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Towards a Portable Drug Discovery Pipeline with SYCL 2020

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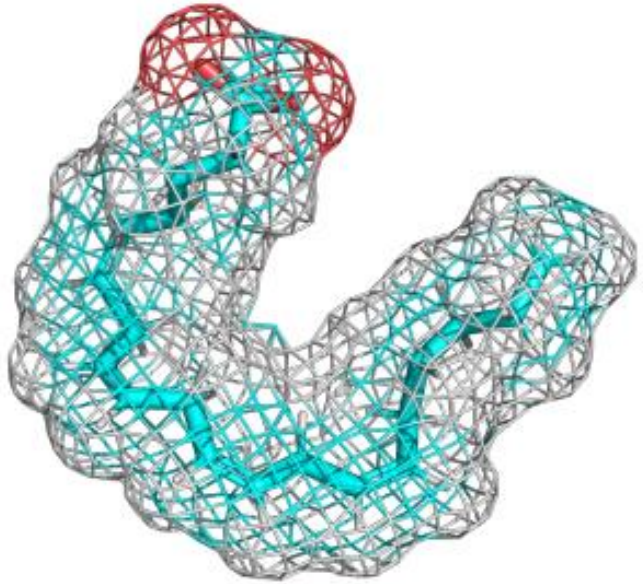
Outline

- 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

Virtual Screening

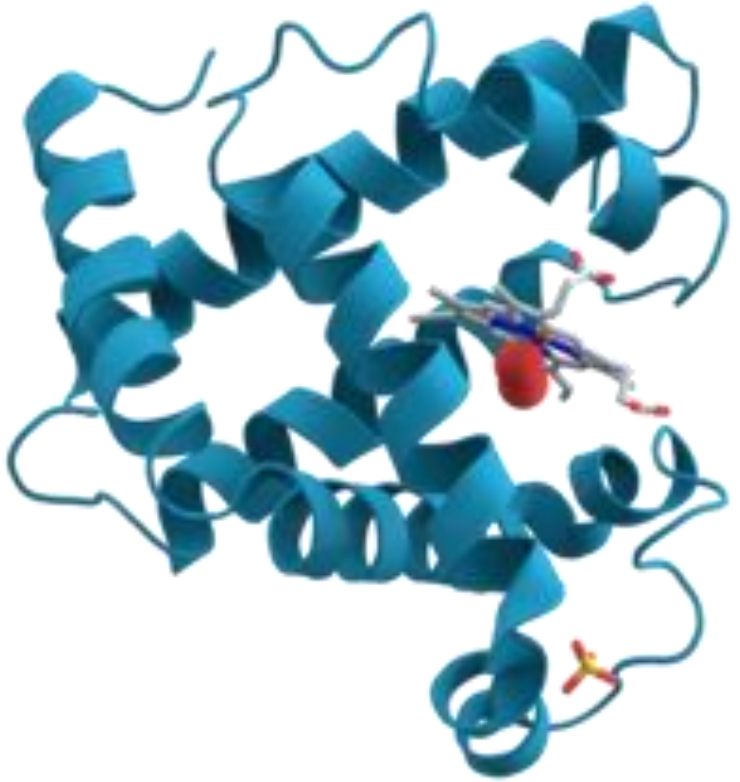
- Initial stages of the drug discovery process
- Ligand: small molecule with usually less than 100 atoms
- Can be view as a graph
  - Atoms as vertices
  - Bond as edges
- Can be generated by chemical reactions
- **Drug Candidate**



Arachidonic Acid ligand example

Virtual Screening

- A protein is a molecule that is composed of one or more chains of amino acid residues
  - Tens of thousand 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**



A representation of the 3D structure of the protein myoglobin

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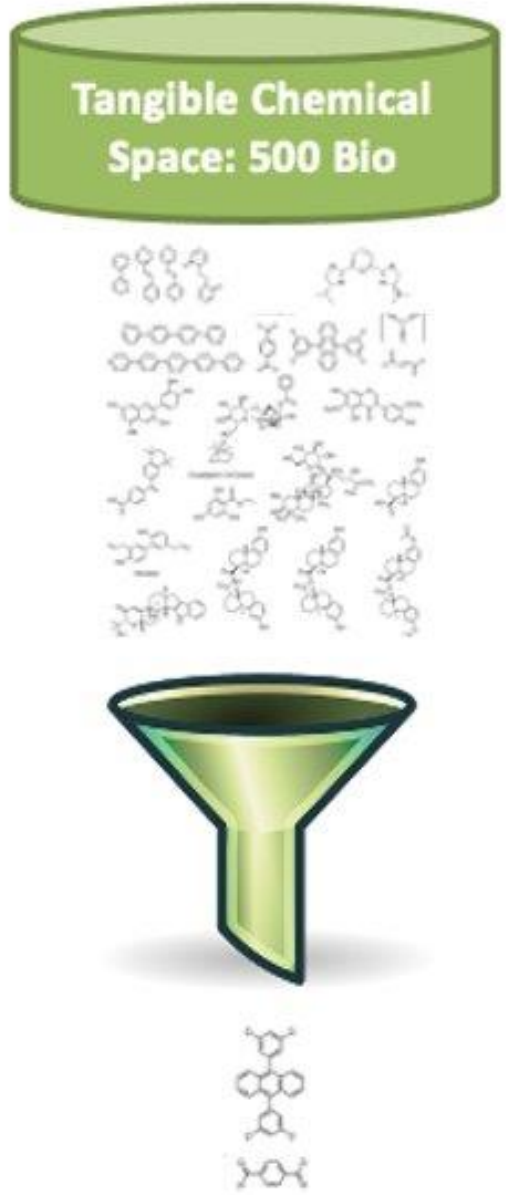
Virtual Screening

- 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



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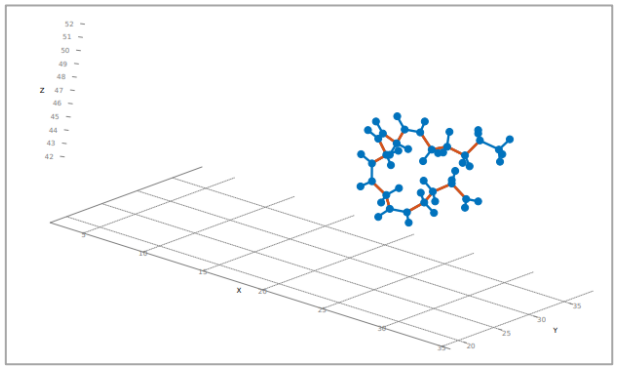
Virtual Screening

Challenges:

- Evaluate as much ligand candidates as possible
- The bond strength depends on the ligand's atoms 3D displacement when it in teracts the with target protein
    - We need to "dock" before "score" it
- A ligand can be change its shape
    - Multiple way to dock the same ligand



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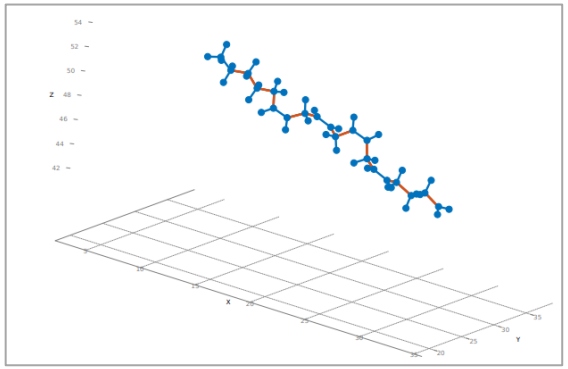
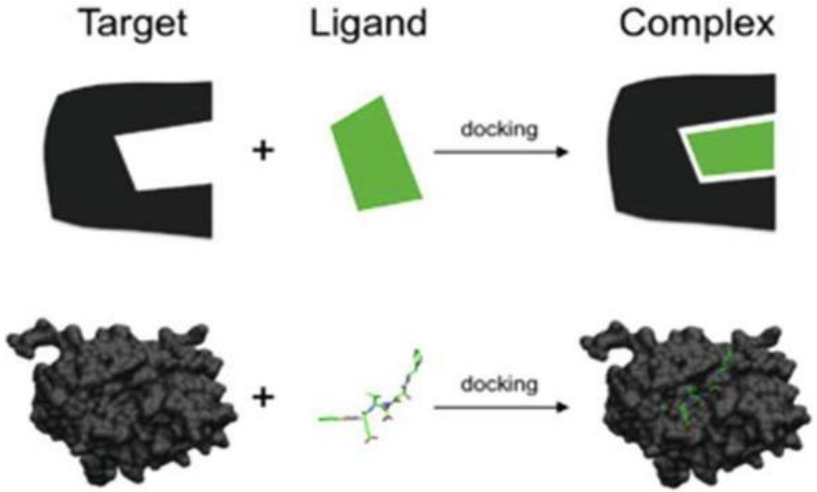


Unfolded

Two conformations of the Arachidonic Acid.



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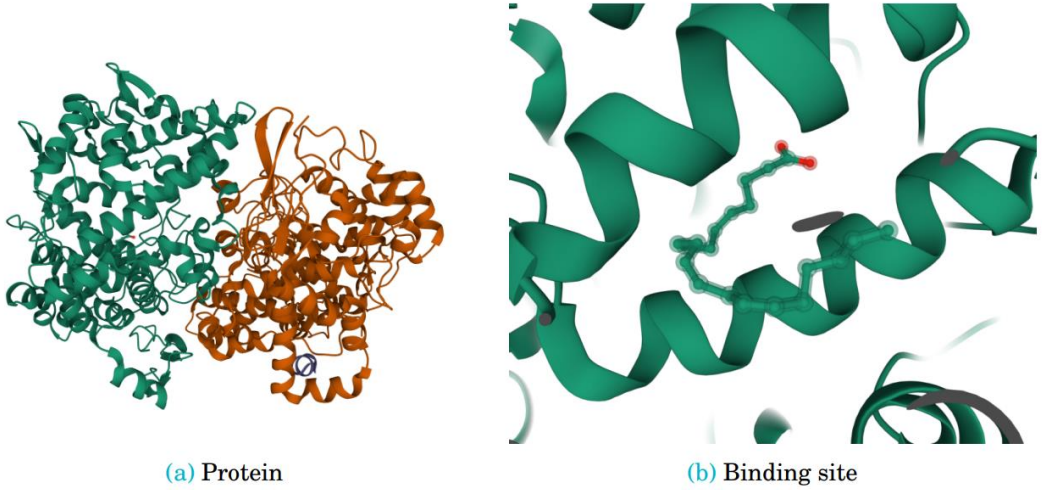
Dock & Score

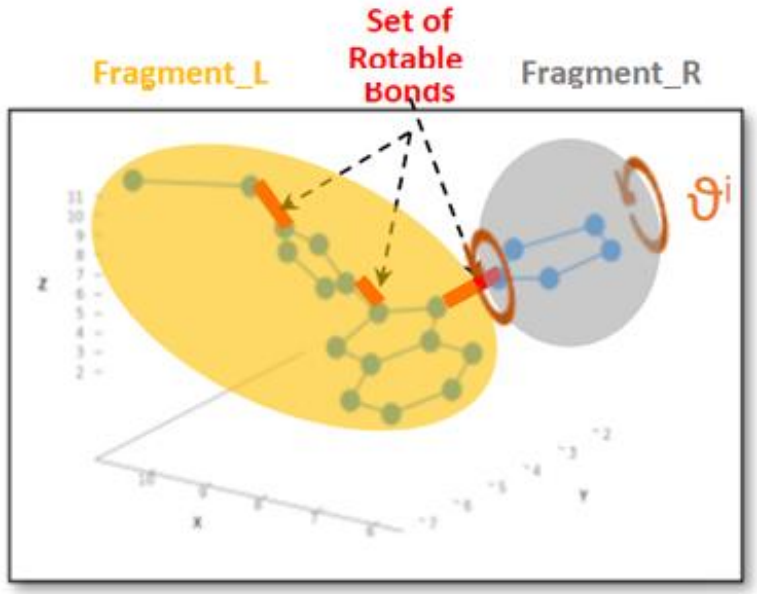
Molecular Docking as "Relaxed" lock and key model:

- 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

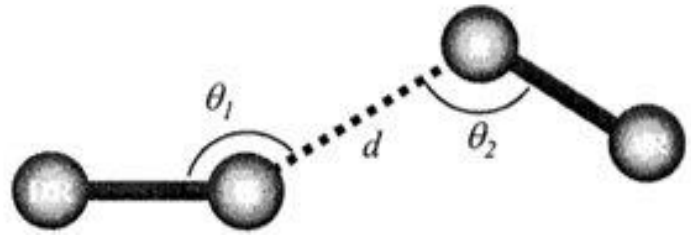


(a) Protein (b) Binding site

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



$\vartheta=[\vartheta^1,\ldots,\vartheta^N]$



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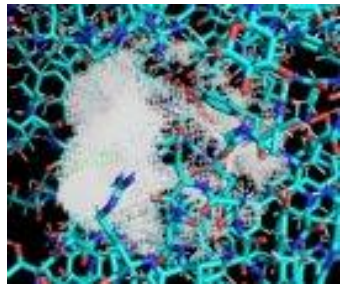
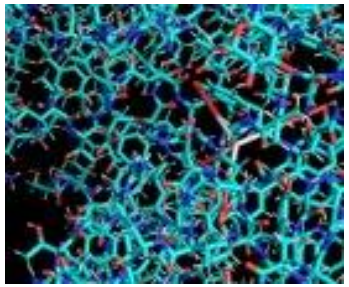
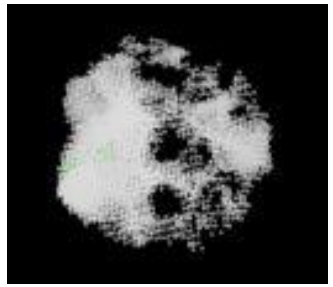
Dock & Score

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;







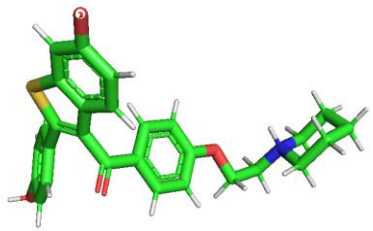
LiGen: Ligand Generator Platform

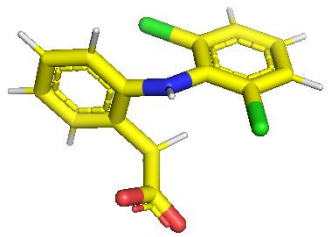
The LiGen drug discovery framework

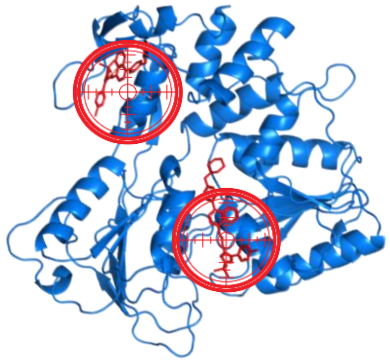
- Owned by Dompe Farmaceutici and co-developed by PoliMi and CINECA
- used for the discovery of drug against different pathogens
    - Zika [ANTAREX], SARS-CoV-2 [EXSCALATE4COV]

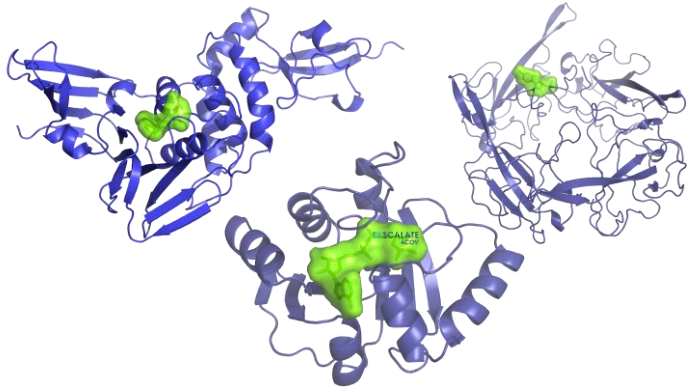
LiGen processing pipeline

- 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.









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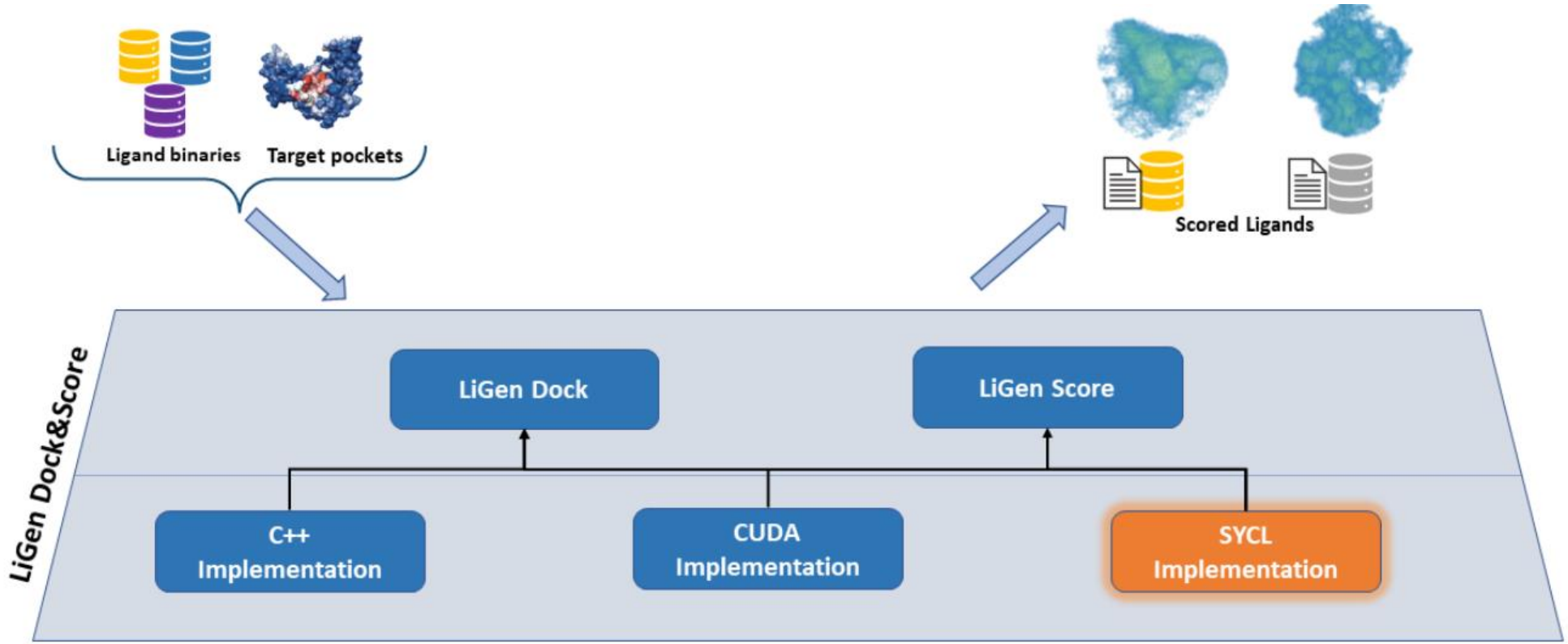
The LiGen Drug Discovery Pipeline



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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

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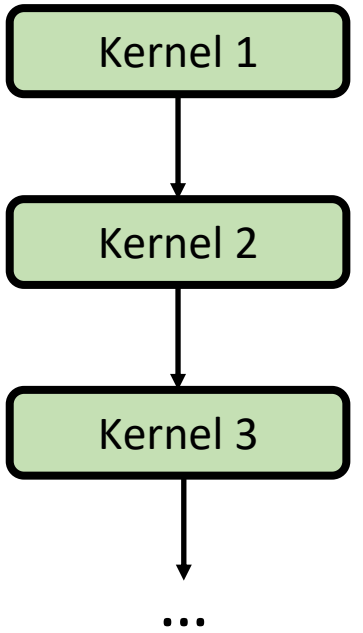
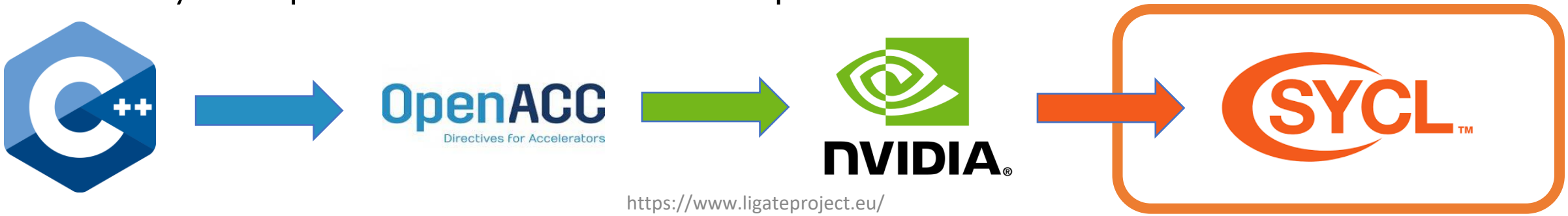
Porting from CUDA to SYCL2020

- 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





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***

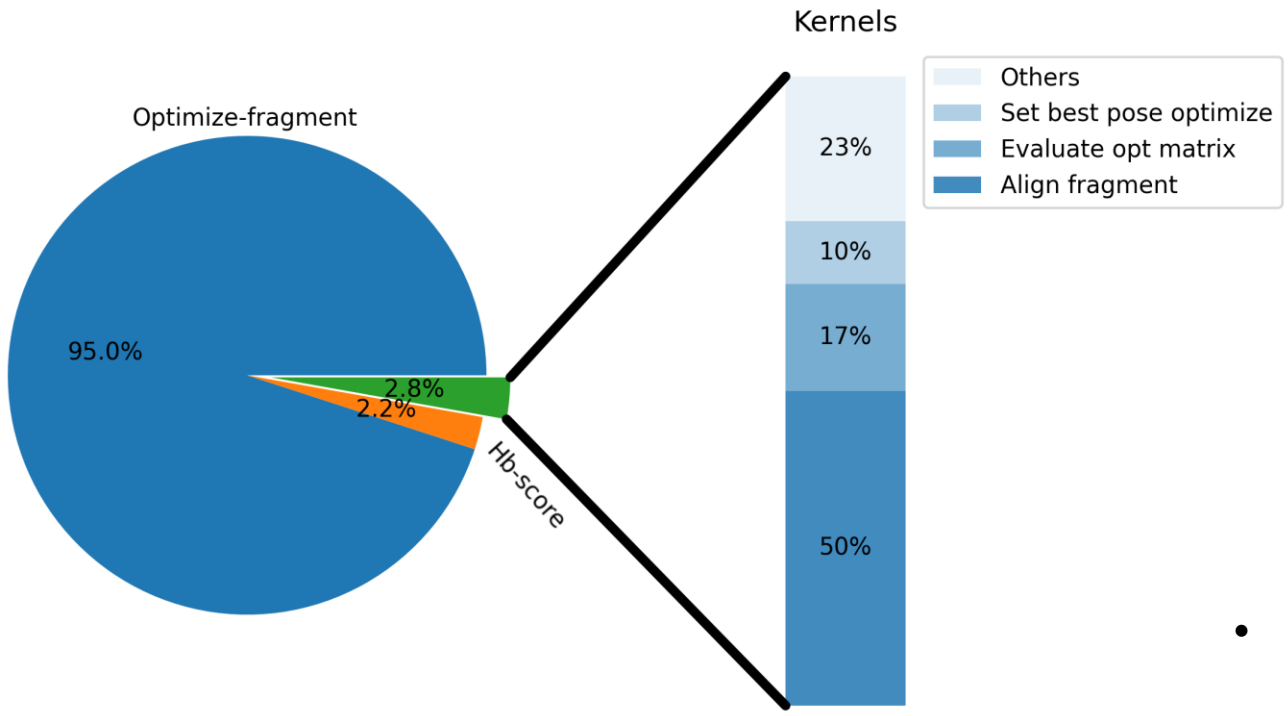
Performance Tuning

- 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

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

Application Performance Evaluation



Runtime per Kernel

- 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

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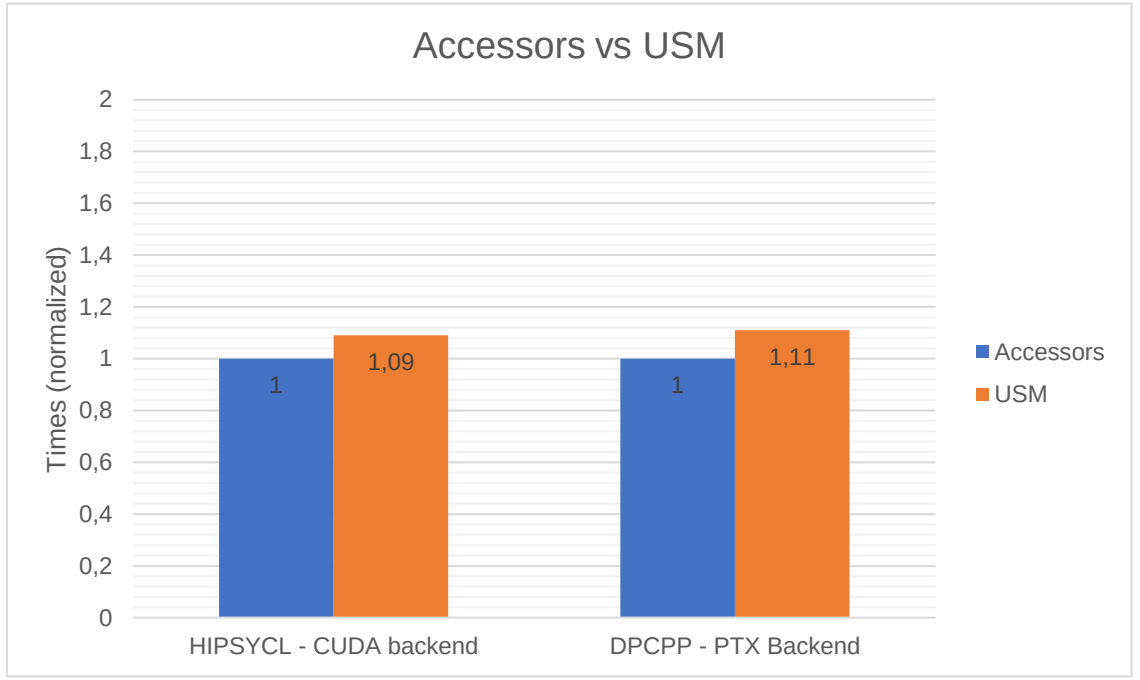
Accessor vs USM Evaluation

- 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



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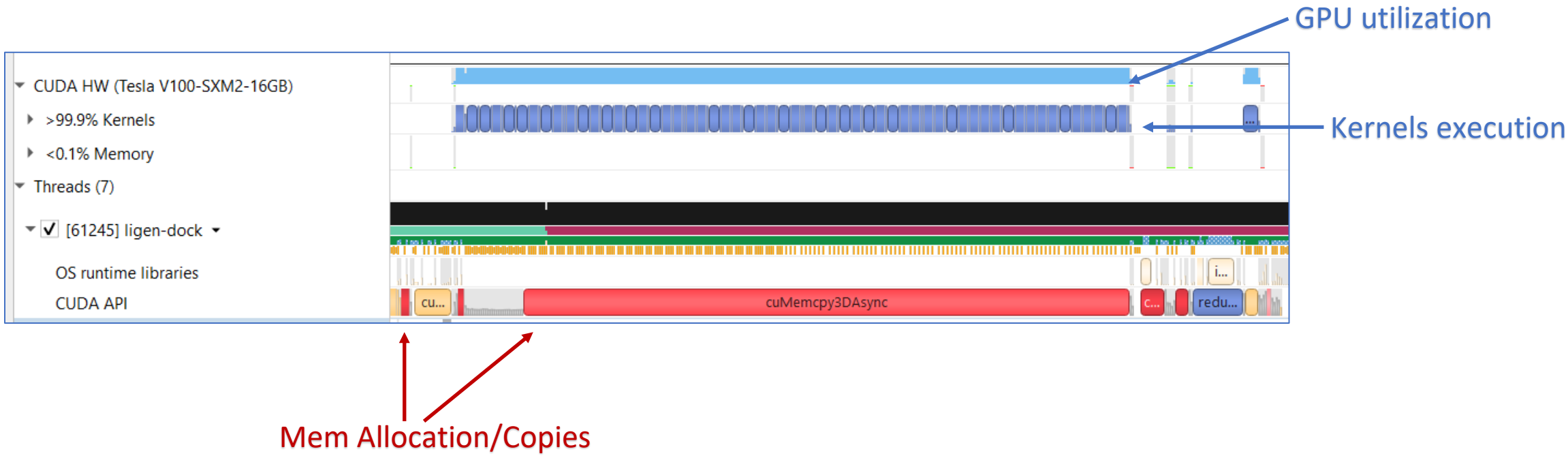
Accessors vs USM Evaluation

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



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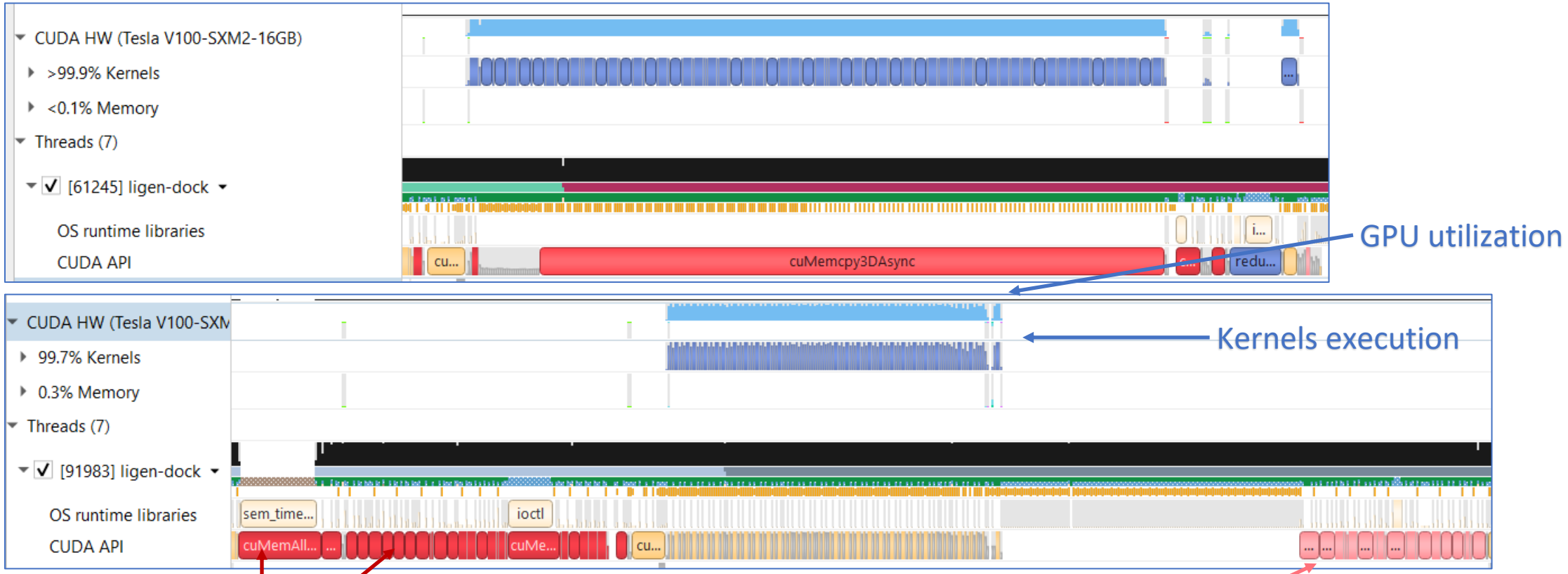
Accessors vs USM Evaluation

- 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



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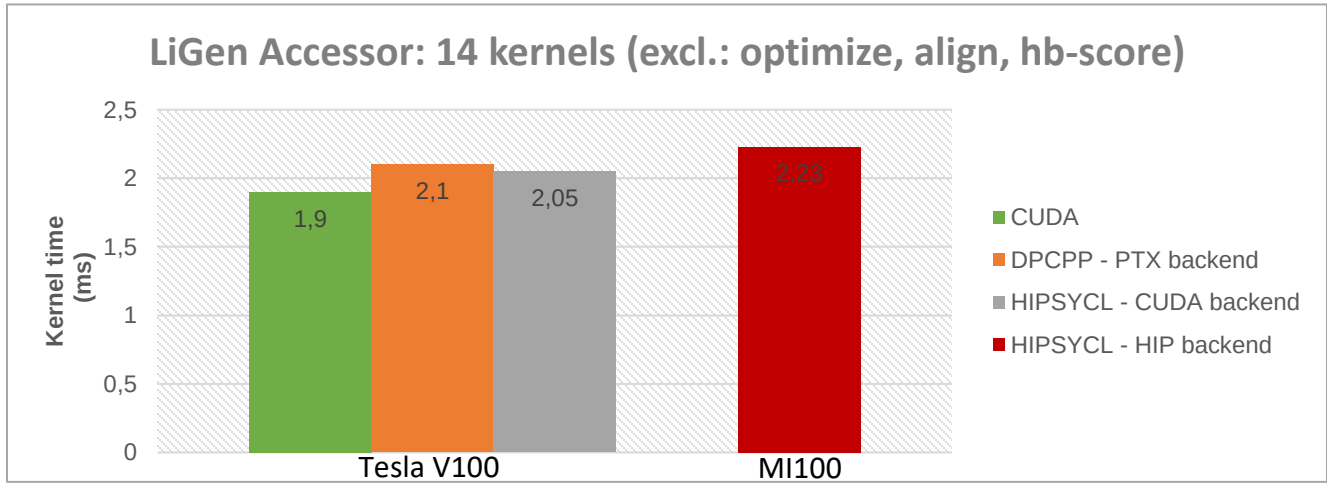
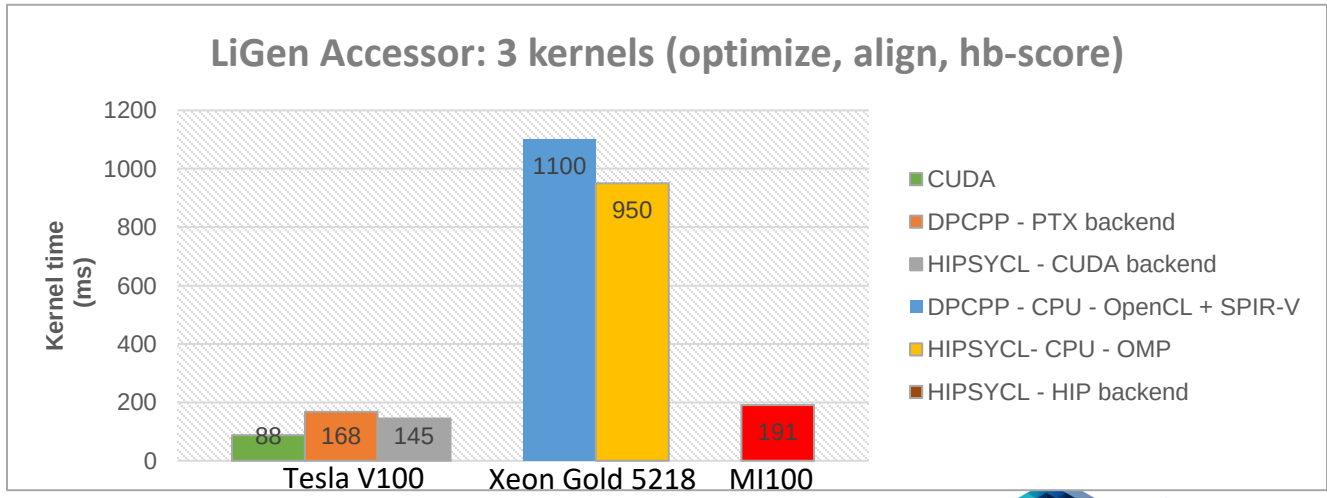
Performance Portability Evaluation

- 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



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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

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