[Halide/LLVM/Clang/dlibC++ Machine Learning Library Toolkit] as HI-END cryo-EM Image Processing Software & Informatics Platform - A Simple Short Communication on Using [Halide/dlibC++ Machine Learning Library Toolkit/IoT/HPC] in a Related Heterogeneous Computing Environment R&D.

“Only those who attempt the absurd will achieve the impossible” . - M. C. Escher.

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Abstract :

As explained in the TITLE mentioned above , we present here a simple commentary/communication on cryo-EM Image Processing Technique using Halide in the context of IoT/HPC Computing Environments.Halide is a language for fast, portable data-parallel computation for HI-END applications.

keywords : cryo-EM Image Processing/Halide/dlibC++/Tensors/IoT/HPC/Heterogeneous Computing Environments.

[I] Our Inspiration & Introduction :

[Information on Halide] :

“Halide is a language for fast, portable computation on images and tensors .”

“Halide is a programming language designed to make it easier to write high-performance image and array processing code on modern machines. Halide currently targets:

- CPU architectures: X86, ARM, MIPS, Hexagon, PowerPC
- Operating systems: Linux, Windows, macOS, Android, iOS, Qualcomm QuRT
- GPU Compute APIs: CUDA, OpenCL, OpenGL, OpenGL Compute Shaders, Apple Metal, Microsoft Direct X 12

Rather than being a standalone programming language, Halide is embedded in C++. This means you write C++ code that builds an in-memory representation of a Halide pipeline using Halide's C++ API. You can then compile this representation to an object file, or JIT-compile it and run it in the same process.” [Source : https://halide-lang.org/]

[Information on cryo-EM Image Processing] :

“Cryogenic electron microscopy (cryo-EM) is an electron microscopy (EM) technique applied on samples cooled to cryogenic temperatures and embedded in an environment of vitreous water. An aqueous sample solution is applied to a grid-mesh and plunge-frozen in liquid ethane. While development of the technique began in the 1970s, recent advances in detector technology and software algorithms have allowed for the determination of biomolecular structures at near-atomic resolution.[1] This has attracted wide attention to the approach as an alternative to X-ray crystallography or NMR spectroscopy for macromolecular structure determination without the need for crystallization. “
[Source : Wikipedia / https://en.wikipedia.org/wiki/Cryogenic_electron_microscopy **]**

“The 2017 Nobel prize in chemistry has been awarded to three scientists ‘for developing cryo-electron microscopy for the high-resolution structure determination of biomolecules in solution’.

The laureates are: Jacques Dubochet from the University of Lausanne, Switzerland; Joachim Frank from Columbia University, New York, US; and Richard Henderson from the Medical Research Council Laboratory of Molecular Biology in Cambridge, UK. They each contributed to developing a technique that allows scientists to see the intricate structures of proteins, nucleic acids and other bio-molecules, and even study how they move and change as they perform their functions.”

[Source : https://www.chemistryworld.com/news/explainer-what-is-cryo-electron-microscopy/3008091.article **]**

[Information on dlibC++ Machine Learning Library Toolkit] :

“ Dlib is a modern C++ toolkit containing machine learning algorithms and tools for creating complex software in C++ to solve real world problems. It is used in both industry and academia in a wide range of domains including robotics, embedded devices, mobile phones, and large high performance computing environments. Dlib's open source licensing allows you to use it in any application, free of charge. “ [Source : http://dlib.net/]

[Information on Tensors] :

“In mathematics, a *tensor* is a geometric object, either a scalar, a geometric vector, or a multi-linear map from other *tensors* to a resulting *tensor*. Vectors and scalars (which are often used in elementary physics and engineering applications) are the simplest *tensors*. “
[Source : *https://en.wikipedia.org/wiki/Tensor*]

https://www.mia.uni-saarland.de/Research/IP_Tensor.shtml

[Information on an Interesting Simple Review of Scientific Literature on Cryo-EM Image Processing R&D] :

Why the need to develop “Excellent Cryo-EM Image Processing” Software/Methods always ? - Some interesting points from the existing scientific literature review on Cryo-EM Image Processing domain – Let us guess - “Who is RIGHT or Who is WRONG” ?

“The structure of a protein known informally as the **HIV trimer** is among the most highly prized goals of structural biology. “ In this context, please read further to understand the pros and cons of cryo-EM Image Processing Technique to probe the frontiers of Nano-Bio Systems.

“The dispute over the proteins' architecture began in early June, when Mao and his colleagues published cryo-EM reconstructions at a resolution of 6-ångströms in *Proceedings of the National Academy of Sciences*[1]. According to their study, the tip of the spike seemed to have a cavity at its centre. “

[Source : Rift widens over structure of HIV’s molecular anchor -Studies of a potential vaccine target bolster claims that an earlier paper was flawed. Brendan Borrell /31 October 2013.]

“Reply to Subramaniam, van Heel, and Henderson: Validity of the cryo-electron microscopy structures of the HIV-1 envelope glycoprotein complex” - “Subramaniam (1), van Heel (2), and Henderson (3) express their opinions and hypotheses about our cryo-electron microscopy (EM) structures of the uncleaved HIV-1 envelope glycoprotein [Env(-)ΔCT] trimer (4, 5). There are no data in these communications, nor elsewhere in the published literature, that contradict our results; however, we conducted systematic additional studies that provide strong evidence disproving their hypotheses. “

[Source : Proc Natl Acad Sci U S A. 2013 Nov 5; 110(45): E4178–E4182. Published online 2013 Oct 8. doi: 10.1073/pnas.1316666110 Microbiology]

[Source : https://www.pnas.org/content/110/30/12438/tab-article-info]
[Source : *www.pnas.org/content/110/45/E4175/tab-article-info*]
[Source : https://app.dimensions.ai/details/publication/pub.1037848964 **]**

Finding trimeric HIV-1 envelope glycoproteins in random noise" - Marin van Heel Published 2013;
[DOI:10.1073/pnas.1314353110.]

"Structural biology needs no introduction for people doing drug discovery. This wasn't always so. Drugs were discovered back in the days when people used to argue about whether those "receptor" thingies were real objects (as opposed to useful conceptual shorthand), and before anyone had any idea of what an enzyme's active site might look like. And even today, there are targets, and whole classes of targets, for which we can't get enough structural information to help us out much. "

[Source : Analytical Chemistry - An HIV Structure Breakthrough? Or "Complete Rubbish"?]

By Derek Lowe 16 August, 2013 -
https://blogs.sciencemag.org/pipeline/archives/2013/08/16/an_hiv_structure_breakthrough_or_complete_rubbish]

CryoEM is very powerful if done right and is very much helpful -

[Source : http://www.biochem.mpg.de/en/rd/baumeister]

www.sciencemag.org SCIENCE VOL 341,443-444,2 AUGUST 2013 - Is High-Tech View of HIV Too Good to Be True?

[Information on one of our R&D works that could solve these type of disputes to some extent] :

"Formalizing Image Processing in Higher Order Logic(hol) by Understanding and Using XML-Hol-Scala-JVM Software Framework Towards Processing of Cryo-EM/TEM/SEM Images Based on Levy Processes a Novel Suggestion"; Author : D.N.T.Kumar .

[Source : http://vixra.org/author/d_n_t_kumar]

[II] Halide based Electron Microscopy Imaging & Informatics Framework involving some Machine Learning Algorithms :

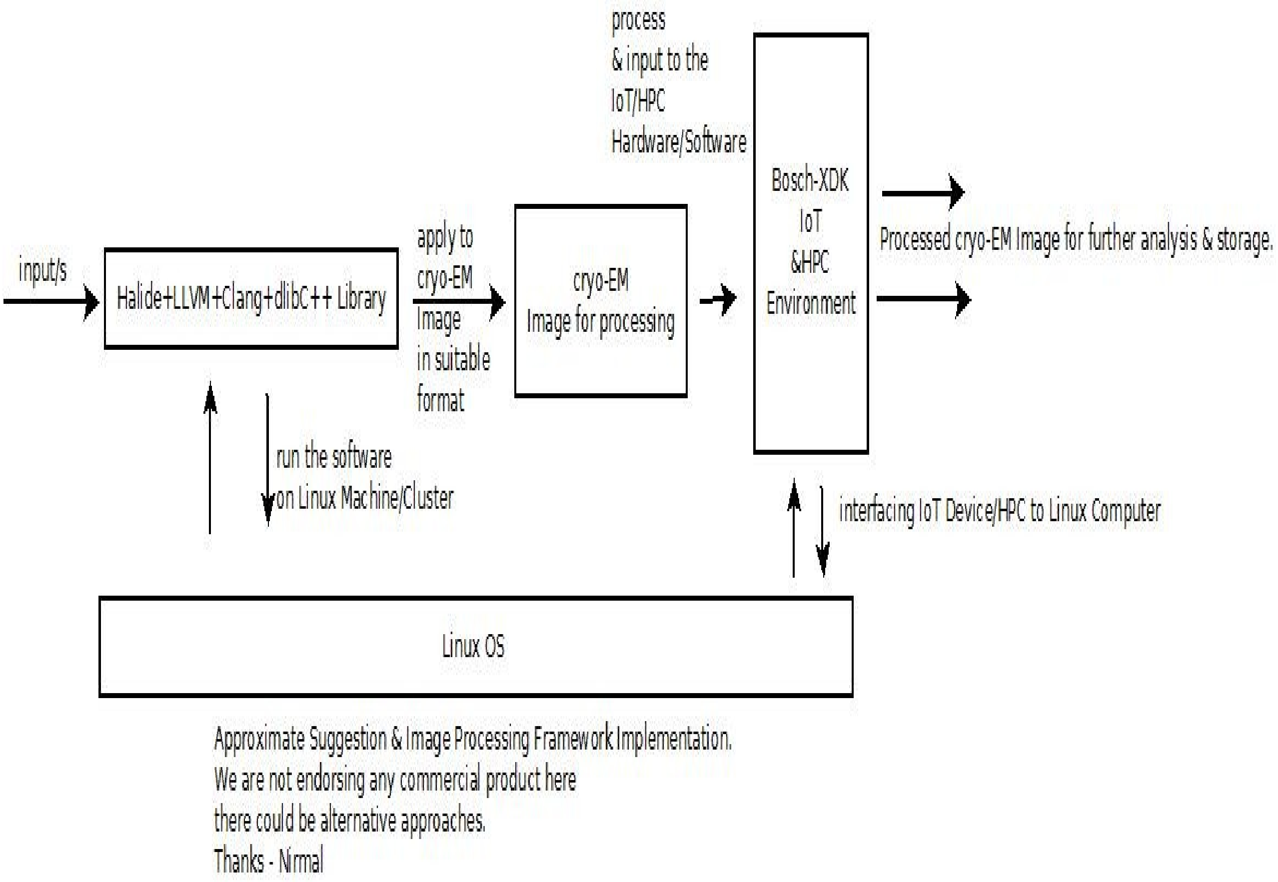

Figure I – [Halide + LLVM+Clang+dlibC++ Machine Learning Library Toolkit] based cryo-EM Image Processing Informatics Framework - Testing in progress at the time of submission.Please Check and Satisfy yourselves.

[III] Additional Information on Mathematics & Software Used :

[a] https://github.com/halide/Halide

[b] The LLVM Compiler Infrastructure Project - *https://llvm.org/*

[c] Clang C Language Family Frontend for LLVM - *https://clang.llvm.org/*

[d] https://en.wikibooks.org/wiki/Software_Tools_For_Molecular_Microscopy

[e] ***Website:*** http://blake.bcm.edu/eman – Try EMAN/EMAN2 - “A suite of scientific image processing tools aimed primarily at single particle reconstruction. This is a technique for determining the 3-D structure of a molecule or macromolecular assembly from thousands to hundreds of thousands of noisy images of individual molecules, generally collected on a transmission electron microscope. EMAN's focus is on providing state of the art single particle reconstruction methods automated to the greatest extent possible. The goal is to permit even novice users to be able to reconstruct macromolecular structures with high veracity and at high resolution “.

Other Options : **Bsoft** cryo-EM Software is also a good option for C/C++ Programming and extensions.For Java based programming use **– ImageJ** or **Fiji** Software.

[f] http://vixra.org/author/nirmal_tej_kumar

[g] http://vixra.org/author/nirmal

[h] http://vixra.org/author/d_n_t_kumar

[i] https://people.csail.mit.edu/tzumao/gradient_halide/

[IV] Conclusion/s With Future Perspectives :

Based on the information and analysis presented above,we can conclude that Halide could be very much useful in exploring the challenging aspects of cryo-EM Image Processing and applications. To the best of our knowledge,this is one of the pioneering papers on [Halide+LLVM+Clang+dlibC++ Library] as Image Processing & Informatics Platform. Though we referred to cryo-EM Image Processing,this approach could be used for other image processing applications as well.

[V] Acknowledgments :

Special Thanks to all Who made this happen in my LIFE. Non-Profit Academic R&D.
No competing financial interest/s is/are declared.

** Please Note : all the references and additional information were used in drafting this short communication.

** Request readers to carefully study, examine and decide the options available through our communication on this important R&D domain.

** As the nature of this communication is a brief technical note ,we are avoiding the details.

[VI] References :

[1] https://www.nature.com/articles/d41586-018-06791-6 - “Cryo-electron microscopy shapes up
As the imaging technique produces ever-sharper protein structures, researchers are racing to develop tools to assess how accurate they are”. [TECHNOLOGY FEATURE 25 September 2018]

[2] https://web.ma.utexas.edu/users/hadani/publications.htm

[3] *https://en.wikipedia.org/wiki/Single_particle_analysis - “Single particle analysis is a group of related computerized image processing techniques used .... Doerschuk PC, Johnson JE (March 2013). "Dynamics in cryo EM reconstructions visualized with maximum-likelihood derived variance maps".*

[4] *https://www.microscopemaster.com/cryo-electron-microscopy.html*-
“Cryo-Electron Microscopy - What it is, How it Works and Pros and Cons”

[5] *https://www.fei.com/life-sciences/history-of-cryo-em/ - “Cryo-EM possesses a long history that includes many groups of researchers who contributed to the evolution and revolution of cryo-EM in equally important …...”*

[6] Understanding JikesRVM in the Context of Cryo-EM/TEM/SEM Imaging Algorithms and Applications – A General Informatics Introduction from a Software Architecture View Point – Kumar DNT & Gagik Shmavonyan.2016.
[Source : International Journal of Applied Research on Information Technology and Computing Year : 2016, Volume : 7, Issue : 1First page : **(1)** Last page : **(7)** Print ISSN : 0975-8070. Online ISSN : 0975-8089. Article DOI : 10.5958/0975-8089.2016.00001.4]

[7] An Insight into Cryo-EM Imaging Process Architecture Using GENTLE Compiler Construction System with an Informatics Design Paradigm – Kumar Nirmal Tej . 2016.[Source : International Journal of Applied Research on Information Technology and Computing Year : 2016, Volume : 7, Issue : 2 First page : **(80)** Last page : **(89)** Print ISSN : 0975-8070. Online ISSN : 0975-8089. Article DOI : 10.5958/0975-8089.2016.00008.7]

[8] A Simple Introduction and Short Communication on Higher Order Logic (HOL)-JVM/Jikes RVM-Based Deep Learning Algorithms and Mechanisms to Probe the Frontiers of Cryo-EM Image Processing: Tasks and Big Data-Related Applications- Kumar D.N.T.[Source : International Journal of Applied Research on Information Technology and Computing Year : 2018, Volume : 9, Issue : 3 First page : **(221)** Last page : **(224)** Print ISSN : 0975-8070. Online ISSN : 0975-8089. Article DOI : 10.5958/0975-8089.2018.00021.0]

[9] “A method for the alignment of heterogeneous macromolecules from electron microscopy”, Maxim Shatsky et al, Journal of Structural Biology 166 (2009) 67–78.

[10] https://itensor.org/ - ITensor—Intelligent Tensor—is a C++ library for implementing tensor network calculations. See the list of recent papers using ITensor.
[11] https://github.com/ITensor – ITensor Source Code .

THE END