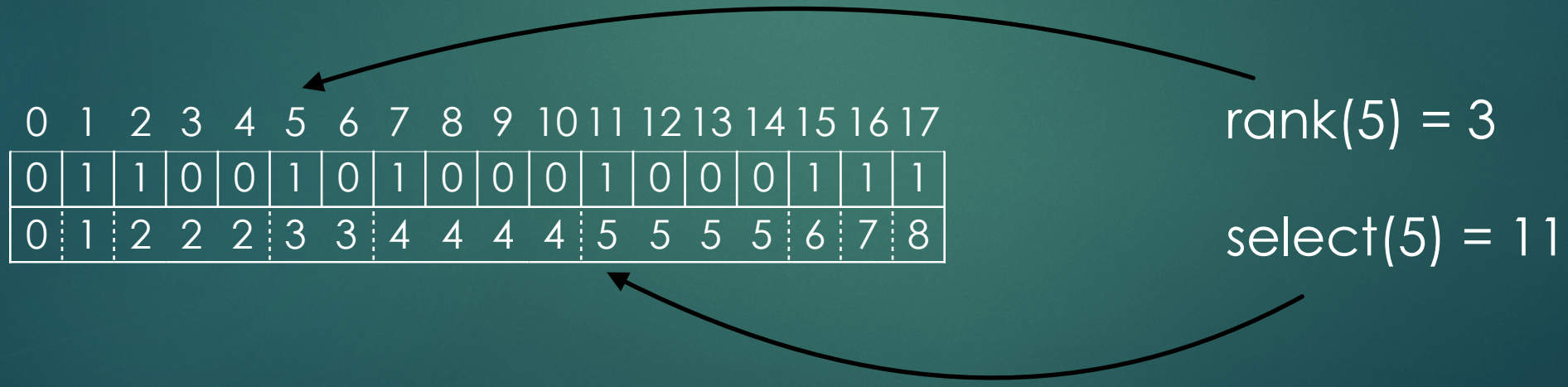
Efficient representation of the colored de Bruijn Graph

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



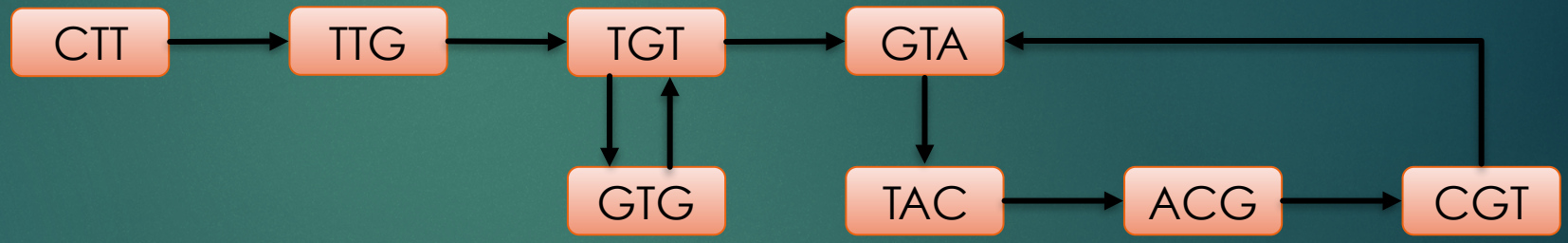
de Bruijn Graph[1-3]

Edge-centric Variant

K = 4

Sample:

CTTGTGTACGTA



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

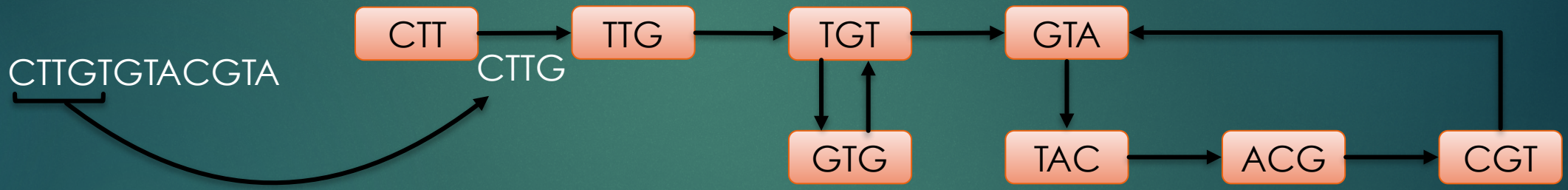
K-mer : unique substring of size k

de Bruijn Graph[1-3]

Edge-centric Variant

K = 4

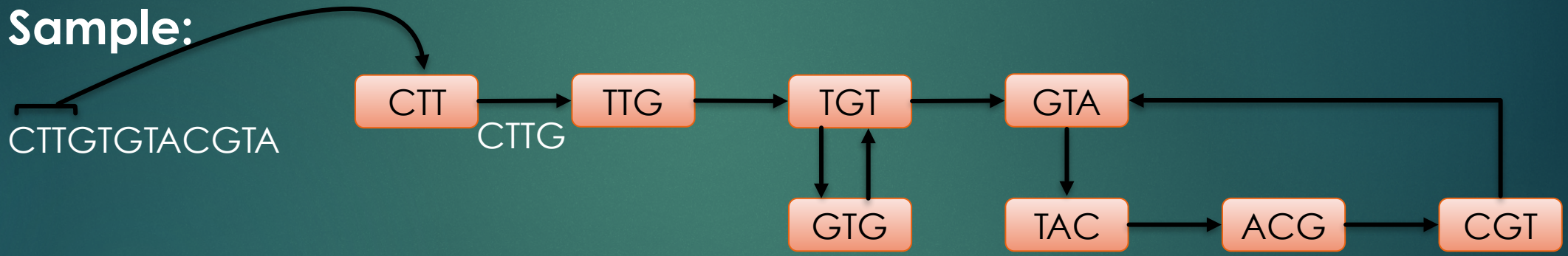
Sample:



de Bruijn Graph[1-3]

Edge-centric Variant

K = 4



de Bruijn Graph[1-3]

Edge-centric Variant

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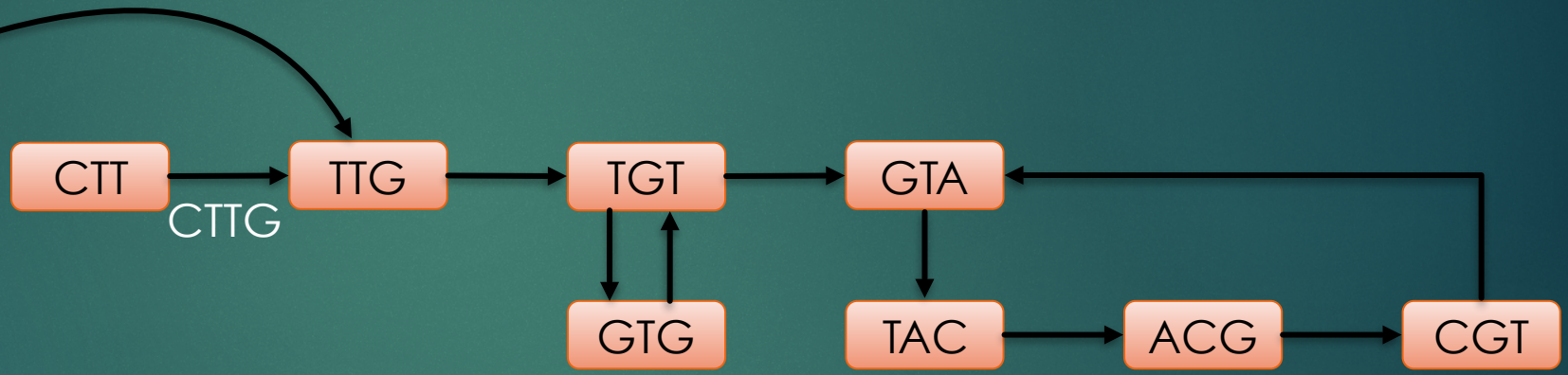
Sample:

CTTGTGTACGTA



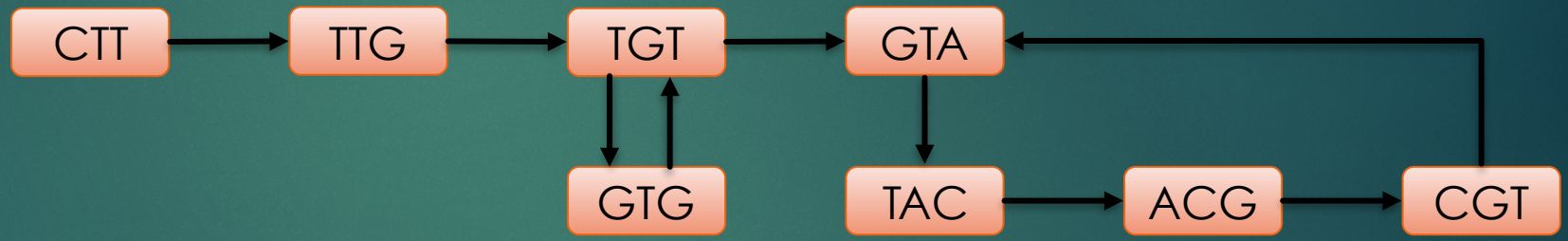
de Bruijn Graph[1-3]

Edge-centric Variant

K = 4

Sample:

CTTGTGTACGTA



- Genome/Transcriptome Assembly
- Sequence Indexing

Rainbowfish

Rainbowfish: A Succinct Colored de Bruijn Graph Representation*

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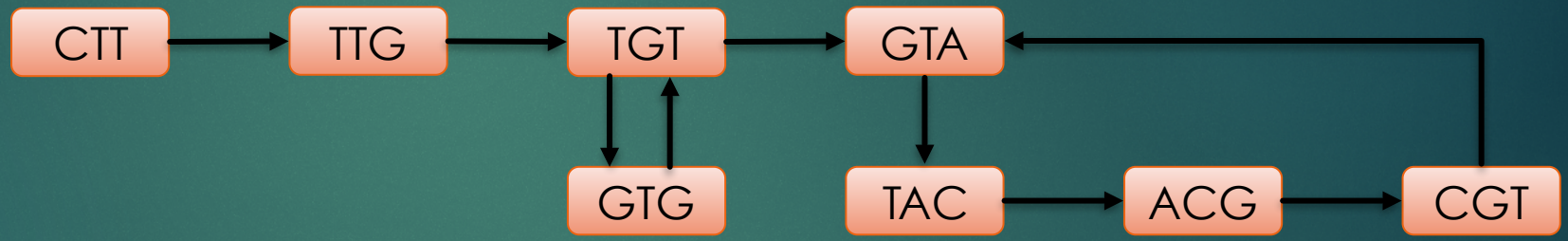
WABI 2017

Colored de Bruijn Graph

K = 4

Sample:

CTTGTGTACGTA

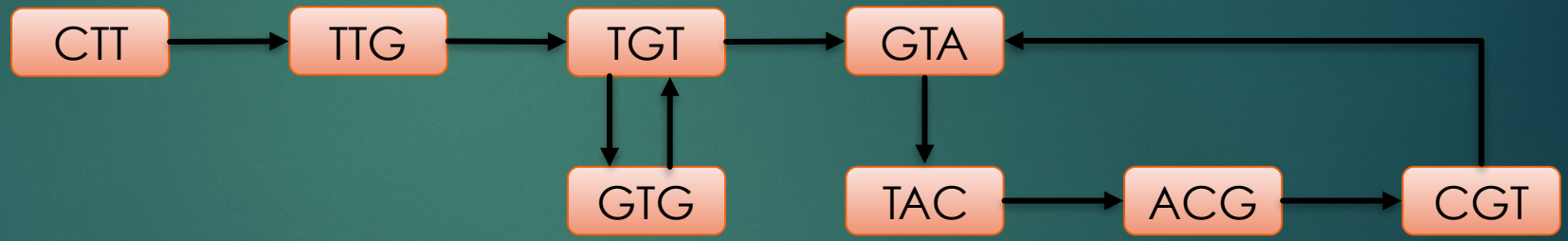


Colored de Bruijn Graph

K = 4

Sample:

- CTTGTGTACGTA

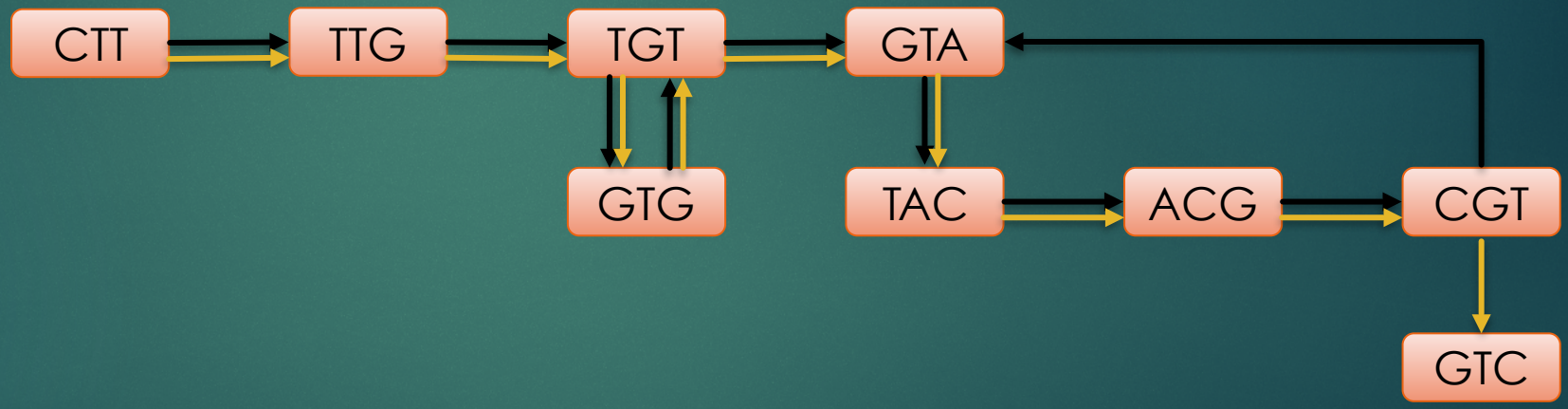


Colored de Bruijn Graph

K = 4

Samples:

- CTTGTGTACGTA
- CTTGTGTACGTC

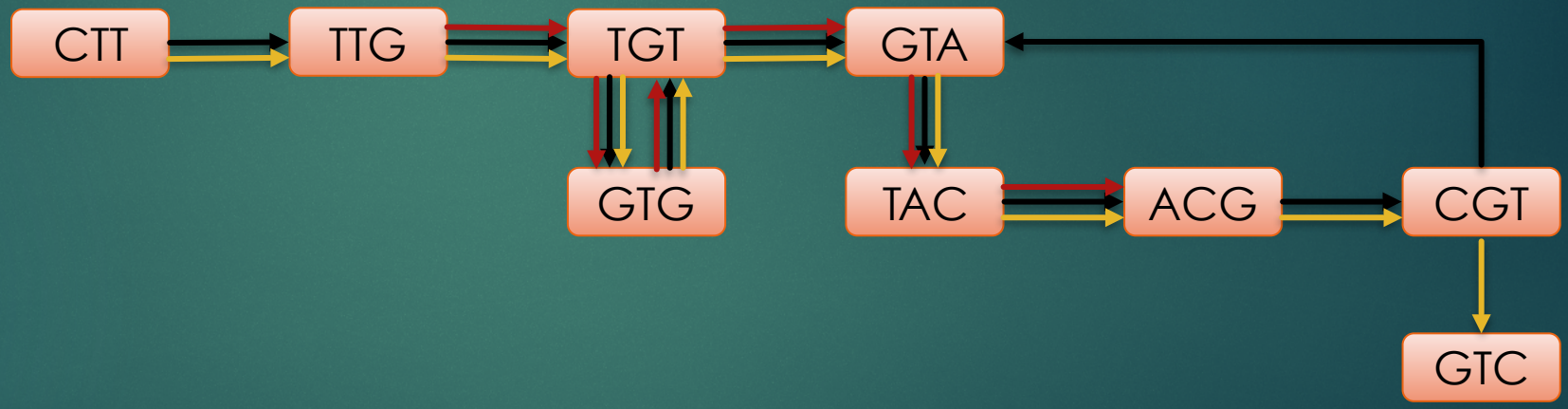


Colored de Bruijn Graph

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

BOSS

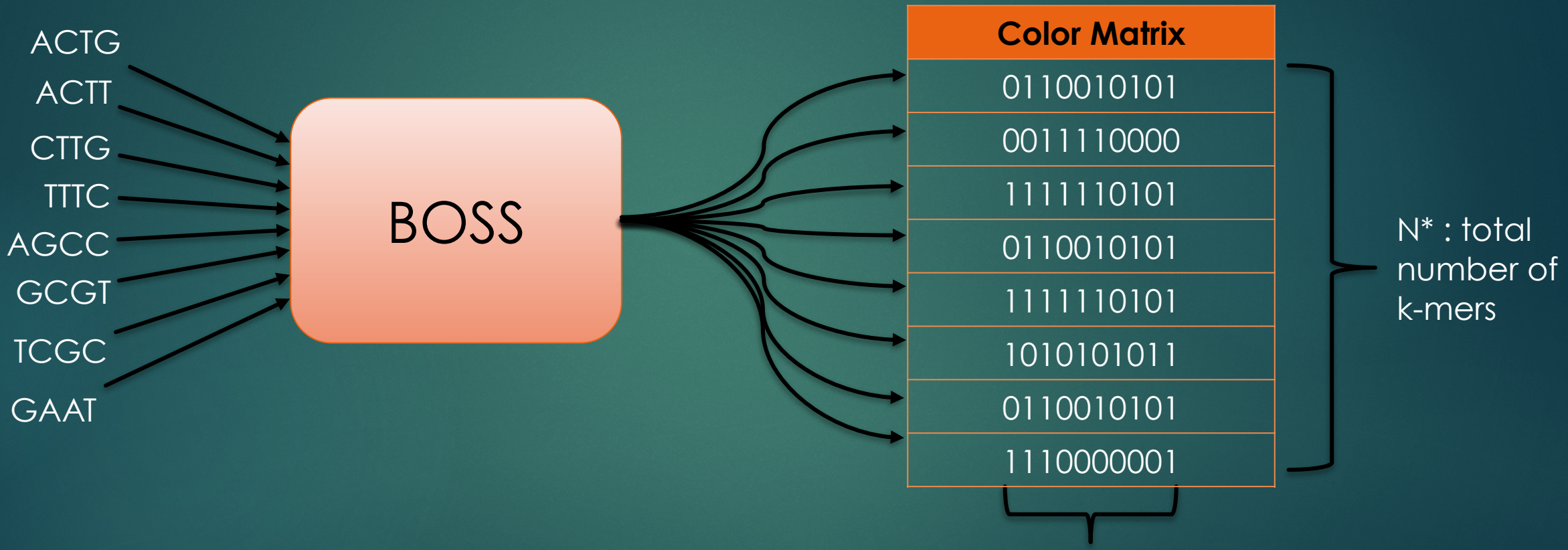
Color Matrix
0110010101
0011110000
1111110101
0110010101
1111110101
1010101011
0110010101
1110000001

N* : total number of k-mers

C : total number of colors (samples)

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

BOSS → VARI



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VARI

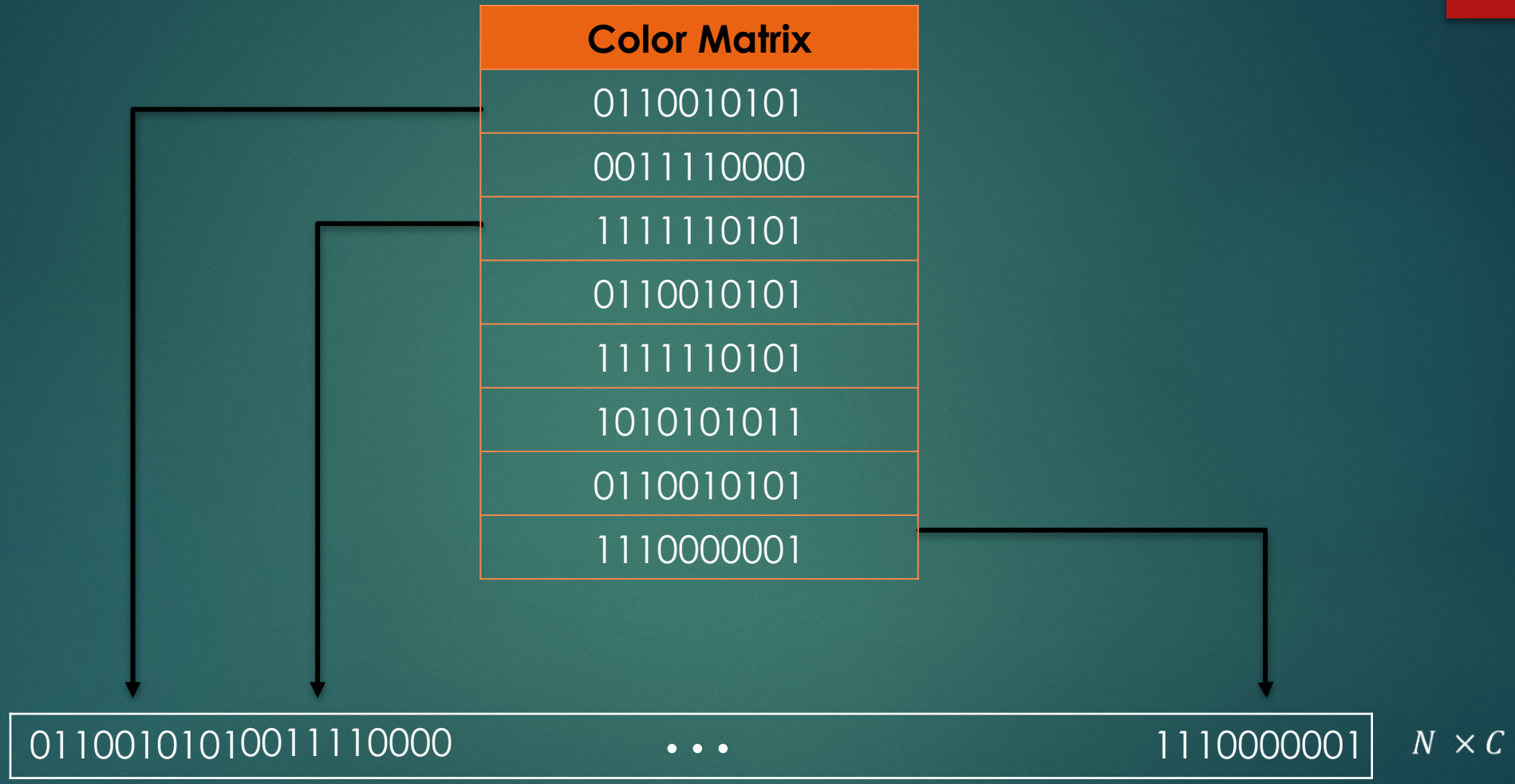
Color Matrix
0110010101
0011110000
1111110101
0110010101
1111110101
1010101011
0110010101
1110000001

VARI

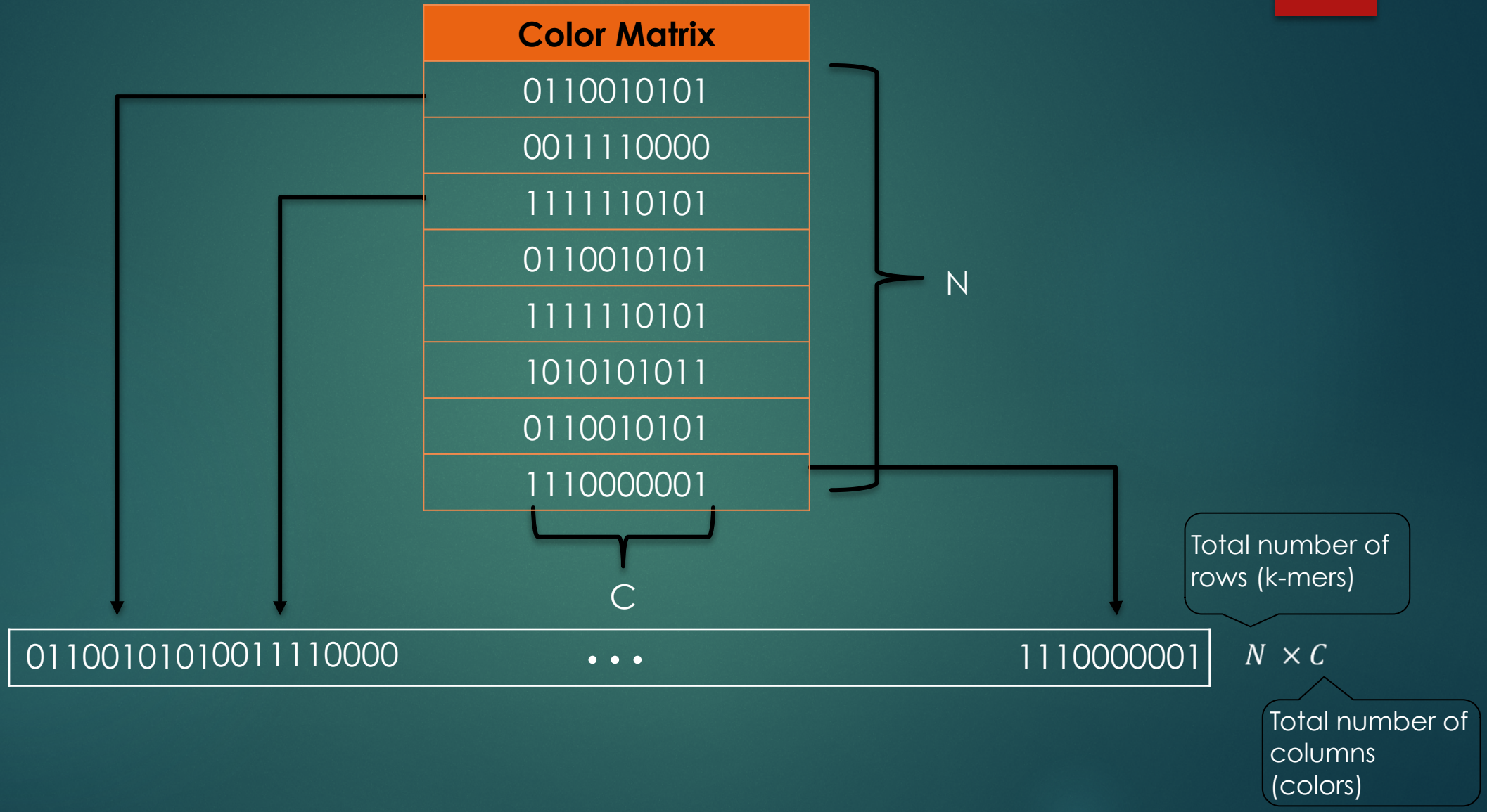
Color Matrix
0110010101
0011110000
1111110101
0110010101
1111110101
1010101011
0110010101
1110000001

0110010101 0011110000 • • • 1110000001

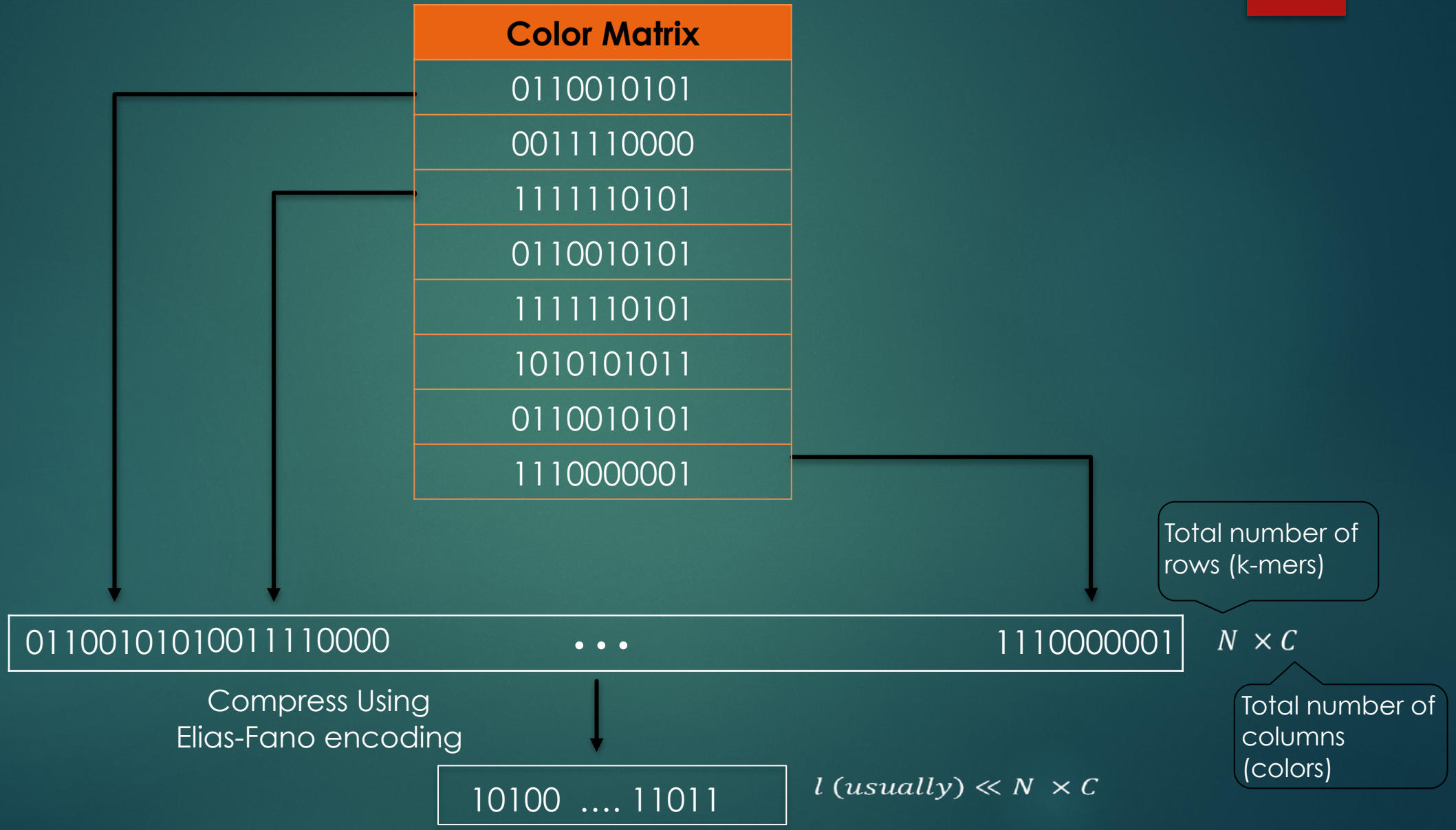
VARI


Color Matrix
0110010101
0011110000
1111110101
0110010101
1111110101
1010101011
0110010101
1110000001
0110010101001111000 0
• • •
1110000001
$N \times C$

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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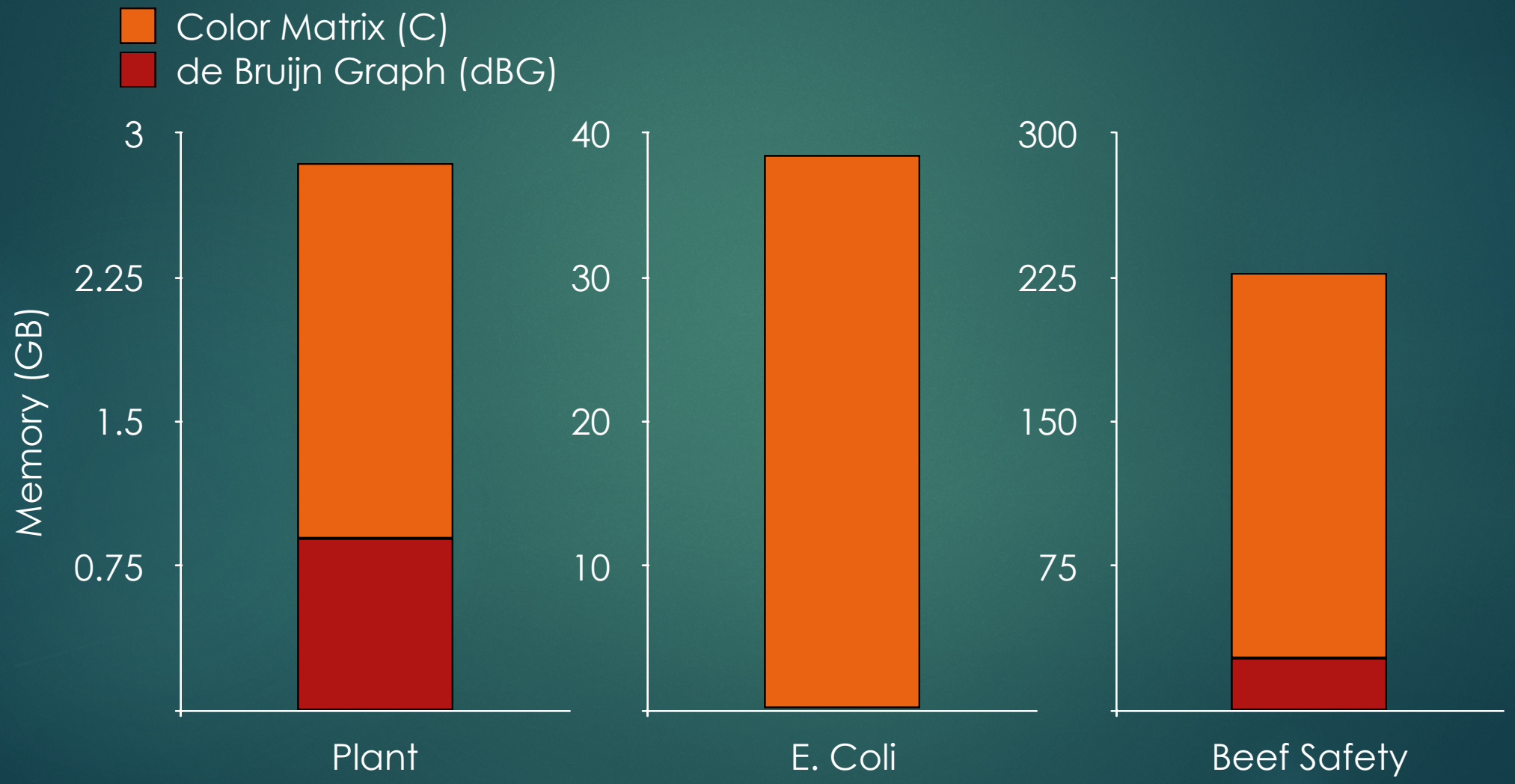
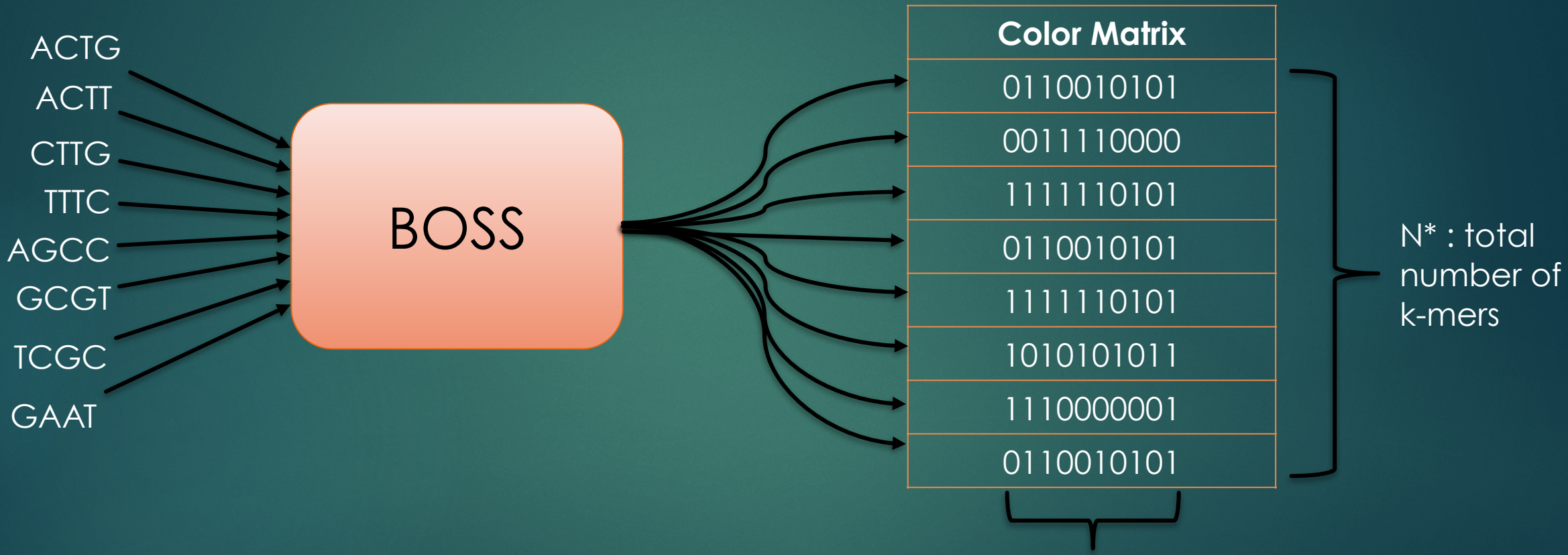
VARI results compared to Cortex

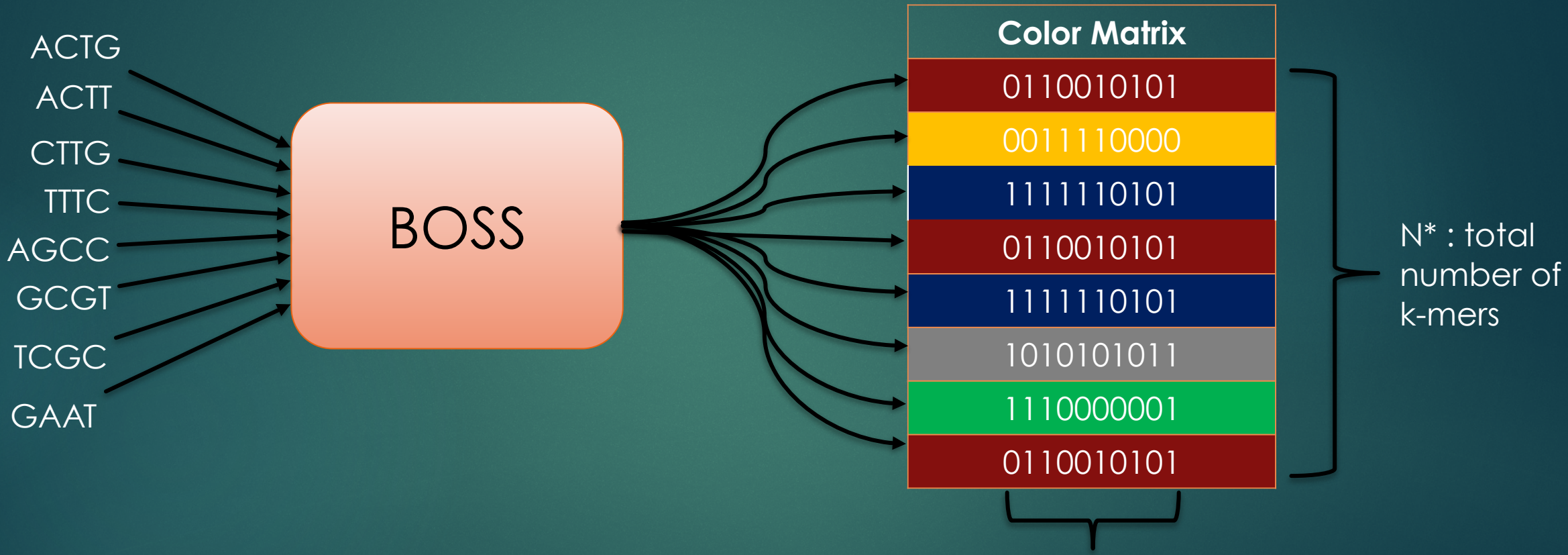


BOSS + VARI



* 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

E = 5

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

C : total number of colors

$l = E \times C$

0110010101	0011110000	1111110101	1010101011	1110000001

Equivalence Bitvector

+

Color Matrix
0
1
2
0
2
3
4
0

N : total number of k-mers

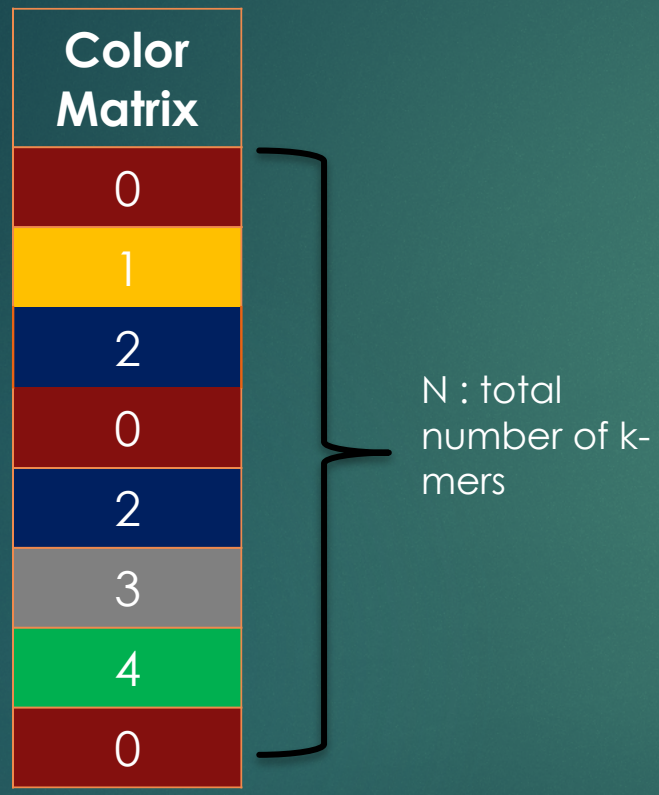
$l = N \times \log_2 E \leq N \times C$

000	001	010	000	010	011	100	000

Label Bitvector

Majority of the space

Rainbowfish
Equivalence Table



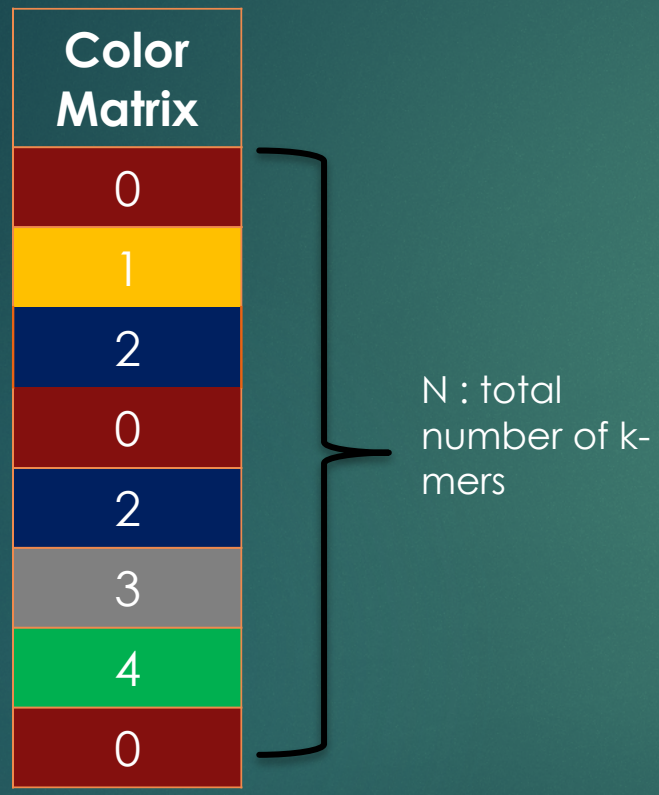
Datasets	$\frac{l}{N \times C}$
E. Coli (10)	0.9
E. Coli (1000)	0.02
E. Coli (5598)	0.004
Plant (4)	1
Beef Safety (88)	< 0.34
Human Txme (95,146)	< 0.0002

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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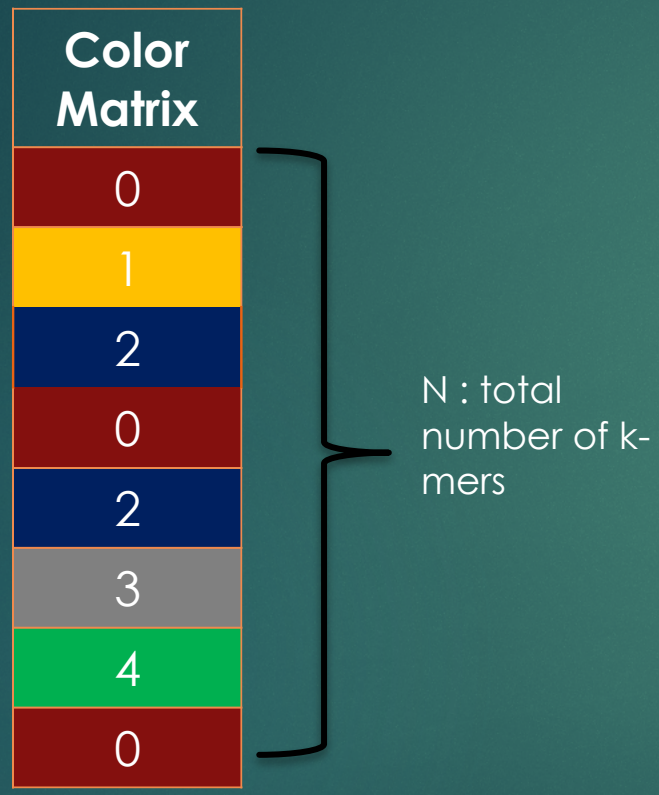
Human Txme (95,146)	< 0.0002

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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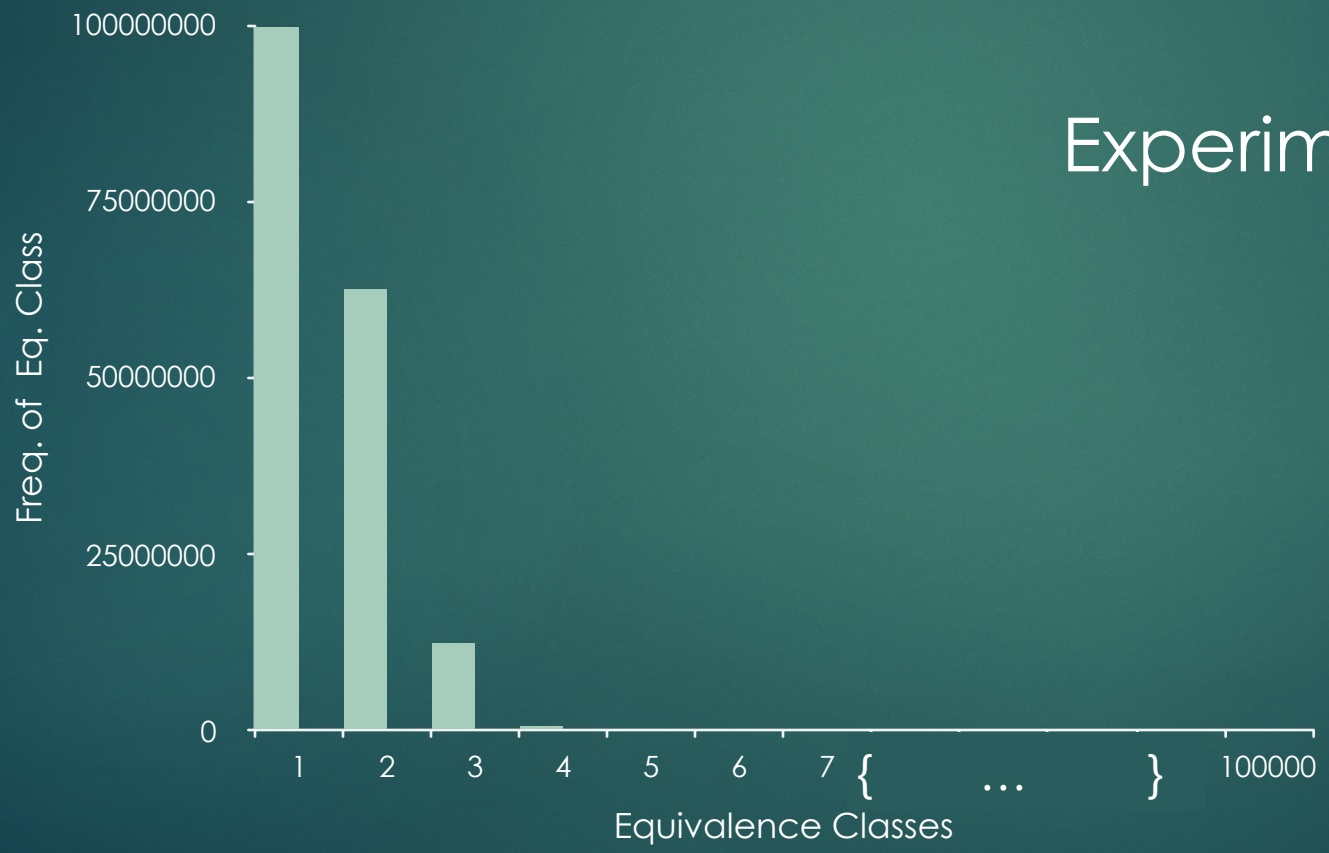
000 001 010 000 010 011 100 000

Label Bitvector

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

Rainbowfish

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

* This idea is briefly discussed in the BFT paper

Rainbowfish

Label & Boundary Bitvectors

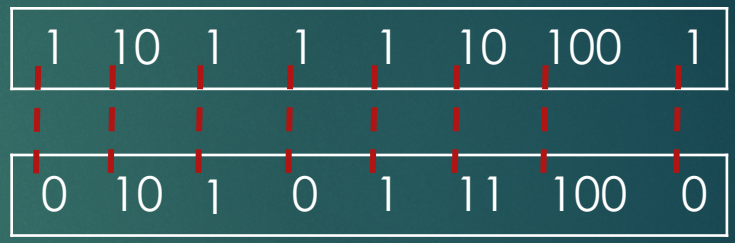
Label	Equivalence Class
0	0110010101
1	1111110101
2	0011110000
3	1010101011
4	1110000001

*

Equivalence Bitvector

Color Matrix
0
2
1
0
1
3
4
0

Boundary Bitvector



Label Bitvector

Label Bitvector

* This idea is briefly discussed in BFT paper

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 $M \leq \min(N, 2^C)$.

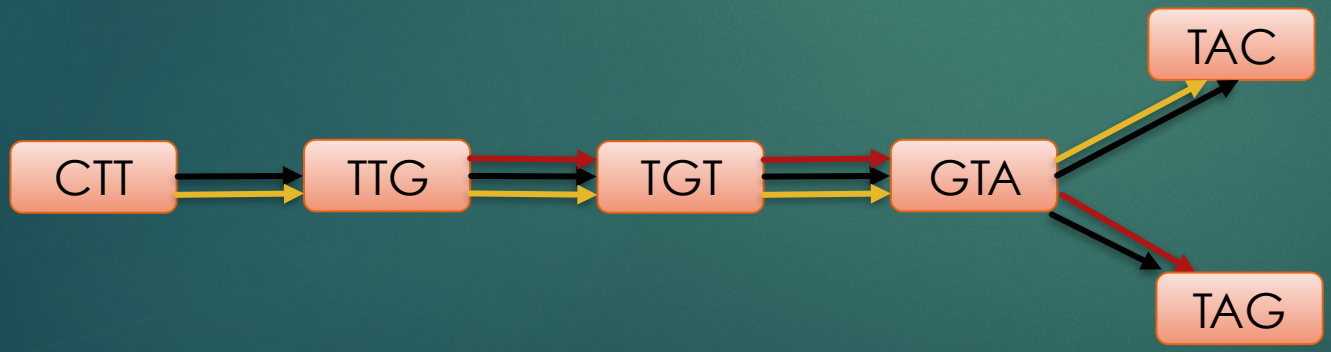
- Counting argument (Lower bound)
  - Count number of ways to map M distinct color class to N set of edges
  - Assign set of M edges a distinct color class : $M!$
  - Assign colors to $N - M$ in any possible manner : $M^{N-M}.M!$
  - To represent any of these we need at least $\log_2(M^{N-M}.M!)$
  -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

Why Is Rainbowfish Succinct

- Succinct Definition + Lemma 1 + Theorem 1 + Theorem 2
- $\mathrm{S} = Z + o(Z)$
- $Z \geq N log_2 M$
- $\mathrm{s} = O\left(MC + NH(X_e)\right) \leq 2N log_2 M$
- $\mathrm{S} = \mathrm{s} + \mathrm{o}(\mathrm{N})$ 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

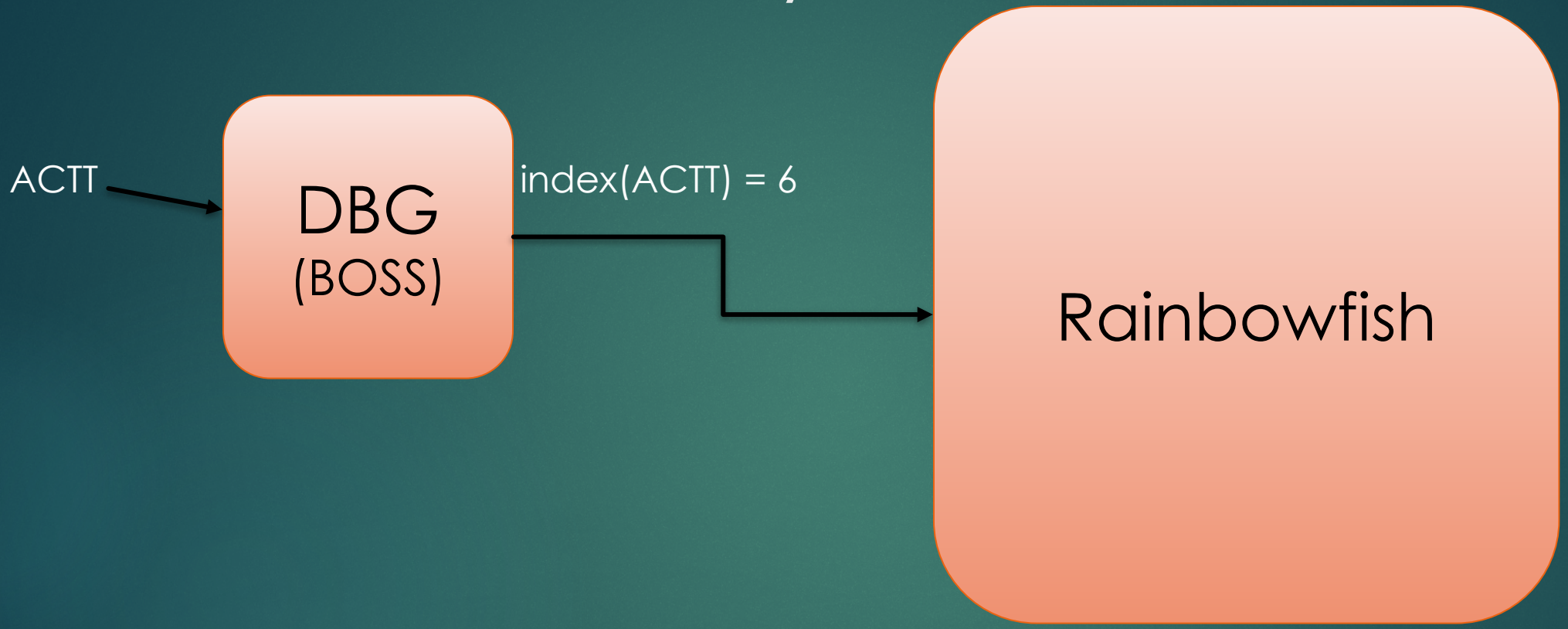
For each k-mer

search(k-mer, color1)

search(k-mer, color2)

Until one of these are false

Rainbowfish Query



Rainbowfish Query

Boundary Bitvector

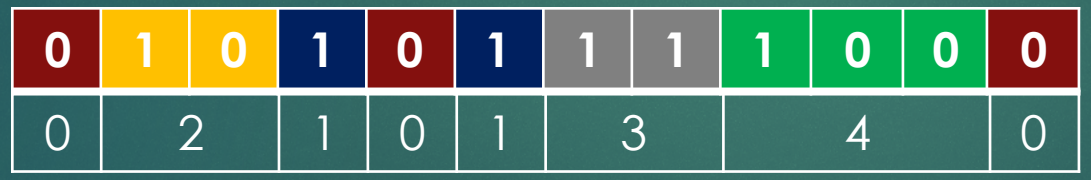
Label Bitvector

Equivalence Bitvector

Rainbowfish Query

index(ACTT) = 6

Boundary Bitvector



Label Bitvector

Equivalence Bitvector

Rainbowfish Query

index(ACTT) = 6

Select(i=6)=8

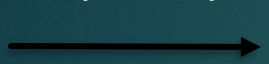
Boundary Bitvector

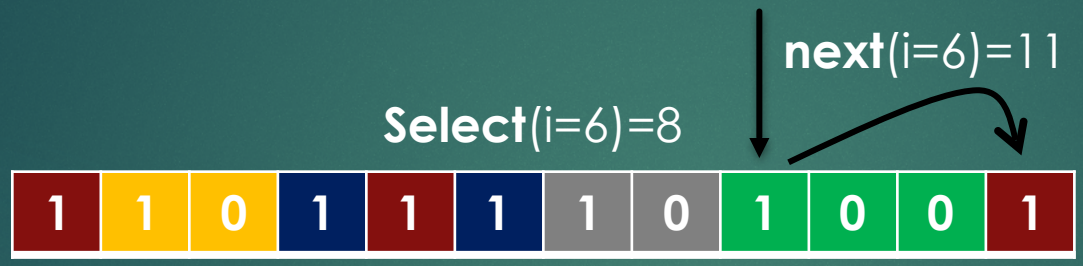
Label Bitvector

Equivalence Bitvector

Rainbowfish Query

index(ACTT) = 6





Boundary Bitvector

0	1	0	1	0	1	1	1	1	0	0	0
0	2		1	0	1	3		4			0

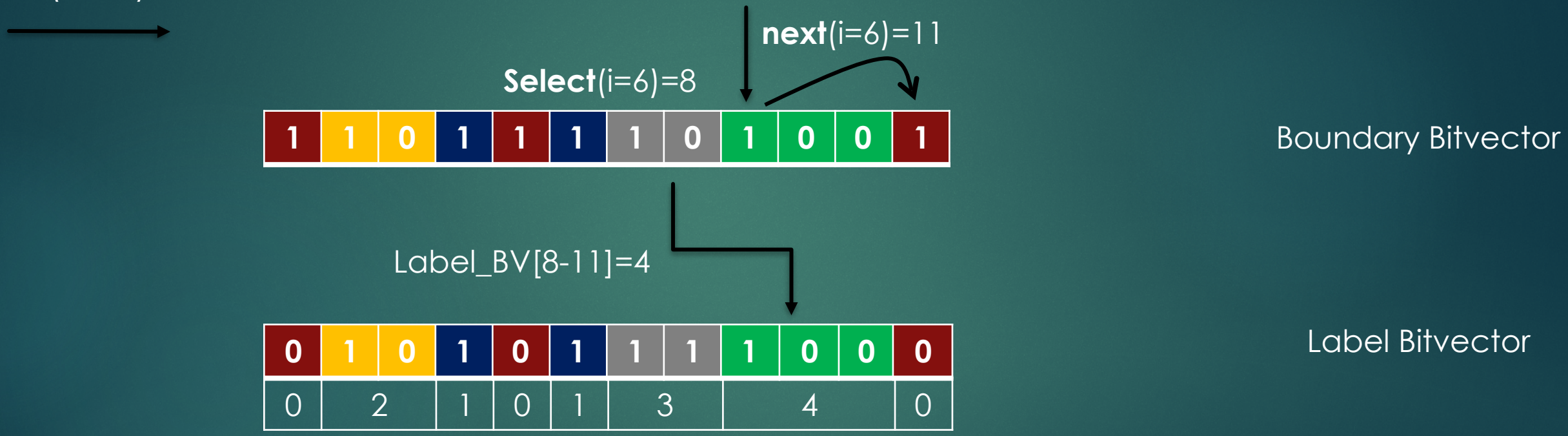
Label Bitvector

0110010101	1111110101	0011110000	1010101011	1110000001

Equivalence Bitvector

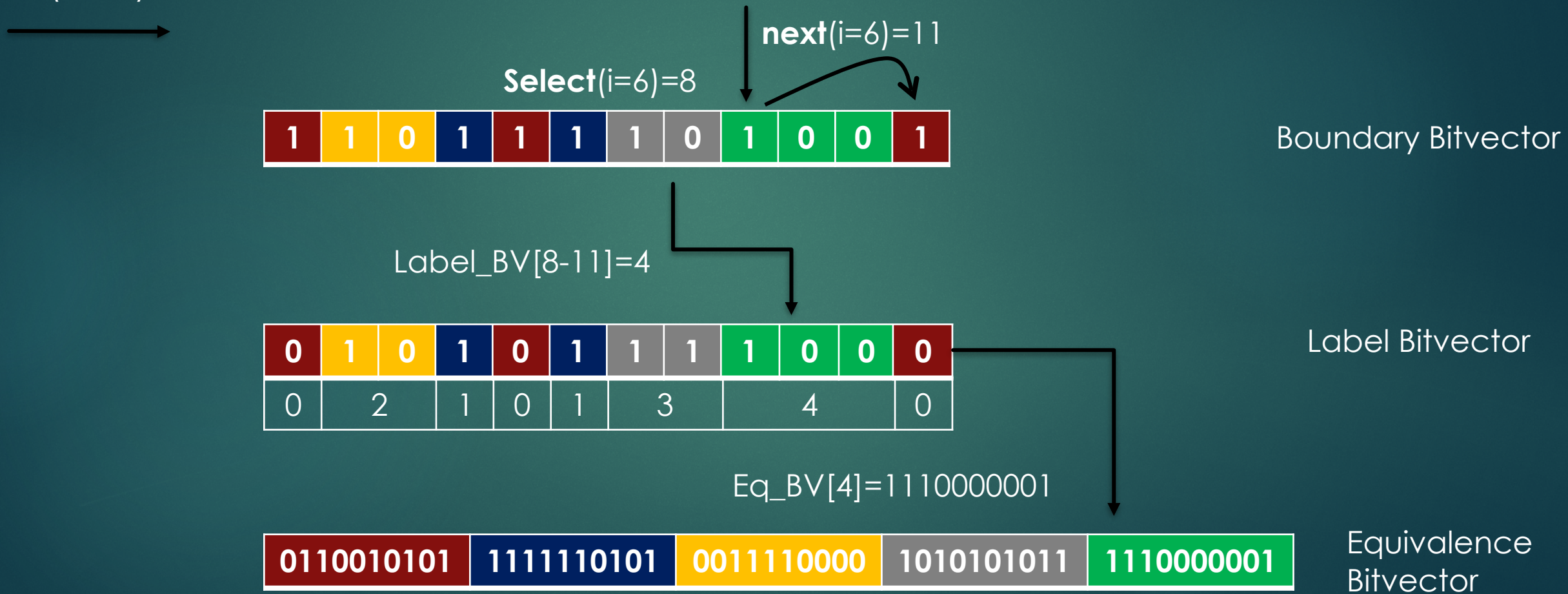
Rainbowfish Query

index(ACTT) = 6



Rainbowfish Query

index(ACTT) = 6



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
Human Txme (95,146)	1,808,435	841	817

* 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
E. Coli 1000	340	270	2,610	2,356
E. Coli 5598	3,141	4,021	8,796	8,201
Plant	108	339	47,040	48,537
Beef Safety	15,375	30,478	NA	NA
Human Txme	13,961	30,804	NA	NA

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