Parallel Methods and Software for Next Generation Sequencing Analysis

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The Big Data Challenge

Then (2005)

ABI 3700

96 ~800 bp reads

76.8 X 10^3 bases

~$1 per kilo base

Now

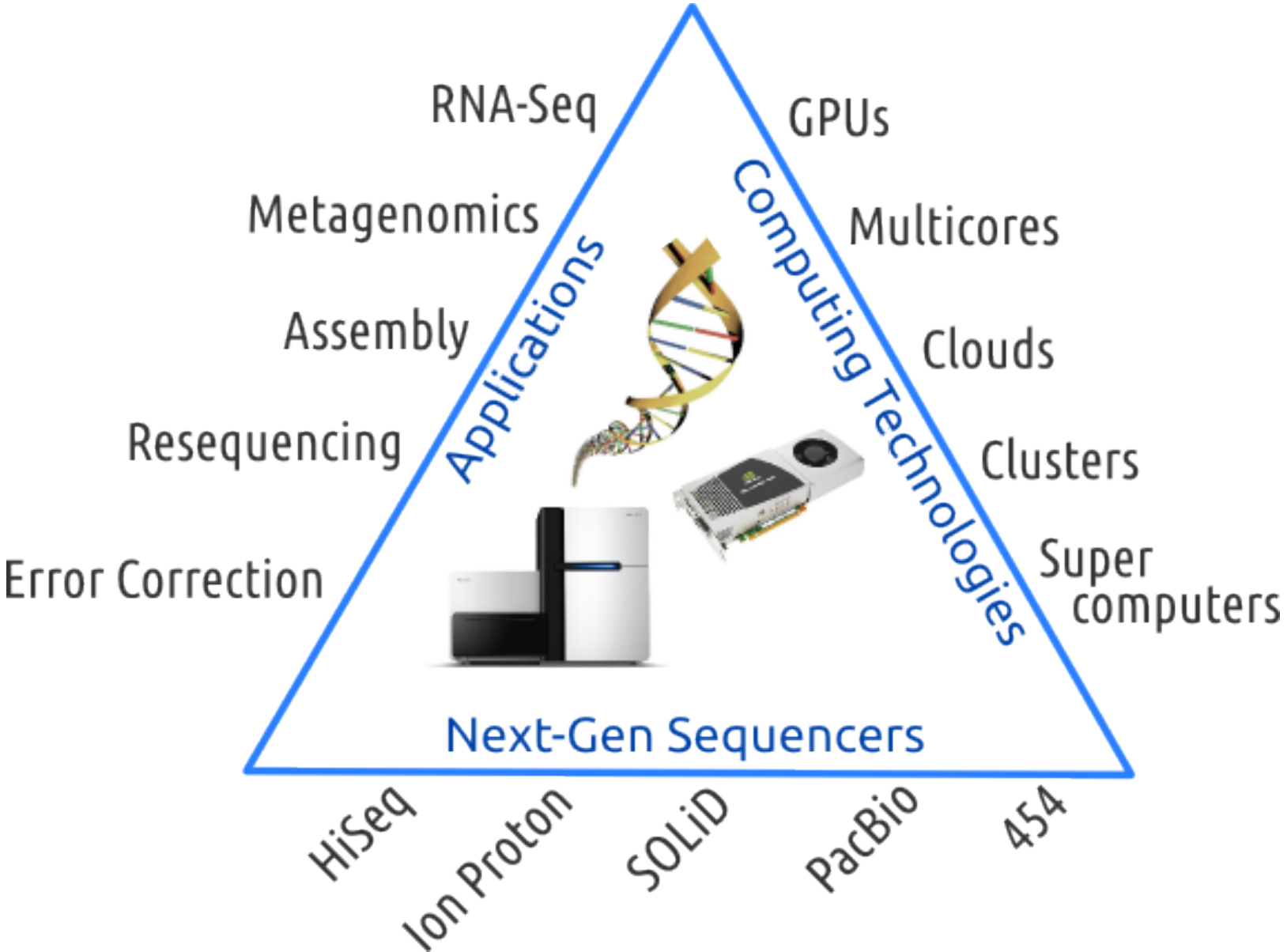
Illumina Hiseq 2500

6 billion 100 bp reads

600 X 10^9 bases

~$1 per 200 million bases

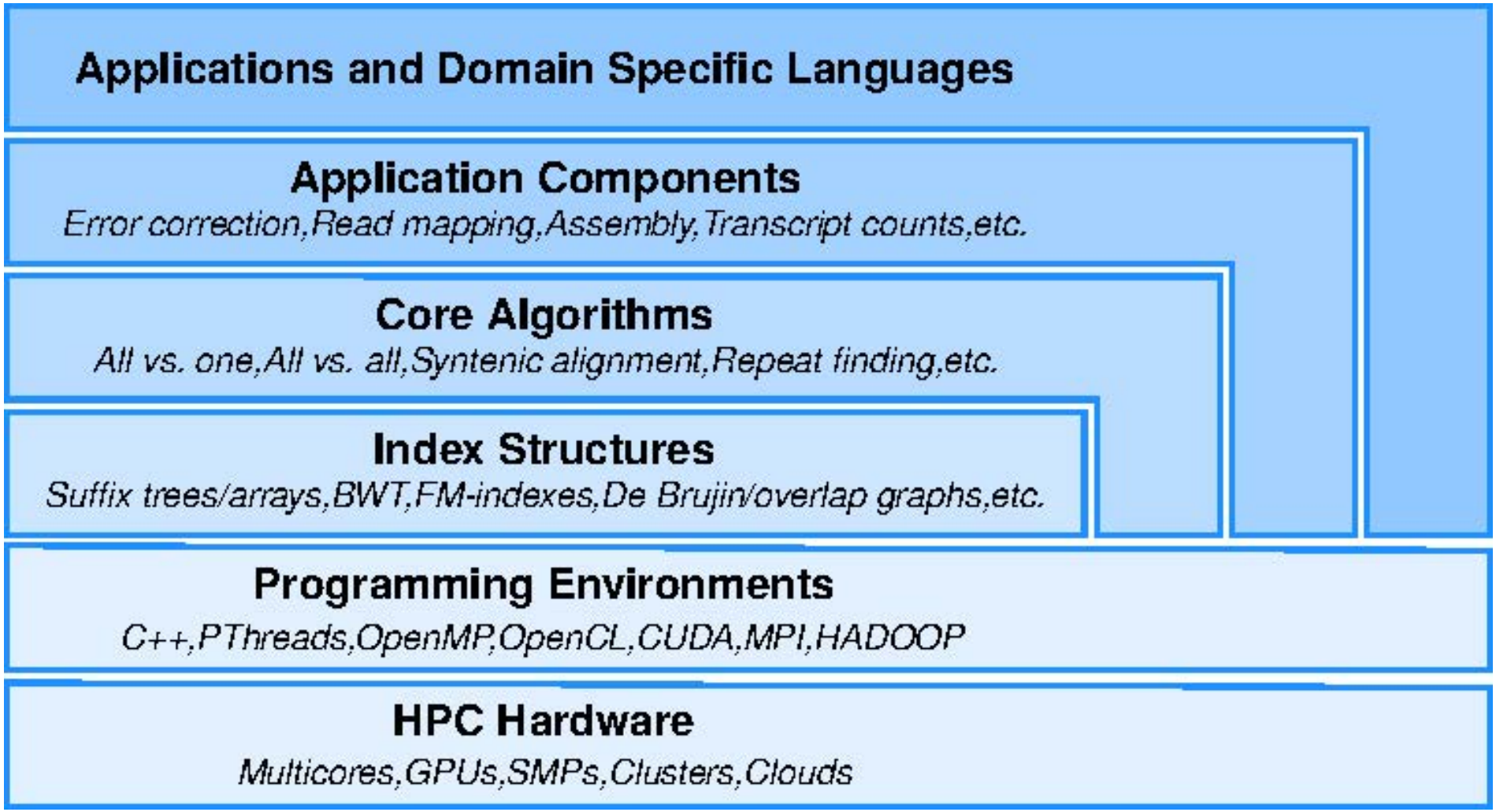
Genomes Galore – Big Data Analytics for High Throughput DNA Sequencing



Goals

- Empower bioinformatics community to migrate to HPC (and, beyond multicore shared memory)
- Preserve ability to create new bioinformatics solutions without loss of control
  - Lower levels provide higher degree of control
  - High levels reduce development time
- Should be useful both for researchers developing new methods and software developers

Software Architecture



Layer 1 – Index Structures

- Index structures on sequences
  - Look up tables, suffix trees, suffix arrays
  - BWT, FM-index
- Core data structures that operate on sequences
  - de Bruijn graphs, overlap graphs, string graphs, Hamming graphs

Layer 2 – Core Algorithms

- Support common algorithmic constructs
- Two types of sequences
  - Short (reads: 25-200bp, 450-700bp, 1000bp+)
  - Ultra-long (genomes, chromosomes, large genomic segments: 10^5 – 10^{10} bp)
- Computations within or across the two types of sequences

Layer 2 – Core Algorithms

- all vs. all between short sequences
  - Common *k*mer
  - Spaced *k*mer (used in mapping)
  - Sharing a good fraction of *k*mers (Jaccard's coeff.)
  - Local alignment (exons within genes, etc.)
  - Suffix-prefix alignment (assembly)
- all (short) vs. one (ultra-long), all vs. few
  - return all mapping locations

Layer 2 – Core Algorithms

- Intra ultra-long
  - repeats, tandem repeats, CpG islands, retrotransposons, gene duplications
- ultra-long vs. ultra-long
  - SNPs, variation detection, large-scale genomic events
- Multiple ultra-long
  - Motif detection, gene content evolution, multi-gene synteny

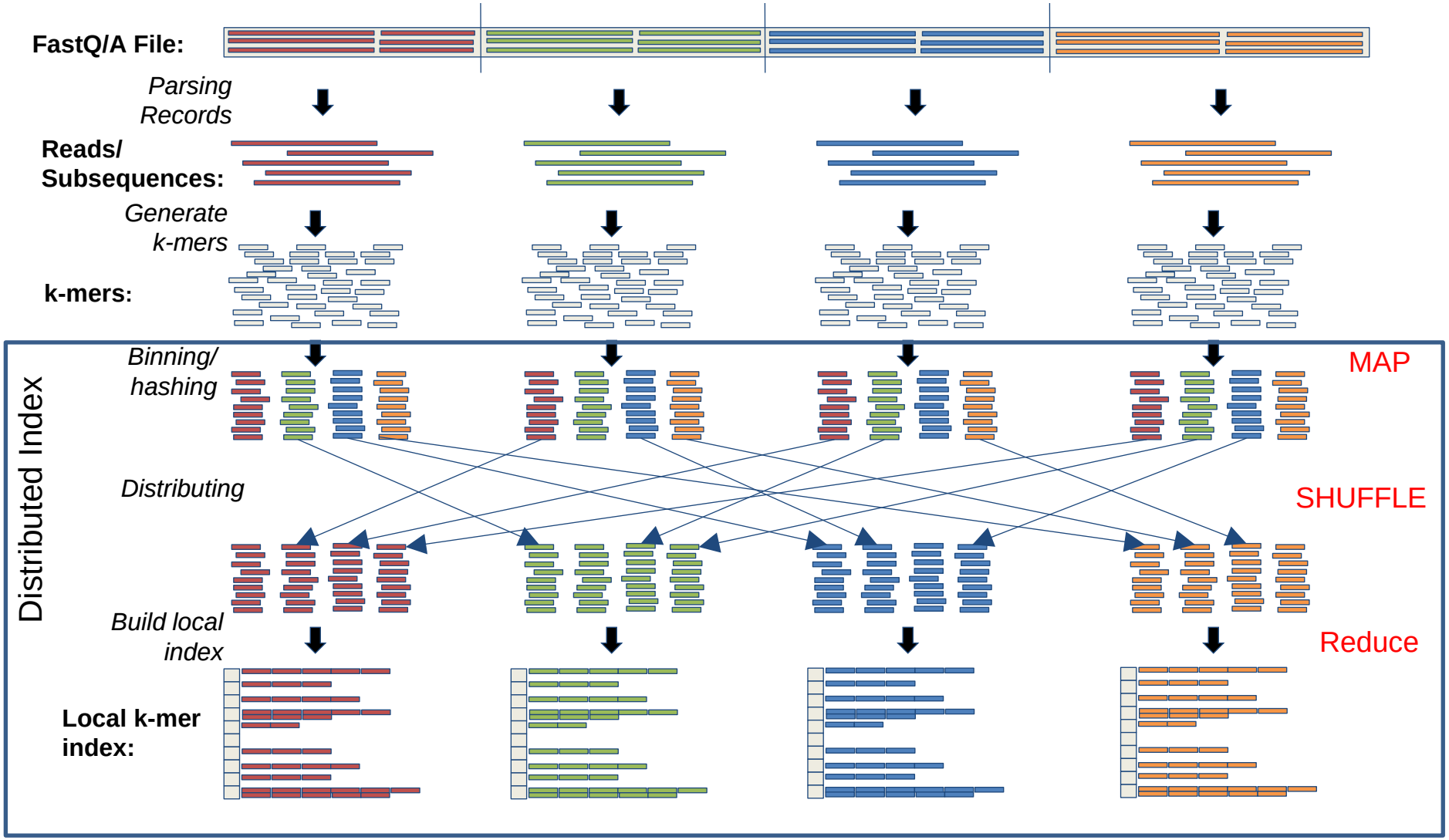
Layer 3 – Application Components

- High level processing tasks envisioned by human researchers
  - Error correction
  - Read mapping
  - Assembly
  - Transcript counts

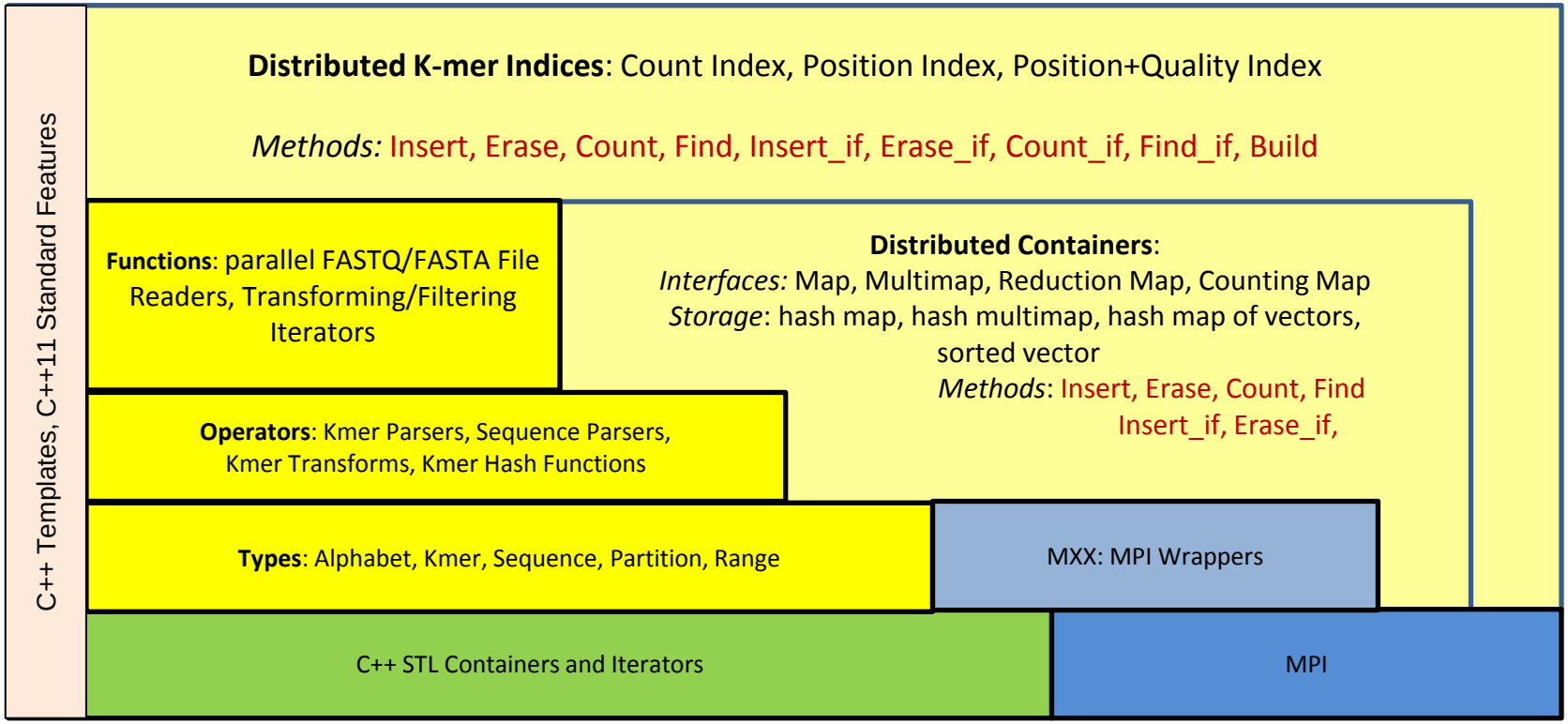
K-mer Indexing

- Create a K-mer Indexing Framework with customizable data
  - **Key:** k-mer or a transformation of a k-mer (e.g. reverse complement)
    - User choice of k, alphabet, and internal data type.
  - **Value (user specified):** read id, position in read, count/frequency, next base in read (i.e. de Bruijn graph edge), quality score, etc
- Define standard k-mer index operations
  - Provide Insert, Erase, Find, and Count operations as well as their conditional counterparts
  - Building blocks for more complex operations on k-mer indices
- Provide high performance implementations of commonly used k-mer indices
  - Indices for Count, Position, and Position and Quality Score

K-mer Indexing Algorithm



K-mer Indexing Framework Design



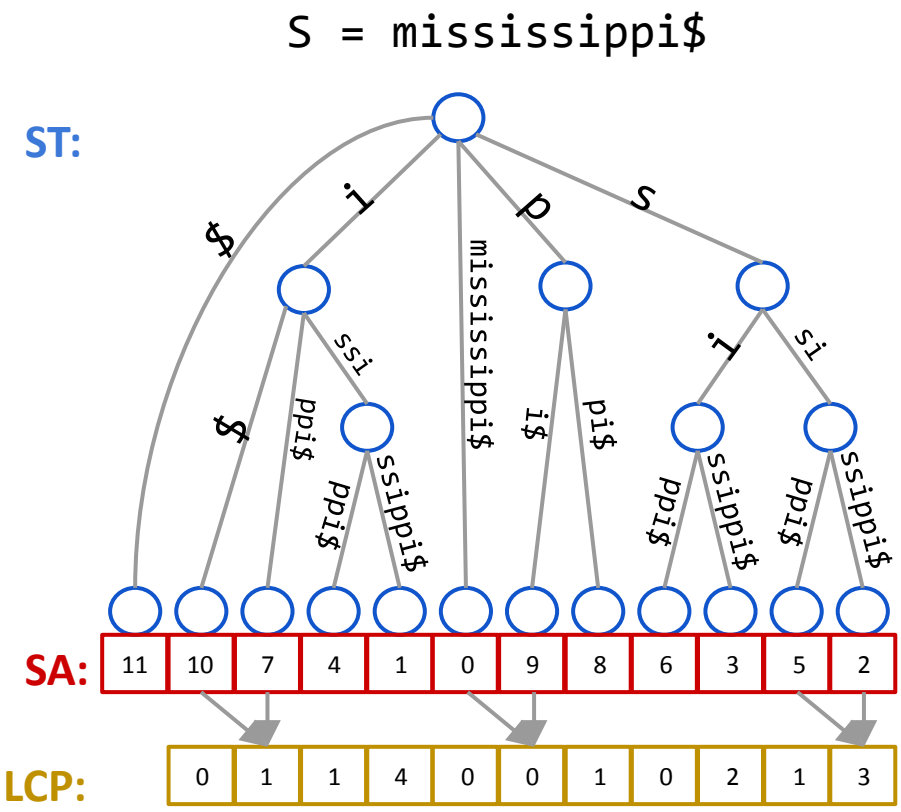
Performance Comparison

	1.9B kmers. Query with 19M kmers (2x E5-2650, 16 cores/node, passmark 15303)			1.7 B kmers, query with 9.1M kmers. Amazon EC2 instance (m2.2xlarge, Xeon X5550 4 cores, passmark 5403)							
	Count Index Hash Map of Vectors			Khmer	Jellyfish	scTurtle	KMC	DSK	Tallymer	BFCounter	Kanalyze
	32 cores	128 cores	1536 cores	8 threads, 1% false pos.	8 threads	8 threads					
Build	47.146	12.238	2.679	1500	700	500	500	1300	5400	1750	2700
Query	2.265	1.243	5.35	300	1400				1000		

- Our k-mer Indices scale to large datasets:
  - A 441GB metagenomics read set with 155.6 billion kmers
  - Count Index construction = 827sec, query for 1% kmers = 3.01 sec
- They flexibly support indices in addition to Count Index

Parallel Suffix Arrays and LCP Arrays

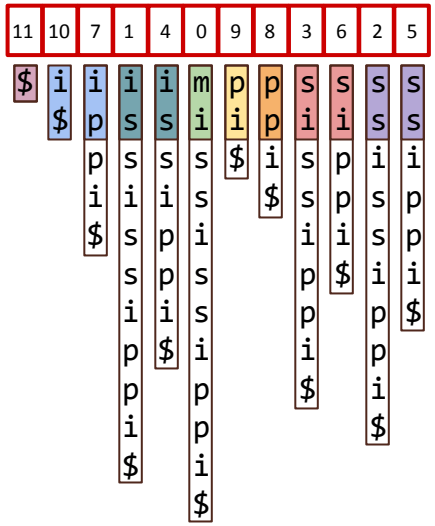
- **Suffix Tree (ST)**
  - trie of all suffixes of a string
- **Suffix Array (SA)**
  - array of sorted suffixes
  - represented by their offset
- **Longest Common Prefix (LCP)**
  - length of prefix match between consecutive suffixes in **SA**



Parallel Suffix Arrays and LCP Arrays

- **Prefix Doubling**

Sorted by prefix 2



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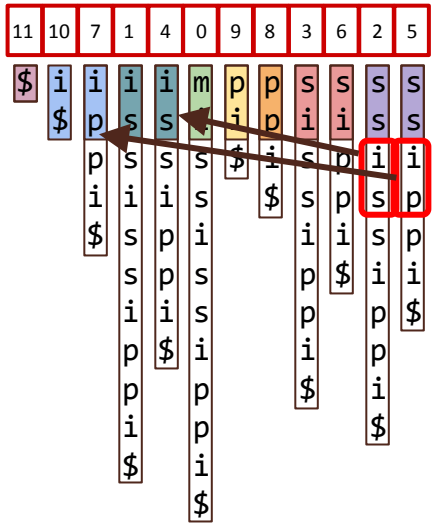

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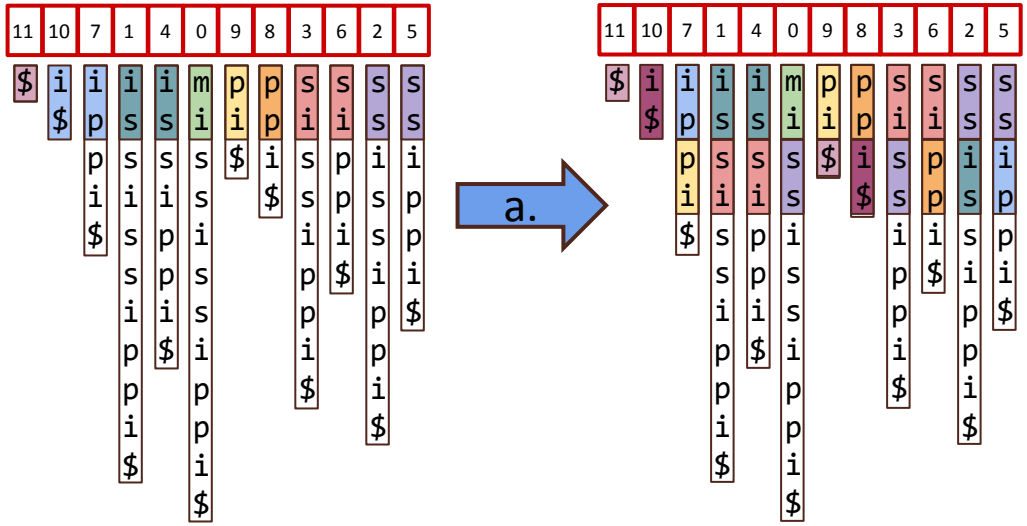

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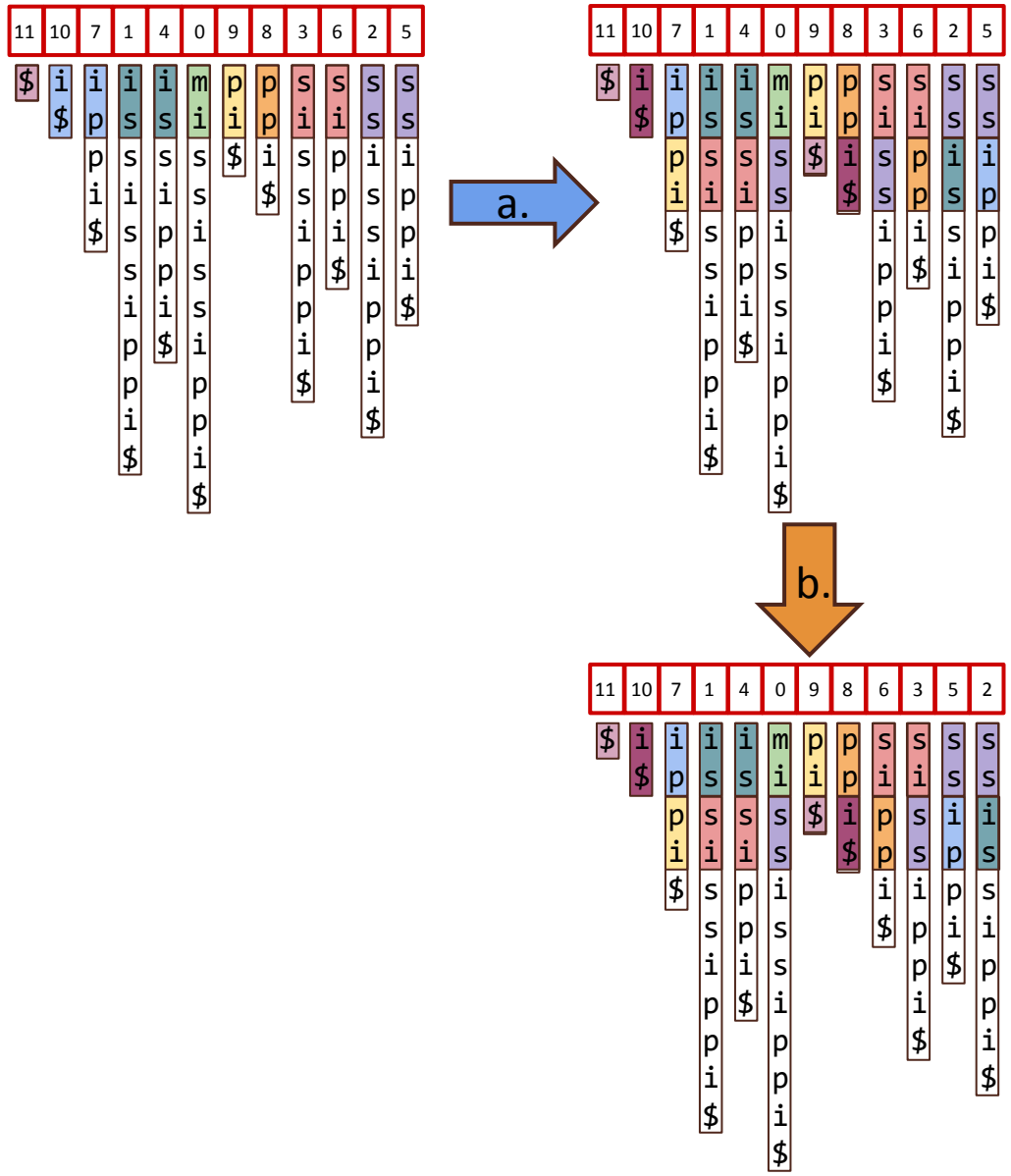

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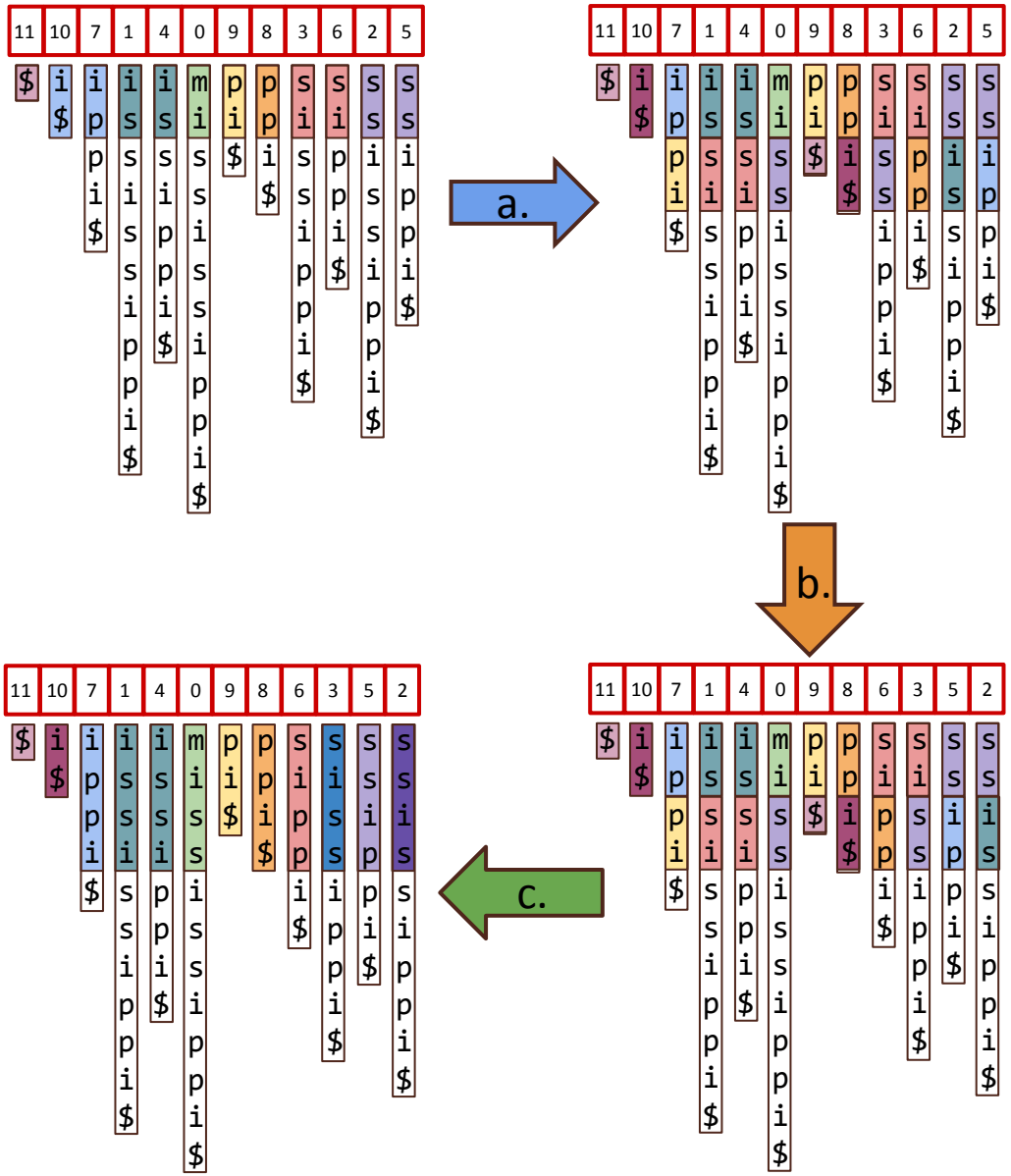
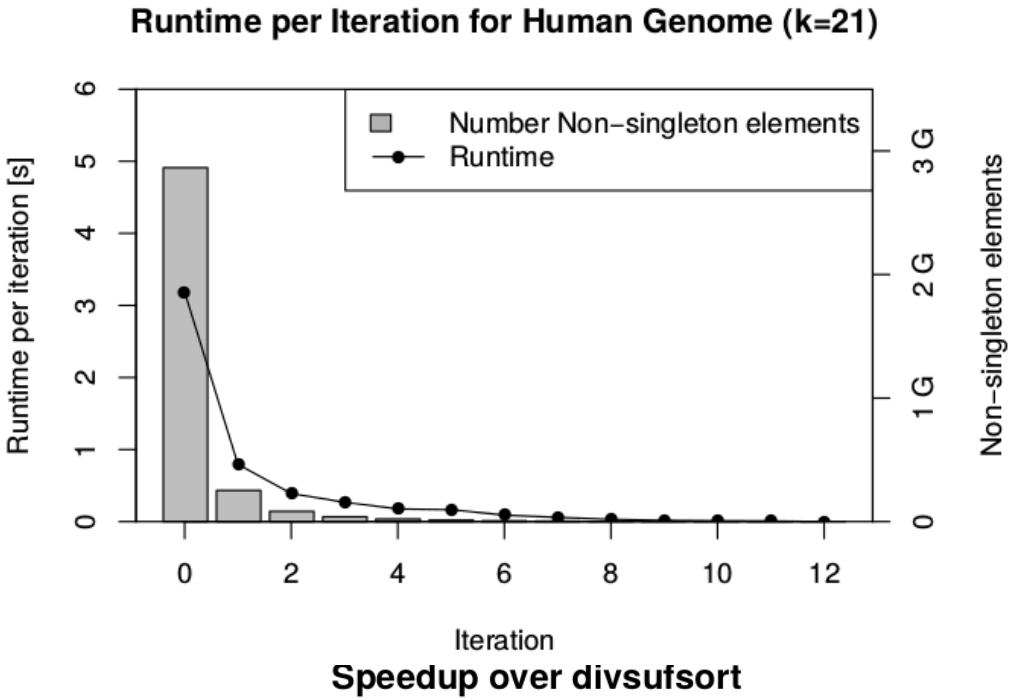


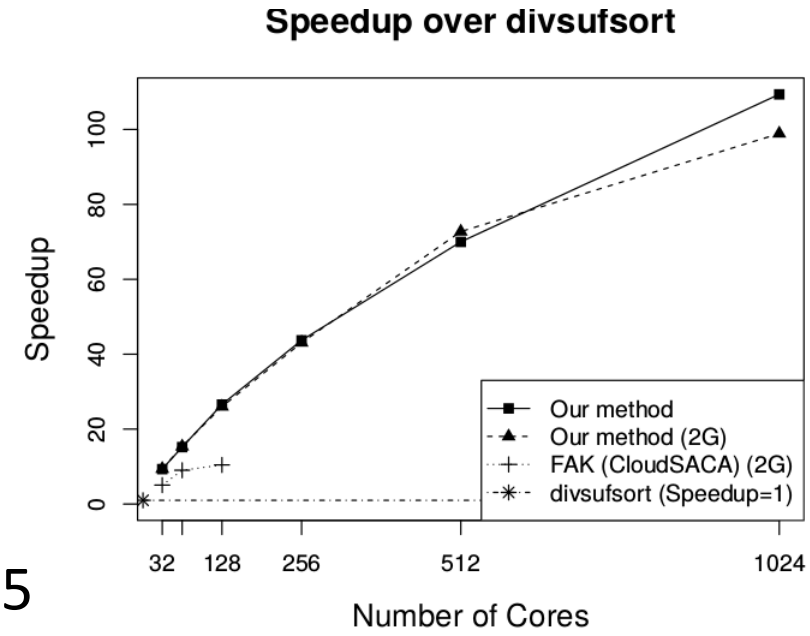
Sorted by prefix 4

Parallel Suffix Arrays and LCP Arrays

Results

- Parallel distributed-memory Suffix Array and LCP Array construction
- Scalability
  - to large inputs
  - to many nodes
- Speedup > 110x
- Indexing of full Human Genome in 8 seconds
- Outperforms all previous approaches

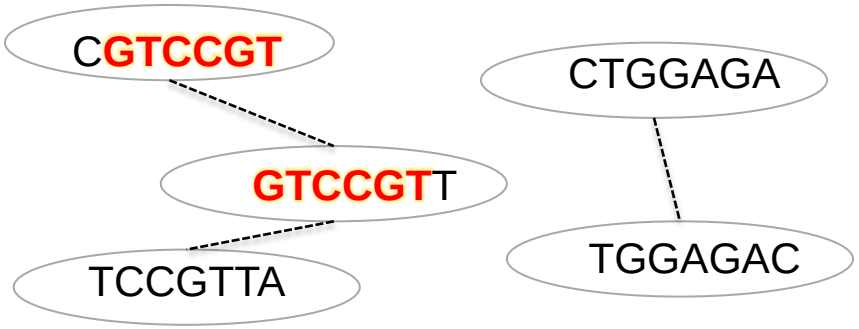




Flick and Aluru, *Supercomputing* 2015

De Bruijn Graph Partitioning

- Soil metagenomics dataset
  - Iowa Corn (1.8 billion reads)
  - Iowa Prairie (3.3 billion reads)
- High species-level heterogeneity
  - Disconnected components in de Bruijn graph (Howe *et al*. 2014)
  - 56 million components in Iowa Prairie dataset
  - 31 million components in Iowa Corn dataset

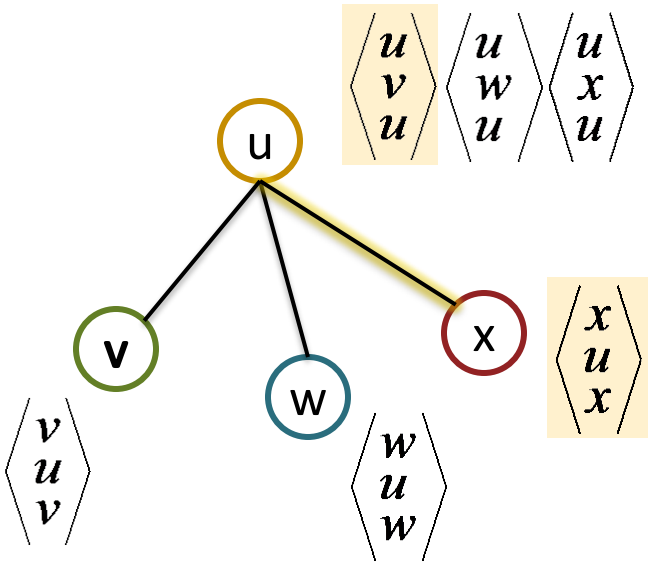


Parallel De Bruijn Graph Partitioning

- Distributed connected component labeling algorithm

Initialization

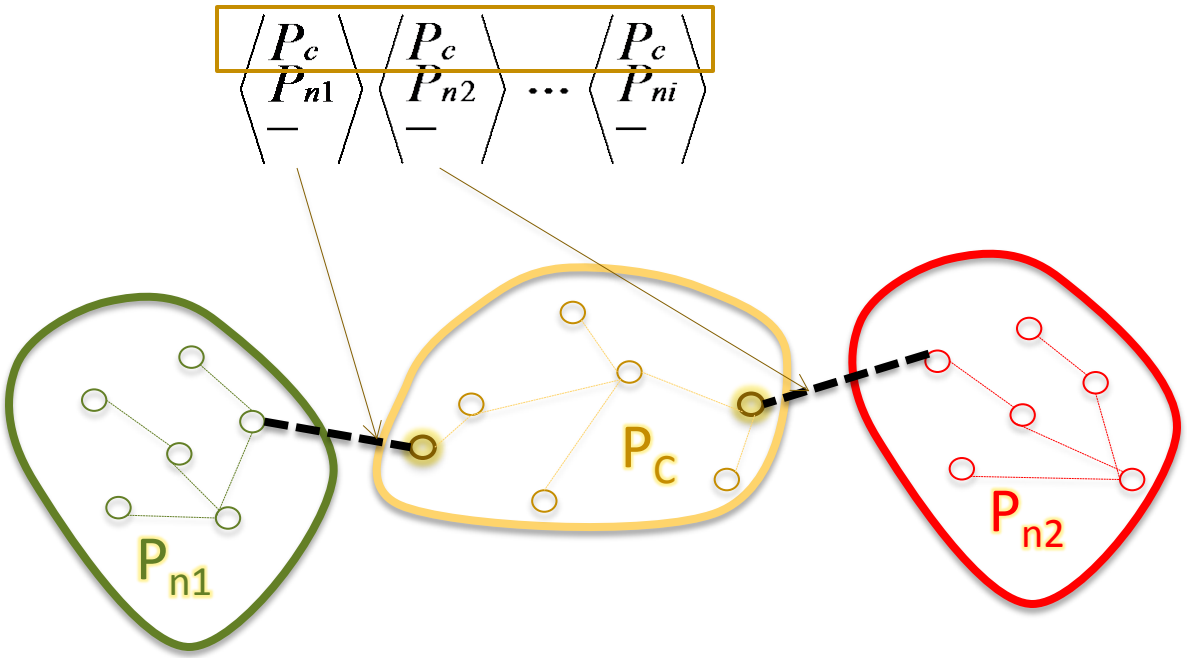
- Vector of tuples
- 2 tuples per edge in the graph
- Partition id of node = node id



⟨ Current partition id
Neighbor partition id
Node id ⟩

Parallel de Bruijn Graph Partitioning

- Each iteration
  - Do a parallel sort of all the tuples by *current partition Id*
  - Within each "bucket", compute minimum *neighbor partition id*
  - Flip the tuples to communicate my new partition id to neighbors in the next iteration



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$$P_c' = \min(P_{n1}, P_{n2} \ldots P_{ni})$$

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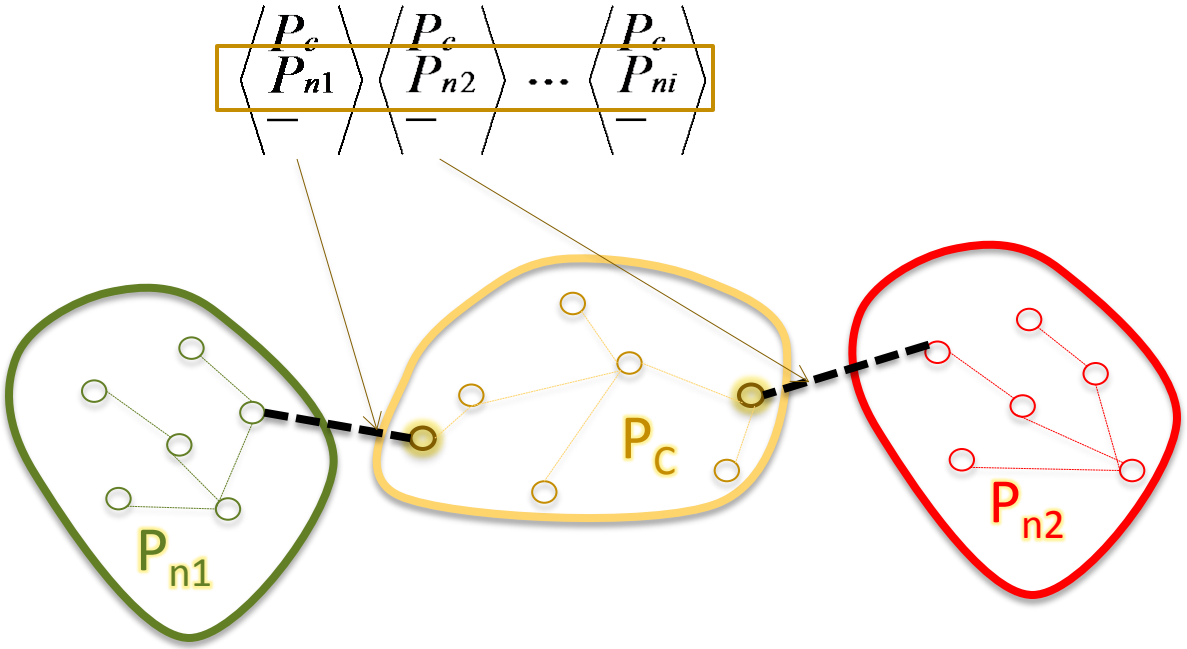

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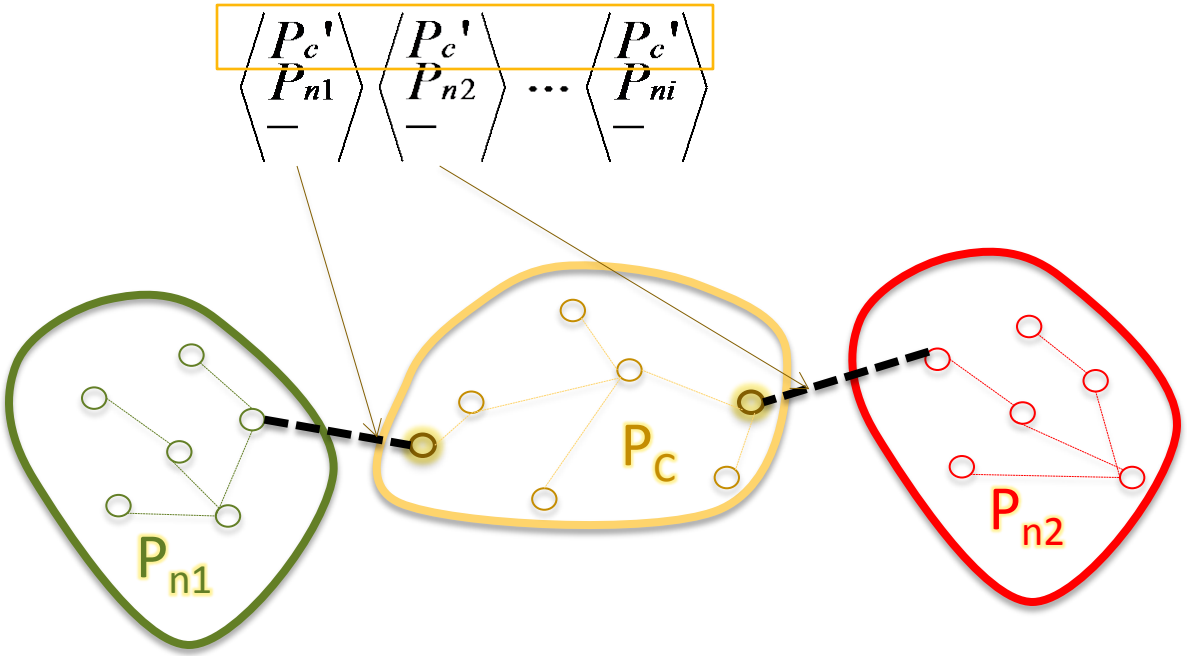

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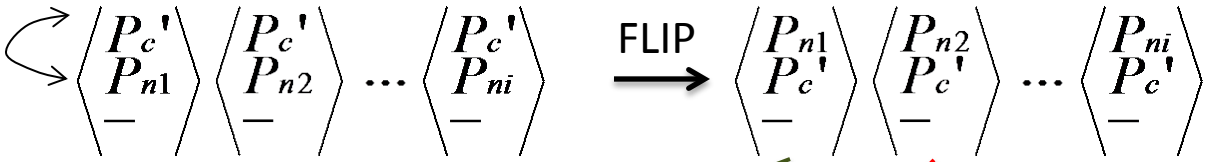

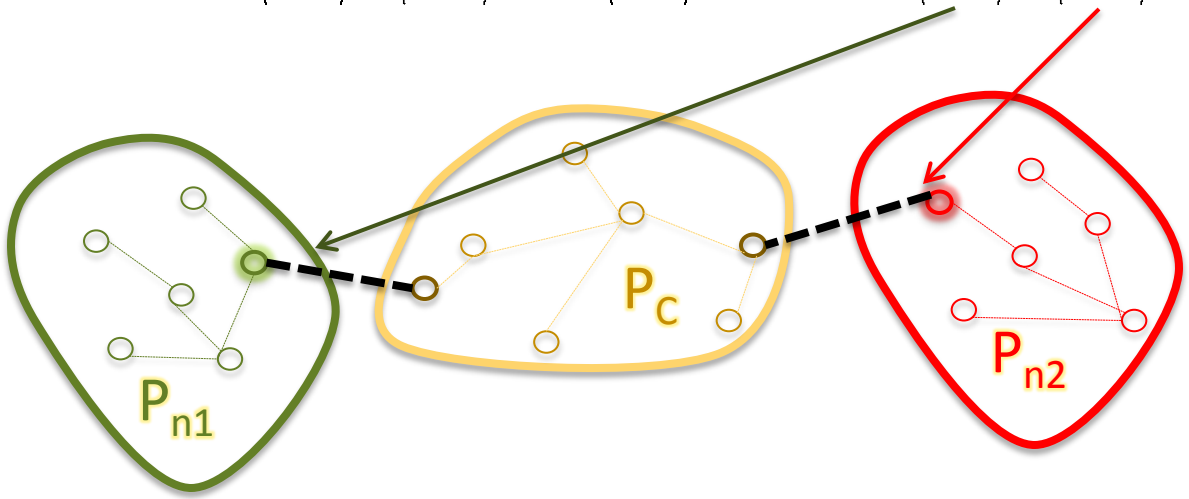

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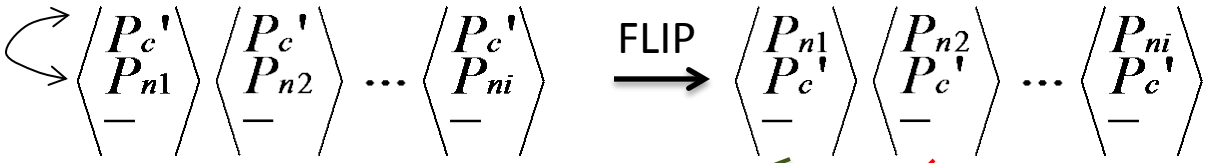
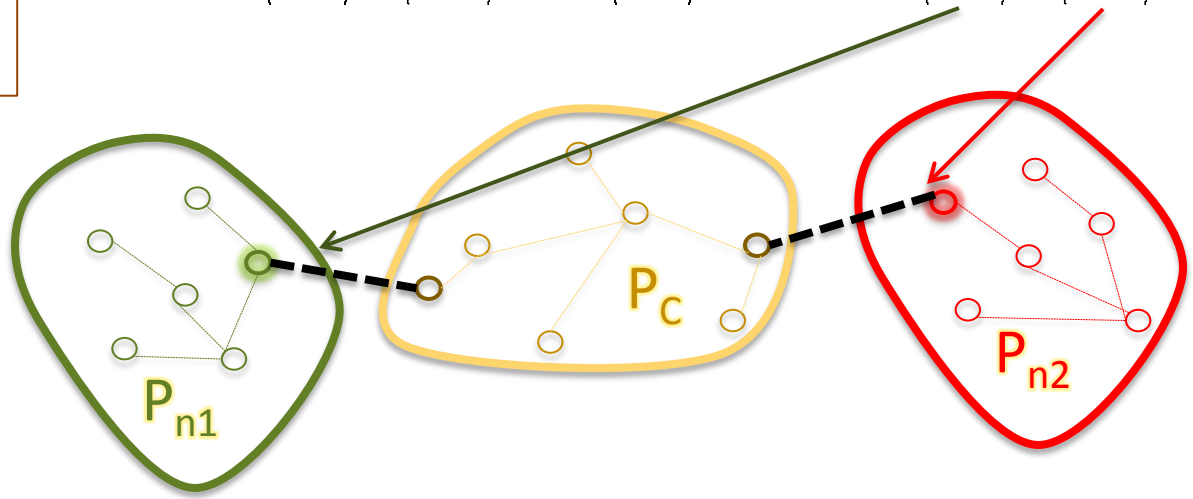
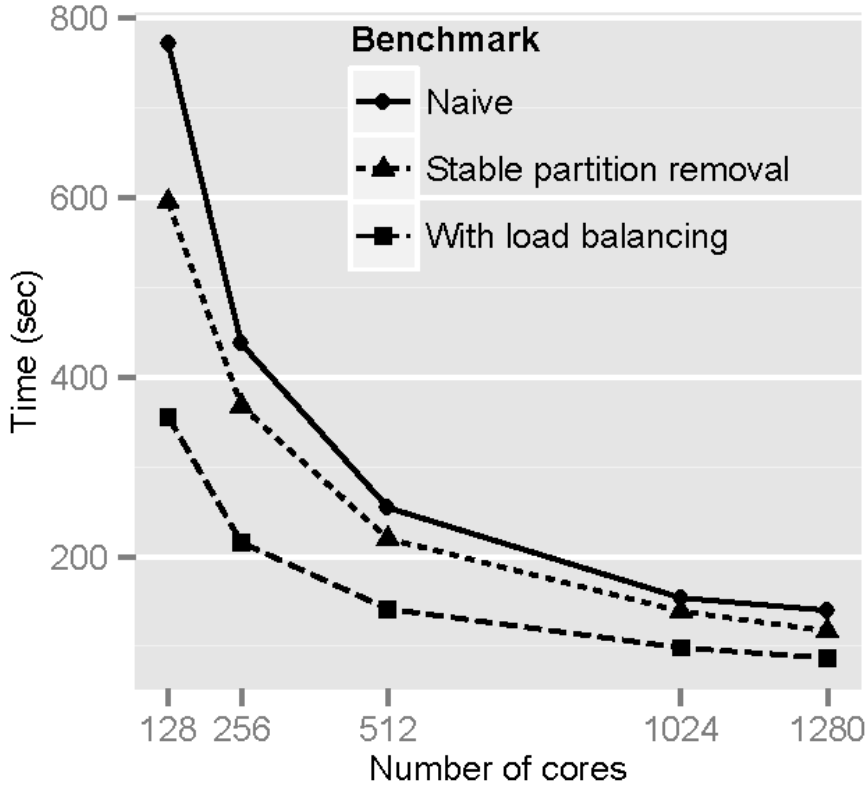
Loop until convergence





Parallel de Bruijn Graph Partitioning

Strong scalability upto 1280 Xeon cores using Infiniband.



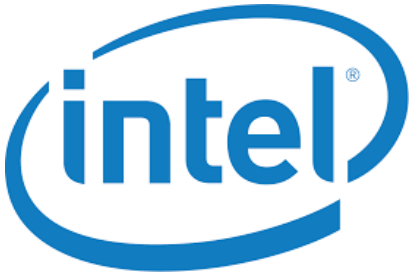
- Partitioned graph with 135 billion edges in 22 minutes (for Iowa corn metagenomics dataset)
- Sequential method takes multiple days.
- Prior methods for connected component labeling don't scale beyond 40 cores on sparse graphs.

Flick, Jain, Pan, and Aluru, *Supercomputing* 2015

Acknowledgements

Research Group:

- Patrick Flick
- Chirag Jain
- Yongchao Liu
- Tony Pan
- Support provided by:



Collaborators:

- Jaroslaw Zola, SUNY Buffalo
- Patrick Schnable, Iowa State
- Charles Sing, U. of Michigan
- Kunle Olukotun, Stanford
- Wu-Chun Feng, V. Tech