deBGR: An Efficient and Near-Exact Representation of the Weighted de Bruijn Graph

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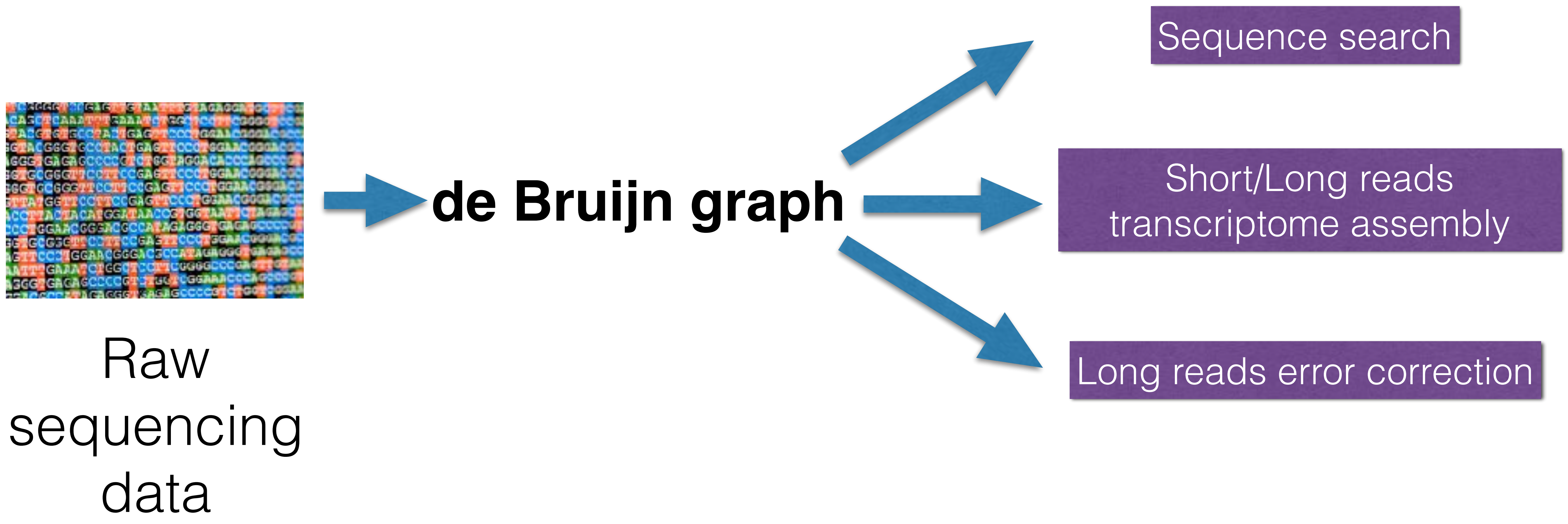
de Bruijn graphs are ubiquitous


Raw sequencing data
de Bruijn graph
Sequence search
Short/Long reads transcriptome assembly
Long reads error correction

A de Bruijn graph is the data representation at the heart of a lot of sequence analyses.

de Bruijn graph (dBG)

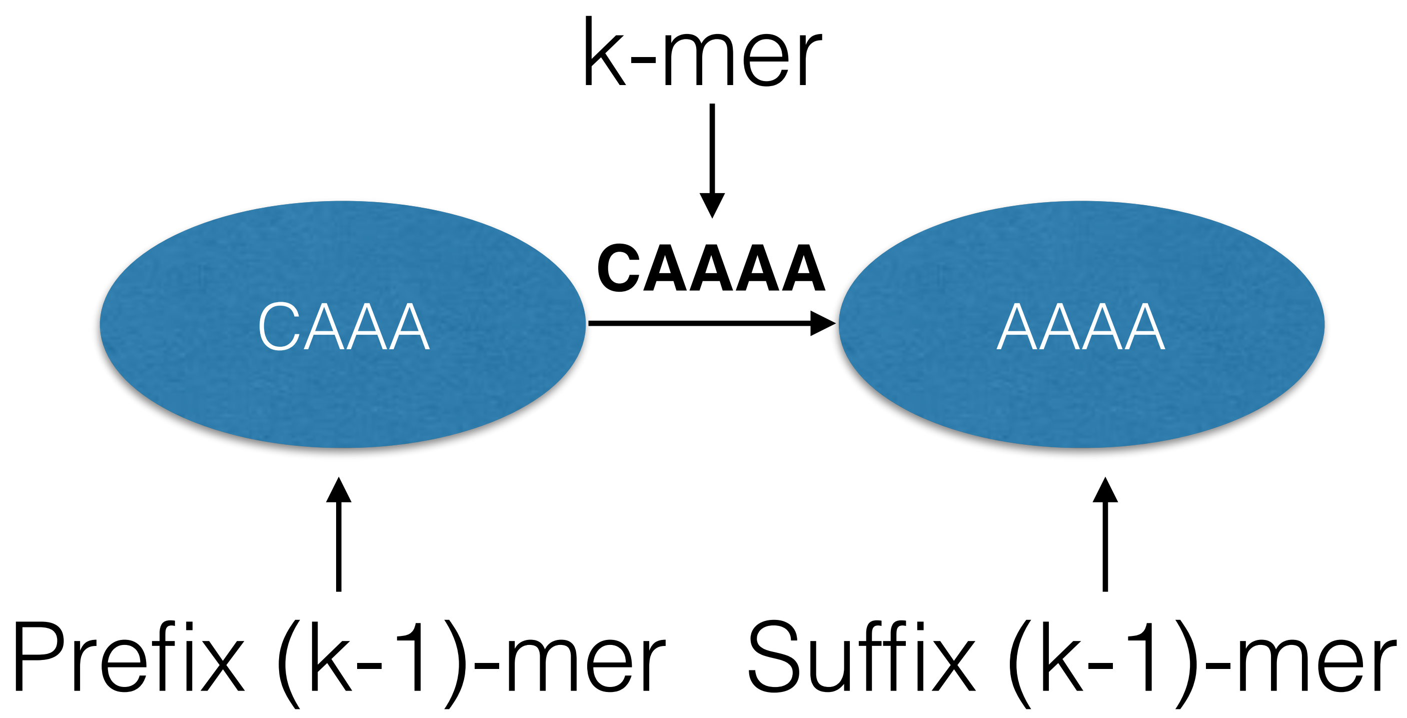
A ***read*** is a string of bases over the DNA alphabet A, C, T, and G. → GGCCAAAATTCG

A **k-mer** is a substring of length k. Here, k is 5. →

```
GGCCA
 GCCAA
  CCAAA
   CAAAA
    AAAAT
     AAATT
      AATTC
       ATTCG
```

de Bruijn graph (dBG)

Read: ….CAAAA….

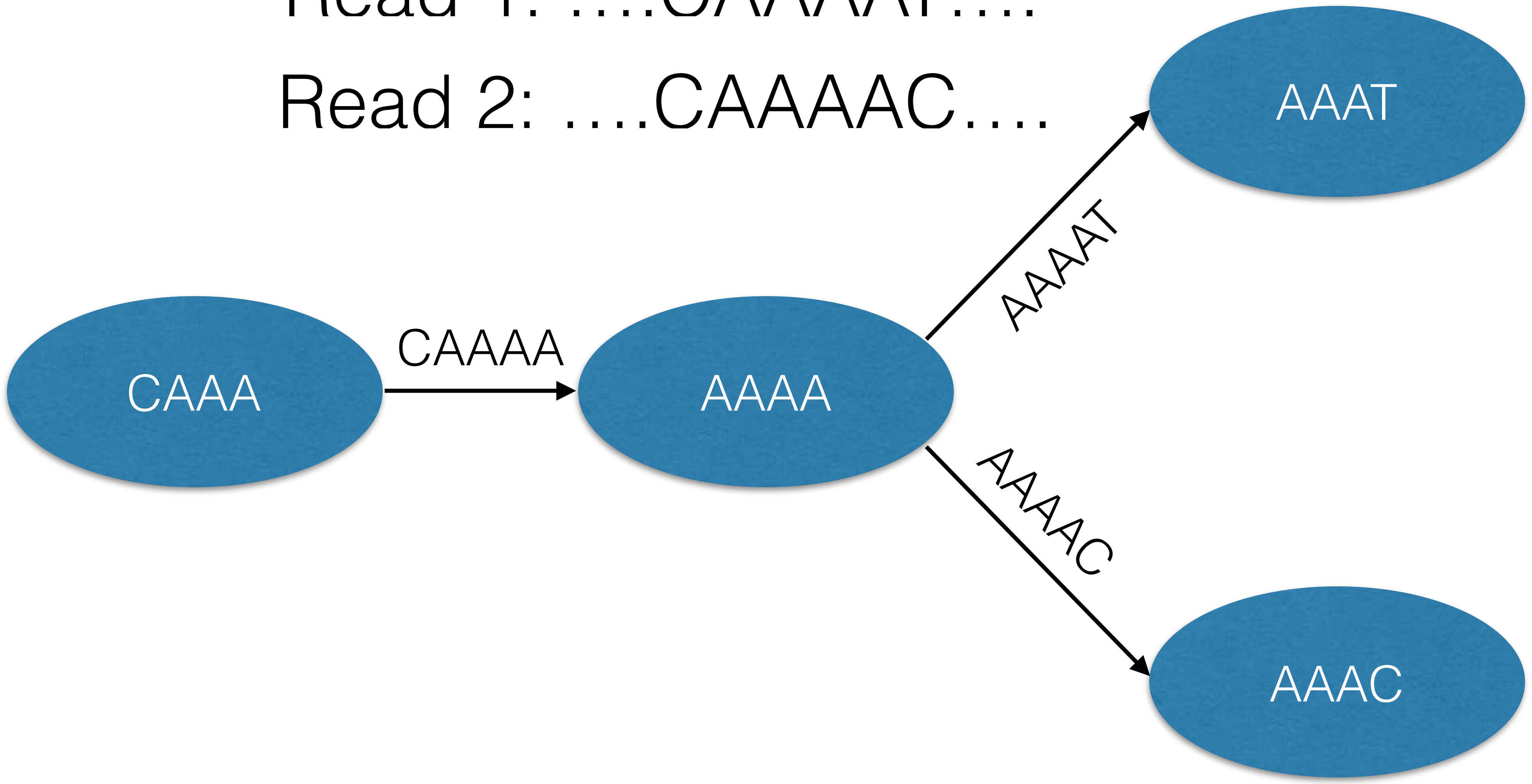


An edge is a k-mer connecting its two k-1 substrings.

de Bruijn graph (dBG)

Read 1: ….CAAAAT….

Read 2: ….CAAAAC….



Weighted de Bruijn graphs

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- Abundance information of each k-mer is critical for transcriptome assembly.

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Weighted de Bruijn graphs pose an extra obligation and opportunity.

Weighted de Bruijn graph (WdBG)

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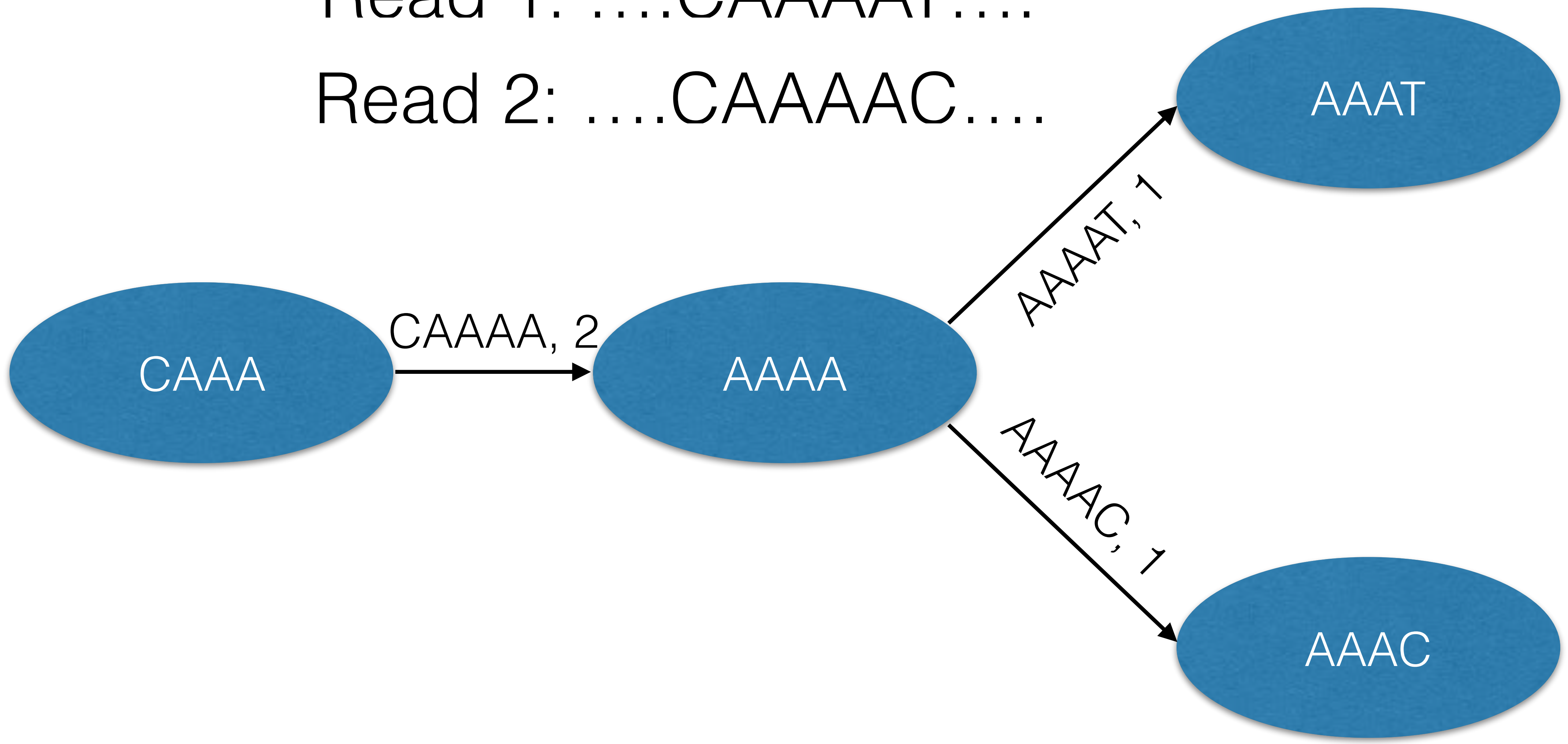
Read 2: ….CAAAAC….



A weighted de Bruijn graph associates each edge (k-mer) its abundance in the underlying dataset.

Measuring dBG representation

de Bruijn graphs store only k-mers, memory usage scales with the number of unique k-mers.

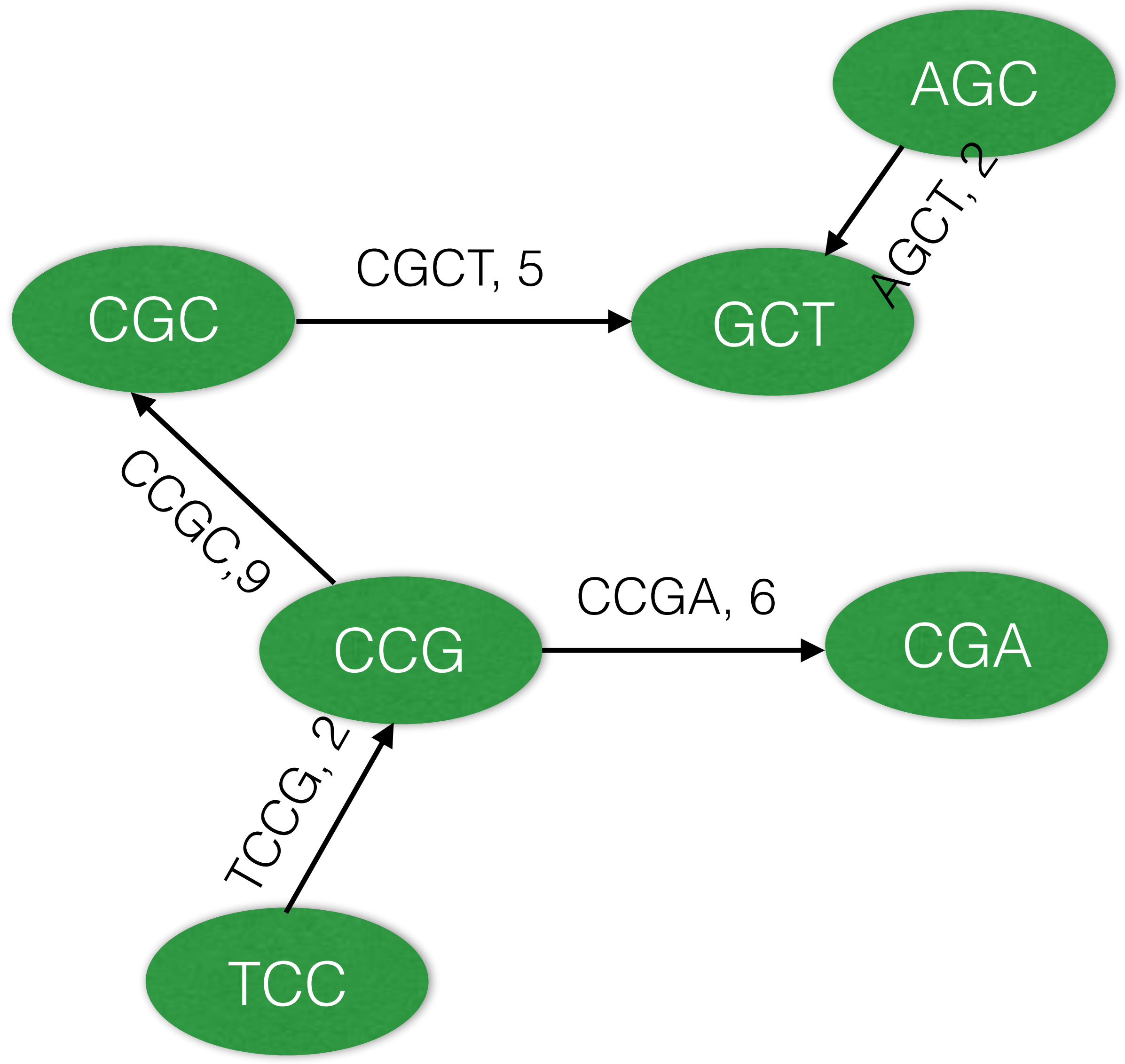
Human genome (few Billion k-mers): >100 GB
Soil metagenomes (few Million species): Few TBs

Beefy server machines are needed to perform weighted de Bruijn graph analysis.

WdBG as a multiset

MultiSet
TCCG, 2
CCGC, 9
CCGA, 6
CGCT, 5
AGCT, 2

(Edge, Abundance)



Weighted de Bruijn graph

Past work on Probabilistic dBG representation

- **Pell et al. 2012**: Represented dBG using a Bloom filter.

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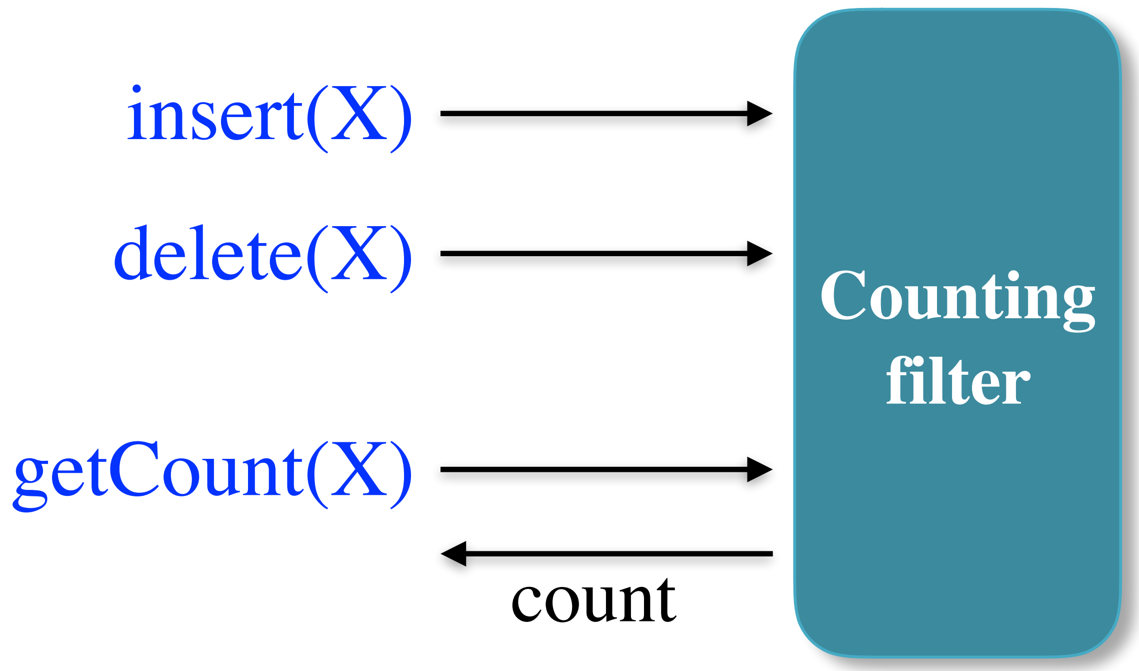
- **Pellow et al. 2016**: Showed how to exploit redundancy in k-mers to reduce the false-positive rate of the Bloom filter without increasing the space.
- **Chikhi and Rikz 2013 and Salikhov et al. 2013:** They showed how to convert a probabilistic representation into an exact one using a small and exact auxiliary data structure.

Counting filters



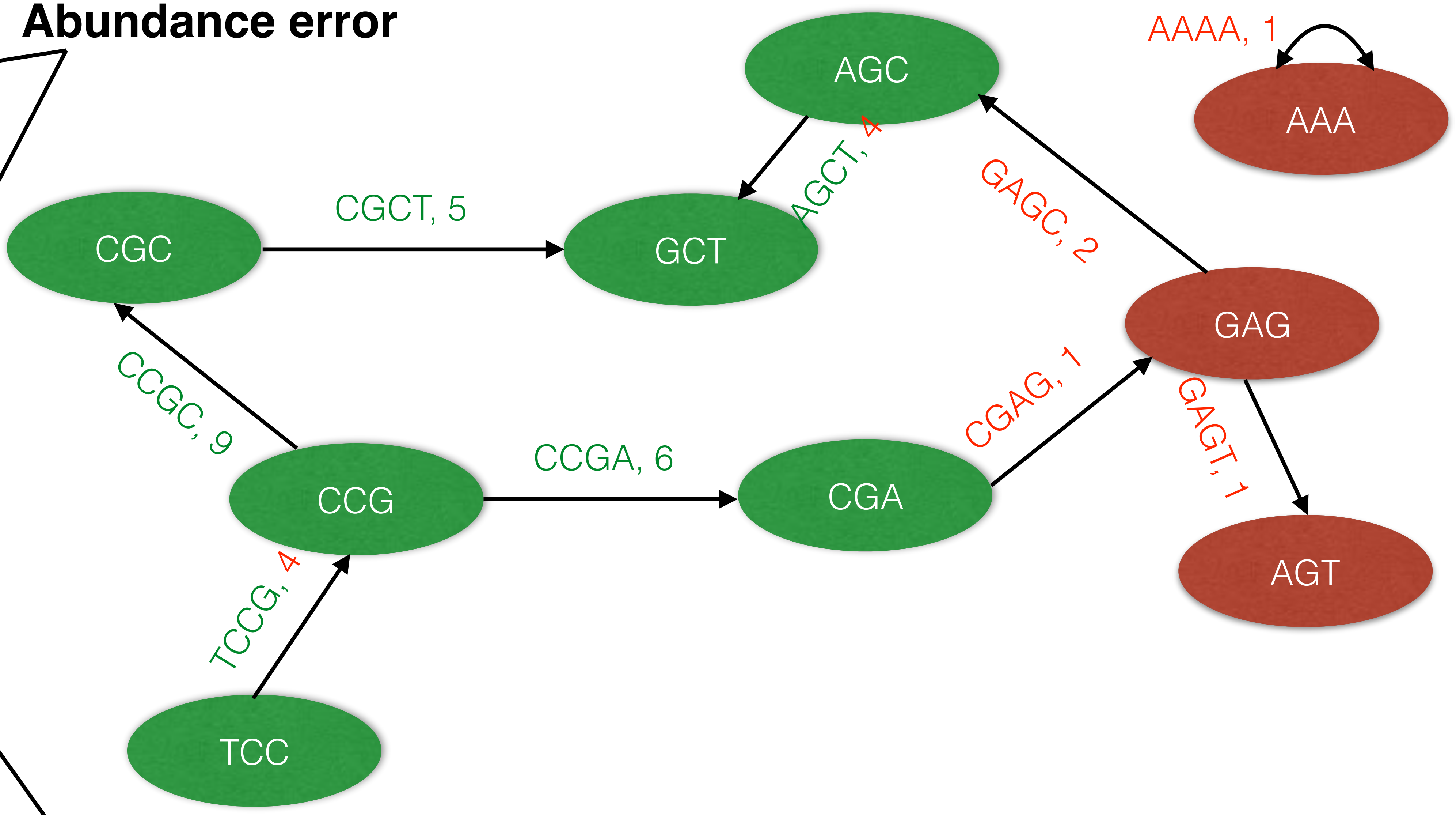
- **A counting filter is a lossy representation of a multiset.**
- **Operations: inserts, count, and delete.**
- **Generalizes AMQs**
  - False positives ≈ over-counts.
- **Counting quotient filter**[Pandey et al. 2017]

Probabilistic weighted de Bruijn graph [Pandey et al. 2017]

Counting quotient filter
TCCG, 4
CCGC, 9
CCGA, 6
CGCT, 5
AGCT, 4
GAGC, 2
CGAG, 1
GAGT, 1
AAAA, 1

Abundance error

Topological errors



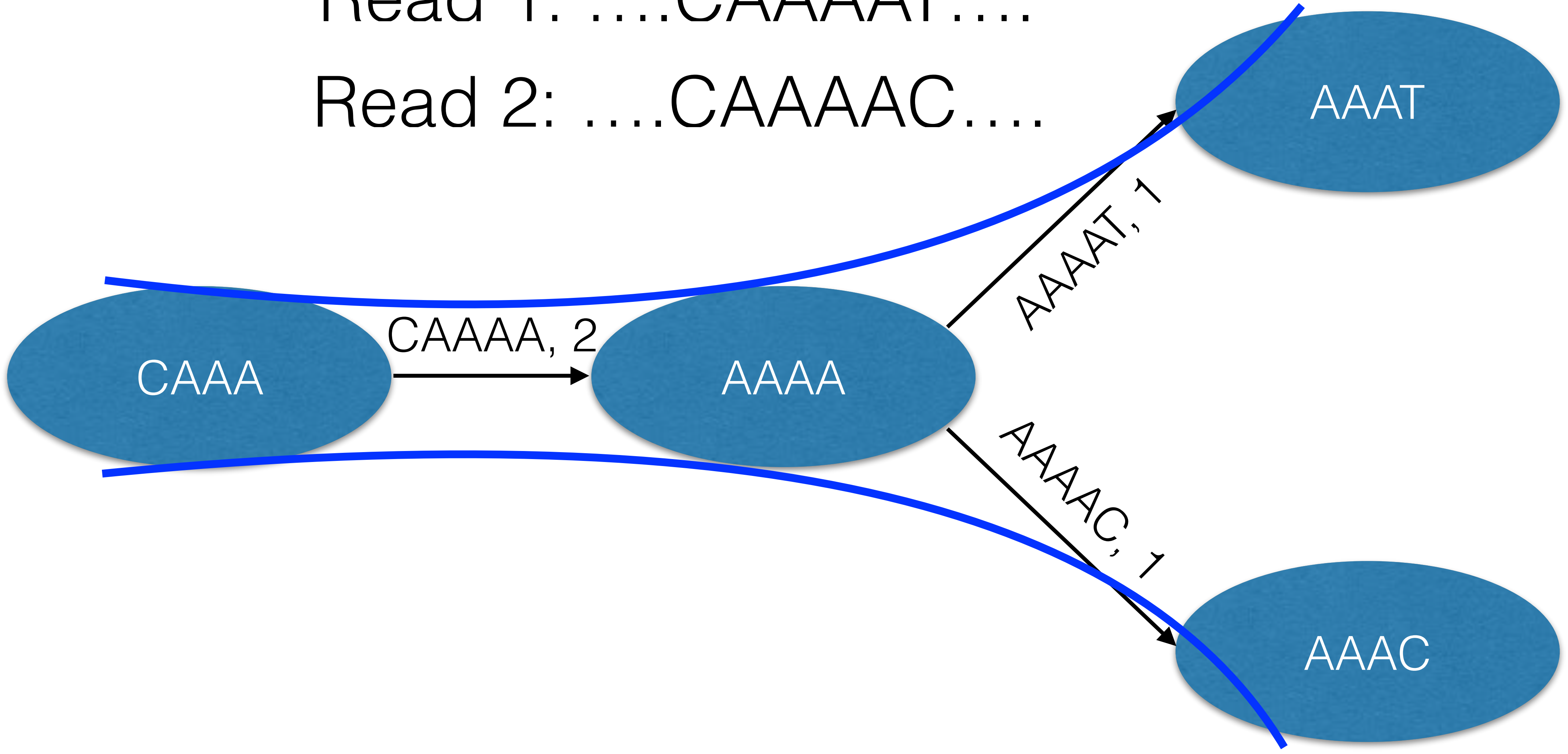
This paper: deBGR

- An **exact representation** of the weighted de Bruijn graph.
  - An algorithm that uses counts in the approximate representation in an AMQ to iteratively **self-correct approximation errors**.
  - It corrects both kinds of errors, **abundance and topological errors** and supports **membership queries**.
  - It **supports deletion** of k-mers from the structure.
  - It takes 18-28% more space than the approximate representation and has **no errors**.

A weighted de Bruijn graph invariant

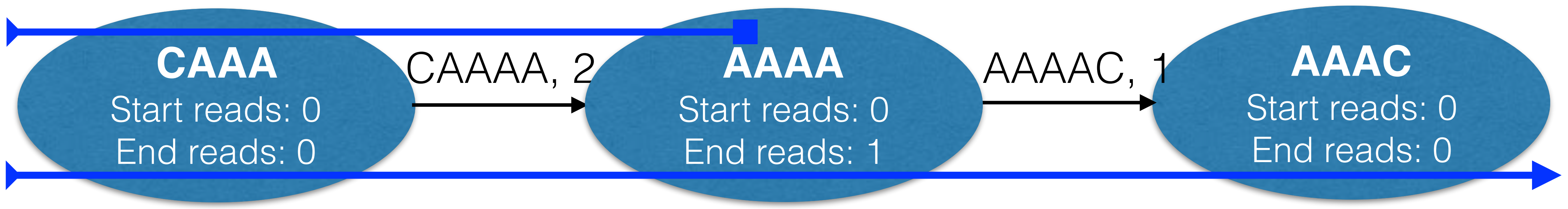
Read 1: ....CAAAAT....

Read 2: ....CAAAAC....



Total incoming abundance = Total outgoing abundance

A weighted de Bruijn graph invariant



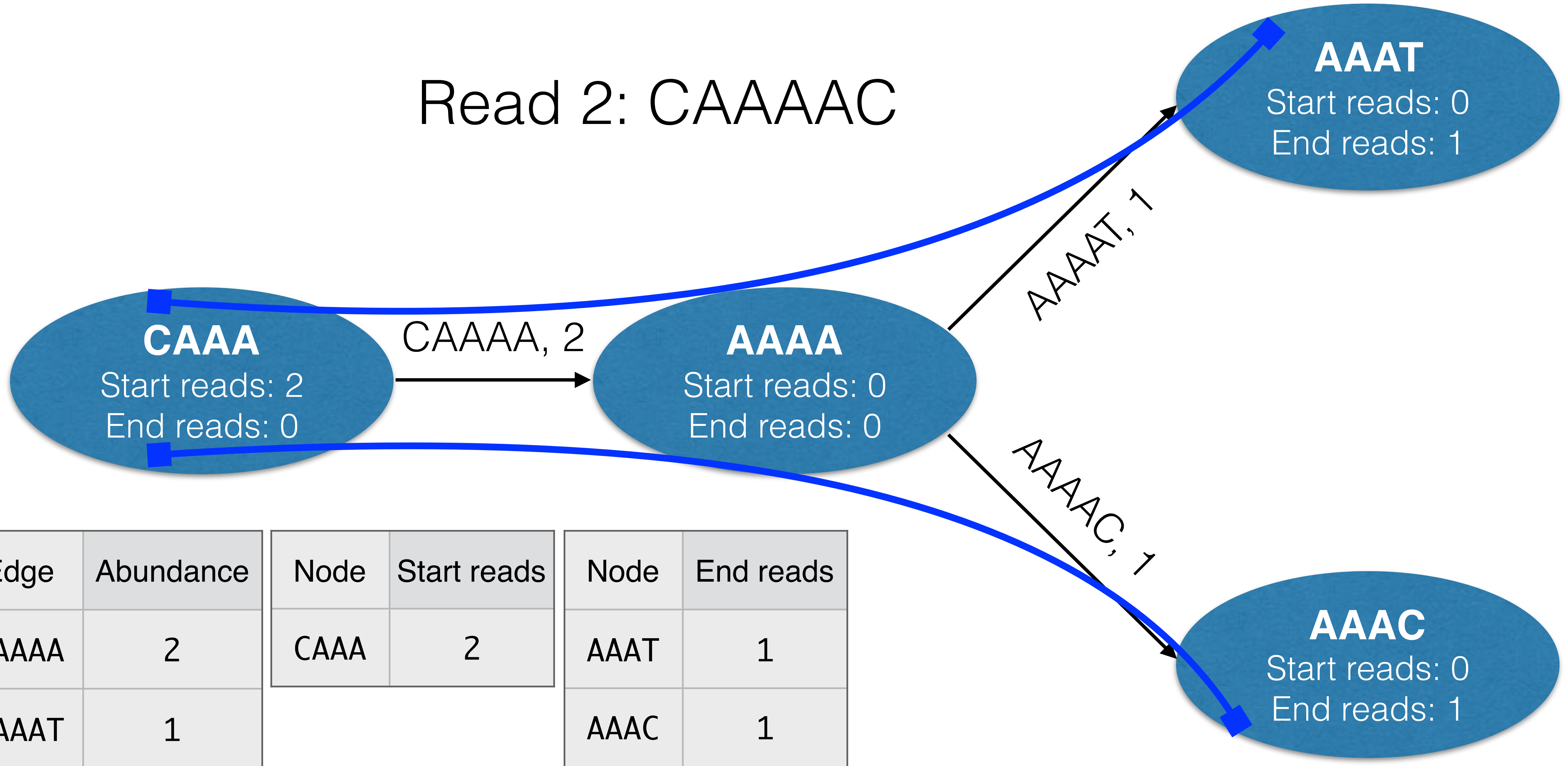
Total incoming abundance = Total outgoing abundance*

***After accounting for read starts and ends.**

WdBG representation in deBGR

Read 1: CAAAAT

Read 2: CAAAAC

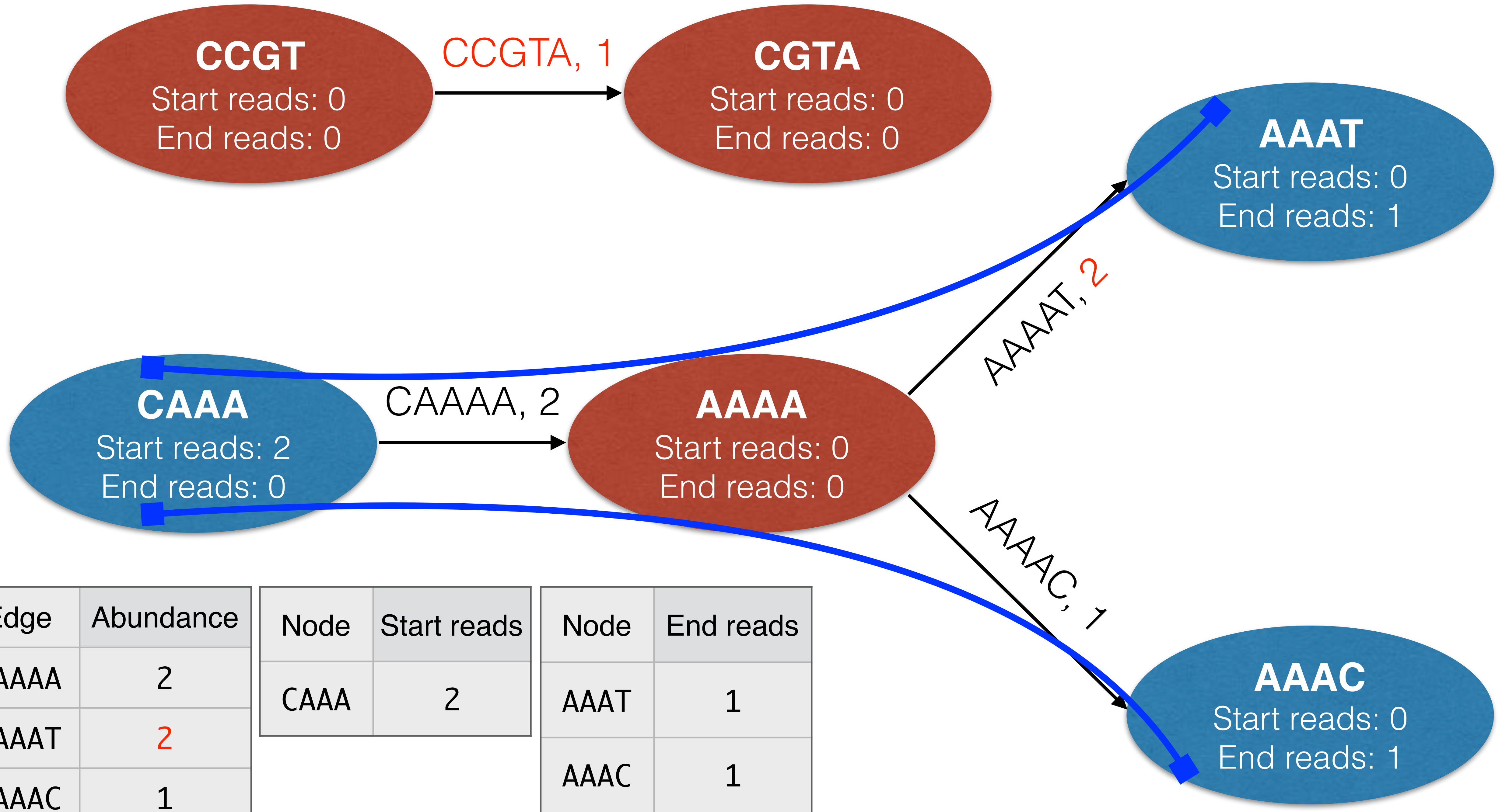


Edge	Abundance
CAAAA	2
AAAAT	1
AAAAC	1

Node	Start reads
CAAA	2

Node	End reads
AAAT	1
AAAC	1

WdBG representation in deBGR

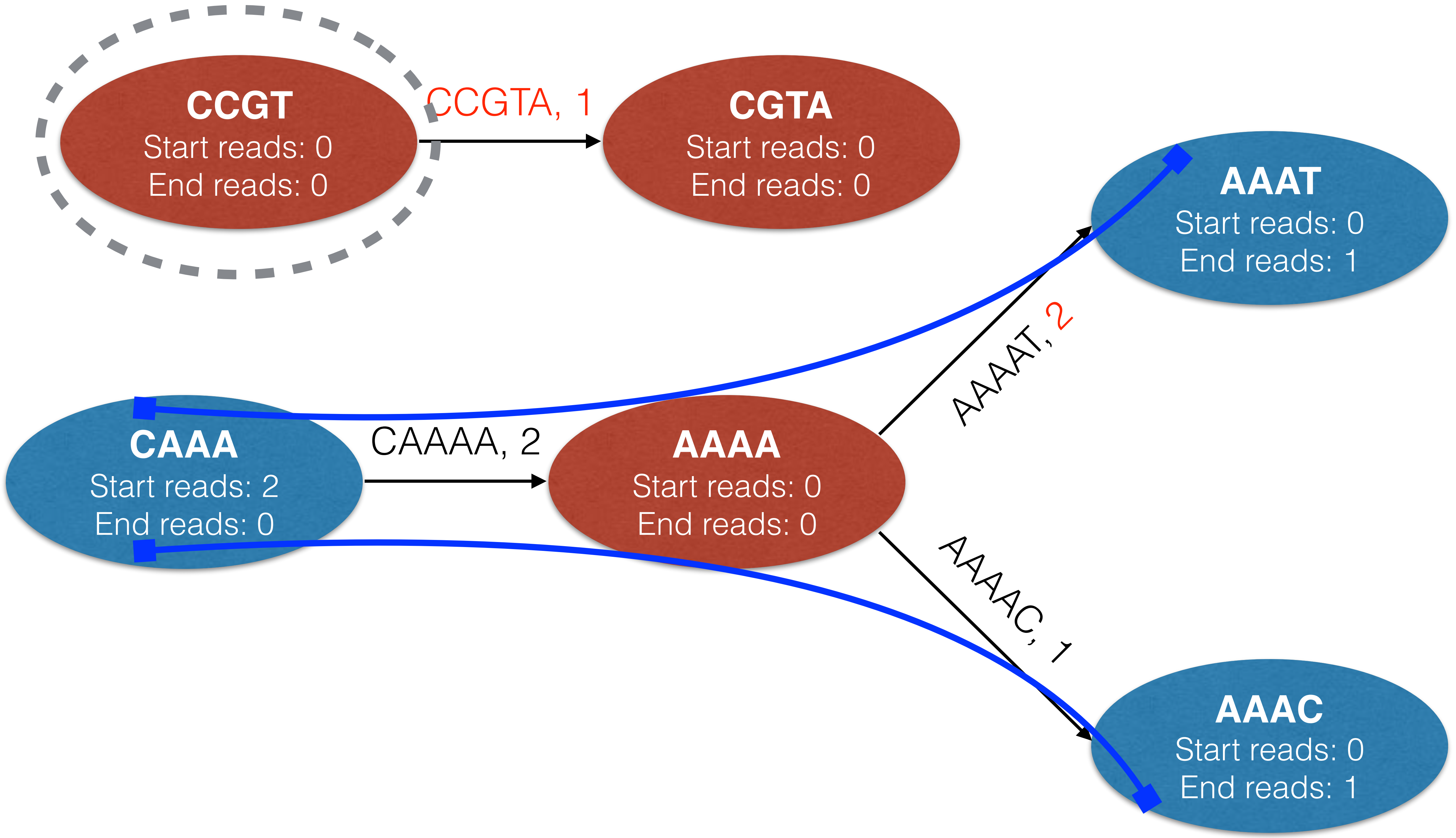


Edge	Abundance
CAAAA	2
AAAAT	2
AAAAC	1
CCGTA	1

Node	Start reads
CAAA	2

Node	End reads
AAAT	1
AAAC	1

Error correction



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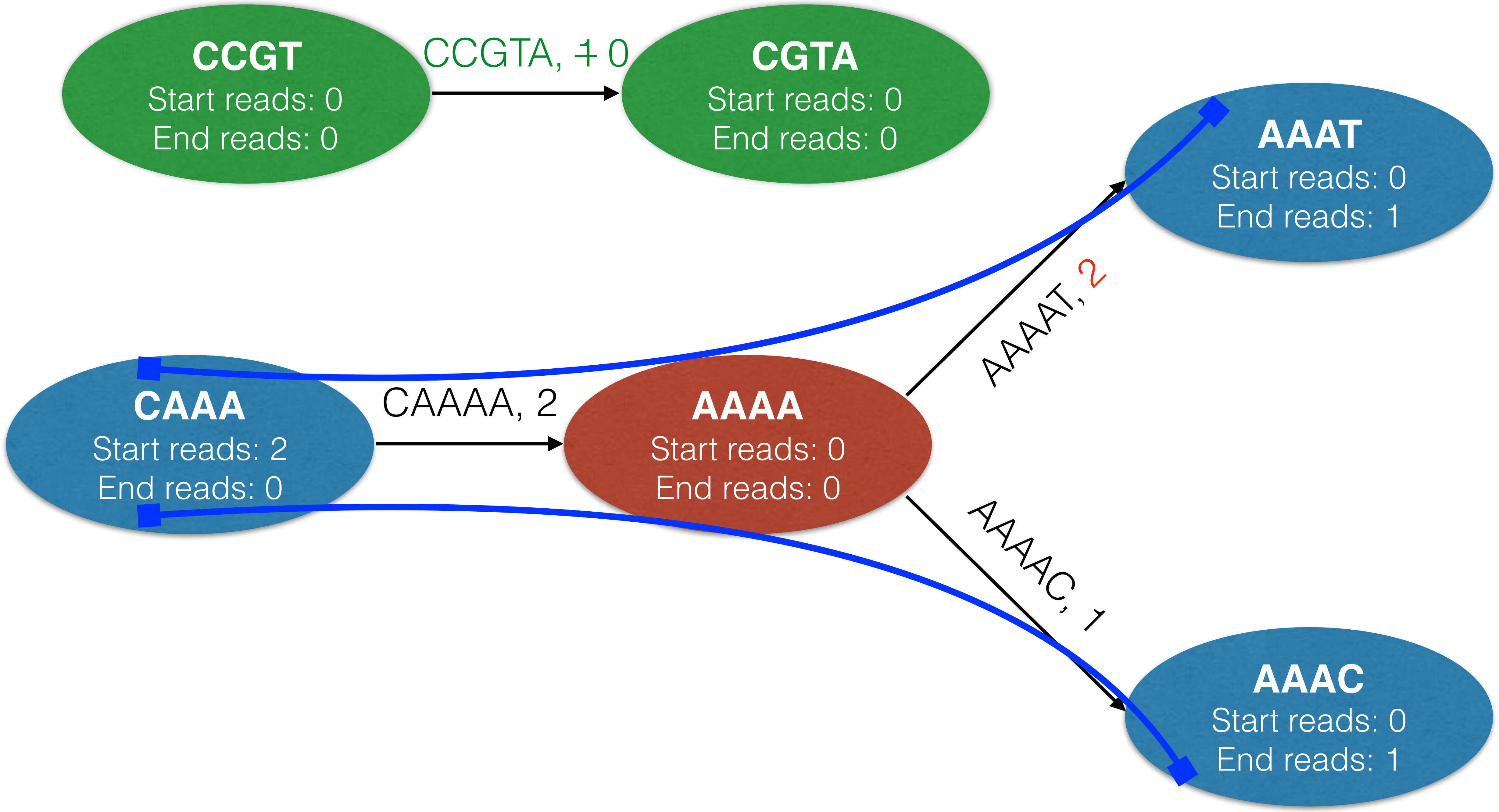

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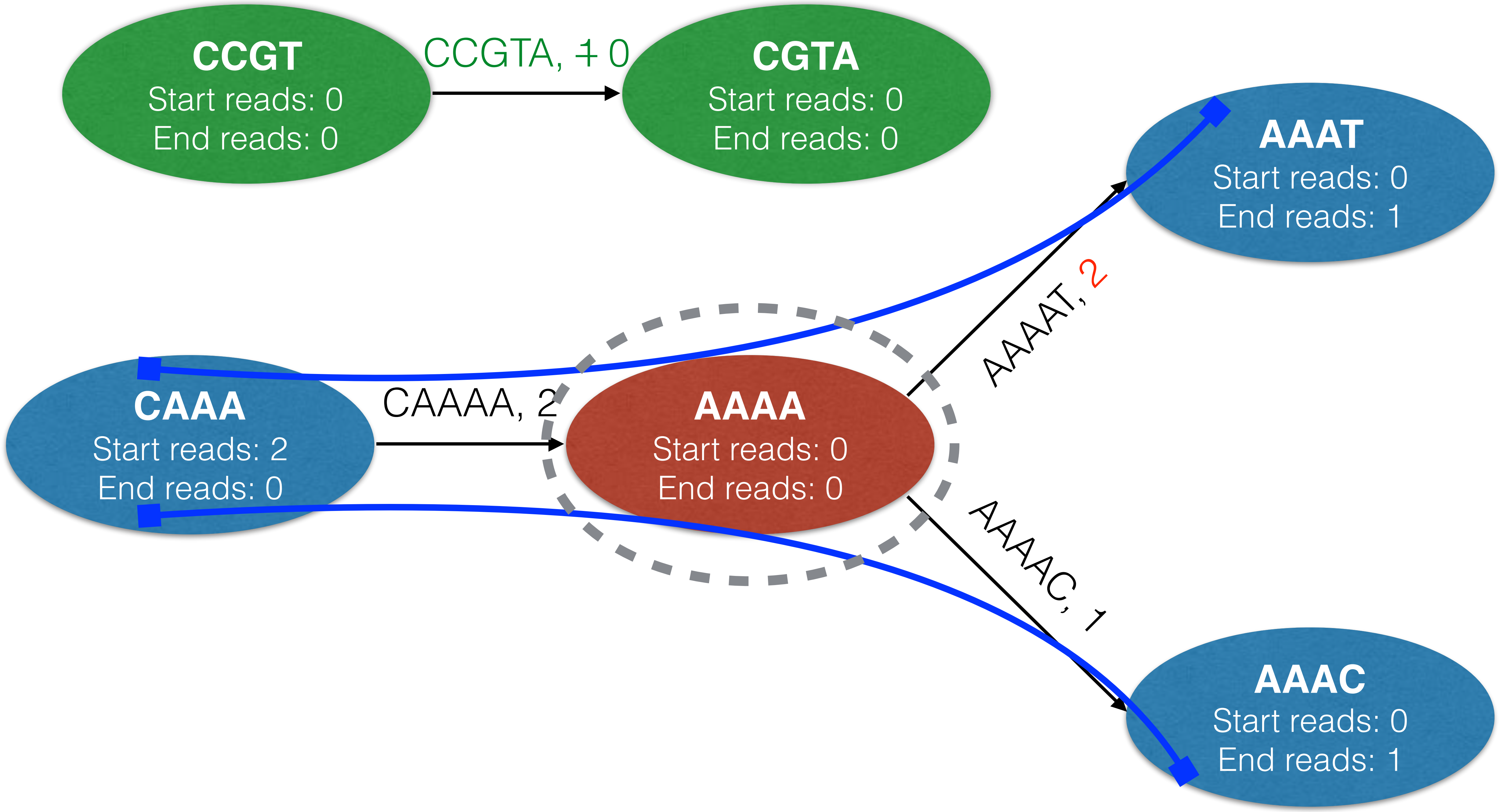

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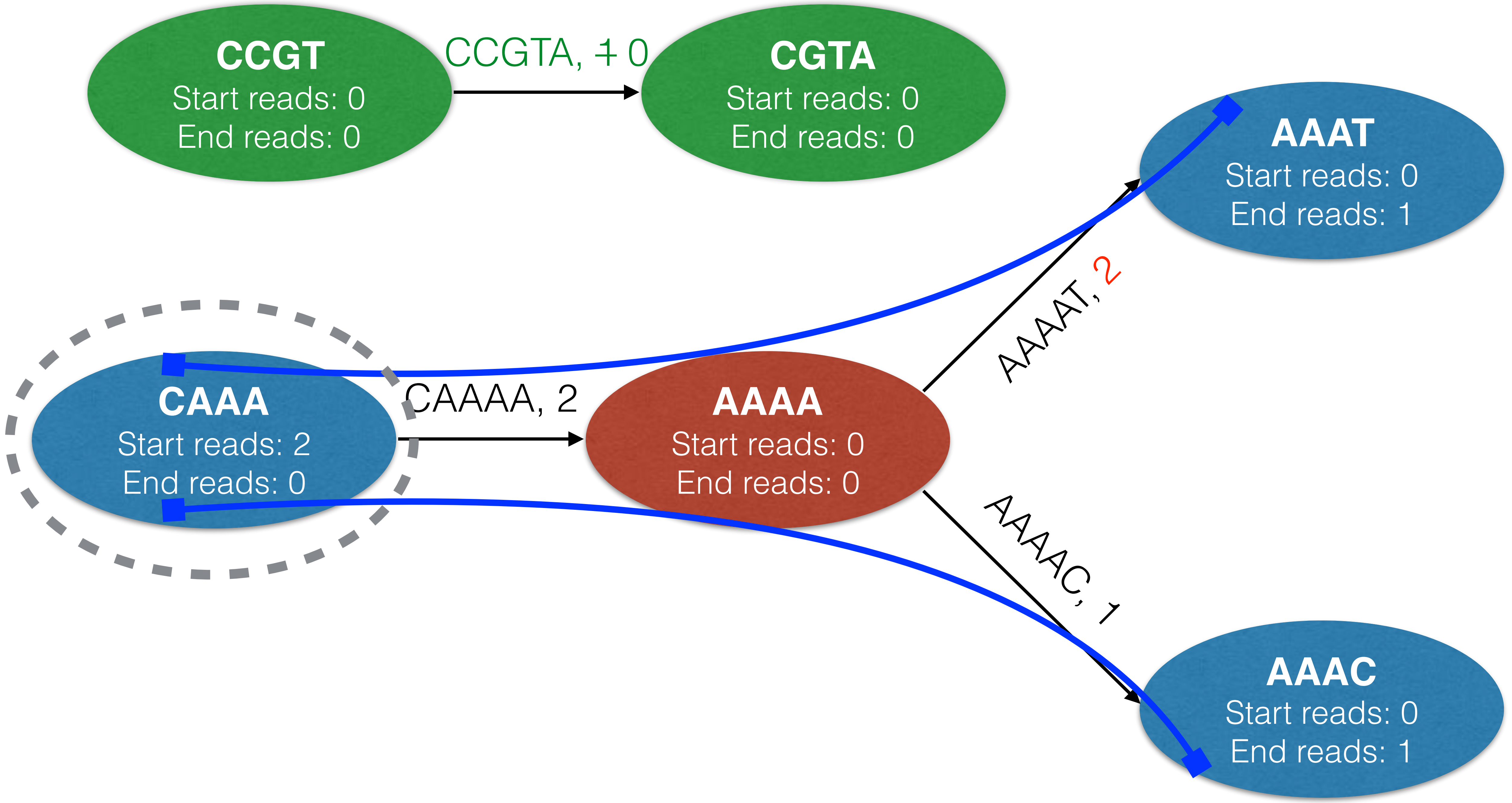

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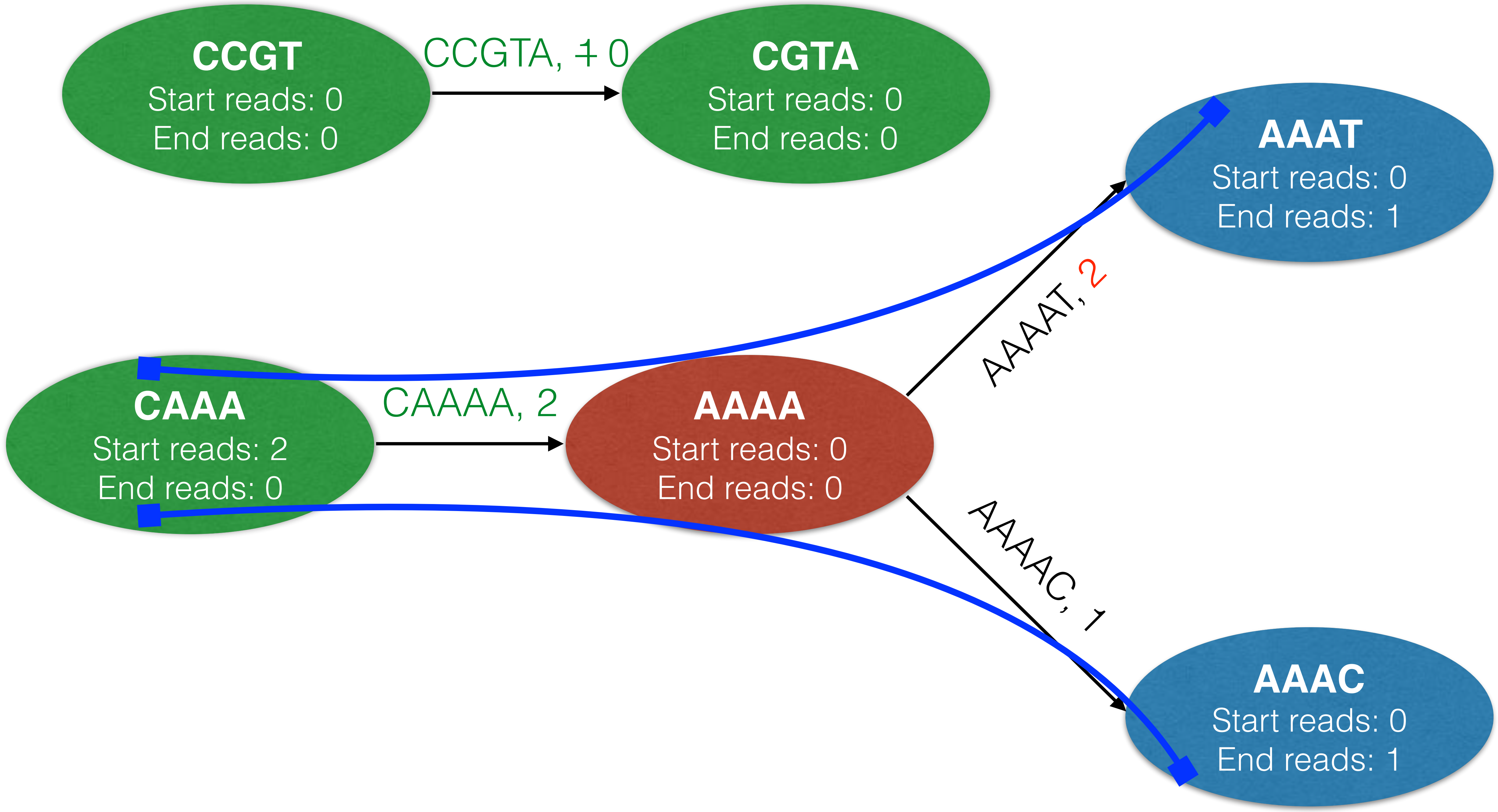

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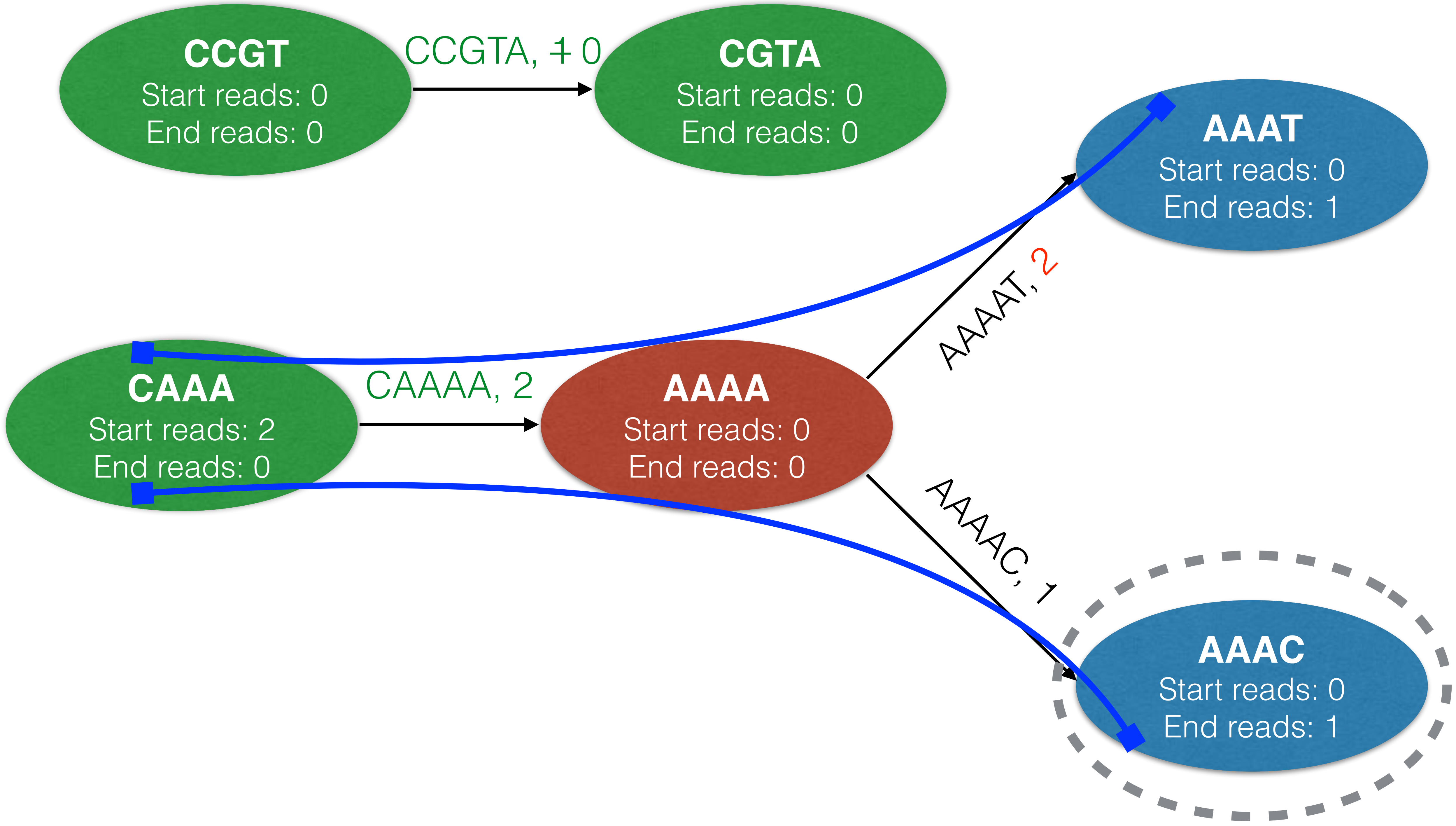

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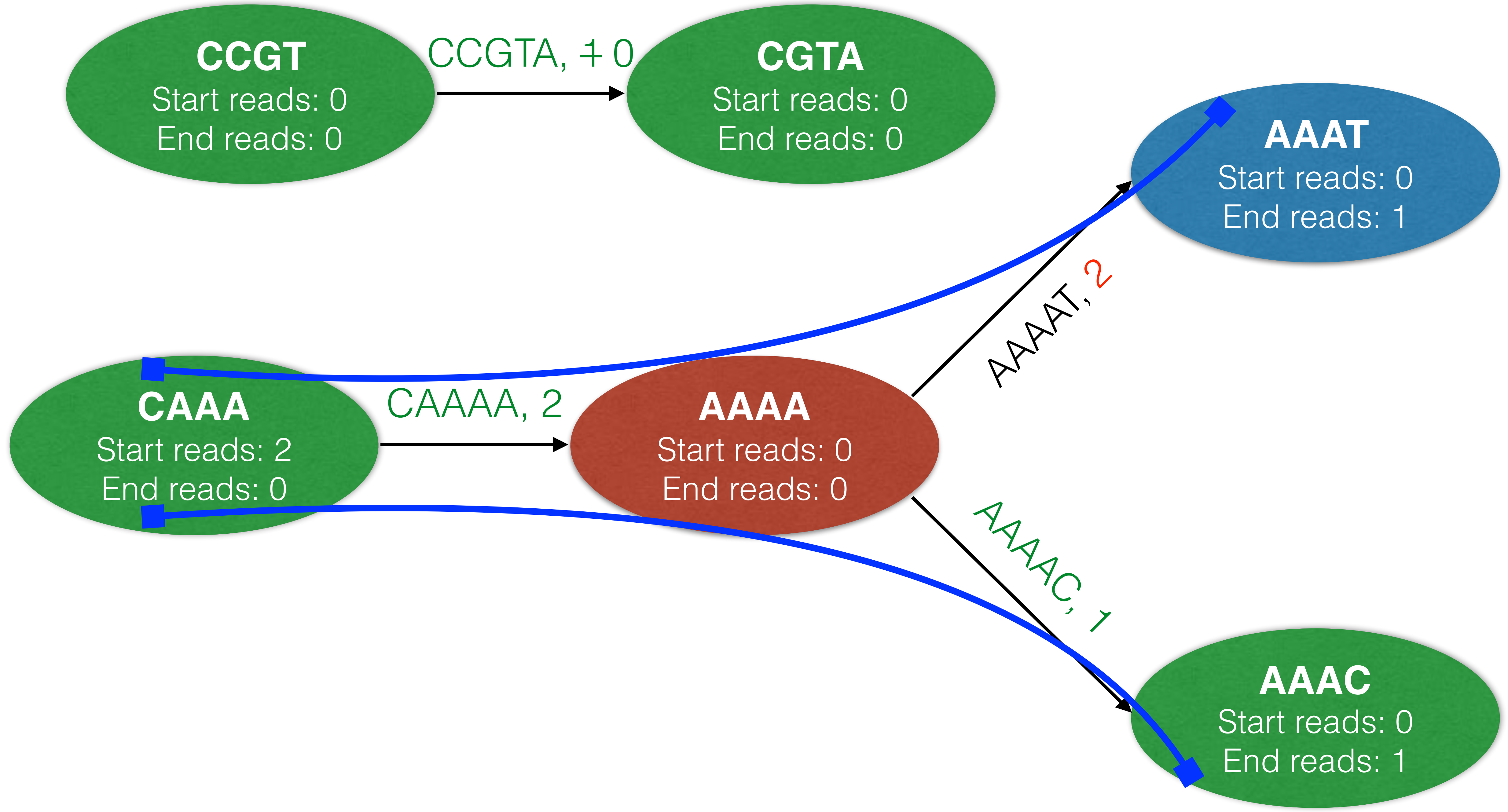

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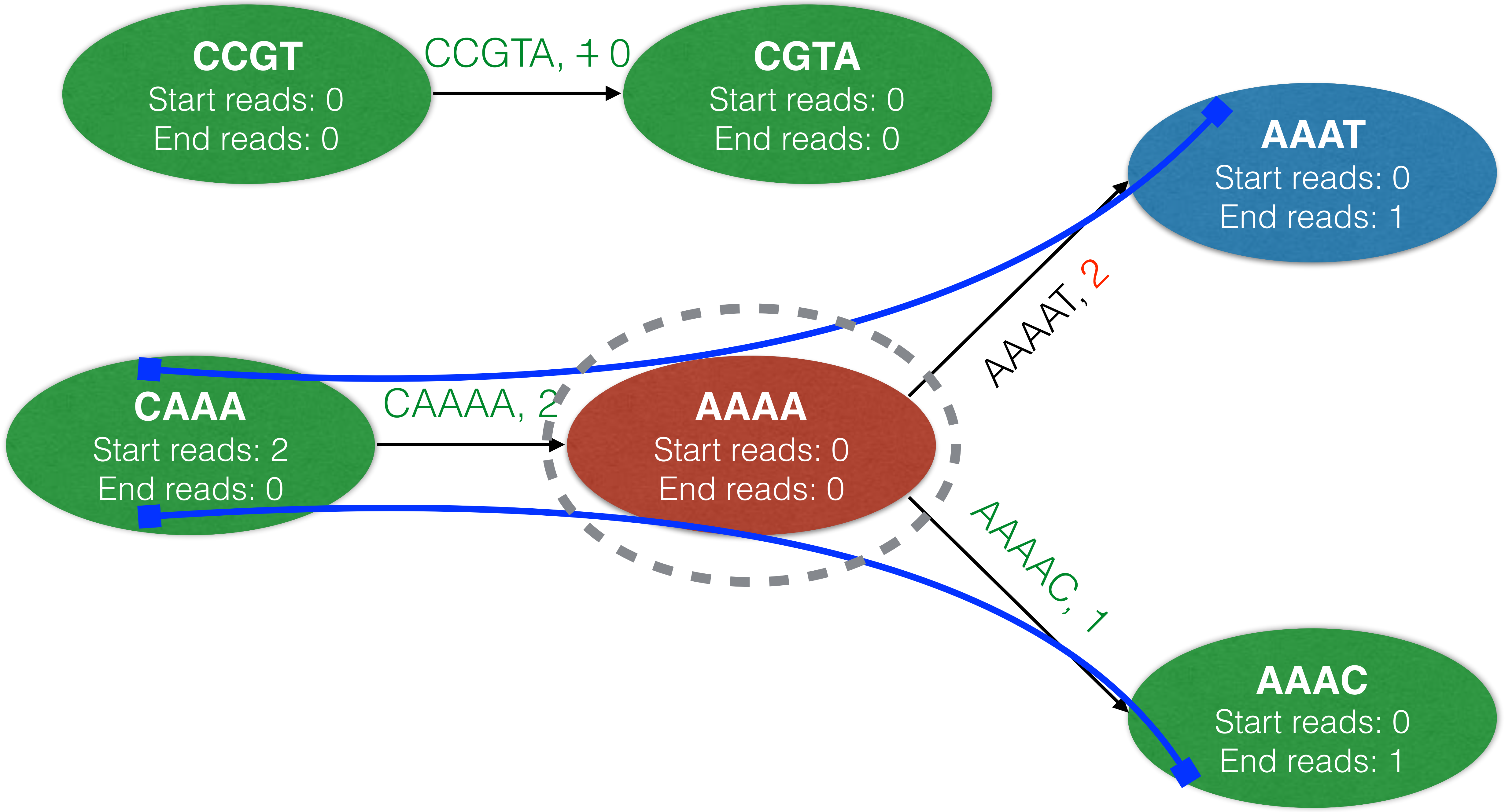

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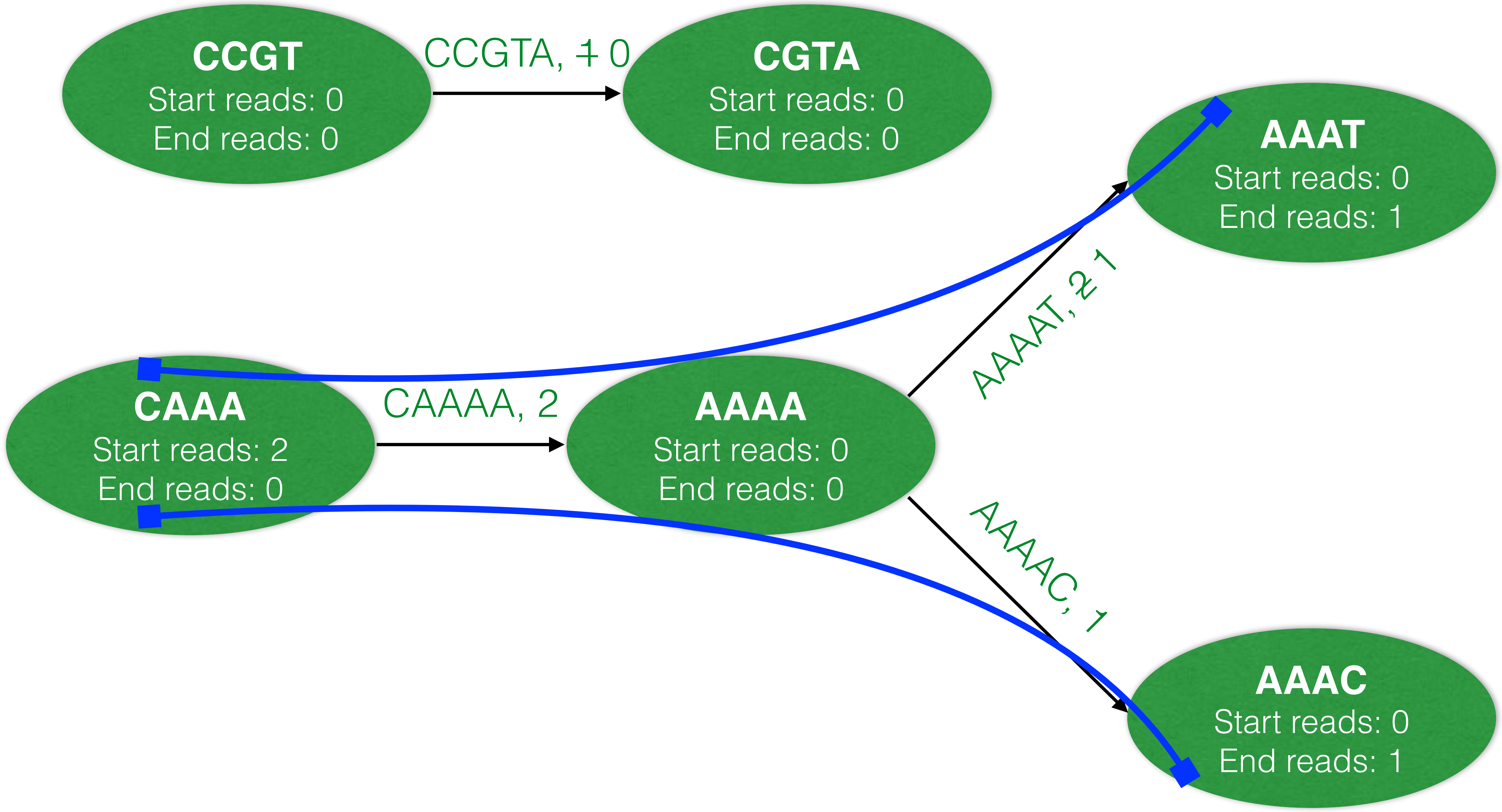


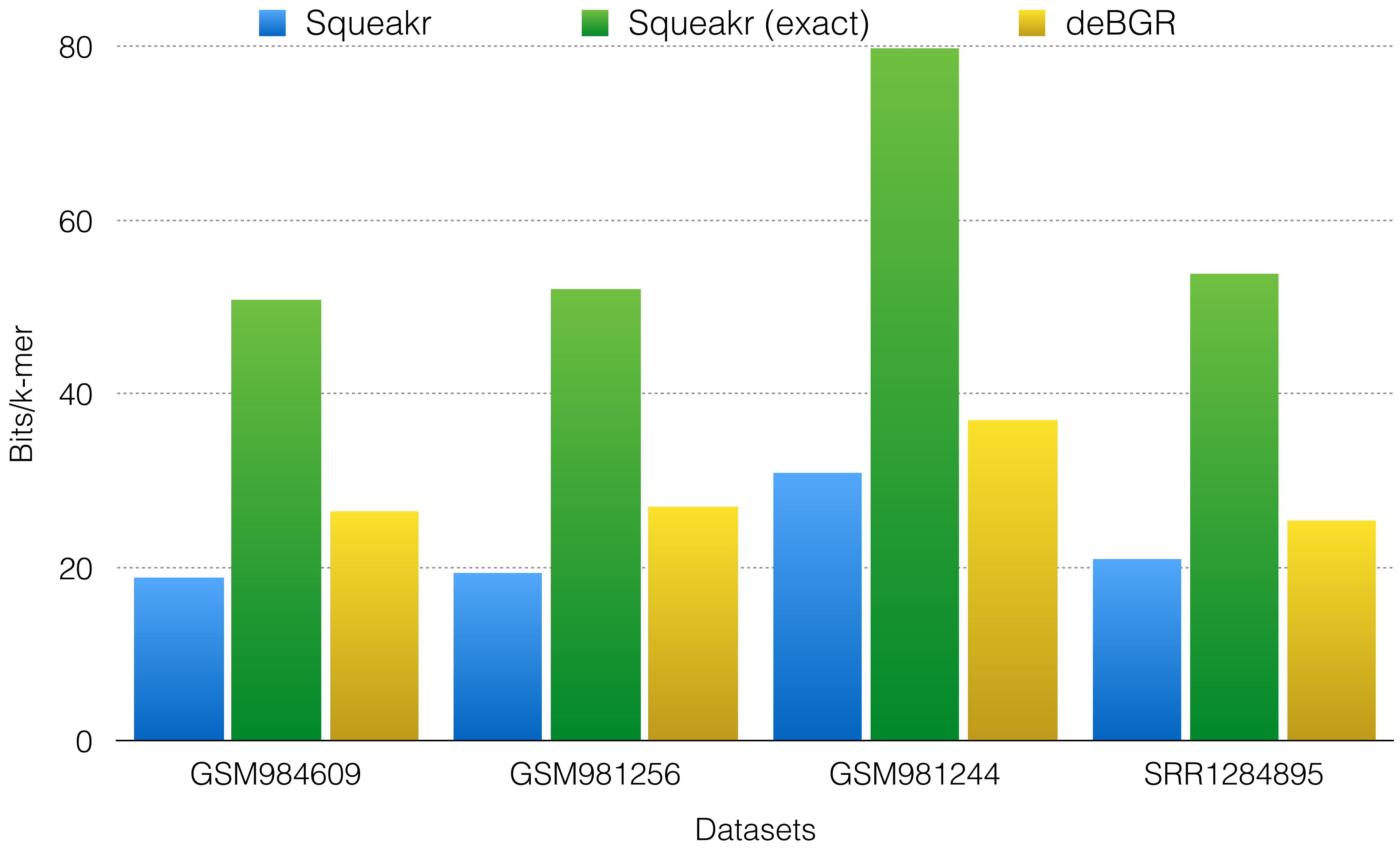
Error correction algorithm

- We use a standard work queue algorithm.
- We bootstrap with a set *C* of edges for which we know the abundance is correct.
- We then expand the set *C* of edges using the weighted de Bruijn graph invariant.
- Please refer to the paper for exact set of rules for error correction.
- Running time: $O(n \cdot \log(n) / \log(1/4\varepsilon))$.

Datasets

Dataset	Size	#k-mer instances	#Distinct k-mers
GSM984609	26 GB	19,662,773,330	1,146,347,598
GSM981256	22 GB	16,470,774,825	1,118,090,824
GSM981244	43 GB	37,897,872,977	1,404,643,983
SRR1284895	33 GB	26,235,129,875	2,079,889,717

Space vs Accuracy



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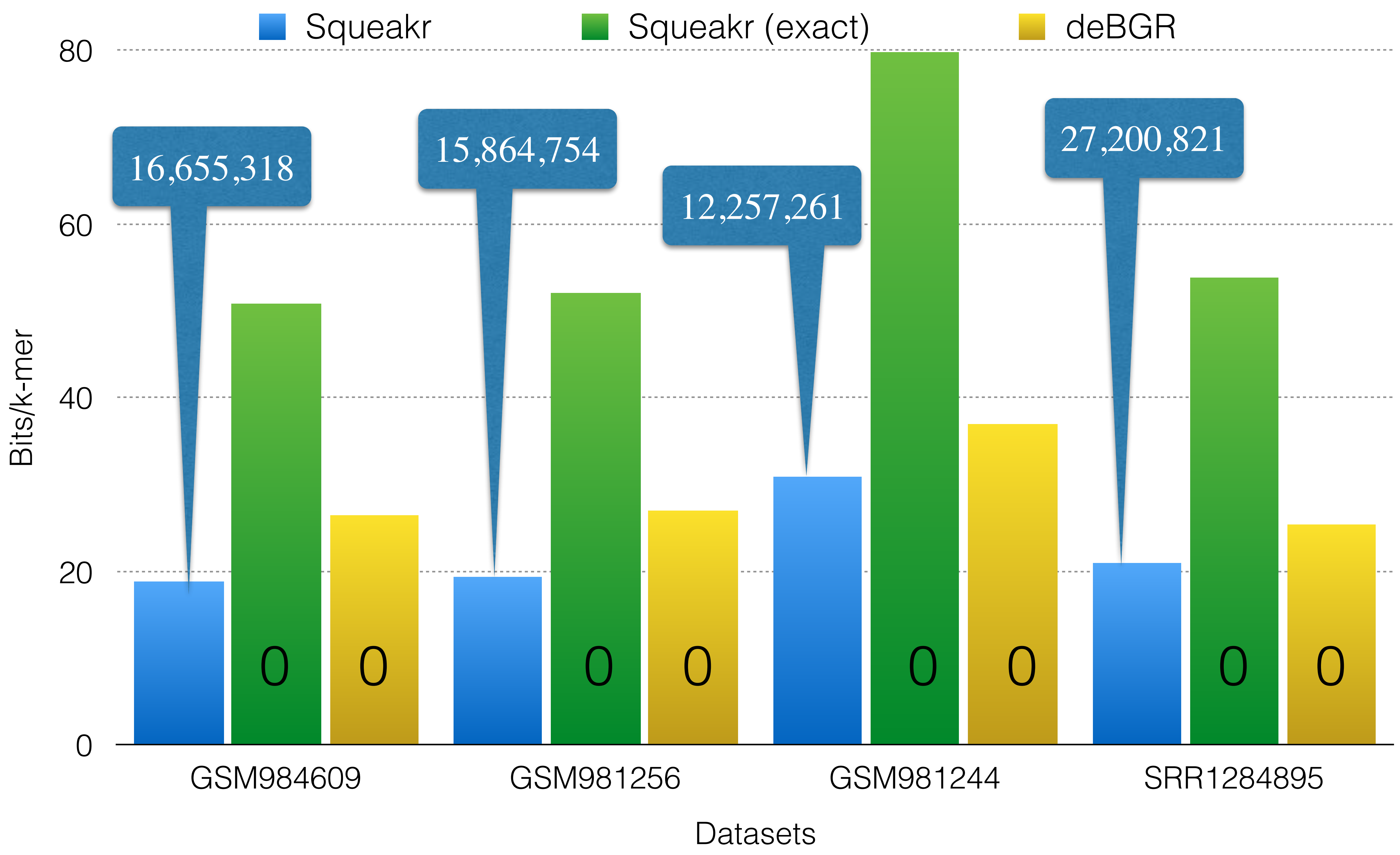

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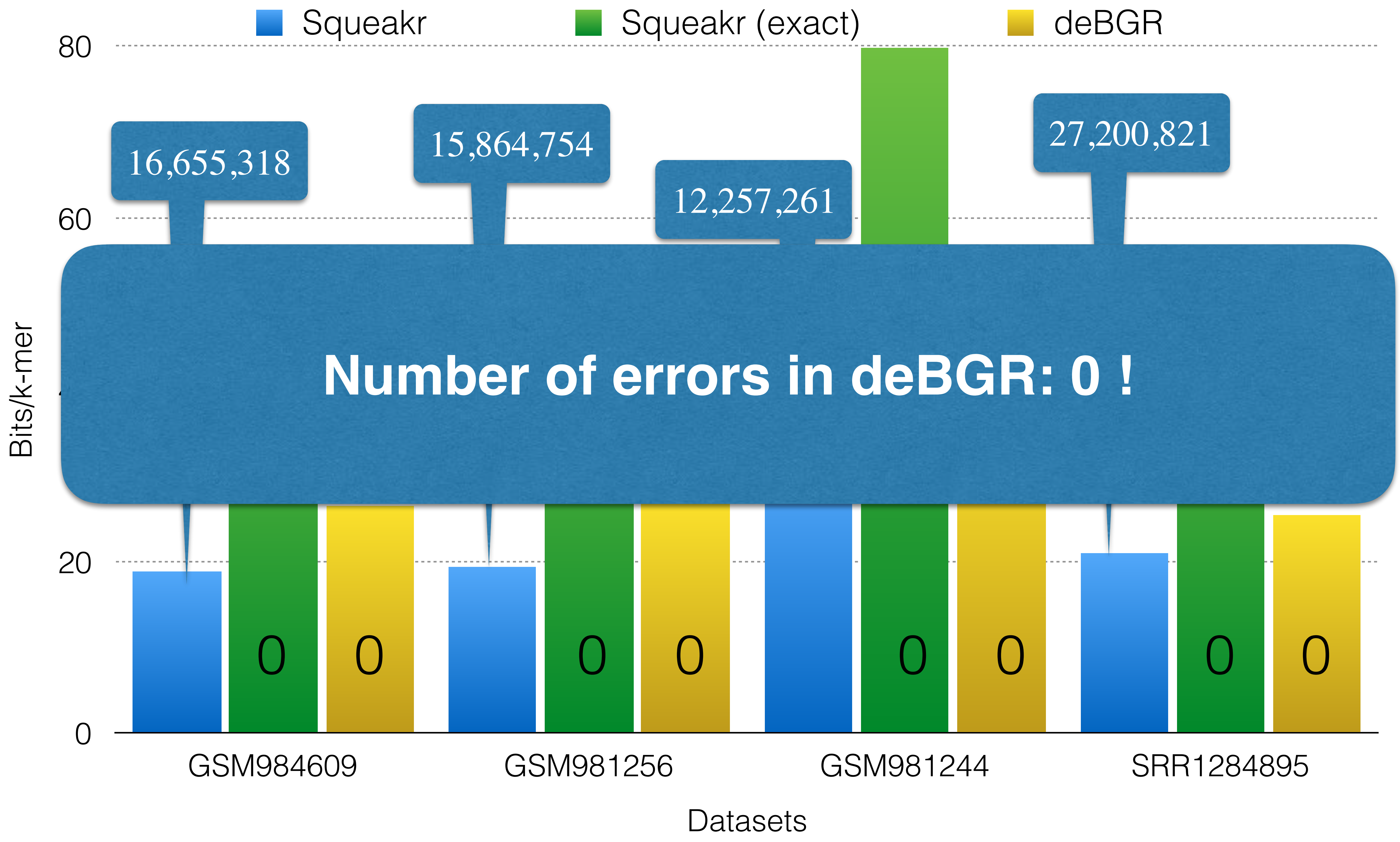

Number of errors in deBGR: 0 !

Conclusion

- Abundance information in important for many data analyses.
- But abundance information is also useful for providing higher de Bruijn graph structural guarantees.
- We show that the abundance information can be used to remove effectively all the errors in an approximate weighted de Bruijn graph representation.

https://github.com/splatlab/debgr