Wide-SIMD Parallelization of Streaming Dataflow, with Applications to Bioinformatics

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Take-Home Message

• **Biological sequence analysis** is a source of high-impact computational problems

• Using SIMD parallel computing for these problems requires dealing with **irregularity**

• **MERCATOR** is an ongoing research effort to make irregular application development on SIMD platforms easier.
Who Am I?

• I study how to accelerate high-impact bioinformatics problems.

• One way to do this is via parallelization on modern architectures (FPGAs, GPUs, ...)

• Along the way, many interesting CS questions...
  – Streaming computation [FCCM’07, JVSP’07,M&M’09]
  – Systolic array design  [FPL’09,FCCM’10,ASAP’10]
  – Deadlock avoidance [SPAA’10,PPoPP’12,DFM’13,JPDC’17]
  – SIMD mapping [ISPDC’14,DFM’15,HPCS’17]
Talk Overview

• **Problems**: DNA comparison and read mapping

• Algorithmic approach – Why SIMD?

• MERCATOR overview and performance

• Research challenges
Molecular Biology is Fundamental

• **Genetic basis** of disease and disease risk
• **Systems biology** – what are your cells doing?
• Studying **natural history** and evolution
• **Engineering** cells’ behavior for medicine, industry, agriculture
The First Step: DNA Sequencing

• Sequencing can tell us what is in a genome...

• ... but also the basis of experiments to probe gene expression, protein binding, chromosome conformation, epigenetic marks, polymorphism, copy number variants ...
**Cost per Raw Megabase of DNA Sequence**

The graph shows the decreasing cost of sequencing DNA over time, following Moore's Law. The cost has decreased from over $10K in 2001 to less than $0.1 in 2017. The graph is sourced from the National Human Genome Research Institute (NIH) and can be found on genome.gov/sequencingcosts.
Problem: Classical Similarity Search

• Given
  – a genome-sized or larger DNA sequence database \( D \)
  – a “query” sequence \( q \) of some length \( L \ll |D| \)

• Does \( q \) appear in \( D \) with at most \( k \) differences, and if so, where?
Typical Parameters

• Database D has size $10^9 - 10^{10}$ bases

• Query q has size $10^2 - 10^4$ bases

• # differences k is 5-25% of $|q|$ (bases added, deleted, changed)
Tools for Similarity Search

- **BLAST** [Altschul et al. 1990, 1996]
- **BLAT** [Kent 2002]

*These tools use variants of same basic search algorithm.*
Problem: Short-Read Mapping

• Given
  – a genome-sized or larger DNA sequence database $D$
  – $N$ “reads” – DNA seqs of some length $L << |D|$

• For each read, *does it appear in $D$ with at most $k$ differences*, and if so, where?
Typical Parameters

• Database D has size $10^9 - 10^{10}$ bases

• Number of reads N is $10^6 - 10^8$

• Length L is 75-150 (may vary among reads)

• # differences k is 0-3 (added, deleted, changed)
Tools for Mapping

- **Bowtie** [Langmead et al. 2009, 2012]
- **BWA** [Li & Durbin 2009, 2010]
- **SOAP2** [Li et al. 2009]

All these tools use variants of same basic search algorithm.
Why Short-Read Mapping?

• Some experimental procedure selects a subset of everything in the database

• Reads are sampled from this subset by your sequencing machine

• Mapping tells you which parts of database are present in your sample
Problem: Alignment-Free Organism ID

• Given
  – a metagenome-sized DNA sequence database $D$
  – $N$ microbial genomes – DNA seqs of some length $L << |D|$

• For each genome, do (some of) its sequences appear in $D$?
Alignment-Free Techniques

• **Min-Hash Sketching** – convert a seq to a small sample (m ~ 1000) of hash values

• **Approximate Containment**: how much of (the sketch for) a genome overlaps (the sketch for) a metagenome?

• MASH (Ondov et al. 2016)
• SourMASH (Brown et al. 2016)
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BLAST operates as a pipeline of computational stages.
Stages of BLAST

• Stage 1: identify *potential match locations* between q, D

• Stage 2: keep only those locations that look somewhat promising

• Stage 3: keep only those locations that actually yield high-similarity alignments
Generating Possible Matches

• Every place where some 11-mer from q matches an 11-mer from D exactly is a candidate.

  accagataca
tagcactcgc
tacgtcagatg
ggttaca

gttaagt
cagatg

gggttagactcag
gattgacag
tggaca

• Can rapidly find all such matching locations using hash table of 11-mers in sequence q
Filtering Candidates

• Uses explicit edit distance computation between q, part of D (Smith-Waterman algo)

• Expensive dynamic programming!

• “Easy” version (substitutions only), followed by hard version (add/delete chars allowed)
BLAST Parallelization

- Can generate candidates in parallel at each DB location, then filter them in parallel.
What About Read Mapping?

• Uses an index (virtual suffix tree) of database

• Matching involves tracing a path down index tree for each read

• (must try several paths if differences are allowed)

• *Can do in parallel for many reads at once!*
Suffix Tree Example

D = acagaccaga$

A

10 $
9 a$
0 aca...
4 acc...
7 aga$
2 agac...
6 caga$
1 cagac...
5 cca...
8 ga$
3 gac...

T
Rapid Matching vs Suffix Tree

• Can find all matches to a read in D in time proportional to read length $L$. Where is $cag$?
Rapid Matching vs Suffix Tree

- Can find all matches to a read in D in time proportional to read length $L$. 

Where is $cag$?
Rapid Matching vs Suffix Tree

- Can find all matches to a read in D in time proportional to read length L.
Rapid Matching vs Suffix Tree

- Can find all matches to a read in D in time proportional to read length L.

Where is cag?
Rapid Matching vs Suffix Tree

- Can find all matches to a read in D in time proportional to read length L.

Where is cag?

D = acagaccagaga$
Extension to Inexact Matching

• To permit matches with k substitutions, try multiple paths, but charge for each mismatch.

• To permit matches with k differences, we do dynamic programming to compute edit distance of read against each path in tree.

• Descent stops for a read when we hit bottom of tree or find that path requires > k differences.
Parallel Alignment is a SIMD Computation

• We process every BLAST starting loc / every read through *same* filtering computation

• *Single Instruction stream, Multiple Data items*
SIMD Targets

• Our work: **NVIDIA GPUs**
  (32 SIMD lanes x 4+ threads x 2-64 cores)

• Other possibilities: any multicore with wide vector instructions (Intel Xeon, AMD, ARM, ...)

• ~All modern processors have wide SIMD!
Batched Traversal (Short Reads)
Batched Traversal
Batched Traversal

Some reads may accumulate > k diffs before others
Batched Traversal

![Diagram showing batched traversal with numbers 9, 0, 4, 7, 2, 6, 1, 5, 8, 3 arranged in a tree structure.]
Batched Traversal

Stop descending when all reads either have > k diffs or are completely matched with fewer diffs
Batched Traversal

Continue on next branch starting from batch on top of stack
Batched Traversal
Batched Traversal
Batched Traversal
Performance?

• Each stage of BLAST costs more but processes less input.

• 98% of threads idle for 110/111 ms
• 1.99% of threads idle for 100/111 ms
• SIMD EFFICIENCY: 1.1%
Irregular Computations

- DNA alignment is an **irregular** computation: different inputs (*i.e.* DB locations, reads) require different amounts of work to process.

- Antithesis of, e.g., linear algebra calculations that are easily vectorized

- **Irregular computations are highly inefficient if naively implemented on SIMD processors.**
The Key Problem

• How can we *efficiently* map irregular computations onto a SIMD architecture?
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Pause for MERCATOR demo
MERCATOR Paradigm

• Application processes a long stream of inputs

• Application graph consists of nodes (computations), edges (data transfer)

• Data flows through graph of computations

• Irregularity: paths differ per input, each input to a node generates 0, 1, or multiple outputs
Handling Irregularity

• Each edge between nodes has a **queue**

• MERCATOR queues inputs to a node until there are enough to fill all its SIMD lanes

• Node is only fired when it has “full ensemble” of inputs in all lanes.
Illustration of Queues
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A Few Complications

• **Shared Code** – two or more nodes may do same thing (e.g. Viola-Jones)

• **Overhead** – queueing isn’t free

• **Asynchrony** – must use multiple processors, each with multiple SIMD lanes

• **Ordering** – are inputs processed “in order”? 
Exploiting Shared Code

• “Module type” ↔ CUDA code

• Multiple nodes with same function have same module type

• *We execute all nodes of a given module type in parallel!*

• [Requires pulling data from each node’s queue concurrently]
Minimizing Overhead

• Queue manipulation is itself parallelized

• Easy case: “read next k inputs from queue into threads 1..k.”

• More fun: “read k total inputs from all queues combined into threads 1..k, and remember which queue each input came from.”
Sneaky Tricks

- Parallel scan
- Branch-free binary search
- Parallel output compaction
  - \([\text{exploits, maintains input ordering}]\)
Results of Synthetic Trial

![Graph showing the results of a synthetic trial. The graph is a 3D surface plot with axes for Filtering rate, Workload (μs per node), and Speedup. The plot demonstrates how speedup changes with varying filtering rates and workloads.]
Dealing with Asynchrony

• Shared input / output buffers

• Output order with multiple processors?

• [Need stream-synchronized signaling]

• Associative (and commutative?) reductions
Applications with Cycles

• App graph can have back edges

• Issue: deadlock prevention

• [topology restrictions, queueing policy]

• Order preservation?
Optimization Opportunities

• Parameter tuning (queue sizes, scheduler, ...)

• Latency-sensitive applications vs occupancy

• Fusing nodes to elide queueing (at what cost to occupancy?)
Want to Play?

• [https://github.com/jdbuhler/mercator](https://github.com/jdbuhler/mercator)

• MERCATOR will be a testing ground for SIMD-aware irregular streaming computation

• Many interesting problems still to be solved!

• → thesis topics