On the representation of de Bruijn Graphs

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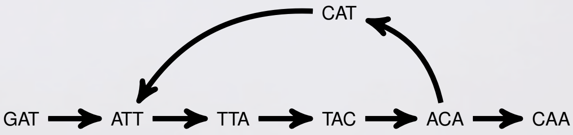
de Bruijn Graph

```
sequence:   GATTACATTACAA
  k-mers:   GAT
   (k=3)     ATT
              TTA
               ...
```

Nodes: *k*-mers (words of length *k*)
Edges: exact suffix-prefix overlaps of length $k - 1$



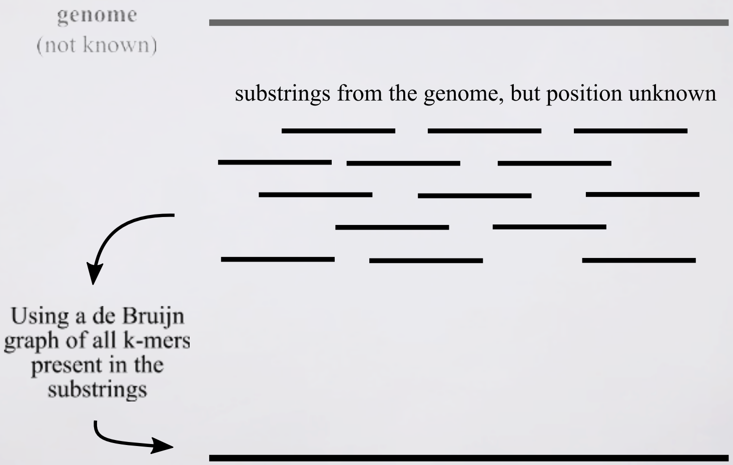
Usages:

- Bioinformatics
  - *de novo* assembly of sequencing data
- Distributed applications

Genome sequencing

```
>1
ACTGA..
>2
TGTAG..
...
```

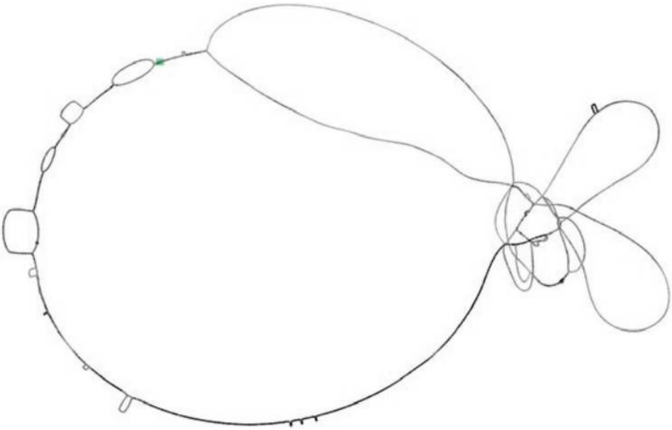
Genome assembly



genome
(not known)

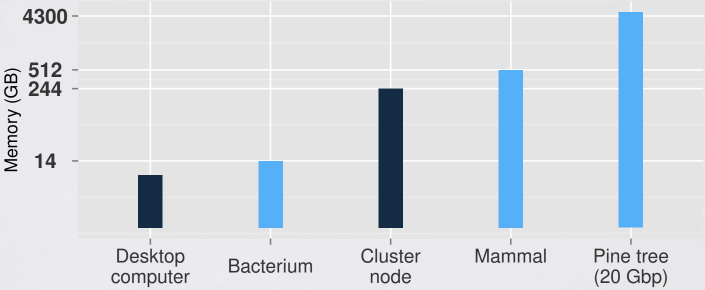
substrings from the genome, but position unknown

Using a de Bruijn graph of all k-mers present in the substrings



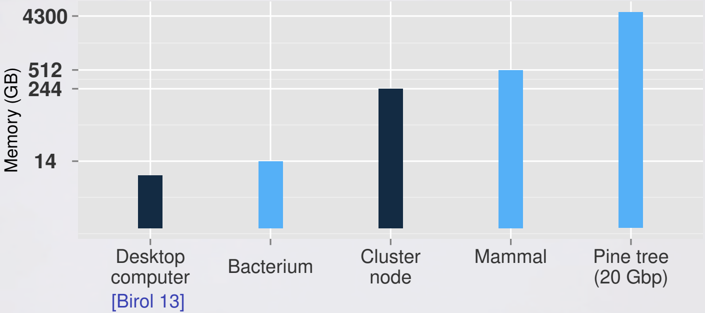
Bacterial genome assembled with a de Bruijn graph.

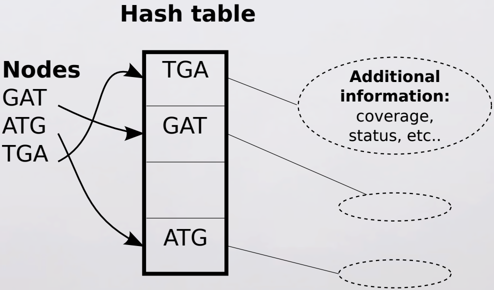
dBGs require a lot of memory



[Birol 13]

dBGs require a lot of memory





How to encode the de Bruijn graph using as little space as possible?

nodes only: $\{GAT, ATT, \ldots\}$

(human genome: $k = 75$, $n = 3 \cdot 10^9$ k-mers)

- Explicit list:

$$2k \cdot n \text{ bits}$$

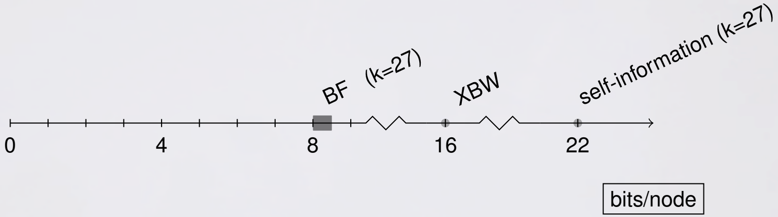
56 GB

- Self-information of n nodes: [Conway, Bromage 11]

$$\log_2 \left(\binom{4^k}{n} \right) \text{ bits}$$

44 GB

Recent techniques



- Bloom filter of nodes (w/ tricks) [Chikhi, Rizk 12], [Salikhov et al. 13]
- XBW (Burrows-Wheeler for trees) variant [Bowe et al. 12]

Why are they doing better?
→ different types of data structures

Data structures

A **membership** data structure is a pair of algorithms $(\mathit{const}, \mathit{contains\_node})$, where:

$$\mathit{data} \leftarrow \mathit{const}(G)$$

contains_node$(\mathit{data}, \mathit{kmer})$ returns $\{$true, false$\}$ whether kmer $\in G$

A **navigational** data structure is $(\mathit{const}, \mathit{neighbors})$, where:

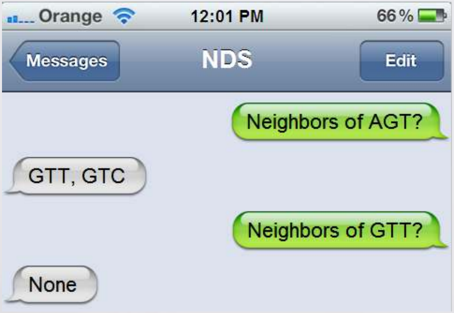
$$\mathit{data} \leftarrow \mathit{const}(G)$$

neighbors$(\mathit{data}, \mathit{kmer})$ returns the neighbors of *kmer* in G

Navigational data structures

	NDS	Membership (e.g. hash table)
Traverse dBG from known nodes	✓	✓
Query **membership** of arbitrary nodes	*x*	✓
Enumerate nodes	*x*	✓

NDS has undefined behavior if query node not present.

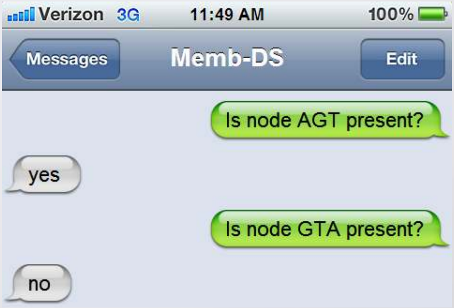


Neighbors of AGT?

GTT, GTC

Neighbors of GTT?

None



Is node AGT present?

yes

Is node GTA present?

no

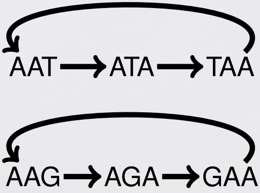
Recent techniques are **NDS** but **not Membership** DS

Why a NDS "beats" the self-information

Consider this example NDS when $k = 3$

“For each node $x = x_1 x_2 x_3$,
out-neighbor: $x_2 x_3 x_1$
in-neighbor: $x_3 x_1 x_2$”

Valid for these two graphs:



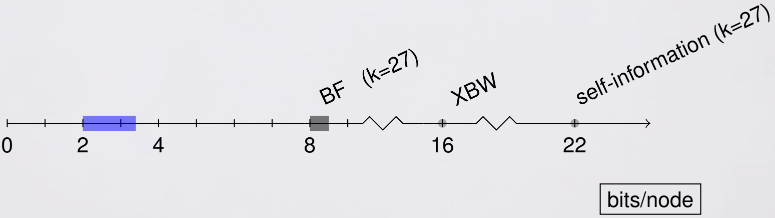
So,

$$1 \text{ NDS} \longleftrightarrow >1 \text{ dBGs}$$

$$1 \text{ Membership DS} \longleftrightarrow 1 \text{ dBG}$$

Lower bounds

We seek dBG representation lower bounds in the NDS model.



NDS lower bound for linear graphs

Linear graphs

Theorem

NDS for linear graphs need at least 2 bits/k-mer of space.

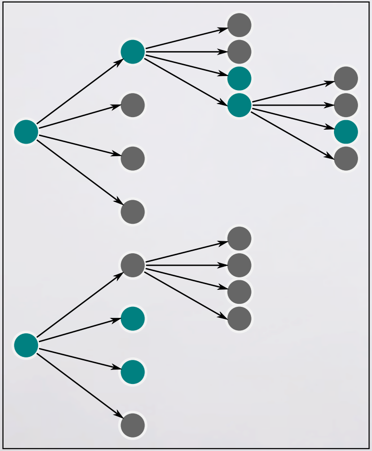
Proof sketch:

- Number of DNA strings that have *n distinct* k-mers and start with same k-mer: $\approx 2^{2n}$ [Gagie 12]
- Number of linear dBGs with n nodes and same left-most node: $\approx 2^{2n}$
- Suppose NDS needs $< 2n$ bits,
- Two graphs have the same NDS (pigeonhole principle)

NDS lower bound

Theorem

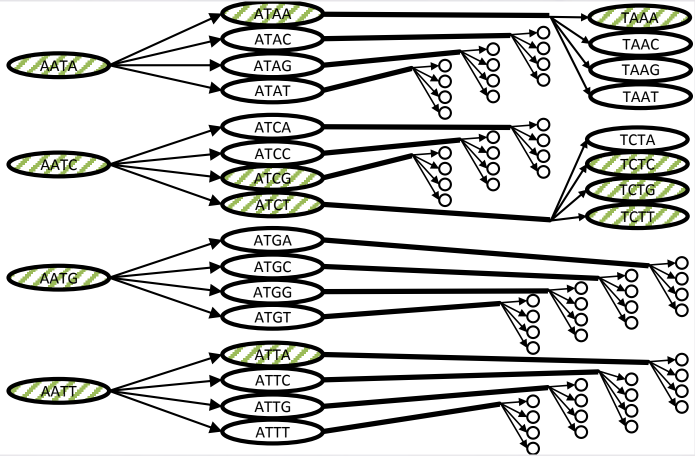
NDS need at least 3.24 bits/k-mer.



Proof sketch:

1. Construct a large family of N graphs, such that for any two graphs, $\exists$ k-mer that appears in both graphs but with different neighbors.
2. Suppose NDS needs $< \log(N)$ bits
3. Two graphs have the same NDS (pigeonhole principle), contradiction

Our construction has $N = 2^{3.24n}$



- Fix an even $k \geq 2$, $\ell = k/2$, $m = 4^{\ell-1}$
- Consider a graph with $\ell + 1$ levels of $\{\mathrm{A}^{\ell-i}\mathrm{T}\alpha,\ \alpha \in \Sigma^{i+\ell-1}\}$
- Select m nodes per level
- $\binom{4m}{m}^{\ell}$ possible graphs
- $\binom{4m}{m}^{\ell} \geq 2^{(c-\epsilon)\ell m}$ with $c = 8 - 3\log 3 \approx 3.24$

Conclusion / Perspectives

Navigational data structures:

- Model for recent dBG data struct.
- Lower bound: 3.24 bits/k-mer
- Gap with known non-parameterized upper bounds (16)

Open questions:

- Closing the gap above
- Entropy-compressed dBG representations

Contact/references:

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