Towards a Portable Drug Discovery Pipeline with SYCL 2020

Luigi Crisci, Majid Salimi Beni, Biagio Cosenza – University of Salerno
Nicolò Scipione, Davide Gadioli, Emanuele Vitali, Gianluca Palermo – Politecnico di Milano
Andrea Rosario Beccari – Dompé Farmaceutici S.p.A.

This project has received funding from the European High-Performance Computing Joint Undertaking (JU) under grant agreement No 956137. The JU receives support from the European Union’s Horizon 2020 research and innovation programme and Italy, Sweden, Austria, Czech Republic, Switzerland.
Outline

• Introduction to LiGen
  • Virtual screening
  • The LiGen drug discovery processing pipeline
• Towards a portable pipeline
  • Porting from CUDA to SYCL 2020
  • Exploiting SYCL 2020 features
• Experimental evaluation
  • Application performance
  • USM vs accessors
  • Performance portability (NVIDIA V100, AMD M100, Intel Xeon)
• Conclusion

https://www.ligateproject.eu/
Virtual Screening

• Initial stages of the drug discovery process
• Ligand: small molecule with usually less than 100 atoms
• Can be viewed as a graph
  • Atoms as vertices
  • Bond as edges
• Can be generated by chemical reactions
• Drug Candidate

Arachidonic Acid ligand example

https://www.ligateproject.eu/
Virtual Screening

- A protein is a molecule that is composed of one or more chains of amino acid residues
  - Tens of thousands of atoms
- Proteins perform a vast array of functions within organisms:
  - Catalysing metabolic reactions,
  - DNA replication,
  - Providing structure to cells and organisms
  - Transporting molecules from one location to another.
- Drug’s target

https://www.ligateproject.eu/

A representation of the 3D structure of the protein myoglobin
Virtual Screening

• A ligand bound into empty spaces of a protein associated with the target disease can change its behaviour, and hence the outcome of disease.

• Virtual screening aims at selecting the most promising ligands from a huge set of possible candidates
  • To forward to the next stages of drug discovery
Virtual Screening

Challenges:

• Evaluate as much ligand candidates as possible

• The bond strength depends on the ligand’s atoms 3D displacement when it interacts with target protein
  • We need to “dock” before “score” it

• A ligand can be change its shape
  • Multiple way to dock the same ligand

Reference
Unfolded
Two conformations of the Arachidonic Acid.
Dock & Score

Molecular Docking as “Relaxed” lock and key model:
- Protein considered a rigid body
- Ligand considered a flexible body
- A ligand is docked on target protein’s binding sites
- Multiple pose for each ligand

Arachidonic Acid bound to the Cyclooxygenase active site of COX-2

https://www.ligateproject.eu/
Dock & Score

**Additive Chemical score**

- Used to evaluate likeness of ligand (pose)-pocket bond
- Takes into account Atomic interactions
  - VdW,
  - Lennard-Jones
  - Metal bonds
  - Hydrogen bonds
  - Solvation effects;

https://www.ligateproject.eu/
LiGen: Ligand Generator Platform

The LiGen drug discovery framework
- Owned by Dompe Farmaceutici and co-developed by PoliMi and CINECA
- used for the discovery of drug against different pathogens
  - Zika [ANTAREX], SARS-CoV-2 [EXSCALATE4COV]

LiGen processing pipeline
- Dock & score as an embarrassing parallel task
- Process each molecule in a pocket, which is a region of interest inside a protein.
- A protein can have multiple pockets and they may have different conformational states, abstracted as different pockets.

https://www.ligateproject.eu/
The LiGen Drug Discovery Pipeline

https://www.ligateproject.eu/
Towards a Portable Pipeline

• The LIGATE project aims at building a portable drug discovery pipeline
  • Funded from the European High-Performance Computing Joint Undertaking Joint Undertaking (JU)
• HPC is heading toward specialization and extreme heterogeneity
• SYCL enables to write platform independent code, while keeping native-comparable performance
Porting from CUDA to SYCL2020

- Originally implemented in C++, then ported to OpenACC and CUDA
- 17 CUDA kernels, dozens of device functions
  - Most kernels have dependency from the previous one
  - Minimal overlapping
- Porting features from CUDA
  - Warp-level primitives -> SYCL 2020 subgroups
  - Custom reductions -> SYCL 2020 reductions
  - Custom group algorithms (all_of, any_of, etc.) -> SYCL2020 group algorithms
  - Dynamic parallelism -> removed without performance difference

https://www.ligateproject.eu/
Exploiting SYCL 2020 Features

• Supporting both Unified Shared Memory (USM) and accessor-based memory management
• Sub-group shuffles and collectives allow us to write more efficient and concise code
• Group algorithms raise efficiency and improve performance portability among architectures
• Reduction native support avoid boilerplate code and improve performance

By using SYCL 2020 reduction and group algorithms we removed more than 430 lines of code

https://www.ligateproject.eu/
Performance Tuning

• Application tuning
  • Block size and number of iteration of the heaviest kernels depending on workload type
  • Up to the scheduler
• Kernel tuning
  • Limited tuning due to high register pressure (e.g., unrolling not effective)
  • Workgroup size
  • Blocking, local memory usage
• Accessors vs USM
  • We developed two version of LiGen, using either Accessor or USM

https://www.ligateproject.eu/
Experimental Setup

• SYCL versions
  • hipSYCL (sha 1046a78777a23ca75c6ea4e92291f1dbe36169ca)
  • DPC++ (release 2021-12)

• Hardware
  • Nvidia Setup
    • IBM POWER9 AC922 at 2.6(3.1) GHz
    • NVIDIA Volta V100 GPU
    • Cuda 11.0
  • AMD Setup
    • Intel Xeon Gold 5218 CPU @ 2.30GHz
    • AMD MI100 GPU

https://www.ligateproject.eu/
Application Performance Evaluation

- **Optimize-fragment kernel**
  - Takes up to 95% of the device time
  - Called iteratively
  - Subgroup reduction, then reduction over group, then reduction across groups
  - Subgroup shifting and reductions
  - About 420 lines of code
  - High register pressure

- **Hb-score kernel**
  - Takes 2.2% of the device time
  - Mostly due to group sorting

---

https://www.ligateproject.eu/
Accessor vs USM Evaluation

• USM version
  • memory management is similar to the CUDA implementation
  • Buffers allocated and initialized at the start
  • Deallocated all together at the end
• Accessor
  • defines each buffer at the start
  • Initialization is managed by the runtime
• No significant differences in the kernel implementations
• Accessor version similar performance compared to the USM version

[Graph showing comparison between Accessors and USM]
Accessors vs USM Evaluation

- Example with DPC++ / PTX backend, on a Tesla V100
- Accessor version (top): memory allocation and free happening across application workflow
Accessors vs USM Evaluation

- Example with DPC++ / PTX backend, on a Tesla V100
- Accessor version (top): memory allocation and free happening across application workflow
- USM version (bottom): allocation at start, deallocation at end

https://www.ligateproject.eu/
Performance Portability Evaluation

- 14 kernels show **excellent performance portability**
  - On NVIDIA V100: portable SYCL version vs manually optimized CUDA **only 7% faster**
  - High performance on both V100 and M100

- Three kernels have **lower performance portability**
  - Optimize and align kernel
    - high register pressure
  - Hb-score kernel
    - sorting kernel

---

**LiGen Accessor: 14 kernels (excl.: optimize, align, hb-score)**

- CUDA
- DPCPP - PTX backend
- HIPSYCL - CUDA backend
- HIPSYCL - HIP backend

**LiGen Accessor: 3 kernels (optimize, align, hb-score)**

- CUDA
- DPCPP - PTX backend
- HIPSYCL - CUDA backend
- DPCPP - CPU - OpenCL + SPIR-V
- HIPSYCL - CPU - OMP
- HIPSYCL - HIP backend

---

[https://www.ligateproject.eu/](https://www.ligateproject.eu/)
Conclusion

• LiGen 3.0 relies on SYCL to provide performance portability
• All CUDA features ported to SYCL
  • successfully runs on a wide range of hardware
• SYCL 2020 features reduced LiGen code complexity
  • reduction and group algorithms allowed us to remove more than 430 lines of code
  • accessors and USM version, very similar in performance
• Performance portability study
  • excellent performance portability on 14 out of 17 kernels
    • manually-tuned CUDA only 7% faster than portable SYCL on V100
  • issues with three kernels because of
    • high register pressure (new Ligen 4.0 pipeline will attack this problem)
    • customized sorting function

https://www.ligateproject.eu/
This project has received funding from the European High-Performance Computing Joint Undertaking (JU) under grant agreement No 956137. The JU receives support from the European Union’s Horizon 2020 research and innovation programme and Italy, Sweden, Austria, Czech Republic, Switzerland.