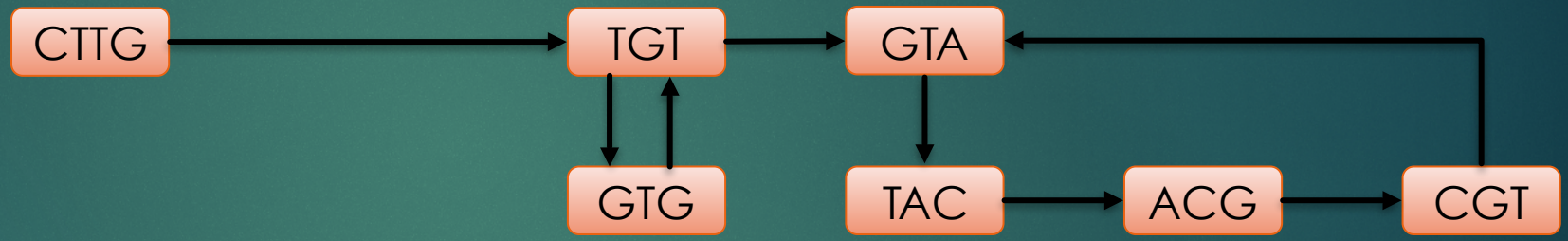

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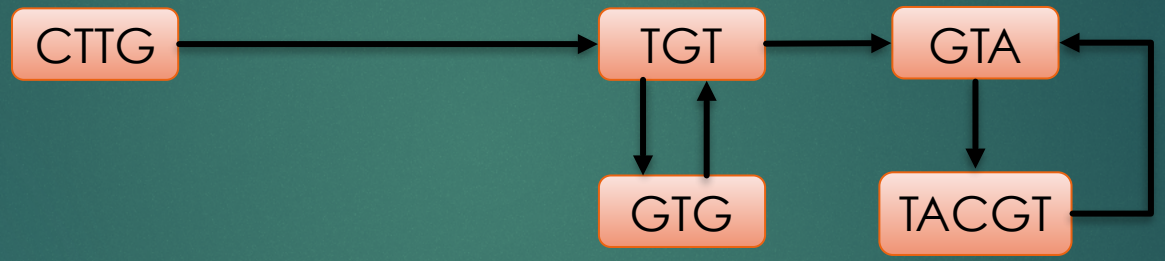

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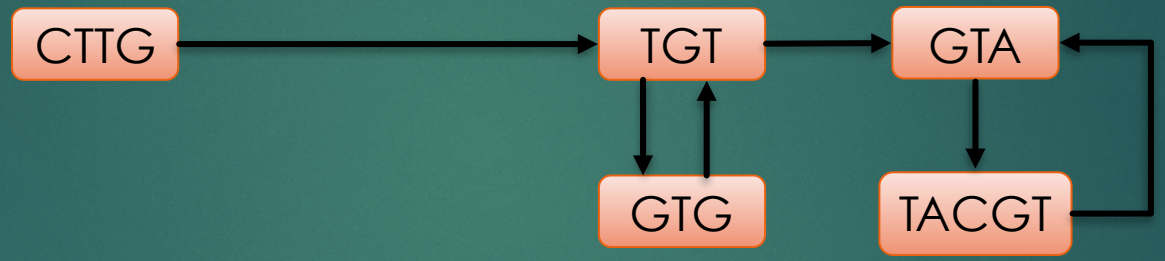

Uniting Info Table

Unitig ID	Unitig Info
0	{ref_y, p_2^y, o_2^y}, {ref_r, p_2^r, o_2^r}, {ref_r, p_2^r, o_2^r}
1	{ref_r, p_3^r, o_3^r}, {ref_g, p_3^g, o_3^g}
⋮	⋮

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K = 4

References:

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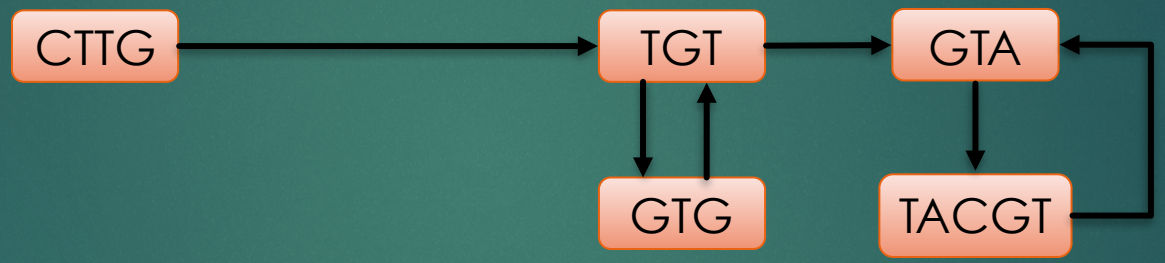

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⋮	⋮

Reduce size of the info table

Compacted de Bruijn Graph

K = 4

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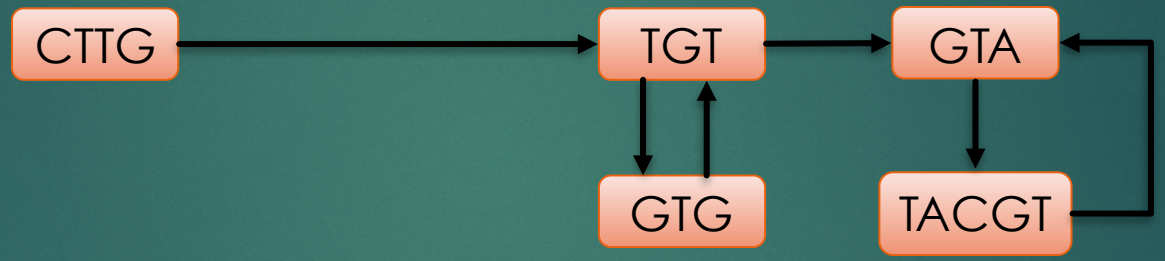

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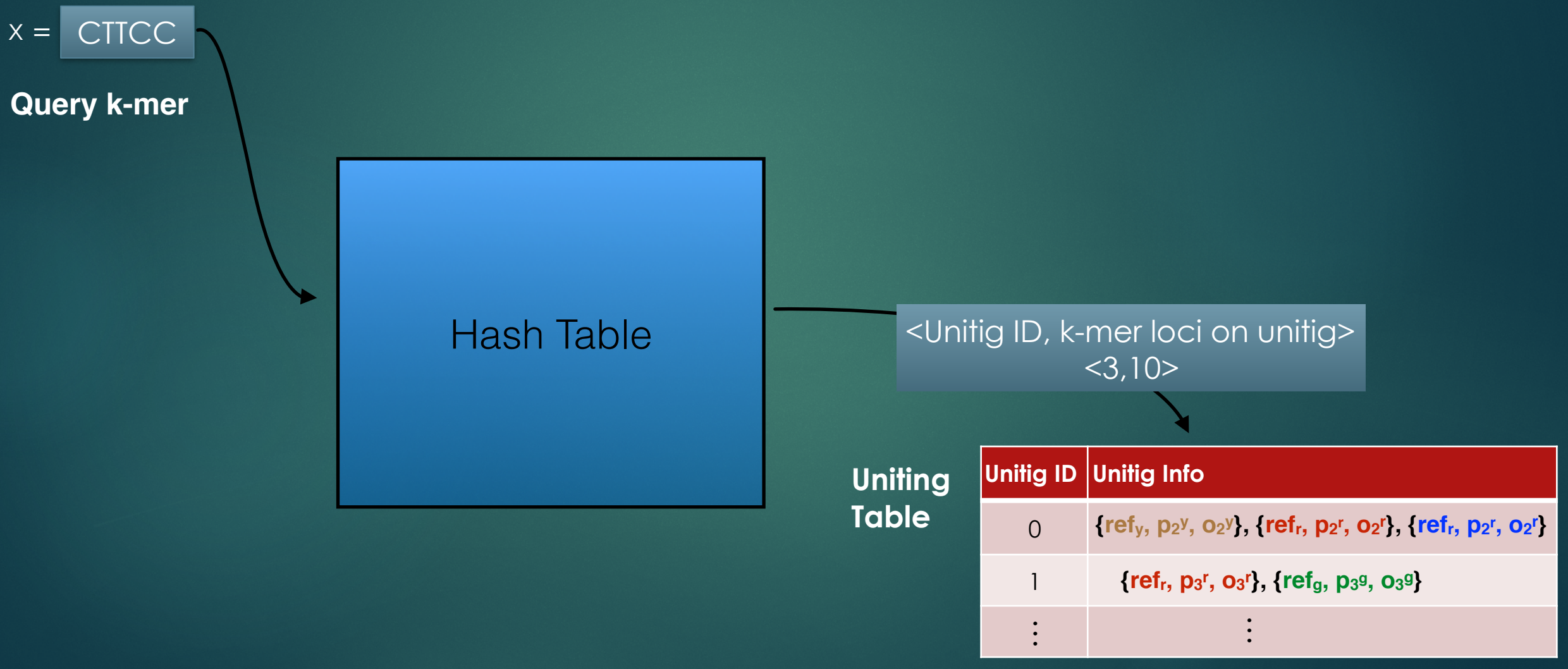
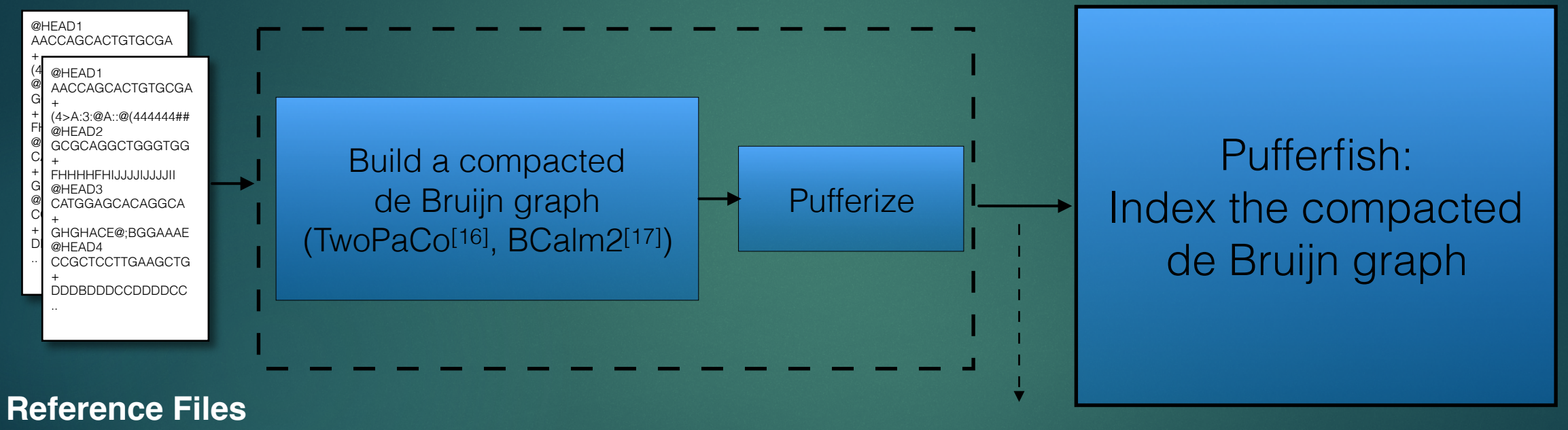
No notion of k-mers

Kallisto[14] and deBGA[13] use Hash Tables to map k-mers to their corresponding unitigs



Pufferfish Pipeline



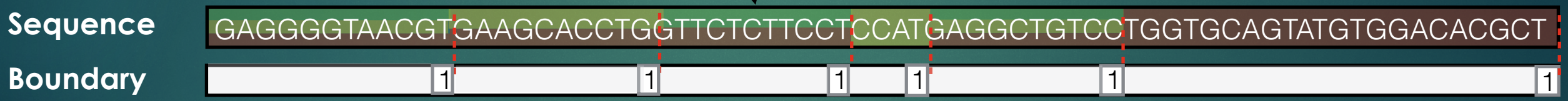
Reference Files

- Unitigs and their ID
- References encoded using unitig IDs

Pufferfish (dense)

x = CTTCC

Query k-mer



rank(p(x))

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Pufferfish (dense)

Awesome MPHF implementation

Fast and scalable minimal perfect hashing for massive key sets

Antoine Limasset[1], Guillaume Rizk[1], Rayan Chikhi[2], and Pierre Peterlongo[1]

1 IRISA Inria Rennes Bretagne Atlantique, GenScale team, Campus de Beaulieu 35042 Rennes, France
2 CNRS, CRIStAL, Université de Lille, Inria Lille - Nord Europe, France

x = CTTCC

Query k-mer

Minimal Perfect Hash Function

h(x)

- Guarantees a unique index in [0,N) for each k-mer
- no collision
- no order preservation
- False Positive Result: Can generate a number in [0, N) for a non-indexed k-mer

Sequence GAGGGGTAACGTGAAGCACCTGGTTCTCTTCCTCCATGAGGCTGTCCTGGTGCAGTATGTGGACACGCT

Boundary 1 1 1 1 1 1

rank(p(x))

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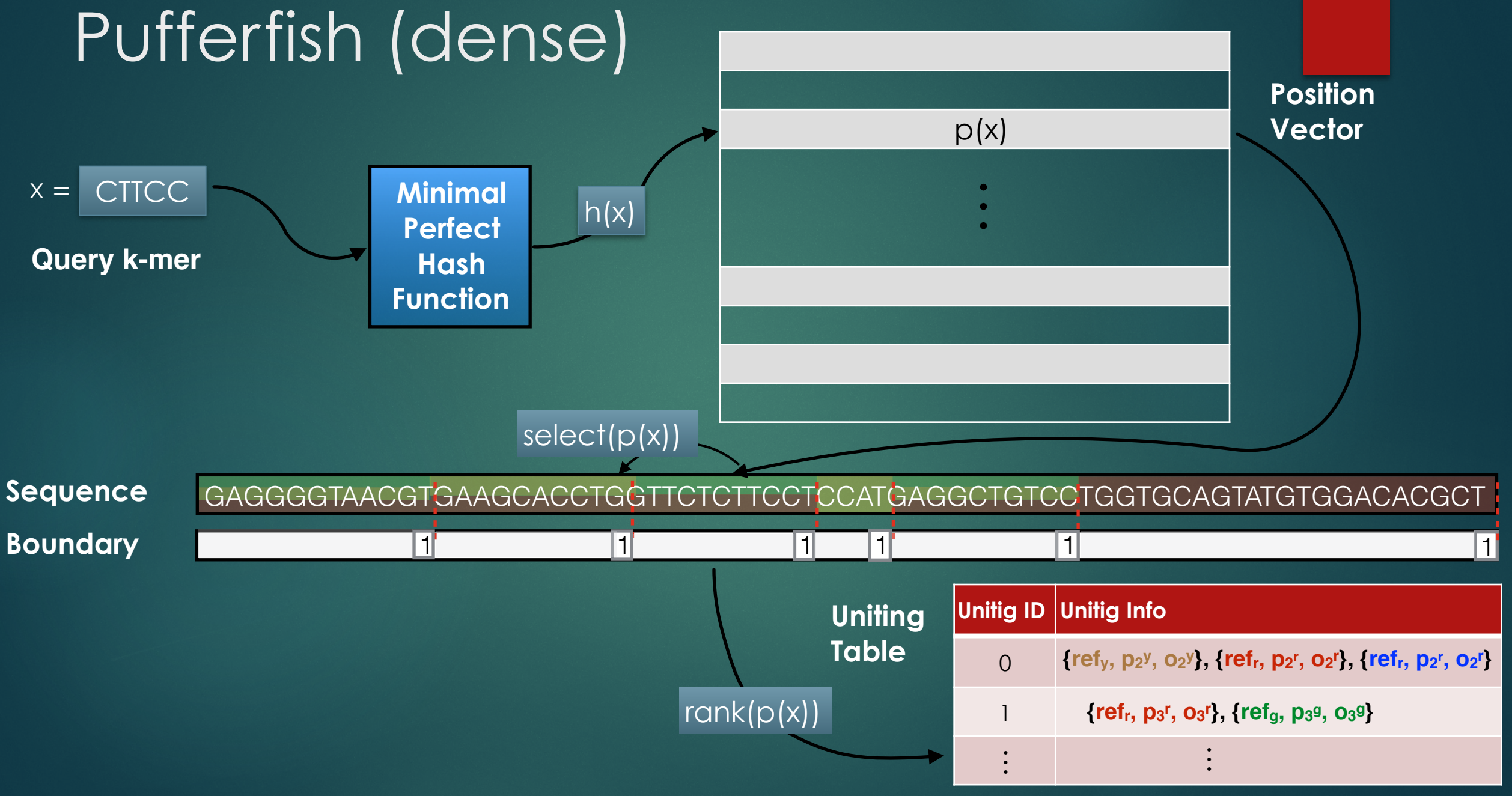

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Pufferfish

Space of index on disk

Tool	Human Transcriptome	Human Genome	Bacterial Genomes
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Pufferfish

Space of index + query in RAM

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What about speed?

Take experimental sequencing reads, and look-up *all* k-mers (k=31). The time reported is to load the index, map all 31-mers, and record the total number of (multi-mapping) hits.

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pufferfish dense	0:02:46	0:10:37	0:06:03

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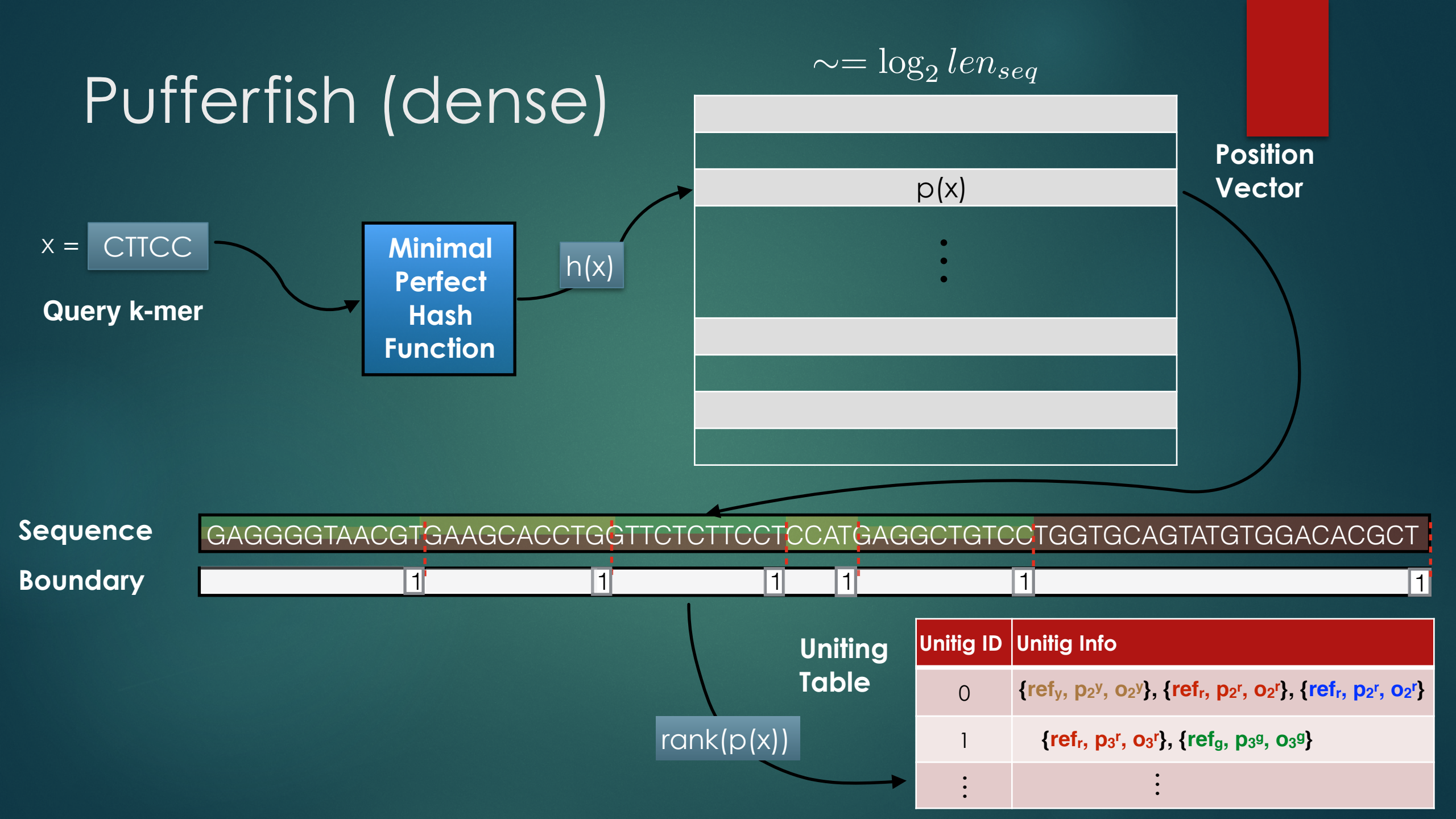

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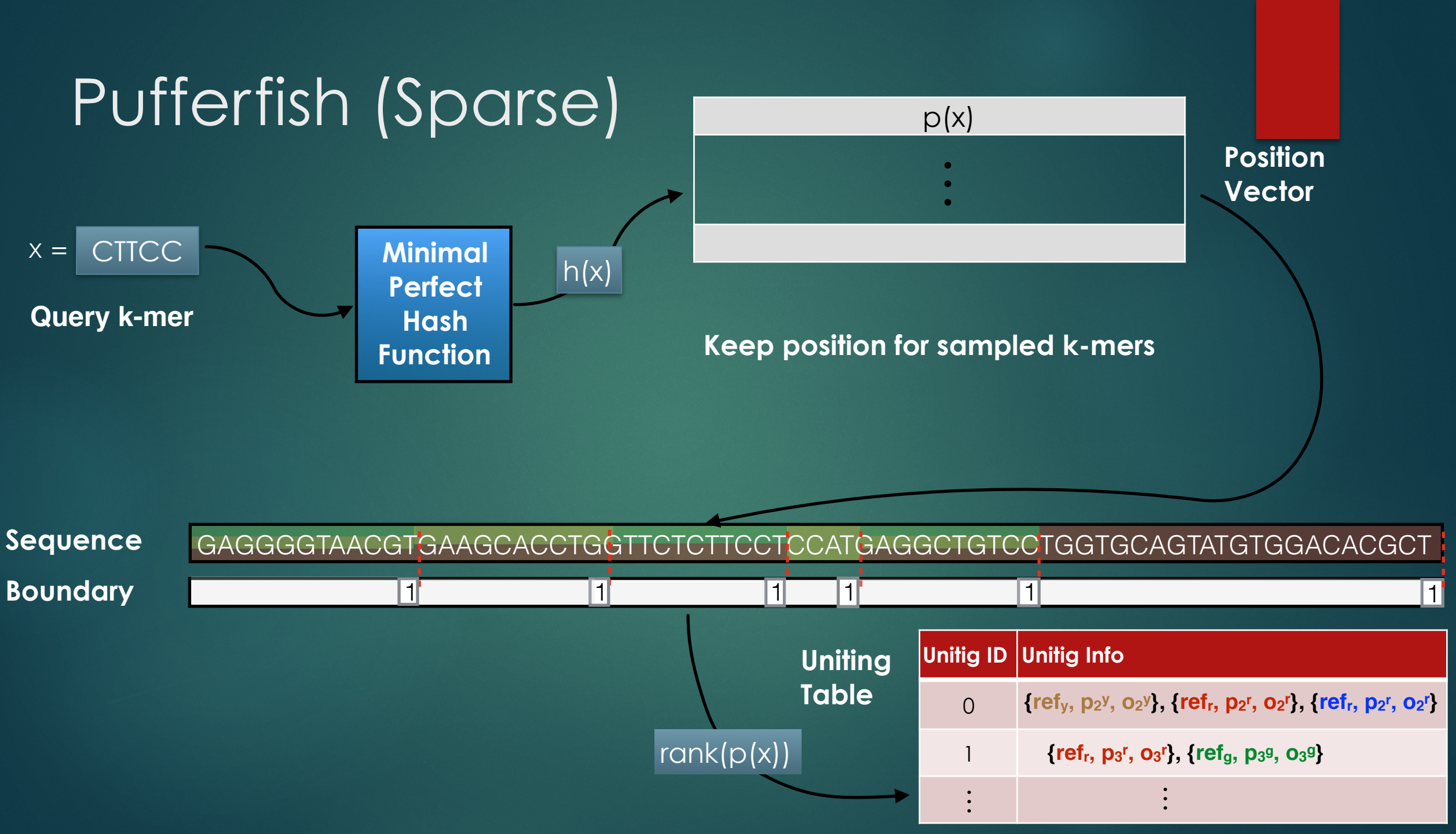
Pufferfish (Sparse)



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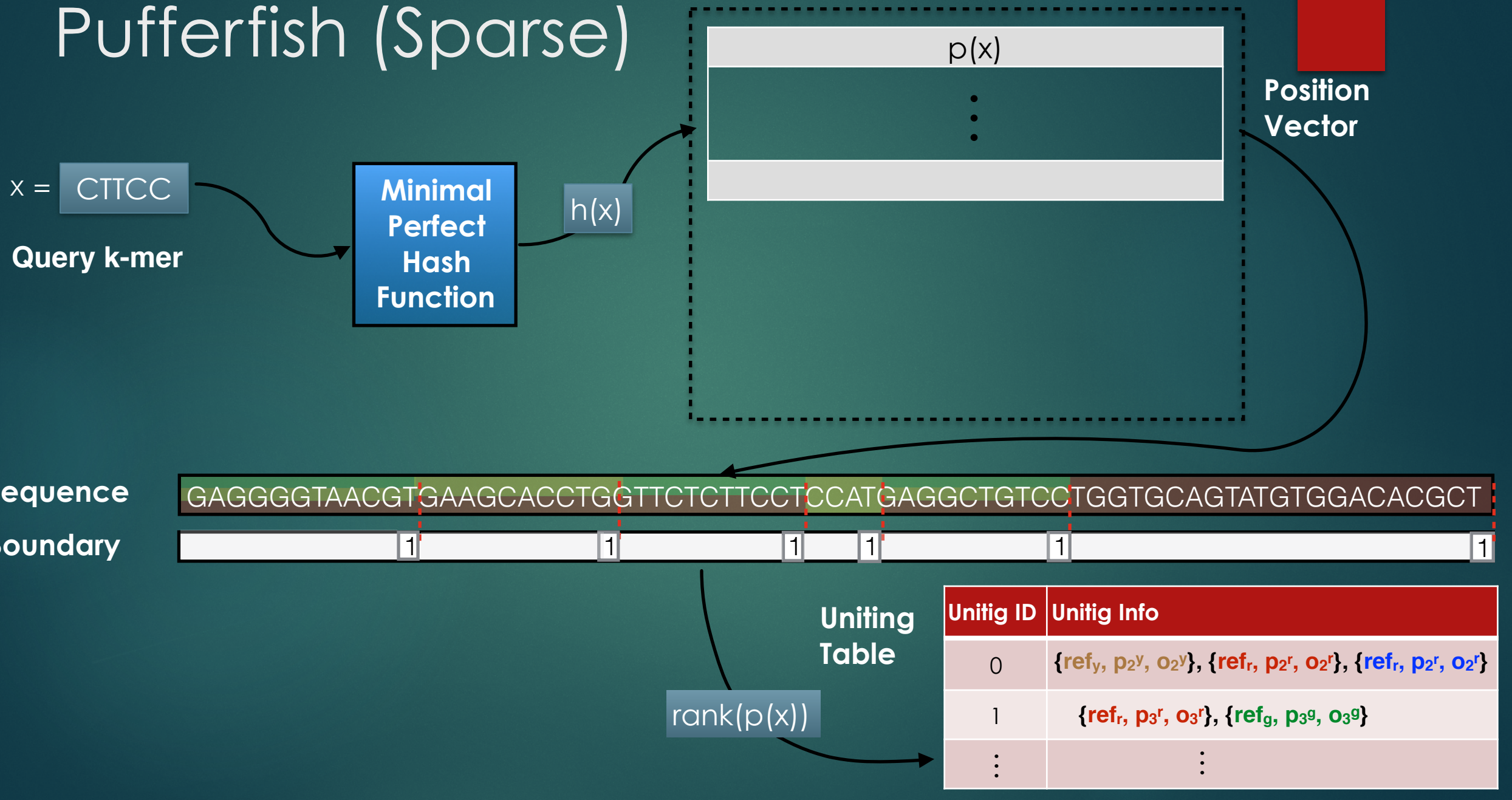

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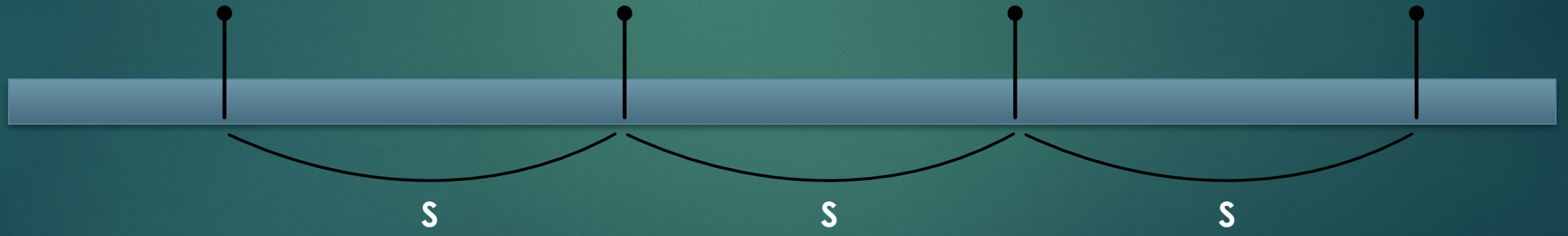

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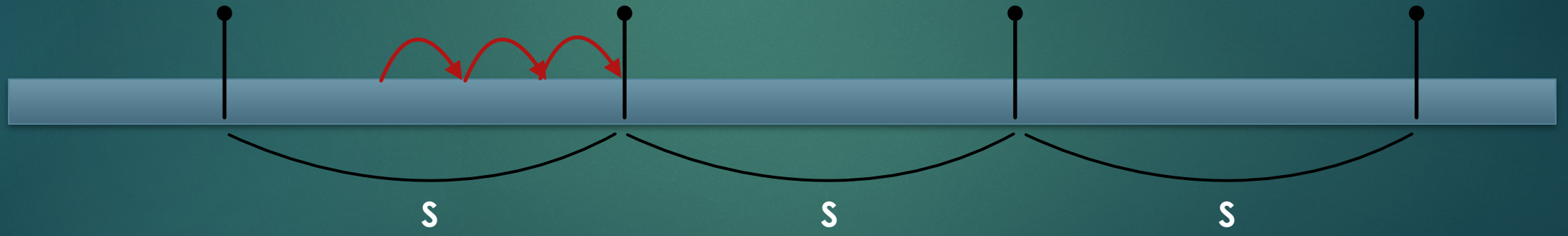

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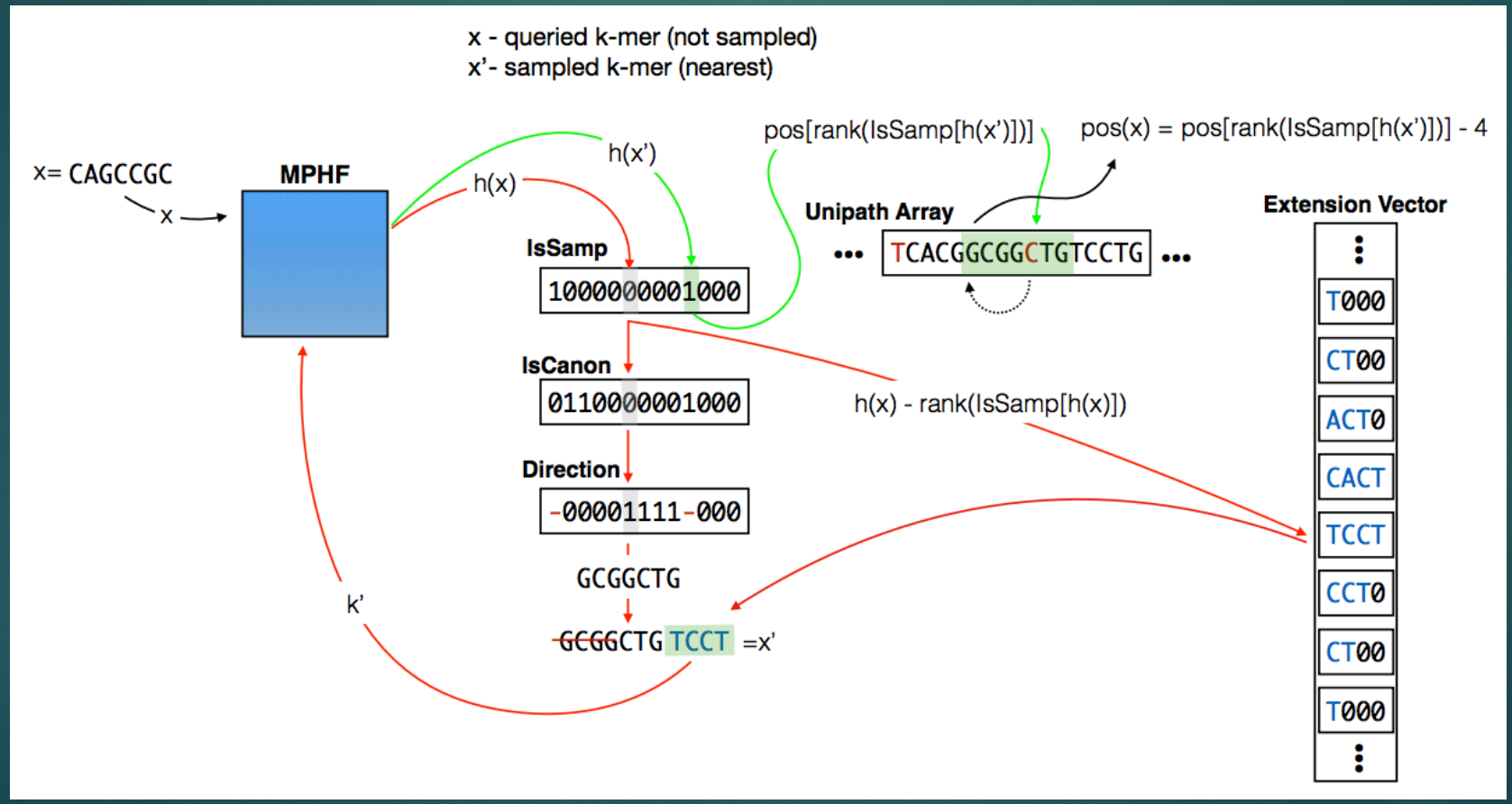
Pufferfish (Sparse)

Main Idea: Successors and predecessors in unipaths are *globally unique*, instead of storing position information for all k-mers, store positions only at sampled "landmarks" and say how to navigate to these landmarks (similar to bi-directional sampling in the FM-index).



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References

- [1] Zerbino, D.R. & Birney, E. Velvet: algorithms for de novo short read assembly using de Bruijn graphs. Genome Res. 18, 821–829 (2008).
- [2] Gnerre, S. et al. High-quality draft assemblies of mammalian genomes from massively parallel sequence data. Proc. Natl. Acad. Sci. USA 108, 1513–1518 (2011). 32. Li, R. et al.
- [3] De novo assembly of human genomes with massively parallel short read sequencing. Genome Res. 20, 265–272 (2010).
- [4] Zamin Iqbal, Mario Caccamo, Isaac Turner, Paul Flicek, and Gil McVean. De novo assembly and genotyping of variants using colored de Bruijn graphs. Nature genetics, 44(2):226–232, 2012.
- [5] Alexander Bowe, Taku Onodera, Kunihiko Sadakane, and Tetsuo Shibuya. Succinct de Bruijn graphs. In Proceedings of the International Workshop on Algorithms in Bioinformatics, pages 225–235. Springer, 2012
- [6] Guillaume Holley, Roland Wittler, and Jens Stoye. Bloom filter trie: an alignment-free and reference-free data structure for pan-genome storage. Algorithms Mol. Biol., 11:3, 2016. **BFT**
- [7] Martin D. Muggli, Alexander Bowe, Noelle R. Noyes, Paul Morley, Keith Belk, Robert Raymond, Travis Gagie, Simon J. Puglisi, and Christina Boucher. Succinct Colored de Bruijn Graphs. 2017.
- [8] Simon Gog. Succinct data structure library. https://github.com/simongog/ sdsl-lite, 2017. [online; accessed 01-Feb-2017

References

- [9] Ben Langmead and Steven L Salzberg. Fast gapped-read alignment with bowtie 2. *Nature methods*, 9(4):357–359, 2012.
- [10] Heng Li. Aligning sequence reads, clone sequences and assembly contigs with bwa-mem. *arXiv preprint arXiv:1303.3997*, 2013.
- [11] Korbinian Schneeberger, Jörg Hagmann, Stephan Ossowski, Norman Warthmann, Sandra Gesing, Oliver Kohlbacher, and Detlef Weigel. Simultaneous alignment of short reads against multiple genomes. *Genome biology*, 10(9):R98, 2009.
- [12] Antoine Limasset, Bastien Cazaux, Eric Rivals, and Pierre Peterlongo. Read mapping on de bruijn graphs. *BMC bioinformatics*, 17(1):237, 2016.
- [13] Bo Liu, Hongzhe Guo, Michael Brudno, and Yadong Wang. debga: read alignment with de bruijn graph-based seed and extension. *Bioinformatics*, 32(21):3224–3232, 2016.
- [14] Nicolas L Bray, Harold Pimentel, Páll Melsted, and Lior Pachter. Near-optimal proba- bilistic RNA-seq quantification. *Nature Biotechnology*, 34(5):525–527, 2016.
- [15] Benedict Paten, Adam M Novak, Jordan M Eizenga, and Erik Garrison. Genome graphs and the evolution of genome inference. *Genome research*, 27(5):665–676, 2017.
- [16] Ilia Minkin, Son Pham, and Paul Medvedev. Twopaco: An efficient algorithm to build the compacted de bruijn graph from many complete genomes. *Bioinformatics*, page btw609, 2016.
- [17] Rayan Chikhi, Antoine Limasset, and Paul Medvedev. Compacting de bruijn graphs from sequencing data quickly and in low memory. *Bioinformatics*, 32(12):i201–i208, 2016.