High Performance Computing and Storage Trends in Life Sciences

SDSC Technology Forum 5/24/18

Robert Sinkovits
San Diego Supercomputer Center
SDSC – a pioneer in supercomputing

- Established as a national supercomputer resource center in 1985 by NSF
- Grant revenues (~$30M/year)
- Employees (~250)
- World leader in data-intensive computing and data management

SDSC Census FY2016

- Total 532
- 67 Affiliates
- 53 Undergrads
- 115 Volunteers
- 50 Others
- 30 Academics (incl. Post Docs)
- 21 Grad Students
- 196 Staff
What does SDSC have to offer

• SDSC operates one of the most powerful supercomputers available to U.S. academic researchers (Comet). This is accompanied by 7 PB of high performance storage.
• SDSC’s Health Cyberinfrastructure Division provides a secure cloud computing environment for working with sensitive data
• We have expertise in many areas of high performance computing, including
  • Software parallelization and optimization
  • Visualization
  • Workflow development
  • Science Gateway (web interfaces to supercomputing) development
• Opportunities for collaboration between domain experts (you) and computational scientists (us)
• We provide training in various formats (half-day workshops, webinars, onsite visits, summer institutes) covering topics in high performance and data intensive computing.
SDSC’s Supercomputers in 1985 and 2018

SDSC builds and maintains some of the largest supercomputers available to academic researchers in the U.S.

1985
Cray XMP-48
800 MFlops

2018
Dell Comet
2.76 PFlops
HPC Today

- **Traditional HPC Disciplines**
  - Physical Sciences
  - Engineering

- **Scientific Applications**
  - Computational fluid dynamics
  - Seismology
  - Climate and weather simulations
  - Structural mechanics and reactive flow

- **Optimized for large files and sequential data access**

*Life Sciences changes things*
Comet overview

Dell PowerEdge R730 GPU nodes

Dell C6320 compute nodes

2 x 160 GB SSD (Intel DC S3500) per node
Comet overview

- **Total peak performance ~2.76 PFlops**
- **Dell primary integrator**
  - Intel Haswell processors w/ AVX2
  - Mellanox FDR InfiniBand
- **1,944 standard compute nodes (46,656 cores)**
  - Dual CPUs, each 12-core, 2.5 GHz
  - 128 GB DDR4-2133 DRAM
  - 2 x 160 GB SSDs (local disk)
- **72 GPU nodes**
  - Same as standard nodes *plus*
  - 36 w/ two dual-GPU NVIDIA K80s
  - 36 with four NVIDIA P100s (June ‘17)
- **4 large-memory nodes**
  - 1.5 TB DDR4-1866 DRAM
  - Four 16-core Haswell processors/node
- **Hybrid fat-tree topology**
  - FDR (56 Gbps) InfiniBand
  - Rack-level (72 nodes, 1,728 cores) full bisection bandwidth
  - 4:1 oversubscription cross-rack
- **Performance Storage (Aeon)**
  - 7.6 PB, 200 GB/s; Lustre
  - Scratch & Persistent Storage segments
- **Durable Storage (Aeon)**
  - 6 PB, 100 GB/s; Lustre
  - Automatic backups of critical data
- **Home directory storage**
- **Gateway hosting nodes**
- **Virtual image repository**
- **100 Gbps external connectivity to Internet2 & ESNet**
IT Infrastructure Affects the Pace of Scientific Discovery

- **Life Sciences Data Sets**
  - Random and sequential access patterns
  - Small and large files
  - Low latency

- **Flexible Infrastructure**
  - High performance file system
  - Flash based storage
  - Cloud scalability

- **Results**
  - Support for advanced analytics
  - Improved researcher productivity
  - Reduced time to discovery

*Ideal for flash technology*
CC* BioBurst for TSCC

- NSF Campus Cyberinfrastructure (CC*) Award (ACI-1659104)
- Objective is to augment campus cluster (TSCC) with capabilities to address the growing bioinformatics workload
- Award value: $500K
- Award start date: Feb 1, 2017
Objective

• The overall objective of BioBurst
  • Improve research productivity by providing a separately-scheduled campus computing resource designed to address performance bottlenecks found in a class of applications important to campus researchers, including genomics, transcriptomics, and other bioinformatics pipelines.

• Specifically, the small block / small file I/O problem with codes such as GATK
Key Features

More specifically, BioBurst will incorporate the following major components and operational characteristics:

• A software-defined I/O accelerator appliance with 40 terabytes of non-volatile (“flash”) memory and software designed to alleviate the small-block/small-file random access I/O problem characteristic of many bioinformatics codes;
  - Derived from Exascale program “burst buffer” technology
• An FPGA-based computational accelerator node (Edico Genome DRAGEN) that has been shown to conduct demultiplexing, mapping, and variant calling of a single human genome in 22 minutes as compared to ~10 hours on standard computing hardware [2];
• 672 commodity (x86) computing cores providing a separately scheduled resource for running various bioinformatics computations;
• Integration with a Lustre parallel file system, which supports streaming I/O, and has the capacity to stage large amounts of data characteristic of many bioinformatics studies
Overall Architecture
More Detail

DDN IME System

Home File System
40 TB

10GbE Switch

Juniper EX4550
32-port

10GbE Switch

EDR IB Switch

Mellanox MSB-7700
36-port

I/O Accelerator

Core Ethernet Switch

Core Ethernet Switch

Lustre Parallel File System
650TB

Arista 7508

New Capability

100 Gb/s InfiniBand

40 Gb/s Ethernet

10 Gb/s Ethernet

NODES:
- 2 x 14-core Xeon
- 128GB DRAM
- 480GB SSD
- 1 x EDR IB
- 1 x 10GbE

DRAGEN NODE:
- FPGA Accelerator
- Custom Firmware

DDN IME System

DDN STORAGE

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IME® I/O Acceleration Architecture

IME’s Active I/O Tier, is inserted right between compute and the parallel file system.

IME software intelligently virtualizes disparate NVMe SSDs into a single pool of shared memory that accelerates I/O, PFS & Applications.

Slide used with permission of DDN
DRAGEN Bio-IT Platform

DRAGEN is a fully reconfigurable FPGA-based platform that can be reconfigured in seconds to host a number of different highly optimized analysis pipelines.

**Ultra-Rapid Genomic Analysis Platform**

- The power of the platform makes it possible to perform an extremely fast and accurate secondary analysis, which results in significant cost savings.
- Pipelines currently available include Whole Genome, Exome, RNASeq, Methylome, Microbiome, Joint Genotyping, Population Calling, Cancer and more.
- DRAGEN accepts FASTQ/BCL, and BAM/CRAM files as input and provides output in standard BAM/VCF/gVCF file formats.
- DRAGEN offers supreme flexibility of data analysis with both the ability to stream BCL data directly from sequencer storage.
- DRAGEN also offers the ability to convert BCL to FASTQ or BAM/CRAM. DRAGEN can read and output compressed or uncompressed files.

Slide used with permission of Edico Genome
### DRAGEN Node Test Results

<table>
<thead>
<tr>
<th>Pipeline</th>
<th>Sample #1 (whole human genome, 48X coverage) Time to Completion in hours</th>
<th>Sample #2 (whole human genome, 49.5X coverage), Time to Completion in hours</th>
</tr>
</thead>
<tbody>
<tr>
<td>SDSC Comet</td>
<td>52.5</td>
<td>Runtime not evaluated on Comet</td>
</tr>
<tr>
<td>Bioburst/DRAGEN</td>
<td>1.5</td>
<td>2</td>
</tr>
</tbody>
</table>

**Notes:**

1. The SDSC Comet pipeline consisted of the following steps/tools for Sample #1:

<table>
<thead>
<tr>
<th>Step</th>
<th>Tool</th>
<th># Cores</th>
<th>Runtime (hours)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>BWA</td>
<td>24</td>
<td>8</td>
</tr>
<tr>
<td>2</td>
<td>MarkDups (Sambamba)</td>
<td>6</td>
<td>3.5</td>
</tr>
<tr>
<td>3</td>
<td>Indel Realignment</td>
<td>2</td>
<td>11</td>
</tr>
<tr>
<td>4</td>
<td>BQSR Step 1</td>
<td>12</td>
<td>3</td>
</tr>
<tr>
<td>5</td>
<td>BQSR Step 2</td>
<td>2</td>
<td>12</td>
</tr>
<tr>
<td>6</td>
<td>GATK 3.6 Haplotype Caller</td>
<td>12</td>
<td>15</td>
</tr>
</tbody>
</table>

2. The BioBurst/DRAGEN pipeline consisted of the Edico Genome map/align and variant calling pipeline implementation (version 2.5.3) running on the single BioBurst DRAGEN node.
IOR Benchmark (IME vs. Lustre)
GATK (IME vs. Lustre)

GATK (4/node): LFS vs IME on 1 node

- LFS
- IME

Percentage of analysis completed

Hours
Comet awards by NSF domain

Molecular bioscience (MCB), primarily molecular dynamics simulations, accounts for the largest fraction of Comet usage.

Much of the work in chemistry (CHE) involves quantum simulations of systems of interest to life science researchers.

Chemical and Thermal Systems (CTS) also encompasses many of the molecular dynamics simulations being carried out on proteins, lipid bilayers and other biological systems.
Structural variants associated with autism

Whole genome sequencing of 9274 subjects from 2600 families show that inherited structural variations are preferentially transferred to affected offspring.

Brandler et al., Science 360 327-331 (2018)
Blocking cancer pathways

Researchers from UCSD School of Medicine and SDSC carried out quantum chemistry simulations showing that Cisplatin can block the MEK 1/2 cellular signaling pathway, thereby blunting the effects of KRAS and BRAF oncogenes.

Platinum (large light grey sphere) in Cisplatin outcompetes copper to bind in a therapeutic way with MEK (mitogen-activated protein kinase) and block a cancer-causing pathway (sulfur = yellow, nitrogen = blue, hydrogen = white spheres). Image courtesy of Andreas Goetz and Igor Tsigelny, SDSC.

Yamamoto, Tsigelny, Goetz and Howell, Oncotarget 2015 6 (27), http://dx.doi.org/10.18632/oncotarget.4355
Understanding ion channels

Klaus Schulten (U. Illinois) uses Comet to study ion channels, membrane proteins found in all three domains of life (bacteria, archaea, eukaryotes) that are essential for basic cellular processes.

Glutamate ions (blue spheres) permeating bacterial (E. coli) mechanosensitive channel of small conductance (MscS) protein channel
Binding enthalpy calculation

Michael Gilson’s lab (UCSD) is using Comet’s GPU nodes to calculate the binding enthalpy and free energy for host-guest systems – small cavity shaped molecules that bind other small molecules.

Structure of host (left) and guest (right). The protonation state is shown for each guest and reflects the dominant species under experimental conditions.

Simulations of biological membranes

Wonpil Im (U. Kansas) has been making extensive use of Comet to perform molecular dynamics simulations on biological membranes to study their mechanical properties and the interactions between lipids and proteins.

This work can lead to a better understanding of how amyloid plaques form in the brains of Alzheimer patients
Protein Lyophilization (freeze-drying)

Pablo Debenedetti (Princeton) uses Comet to study lyophilization (freeze-drying), a standard technique used to increase the storage life of labile biochemical, including therapeutic proteins, by the pharmaceutical industry.

Top left: Trp-cage miniprotein structure. Top right: Mean-squared fluctuation for each residue in Trp-cage for the hydrated and dehydrated powder system. Bottom left: Lysozyme protein structure. Bottom right: Water sorption isotherm for lysozyme.
Self-cleavage of bacterial ribozyme

Sharon Hammes-Schiffer (UIUC) uses Comet’s GPU nodes to perform molecular dynamics simulations of the self-cleavage reaction of the *glmS* ribozyme, which is essential for hydrocarbon synthesis in gram positive bacteria.

The *glmS* ribozyme structure shown and its active site. Red arrows indicate reaction directions: A-1(O2') is deprotonated by a general base and attacks the scissile phosphate, while G1 is protonated by the cofactor GlcN6P and eventually dissociates.
Studying flu at the molecular scale

Rommie Amaro (UCSD) uses Comet to understand how molecular structure of the flu virus affects infectivity.

Atomic model built from experimentally determined structure. Brownian dynamics then used to understand how glycoprotein stalk height impacts substrate binding.

Alasdair Steven, NIH
PDB_REDO – more accurate X-ray structures

The PDB_REDO project (Anastassis Perrakis, Netherlands Cancer Institute, with support from Janssen) aims to periodically update all X-ray structures in the PDB using more accurate algorithms. The calculations on the larger structures require Singularity and access to Comet’s large memory nodes.

PDB ID 3ZFE: Human enterovirus 71 in complex with capsid binding inhibitor WIN51711

PDB ID 1O04: Cys302Ser mutant of human mitochondrial aldehyde dehydrogenase complexed with NAD+ and Mg2+

PDB ID 1GKP: D-hydantoinase (Dihydropyrimidinas E) from Thermus Sp.
CIPRES phylogenetics gateway

- >19,000 CIPRES users have run on NSF-funded supercomputers, including >7,500 in the past year!
- >2,700 publications have been enabled by CIPRES use!

- **US statistics from 2015**
  - 49 states + 2 territories + DC
  - 252 universities & colleges
  - 18 institutes
  - 22 museums, gardens, & zoos
  - 21 government agencies
  - 4 high schools

- **Non-US statistics from 2015**
  - 85 countries
  - 603 universities & colleges
  - 161 institutes
  - 80 museums, gardens, & zoos
  - 134 government agencies
Tree was generated with RAxML on 48 cores of Comet in a 3-day run via CIPRES.

Phyla with red dots are based upon metagenomic analyses without isolated representatives.

<- You are here in Opisthokonta, which includes animals & fungi.
Thank You