Shepard - A Fast Exact Match Short Read Aligner

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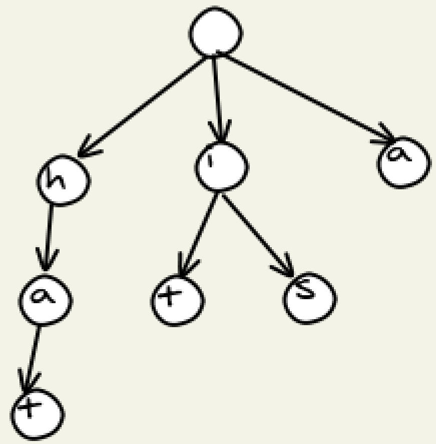
Overview

- The Challenge
- What is Shepard?
  - Software for Minimal Perfect Hash Table Creation
  - FPGA hardware pipeline for fast Hash Table lookups
- How fast is it?
- What's next?

The Challenge

- Align millions of short DNA sequences to a reference genome.
- Current aligners (simplified):



- Our Solution:
  - One giant hash table

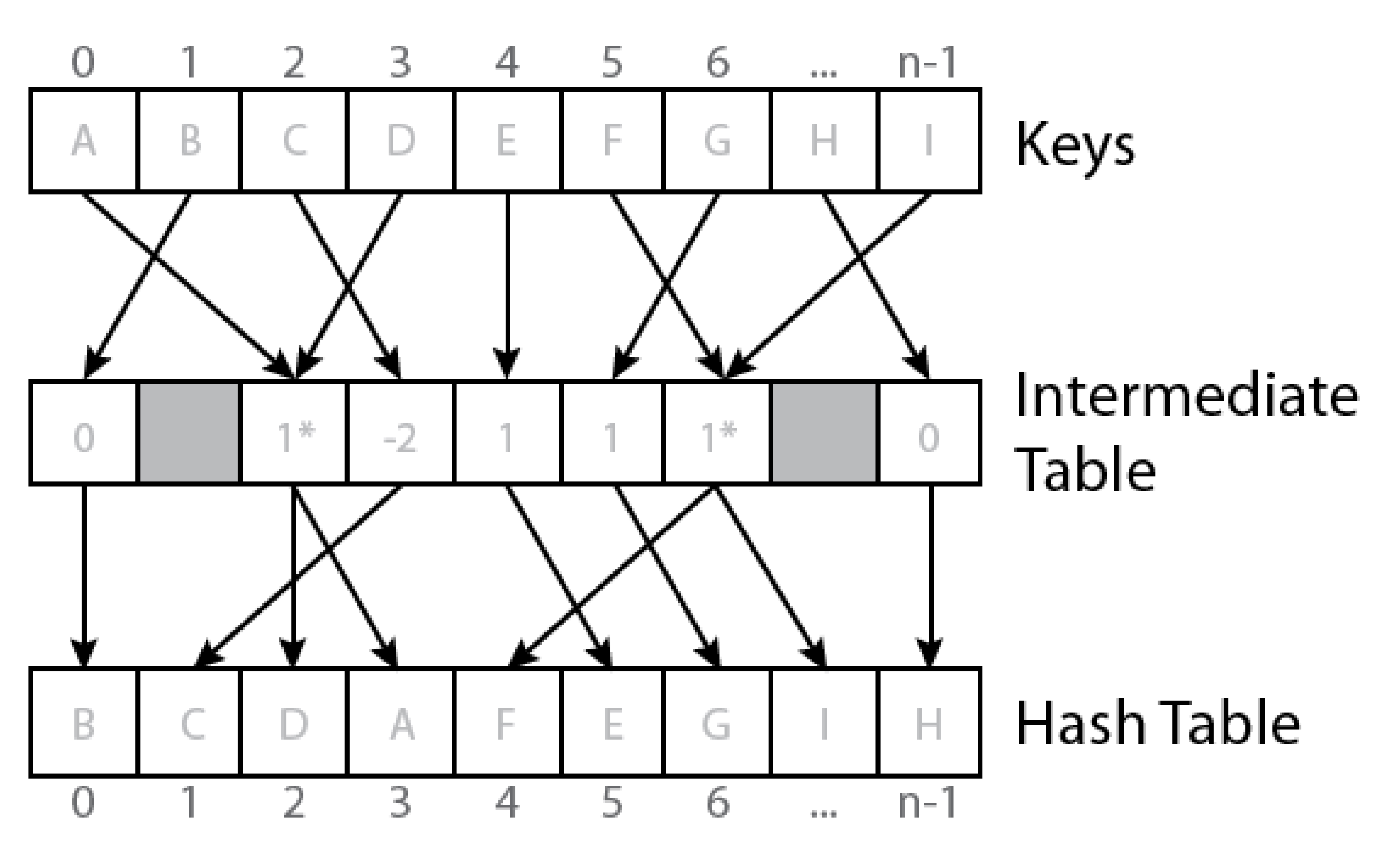
What is a MPH?

- MPH = Minimal Perfect Hash
- Given a **fixed set of keys**…
  - Perfect Hashes have no collisions
  - Minimal Perfect Hashes contain no empty buckets (they are memory efficient)
- For large sets of keys, you can create a general MPH in O(n) time.
  - General MPH algorithms require using an intermediate table.
  - **The intermediate table is the MPH.**

Minimal Perfect Hash Function Example

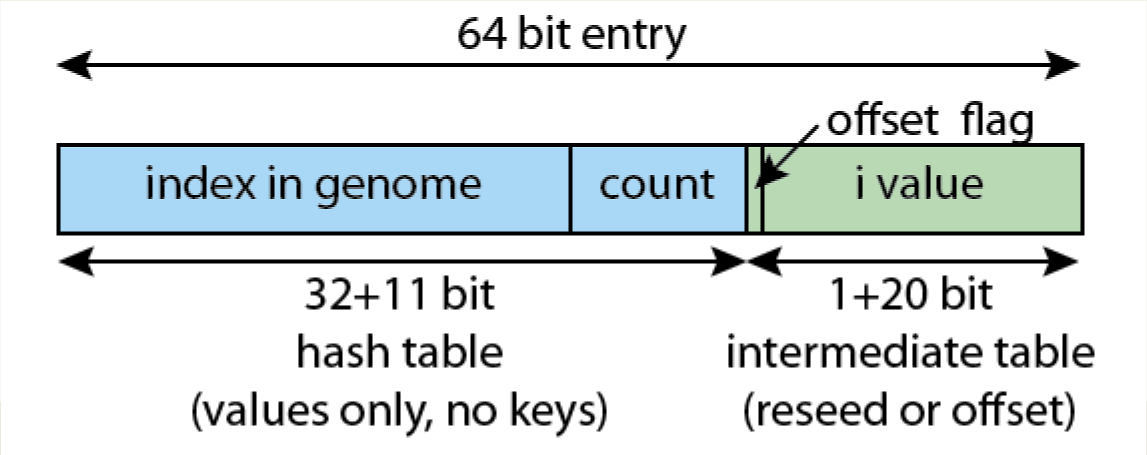
- Hash the key once to retrieve a few bits of information stored in the intermediate table
- Do one of the following:
  - Rehash with the new seed from the intermediate table (any buckets that had a collision would be rehashed*)
  - Add the offset from the intermediate table to the initial index.
- The MPH is created by choosing values for the intermediate table so that a given set of keys will not collide!

Minimal Perfect Hash Example



Shepard's Software

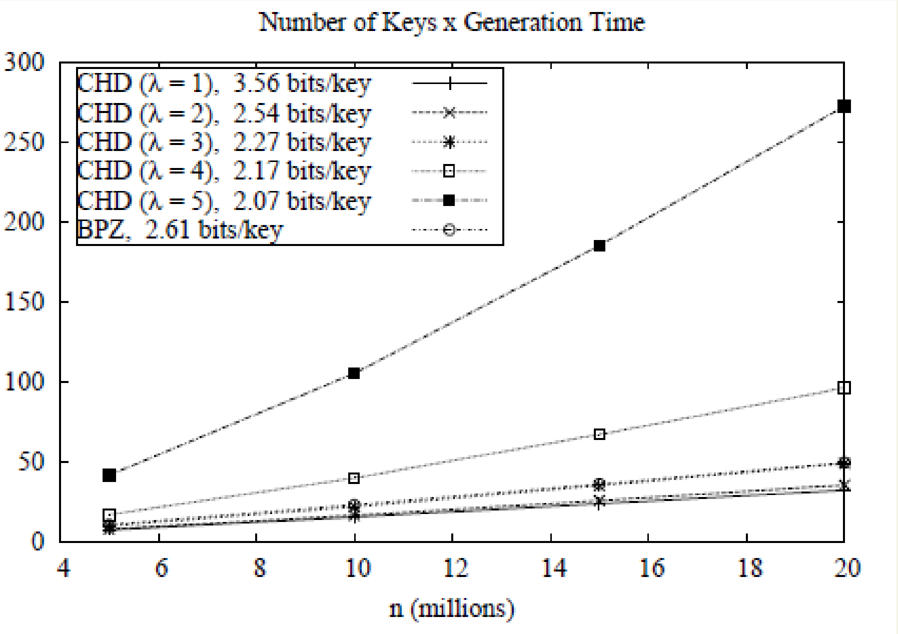
- Differences between our algorithm and other general purpose MPH algorithms (CHD)
  - CHD compresses the intermediate table down to between 2 and 4 bits per entry
  - Shepard does not compress (no need); if entries are 8 byte aligned, there are 20 bits per entry available for the intermediate table



Speed of Shepard's Hash Table Construction

- Current MPH creation using C code (CHD)
  - 800,000 entries / sec
    *only 20 million entries

- Shepard MPH C code
  - 300,000 entries / sec
    *using 2.8 billion entries
  - For 2.8 billion entries, takes ~2.5 hours



(d) $\alpha = 1.00$, Space lower bound $= 1.44$.

Graph from: Hash, displace, and compress
Djamal Belazzougui et al

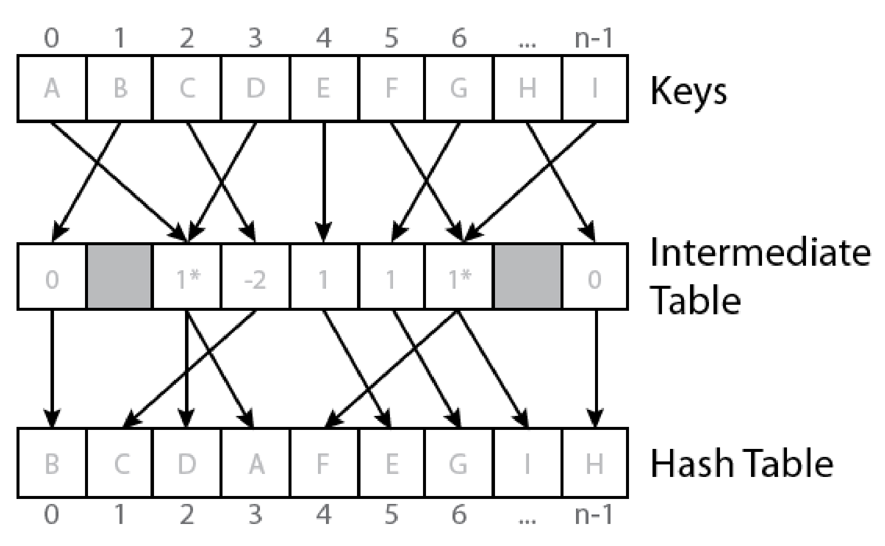
Future Work

- Hardware Pipeline for Hash Table Creation
  - The 6 stages for hash table creation are simple for-loops
  - Assuming:
    - ~40 memory operations per entry in construction
    - Application is memory bound
    - Convey HC-1 can perform 10 billion memory ops / sec
  - We could create the hash table in **about 12 seconds**, more than 250x faster than CHD
  - Concurrency Issues

Software Implementation

Algorithm 1 Pseudocode of the Shepard Pipeline

procedure ALIGN($reads, genome, hashtable, results$)
    for ($i = 0; i < length(reads); i++$) **do**
        $r \leftarrow reads[i]$; ▷ Stage 1
        $h \leftarrow hash(r, seed = 0)$; ▷ Stage 2
        $ivalue \leftarrow intermediateTable[h]$;
        if ($ivalue$ is an offset) **then** ▷ Stage 3
            $index \leftarrow hash(r, seed = 0) + ivalue$;
        else
            $index \leftarrow hash(r, seed = ivalue)$;
        end if
        $entry \leftarrow hashtable[index]$;
        $check \leftarrow genome[entry.index]$; ▷ Stage 4
        if ($r == check$) **then** ▷ Stage 5
            $results[i] \leftarrow entry$;
        else
            $results[i] \leftarrow NULL$;
        end if
    end for
end procedure



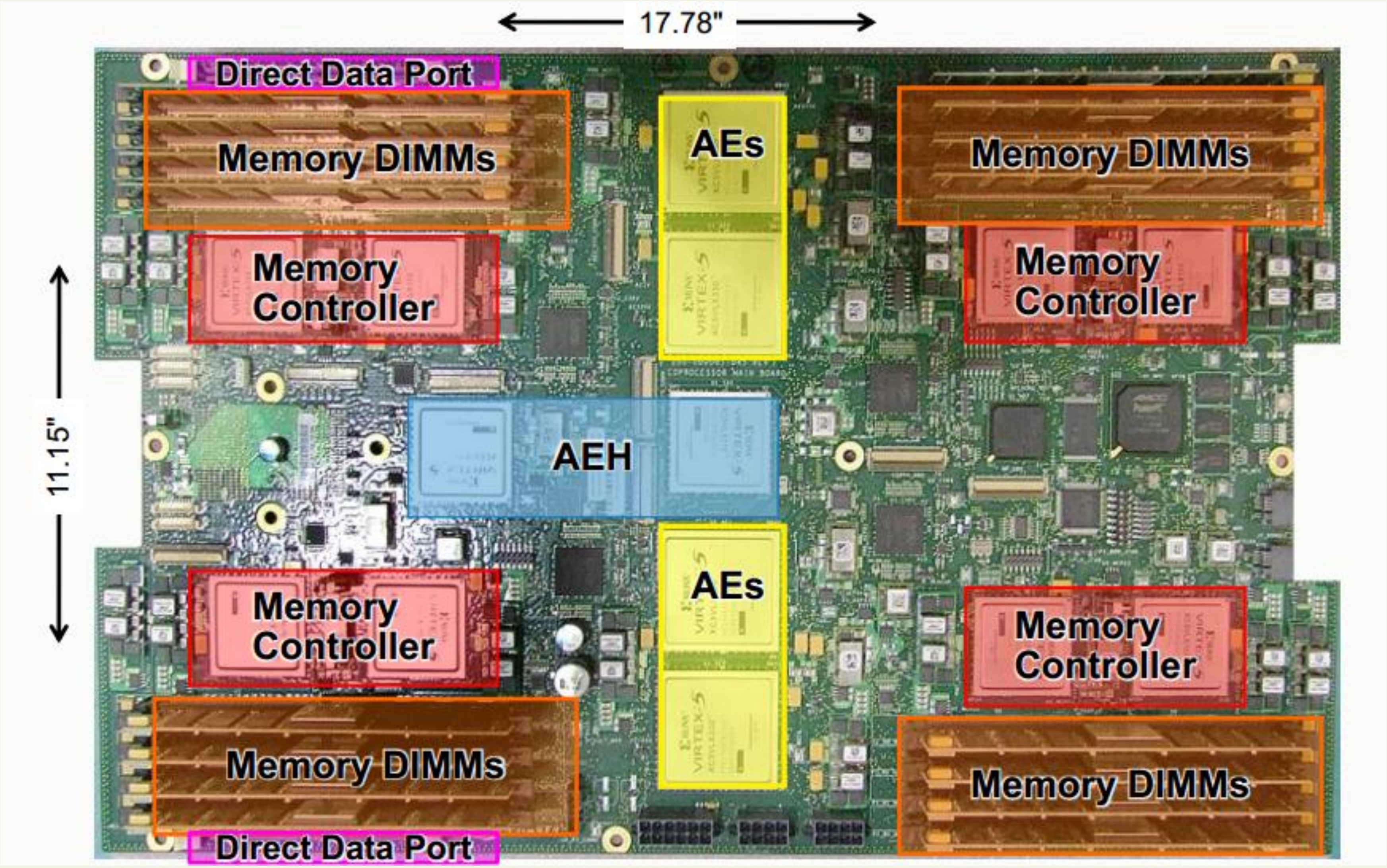
Software Implementation

- Speed
  - Single threaded:
    - 1,000,000 reads / second (using total program execution time)
  - Performance increases when using multiple threads

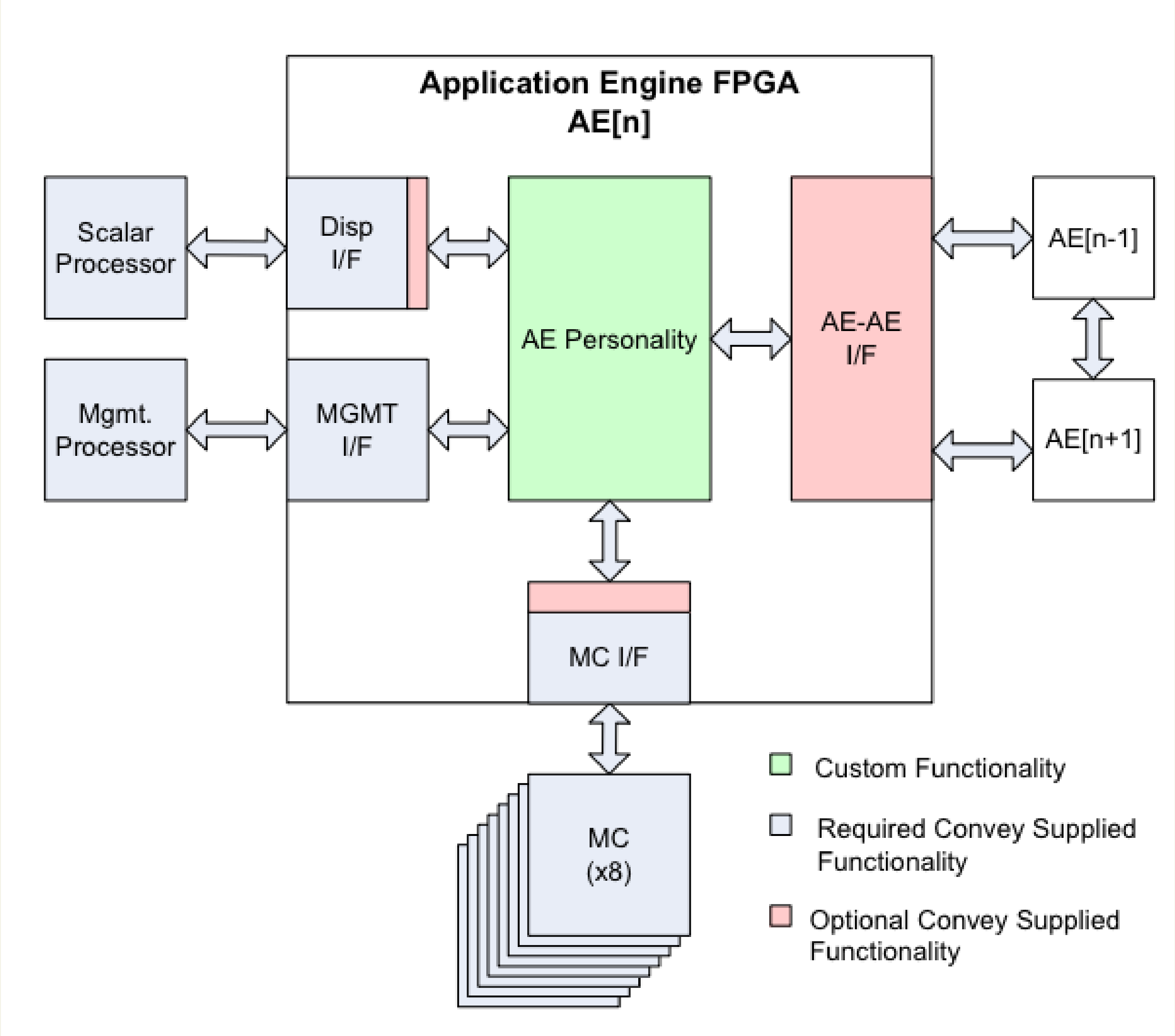
PERFORMANCE COMPARISON OF POPULAR SHORT READ ALIGNERS.

Tool	Platform	Speed (reads/s)	% Aligned	Memory (GB)
MAQ [4]	CPU	50	93.2	1.2
SOAP	CPU	70	93.8	14.7
SOAP2 [5]	CPU	2,000	93.6	5.4
Bowtie [6]	CPU	2,500	91.7	2.3
SOAP3 [9]	GPU	6,000,000	96.8	3.2

The Convey HC-1



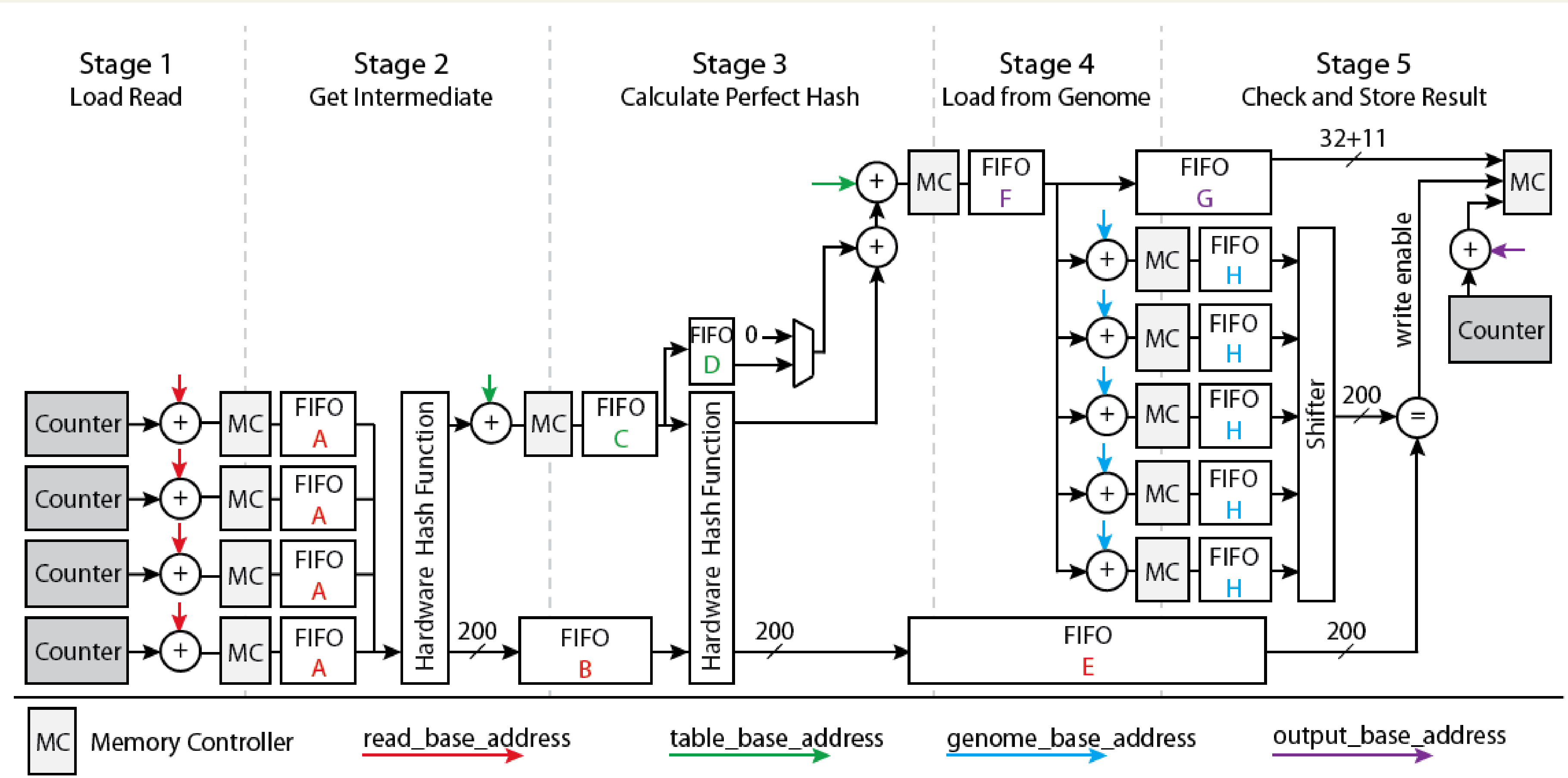
The Convey HC-1



Convey Custom AE Development Process

- It's simple!
- Take your original program, pull out a kernel written in C/C++
- Turn the kernel into a CAE instruction (define ISA)
- Write a software simulator of the program
  - Emulates custom hardware
  - Validates memory accesses
  - Validates AEG registers
- Write hardware description in Verilog or VHDL
  - Use the software simulator to test your design (quick)
  - Build a bitfile (slow)

Hardware Implementation

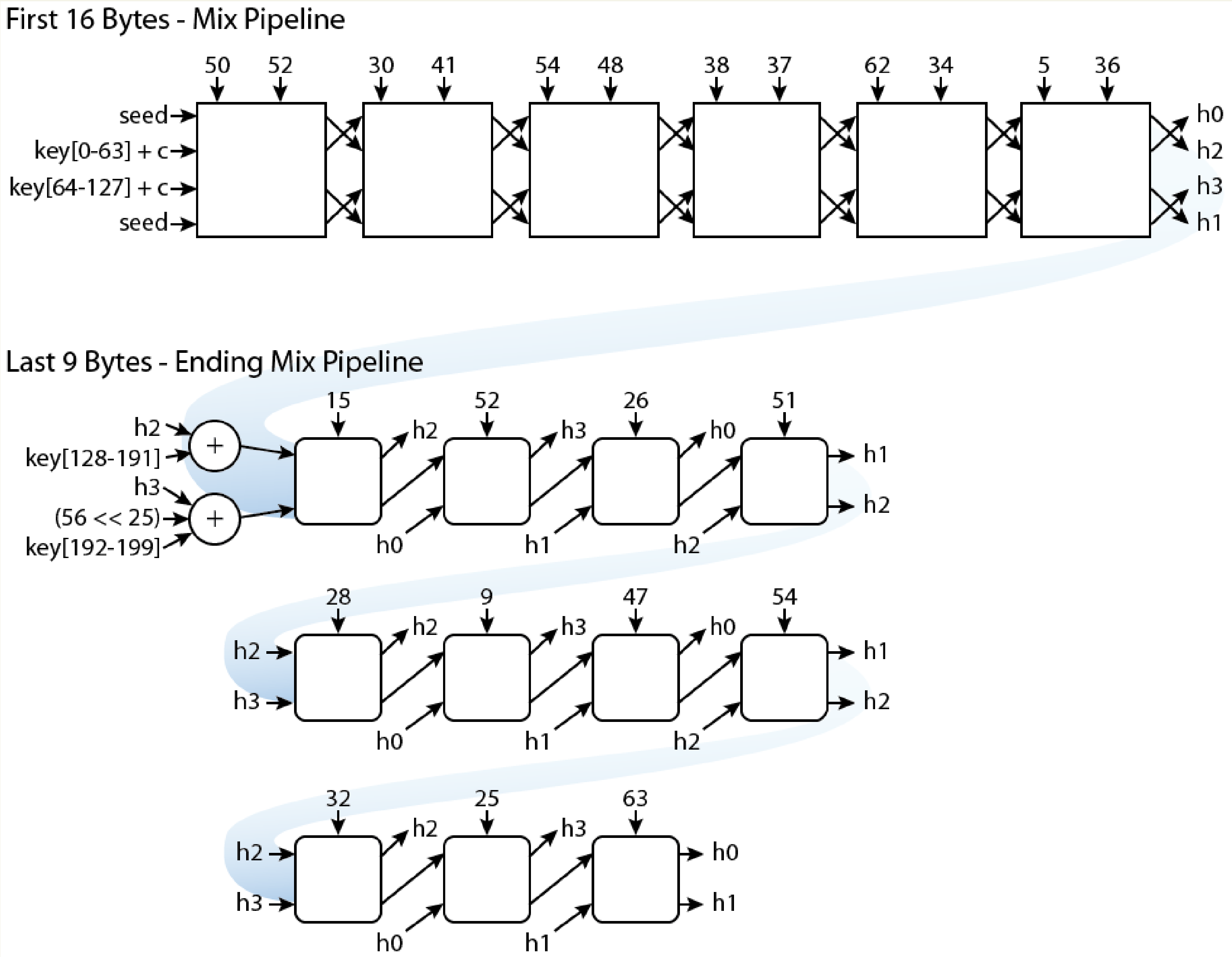


Hash Function Pipeline

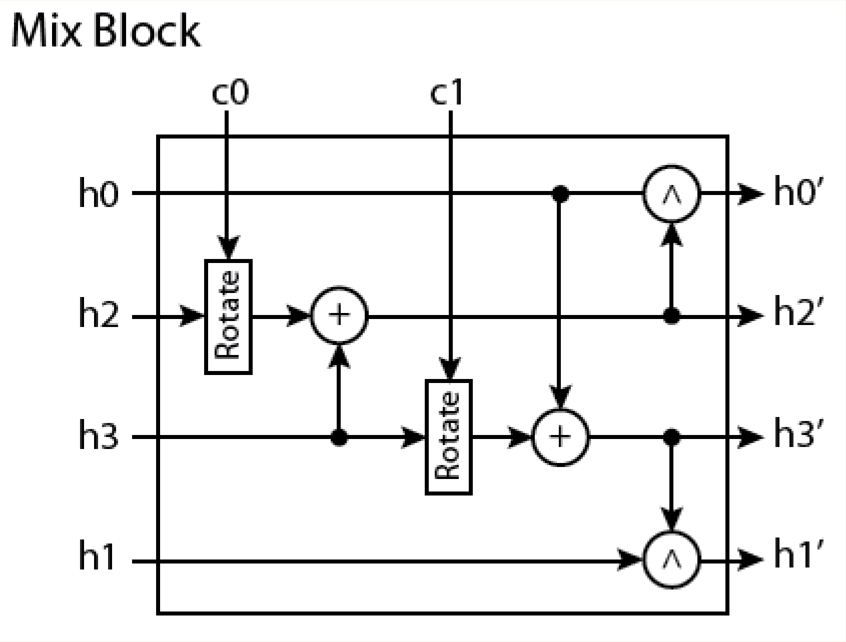
- Jenkin’s Spooky Hash
- Fixed the pipeline specifically for 100 base pair reads (25 bytes)

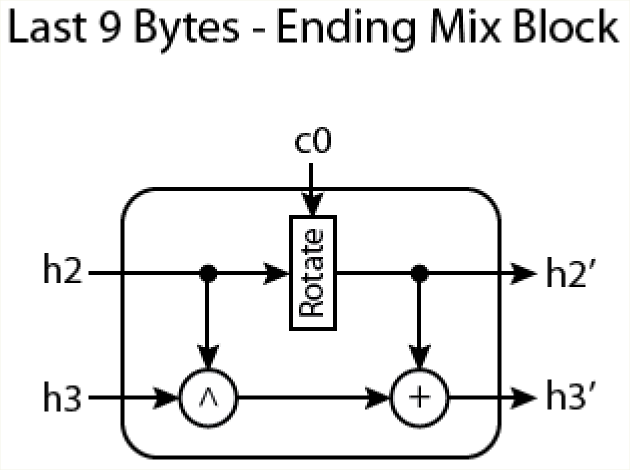
- Hash function consists of rotations, additions, and XOR

Hash Function Pipeline Implementation



Hash Function Pipeline Implementation





Speed

- 350,000,000 reads per second

PERFORMANCE COMPARISON OF POPULAR SHORT READ ALIGNERS.

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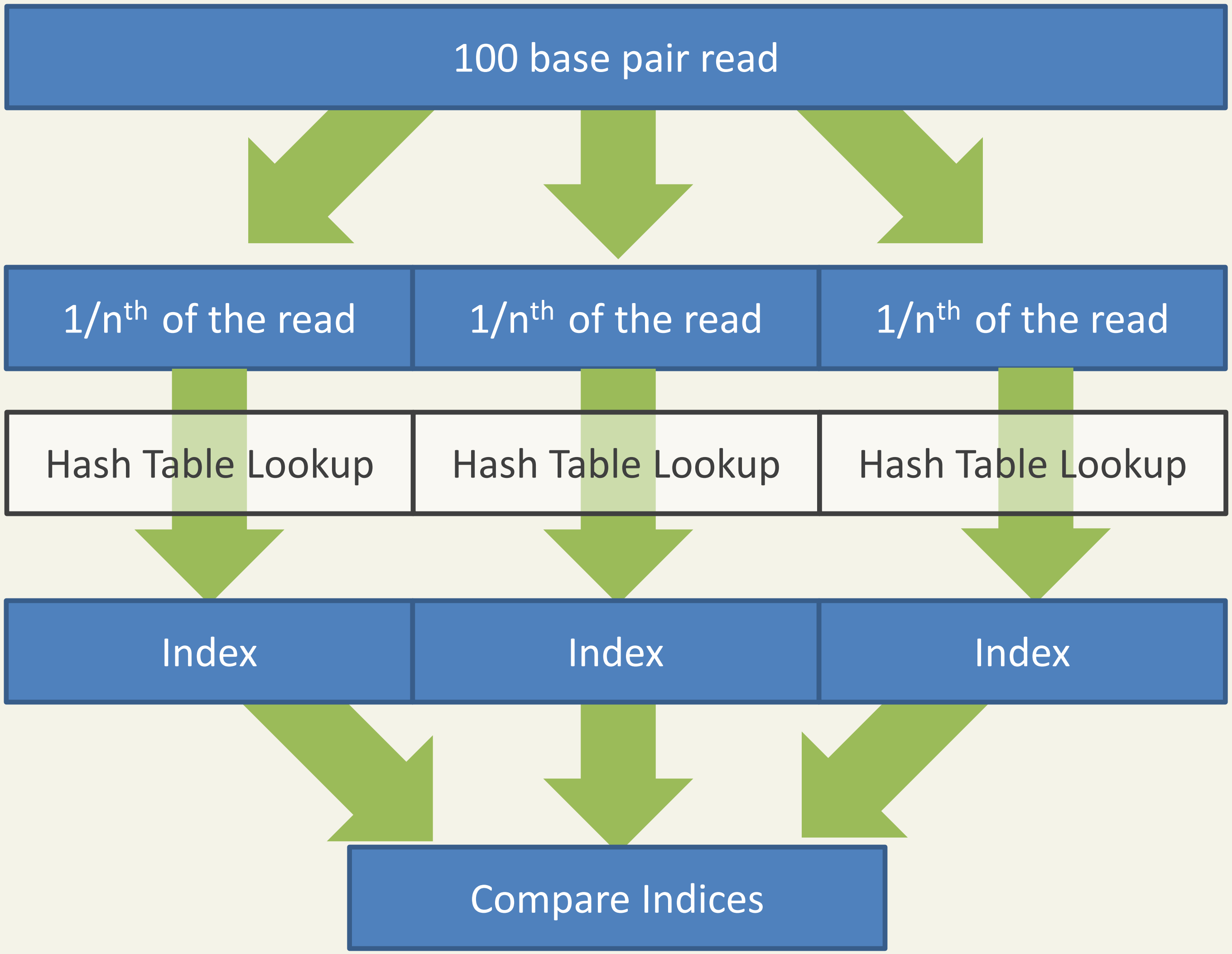
SOAP3 [9]	GPU	6,000,000	96.8	3.2
Shepard	FPGA	350,000,000	25.2	23.3

- Exact matches only!
- *% aligned* depends on the quality of the reference genome and the read data
- Had we used better read data (such as the data used in the SOAP3 paper), the *% aligned* would be as high as 60.3%

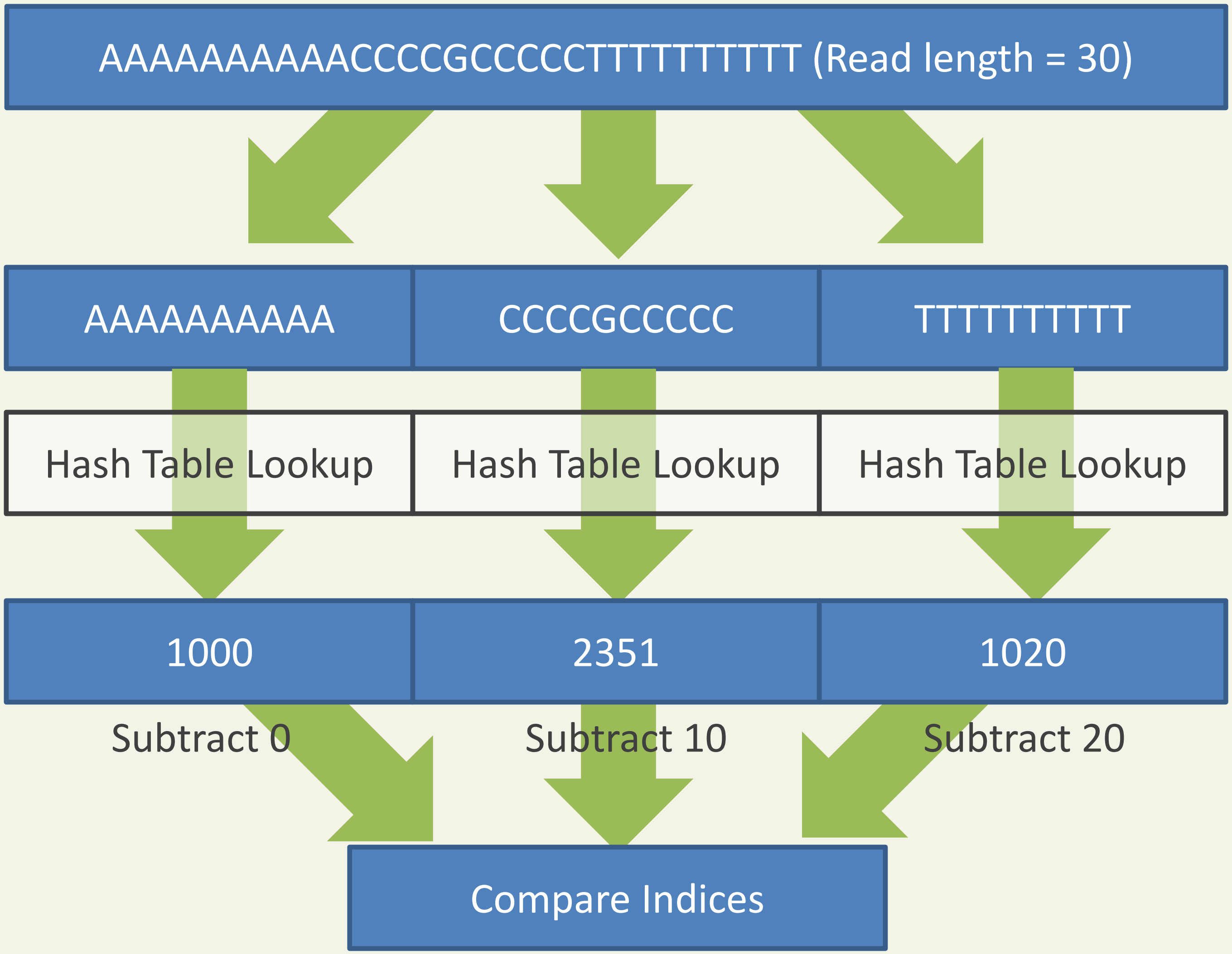
Future Work

- Let's update the pipeline to allow mismatches!
- The idea:
  - Split the read into **n** parts. Use a hash table to lookup the index of these parts.
  - Compare the indices of the parts. If any of the indices match, we can compare the read to the genome to see how many mismatches occurred!
- The time cost lies in the extra 2***n** memory operations that must be performed.
  - Our original design only used 12 of the 16 memory controllers, so if n=3, we would incur no time penalty!
  - We get a "free lunch" by using all of the available resources.

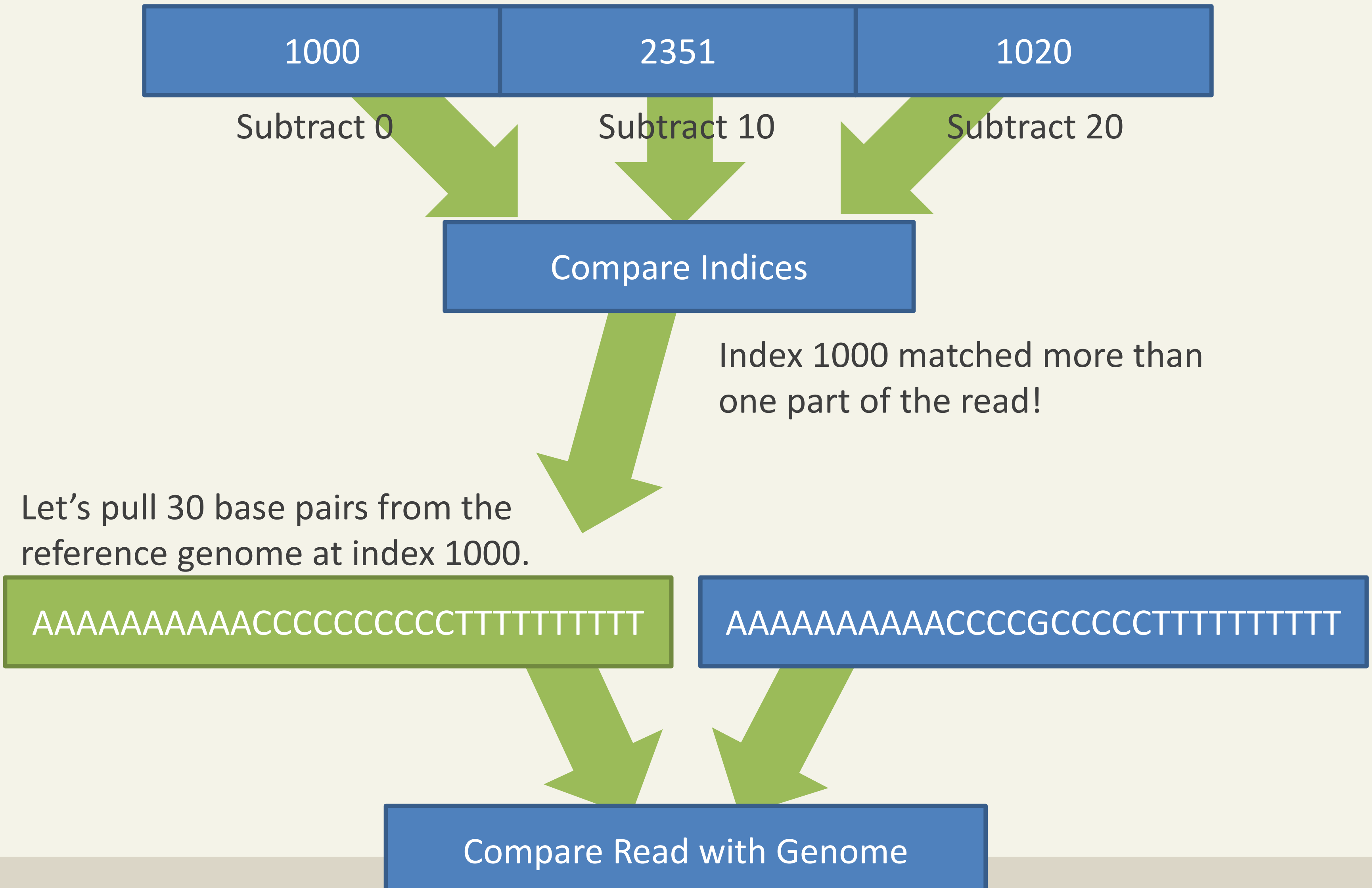
Future Work


100 base pair read
1/nth of the read
1/nth of the read
1/nth of the read
Hash Table Lookup
Hash Table Lookup
Hash Table Lookup
Index
Index
Index
Compare Indices

Future Work Example



Future Work Example



Future Work Example

- The comparison of the genome and a read is fairly simple in hardware for mismatches:
  - XOR the genome with the read
  - Count the number of 1's. If all 0's, it's an exact match.

- It becomes slightly more complex for insertions/deletions, but the same approach can be taken for comparison

Future Work Risks

- What affect will the presence of duplicates have on the alignment %?
  - At 100 base pairs, 2.36% of the genome is a duplicate of itself.
  - At 36 base pairs, 11% of the genome is a duplicate of itself.

- Let’s test in software and find out!

Conclusion (1/2)

- We implemented our own software to create MPH table:
  - Our Speed: 300,000 entries / sec
  - Other software (CHD): 800,000 entries / sec

- Future Work
  - Increase the speed to 250,000,000 entries / sec
  - This would allow us to make the pre-processing step part of the alignment process!
  - Instead of using a generic human reference genome, people may be able to use the DNA sequence of a blood family member as a reference in order to increase the percentage of exact matches.
  - The multi-port cache is useful IP for future projects utilizing the Convey HC-1 (allows atomic read-write)

Conclusion (2/2)

- We implemented our own hardware for read alignment:
  - Speed: 350,000,000 reads / sec
  - Alignment: 25%
  - About 60x speedup over SOAP3 (GPU)
  - Over 100,000x speedup over Bowtie (CPU)
  - Con: exact match only

- Future Work
  - Increase the alignment percentage by gaining the ability to detect mismatches, insertions, and deletions using the hashing approach.
  - This would make the project applicable to real-world sequence alignment. We can alter the pipeline without loosing too much speed.

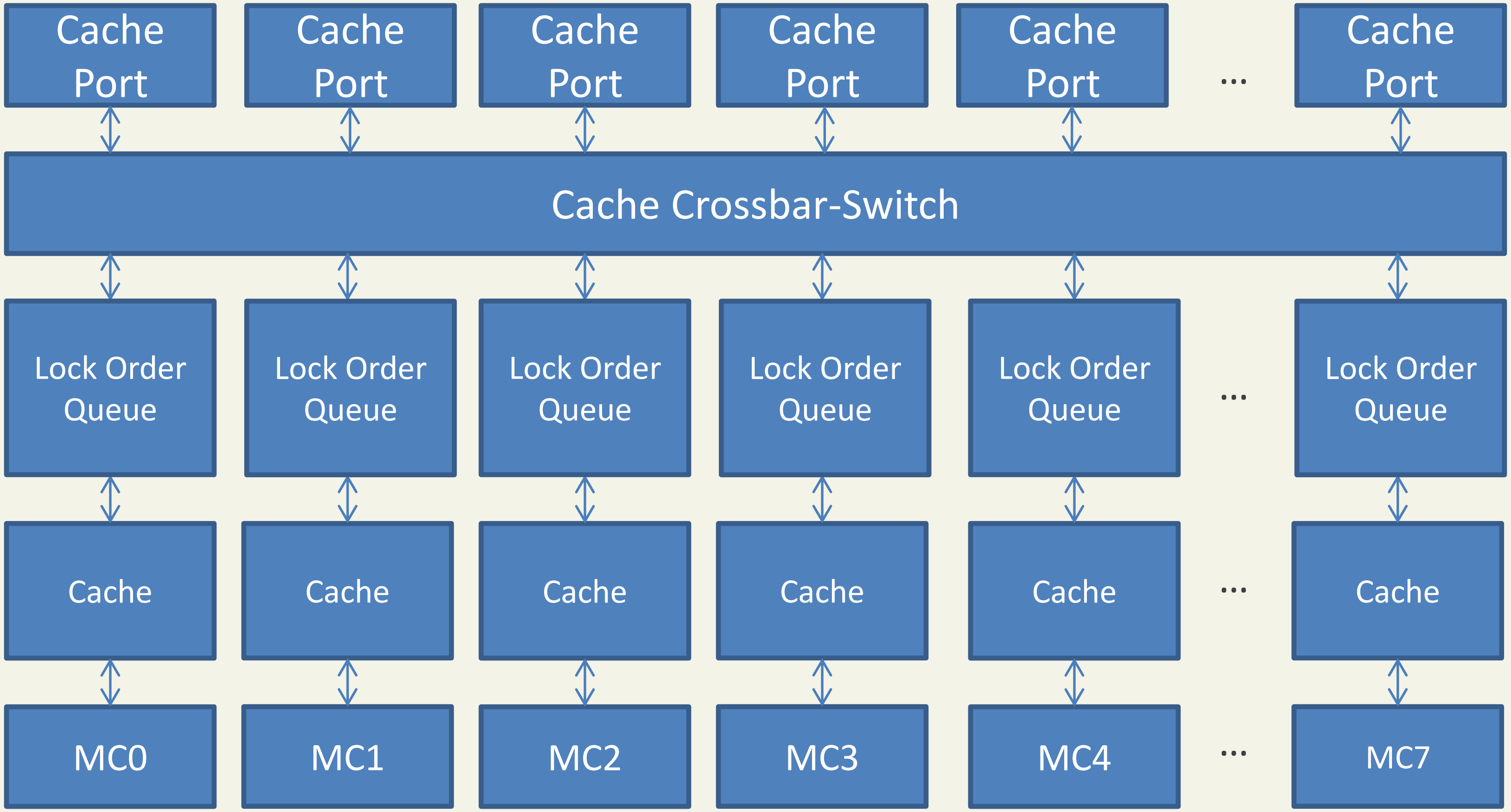
Questions

Future Work

Future Work - Concurrency Solution

- Divide the hash table and keys in four, one for each of the four FPGAs (AEs) on the Convey HC-1
  - Use the first two bits of the key to separate the hash table
  - Need to keep track of the size of each hash table, though they should be roughly the same size
  - This gets rid of AE to AE concurrency issues by separating the problem
- For stages 2, 4, and 5, implement a cache on each AE for handling the rare case of a concurrency issues.

Future Work - The Cache



Future Work - The Cache

- 16 Cache ports
- Use the Write Complete interface
- No crossbar, no read order queue, no strong order queue
- Write back on replace
- The cache would need the ability to Lock certain cache lines to a given Cache Port. Store the lock with the cache line.

- Lock Order Queue
  - If a request for a memory address comes in, and the cache is locked, the request waits until it is unlocked

- The cache will provide an **infrastructure** that we can use more generally in other projects utilizing the Convey HC-1. It allows strongly-ordered memory operations across multiple Memory Controllers.

Construction Algorithm Visualized!

Algorithm

- Stage 1 (create unique)
  – Create a list of all N of your <key, value> pairs to be added to the hash table
- Stage 2
  – Hash every key into a bucket to see which spaces in the hash table will have collisions
  – This amounts to having an array of size N initialized to all zeros. Then, you hash every key and increment the value at that index.
- Stage 2a
  – Count the number of buckets of each size. Since the max bucket size is small (< 20), this can be done during Stage 2.

Algorithm (Continued)

- Stage 3 (sorting)
  - Sort the keys by bucket size (largest to smallest)
  - Using the collision count values from stage 2 and the size of each bucket, this can be done in O(N) time.
- Stage 4 (reseed big buckets)
  - For each bucket size >= 2, starting with the largest, reseed the bucket
  - This involves initializing an bit array with all 0's.
  - For each bucket (contains 2 or more keys), rehash all the keys from the bucket with a new seed. Check the bit array that all keys have a spot in the final array
  - Store the new seed in the intermediate table.

Algorithm (Continued)

- Stage 5 (displace singular buckets)
  - For each bucket size = 1, find the next available empty space in the bit array
  - Place the key in this position, recording the offset from the original location in the intermediate table
- Stage 6 (add values to hash table)
  - The intermediate table is your a MPHF
  - Simply place the values in the final output table.

Example

- We are going to create a MPH Table for the following keys:
  - Armadillo
  - Bird
  - Cat
  - Dog
  - Elephant
  - Frog
  - Garage
  - Horse
  - Iguana
  - Jaguar

Stage 2

- Keys:
- Hash(seed=0)

Bucket Size	Number
0	10
1	0
2	0

Counts
0
0
0
0
0
0
0
0
0
0

Stage 2

- Keys:
  - Armadillo
- Hash(seed=0)
  - 1

Bucket Size	Number
0	9
1	1
2	0

Counts
0
1
0
0
0
0
0
0
0
0

Stage 2

- Keys:
  - Armadillo
  - Bird
- Hash(seed=0)
  - 1
  - 5

Bucket Size	Number
0	8
1	2
2	0

Counts
0
1
0
0
0
1
0
0
0
0

Stage 2

- Keys:
  - Armadillo
  - Bird
  - Cat

- Hash(seed=0)
  - 1
  - 5
  - 4

Bucket Size	Number
0	7
1	3
2	0

Counts
0
1
0
0
1
1
0
0
0
0

Stage 2

- Keys:
  - Armadillo
  - Bird
  - Cat
  - Dog
- Hash(seed=0)
  - 1
  - 5
  - 4
  - 8

Bucket Size	Number
0	6
1	4
2	0

Counts
0
1
0
0
1
1
0
0
1
0

Stage 2

- Keys:
  - Armadillo
  - Bird
  - Cat
  - Dog
  - Elephant
- Hash(seed=0)
  - 1
  - 5
  - 4
  - 8
  - 3

Bucket Size	Number
0	5
1	5
2	0

Counts
0
1
0
1
1
1
0
0
1
0

Stage 2

- Keys:
  - Armadillo
  - Bird
  - Cat
  - Dog
  - Elephant
  - Frog
- Hash(seed=0)
  - 1
  - 5
  - 4
  - 8
  - 3
  - 1

Bucket Size	Number
0	5
1	4
2	1

Counts
0
2
0
1
1
1
0
0
1
0

Stage 2

- Keys:
  - Armadillo
  - Bird
  - Cat
  - Dog
  - Elephant
  - Frog
  - Garage

- Hash(seed=0)
  - 1
  - 5
  - 4
  - 8
  - 3
  - 1
  - 9

Bucket Size	Number
0	4
1	5
2	1

Counts
0
2
0
1
1
1
0
0
1
1

Stage 2

- Keys:
  - Armadillo
  - Bird
  - Cat
  - Dog
  - Elephant
  - Frog
  - Garage
  - Horse

- Hash(seed=0)
  - 1
  - 5
  - 4
  - 8
  - 3
  - 1
  - 9
  - 5

Bucket Size	Number
0	4
1	4
2	2

Counts
0
2
0
1
1
2
0
0
1
1

Stage 2

- Keys:
  - Armadillo
  - Bird
  - Cat
  - Dog
  - Elephant
  - Frog
  - Garage
  - Horse
  - Iguana

- Hash(seed=0)
  - 1
  - 5
  - 4
  - 8
  - 3
  - 1
  - 9
  - 5
  - 0

Bucket Size	Number
0	3
1	5
2	2

Counts
1
2
0
1
1
2
0
0
1
1

Stage 2

- Keys:
  - Armadillo
  - Bird
  - Cat
  - Dog
  - Elephant
  - Frog
  - Garage
  - Horse
  - Iguana
  - Jaguar
- Hash(seed=0)
  - 1
  - 5
  - 4
  - 8
  - 3
  - 1
  - 9
  - 5
  - 0
  - 7

Bucket Size	Number
0	2
1	6
2	2

Counts
1
2
0
1
1
2
0
1
1
1

Stage 2

- Keys:
  - Armadillo
  - Bird
  - Cat
  - Dog
  - Elephant
  - Frog
  - Garage
  - Horse
  - Iguana
  - Jaguar

- Hash(seed=0)
  - 1
  - 5
  - 4
  - 8
  - 3
  - 1
  - 9
  - 5
  - 0
  - 7

Bucket Size	Number
0	2
1	6
2	2

Counts
1
2
0
1
1
2
0
1
1
1

Stage 3

- Keys:
  - Armadillo
  - Bird
  - Cat
  - Dog
  - Elephant
  - Frog
  - Garage
  - Horse
  - Iguana
  - Jaguar

Bucket Size	Number
0	2
1	6
2	2

New Index
-
-
-
-
-
-
-
-
-
-

Counts
1
2
0
1
1
2
0
1
1
1

Stage 3

- Keys:
  - Armadillo
  - Bird
  - Cat
  - Dog
  - Elephant
  - Frog
  - Garage
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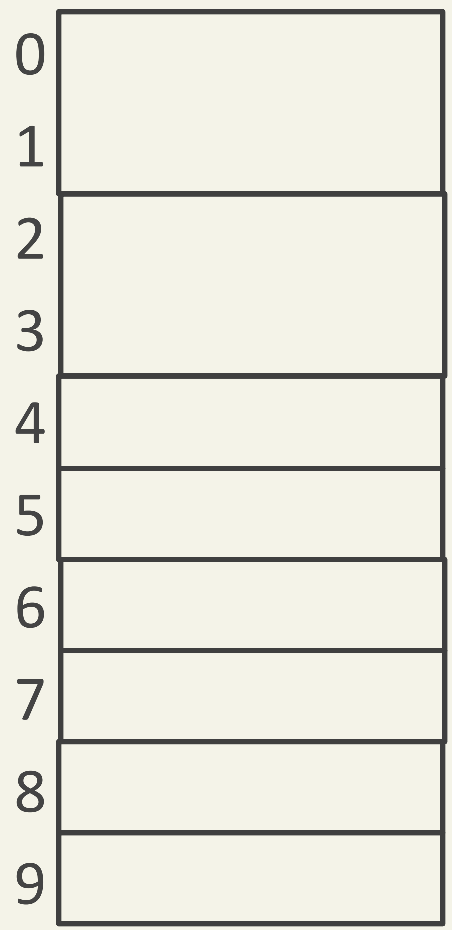

Bucket Size	Number
0	2
1	6
2	2

New Index
4
-
-
-
-
-
-
-
-
-

Counts
1
2
0
1
1
2
0
1
1
1

Stage 3

- Keys:
  - Armadillo
  - Bird
  - Cat
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  - Elephant
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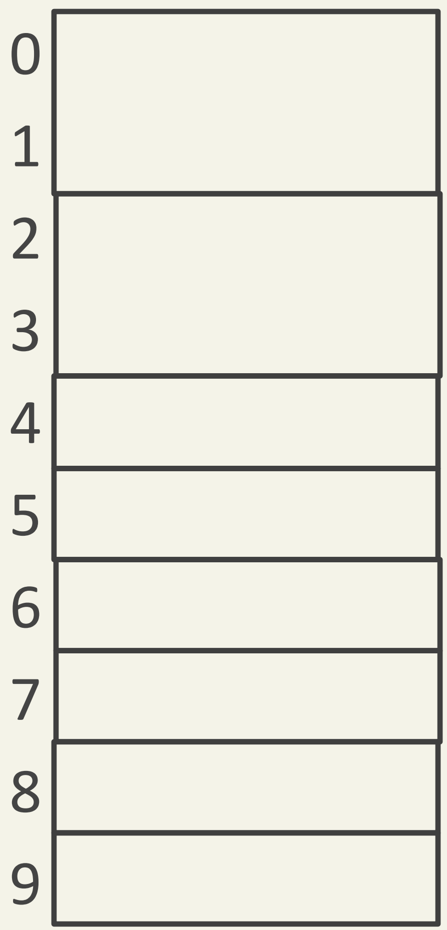
  - Horse
  - Iguana
  - Jaguar



Bucket Size	Number
0	2
1	6
2	2

New Index
4
0
-
-
-
-
-
-
-
-

Counts
1
2
0
1
1
2
0
1
1
1

Stage 3

- Keys:
  - Armadillo
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  - Elephant
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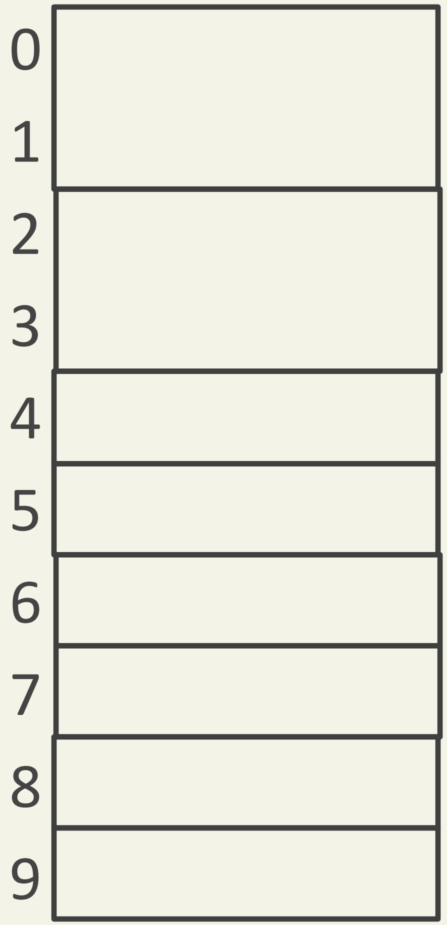

Bucket Size	Number
0	2
1	6
2	2

New Index
4
0
-
5
-
-
-
-
-
-

Counts
1
2
0
1
1
2
0
1
1
1

Stage 3

- Keys:
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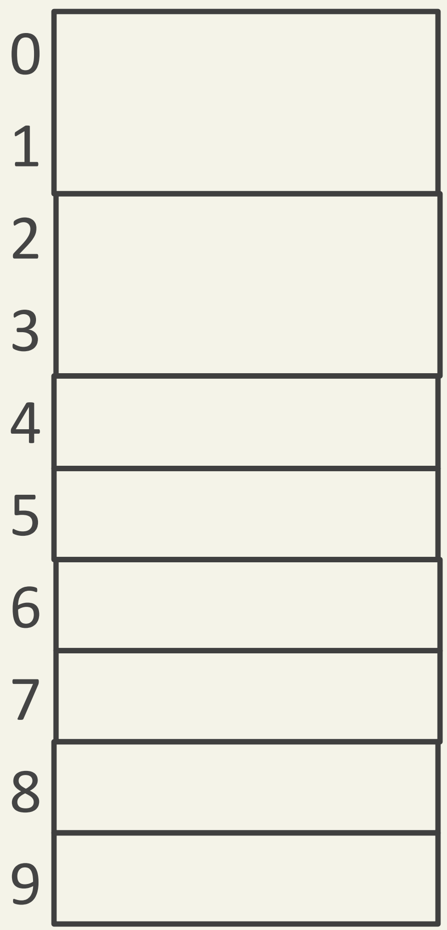

Bucket Size	Number
0	2
1	6
2	2

New Index
4
0
-
5
6
-
-
-
-
-

Counts
1
2
0
1
1
2
0
1
1
1

Stage 3

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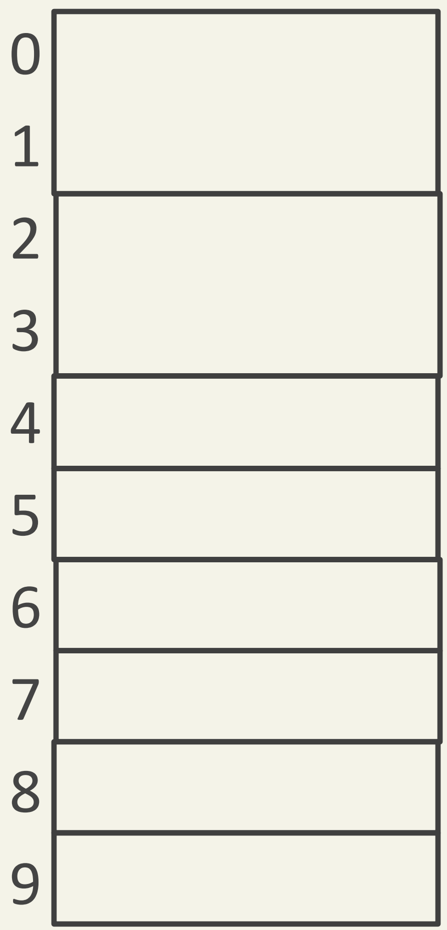

Bucket Size	Number
0	2
1	6
2	2

New Index
4
0
-
5
6
2
-
-
-
-

Counts
1
2
0
1
1
2
0
1
1
1

Stage 3

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  - Elephant
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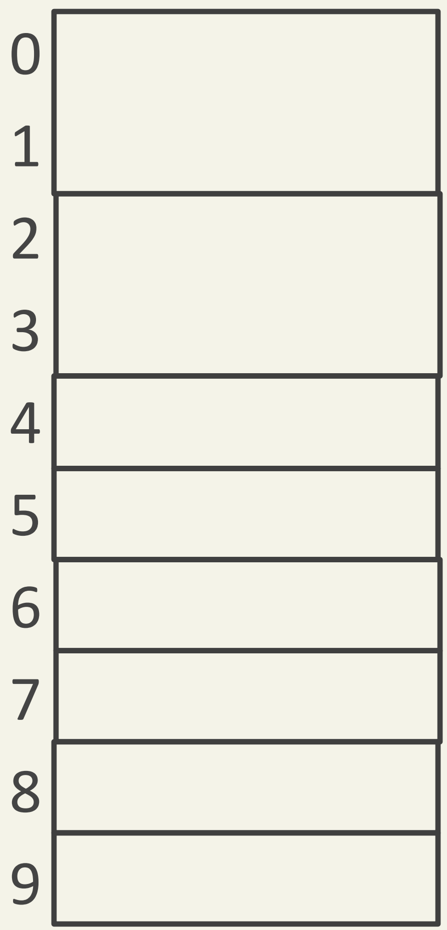
  - Horse
  - Iguana
  - Jaguar



Bucket Size	Number
0	2
1	6
2	2

New Index
4
0
-
5
6
2
-
7
-
-

Counts
1
2
0
1
1
2
0
1
1
1

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  - Garage
  - Horse
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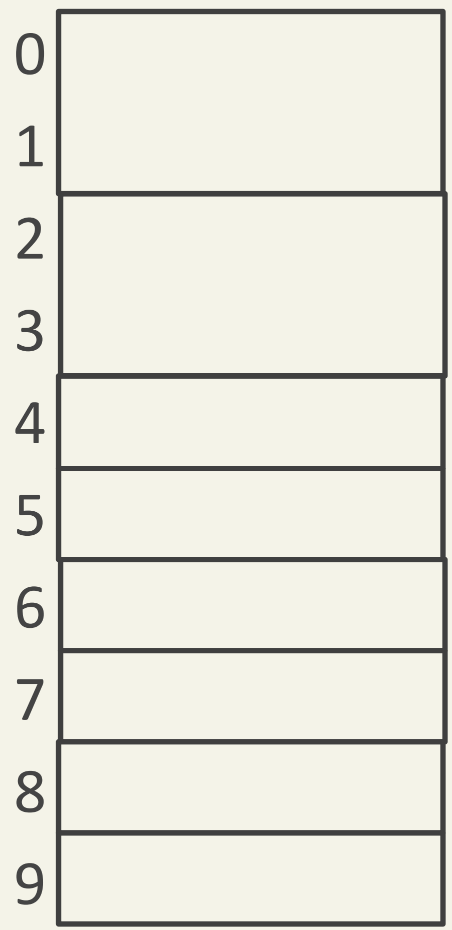


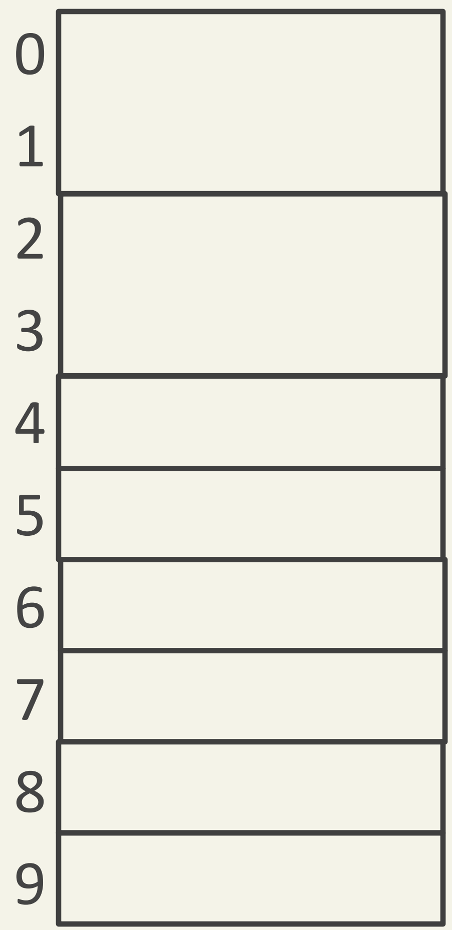
Bucket Size	Number
0	2
1	6
2	2

New Index
4
0
-
5
6
2
-
7
8
-

Counts
1
2
0
1
1
2
0
1
1
1

Stage 3

- Keys:
  - Armadillo
  - Bird
  - Cat
  - Dog
  - Elephant
  - Frog
  - Garage
  - Horse
  - Iguana
  - Jaguar



Bucket Size	Number
0	2
1	6
2	2

New Index
4
0
-
5
6
2
-
7
8
9

Counts
1
2
0
1
1
2
0
1
1
1

Stage 3

- Keys:
  - 1– Armadillo
  - 5– Bird
  - 4– Cat
  - 8– Dog
  - 3– Elephant
  - 1– Frog
  - 9– Garage
  - 5– Horse
  - 0– Iguana
  - 7– Jaguar

- Sorted Keys:
  - Armadillo
  - Frog
  - Bird
  - Horse
  - Iguana
  - Elephant
  - Cat
  - Jaguar
  - Dog
  - Garage

Bucket Size	Number
0	2
1	6
2	2

New Index	Counts
4	1
0	2
-	0
5	1
6	1
2	2
-	0
7	1
8	1
9	1

Stage 4

- From largest to smallest
  - Armadillo – 1 -> 2
  - Frog – 1 -> 7
  - Bird – 5
  - Horse – 5
  - Iguana – 0
  - Elephant – 3
  - Cat – 4
  - Jaguar – 7
  - Dog – 8
  - Garage – 9

Intermediate Table
0
0
0
0
0
0
0
0
0
0

Bit Array
0
0
0
0
0
0
0
0
0
0

Stage 4

- From largest to smallest
  - Armadillo – 1 -> 2
  - Frog – 1 -> 7
  - Bird – 5
  - Horse – 5
  - Iguana – 0
  - Elephant – 3
  - Cat – 4
  - Jaguar – 7
  - Dog – 8
  - Garage – 9

Intermediate Table
0
reseed = 1
0
0
0
0
0
0
0
0

Bit Array
0
0
1
0
0
0
0
1
0
0

Stage 4

- From largest to smallest
  - Armadillo – 1 -> 2
  - Frog – 1 -> 7
  - Bird – 5 -> 1
  - Horse – 5 -> 9
  - Iguana – 0
  - Elephant – 3
  - Cat – 4
  - Jaguar – 7
  - Dog – 8
  - Garage – 9

Intermediate Table
0
reseed = 1
0
0
0
reseed = 1
0
0
0
0

Bit Array
0
1
1
0
0
0
0
1
0
1

Stage 5

- From largest to smallest
  - Armadillo – 1 -> 2
  - Frog – 1 -> 7
  - Bird – 5 -> 1
  - Horse – 5 -> 9
  - Iguana – 0 -> 0
  - Elephant – 3
  - Cat – 4
  - Jaguar – 7
  - Dog – 8
  - Garage – 9

Intermediate Table
offset = 0
reseed = 1
0
0
0
reseed = 1
0
0
0
0

Bit Array
1
1
1
0
0
0
0
1
0
1

Stage 5

- From largest to smallest
  - Armadillo – 1 -> 2
  - Frog – 1 -> 7
  - Bird – 5 -> 1
  - Horse – 5 -> 9
  - Iguana – 0 -> 0
  - Elephant – 3 -> 0
  - Cat – 4
  - Jaguar – 7
  - Dog – 8
  - Garage – 9

Intermediate Table
offset = 0
reseed = 1
0
offset = 0
0
reseed = 1
0
0
0
0

Bit Array
1
1
1
1
0
0
0
1
0
1

Stage 5

- From largest to smallest
  - Armadillo — 1 -> 2
  - Frog — 1 -> 7
  - Bird — 5 -> 1
  - Horse — 5 -> 9
  - Iguana — 0 -> 0
  - Elephant — 3 -> 0
  - Cat — 4 -> 0
  - Jaguar — 7
  - Dog — 8
  - Garage — 9

Intermediate Table
offset = 0
reseed = 1
0
offset = 0
offset = 0
reseed = 1
0
0
0
0

Bit Array
1
1
1
1
1
0
0
1
0
1

Stage 5

- From largest to smallest
  - Armadillo – 1 -> 2
  - Frog – 1 -> 7
  - Bird – 5 -> 1
  - Horse – 5 -> 9
  - Iguana – 0 -> 0
  - Elephant – 3 -> 0
  - Cat – 4 -> 0
  - Jaguar – 7 -> 5
  - Dog – 8
  - Garage – 9

Intermediate Table
offset = 0
reseed = 1
0
offset = 0
offset = 0
reseed = 1
0
offset = -2
0
0

Bit Array
1
1
1
1
1
1
0
1
0
1

Stage 5

- From largest to smallest
  - Armadillo – 1 -> 2
  - Frog – 1 -> 7
  - Bird – 5 -> 1
  - Horse – 5 -> 9
  - Iguana – 0 -> 0
  - Elephant – 3 -> 0
  - Cat – 4 -> 0
  - Jaguar – 7 -> 5
  - Dog – 8 -> 6
  - Garage – 9

Intermediate Table
offset = 0
reseed = 1
0
offset = 0
offset = 0
reseed = 1
0
offset = -2
offset = -2
0

Bit Array
1
1
1
1
1
1
1
1
0
1

Stage 5

- From largest to smallest
  - Armadillo – 1 -> 2
  - Frog – 1 -> 7
  - Bird – 5 -> 1
  - Horse – 5 -> 9
  - Iguana – 0 -> 0
  - Elephant – 3 -> 0
  - Cat – 4 -> 0
  - Jaguar – 7 -> 5
  - Dog – 8 -> 6
  - Garage – 9 -> 8

Intermediate Table
offset = 0
reseed = 1
0
offset = 0
offset = 0
reseed = 1
0
offset = -2
offset = -2
offset = -1

Bit Array
1
1
1
1
1
1
1
1
1
1