

# **Higher Order Logic (HOL) Based Analysis of Cryo-EM Images Using Multivariate Analysis, Automatic Data Refinement Libraries Involving Vector Spaces for the HOL-Scala-ImageJ-JikesRVM(JVM) Environment to Probe Nano-Bio Systems – A Technical Note.**

**Nirmal Tej Kumar**

Current Member : ante Inst,UTD,Dallas,TX,USA.  
Independent Consultant : Informatics & Nanotechnology.  
: USA/Israel/BRICS Group of Nations.  
email id: [hmfg2014@gmail.com](mailto:hmfg2014@gmail.com)

## **Abstract :**

Cryo-Electron Microscopy(cryo-EM/Cryo-EM) : is a promising method for the imaging of macromolecules in the electron microscope, especially “single-particle” techniques are powerful and popular.As the title of this technical notes indicates it was proposed to probe the frontiers of “Nano-Bio” Systems by using HOL Platform and its associated mathematical concepts,algorithms and libraries to process Cryo-EM Images.

**Key Words :** Image J/JikesRVM/Java/Scala/MVA/ADR/Vector Spaces/Cryo-EM Images.

## **Introduction :**

Cryo-Electron Microscopy (cryo-EM/Cryo-EM) is increasingly becoming a mainstream technology for studying and investigating the architecture of cells, viruses and protein assemblies at molecular resolution. Further, we observe that recent developments in microscope design and imaging hardware, paired with enhanced image processing and automation capabilities, appear poised to further advance the effectiveness of cryo-EM methods. It is in this context, that the idea of using HOL based informatics platform to process cryo-EM images was proposed.

## **Inspiration :**

I started my R&D work in this domain since 2014 by collaborating with several international researchers to probe “Nano-Bio Systems” and we know for sure that R& D of Cryo-EM Image Processing is a hot topic and very much promising.

“2017 Nobel Prize in Chemistry - A New Era in Cryo-EM”. [It is useful to read this information for inspiration] – {Source <https://www.fei.com/cryo-em/>}

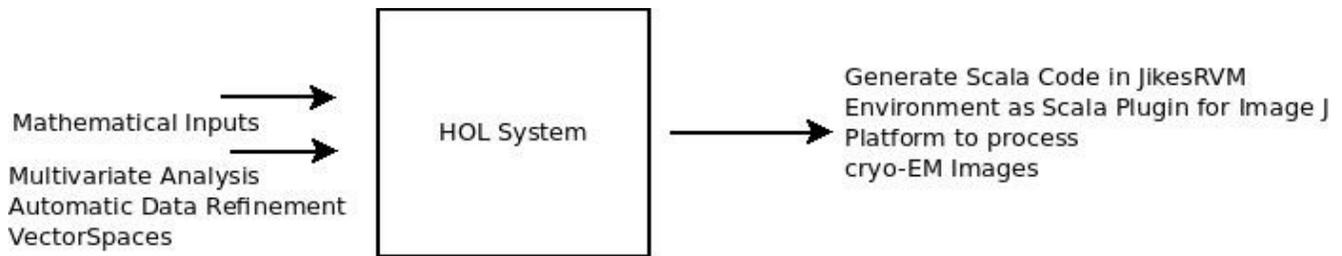
*Please read the following papers to understand and design your own informatics platforms :*

Proc Natl Acad Sci USA. 5 November 2013;110(45):18037–41. Published online 2013 October 8. DOI:10.1073/pnas.1314449110;PMCID: PMC3831464; Biophys Comput Biol.

Tang G, et al. EMAN2: An extensible image processing suite for electron microscopy. J Struct Biol 2007;157(1):38–46.

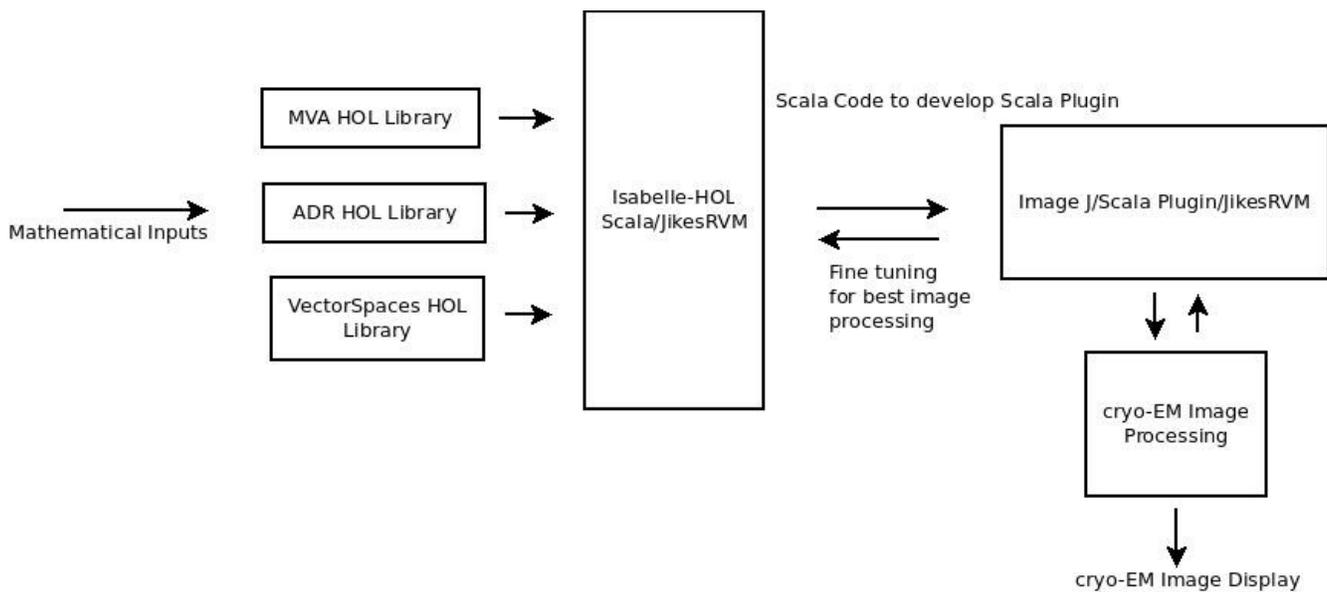
\*\*Kumar, D.N.T. & Shmavonyan, G.s. (2016). Understanding JikesRVM in the Context of Cryo-EM/TEM/SEM Imaging Algorithms and Applications – A General Informatics Introduction from a Software Architecture View Point. International Journal of Applied Research on Information Technology and Computing. 7. 1. 10.5958/0975-8089.2016.00001.4.

## Informatics Framework Design & Implementation :



Simple Block Diagram to process cryo-EM Images using HOL-Scala-ImageJ/JikesRVM

**Figure I – Approximate Informatics & Image Processing Method.**



Simple Block Diagram to Process cryo-EM Images using HOL/Scala/ImageJ/JikesRVM

**Figure II - Approximate Informatics & Image Processing Method**

All the references and information links used in this technical note or short communication are used and the whole paper is based on the links shown below.Refs[1-7].Please make a note I have performed most of my work on Linux based HPC Cluster.

## **Informatics Framework Discussion & Analysis :**

The implementation is illustrated in a simple way as depicted above in the Figures[I] & [II]. To get a clear picture of the idea implemented the readers are kindly requested to study my publications/technical notes/short communications available on Vixra.org besides Ref[2].

<http://vixra.org/pdf/1709.0412v1.pdf> ; <http://vixra.org/pdf/1709.0389v1.pdf> ;

<http://vixra.org/pdf/1709.0376v1.pdf> ; <http://www.vixra.org/pdf/1709.0404v1.pdf>;

<http://vixra.org/pdf/1709.0403v1.pdf>

## **Conclusion :**

In this short communication or technical note, we have demonstrated the feasibility of a possible prototyping solution to process a simple cryo-EM image using cryo-EM image processing software based on “HOL-Scala-ImageJ-JikesRVM” informatics platform. To rapidly prototype and process cryo-EM images with different mathematical imaging algorithms, we needed an excellent testbed so the above mentioned platform was feasible for our R&D. It is our intention to highlight the importance of JikesRVM as testbed for computing and applications using Scala in the context of “Reactive Programming Environments”

## **Additional Information on Mathematics & Software Used :**

[a] <http://isabelle.in.tum.de/> - HOL Informatics Platform .

[b] [http://isabelle.in.tum.de/website-Isabelle2013-1/dist/library/HOL/HOL-Multivariate\\_Analysis/outline.pdf](http://isabelle.in.tum.de/website-Isabelle2013-1/dist/library/HOL/HOL-Multivariate_Analysis/outline.pdf) – Multivariate Analysis Library for HOL Platform.

[c] <https://www.isa-afp.org/entries/VectorSpace.html> – VectorSpace Library for HOL Platform.

[d] [https://www.isa-afp.org/entries/Automatic\\_Refinement.html](https://www.isa-afp.org/entries/Automatic_Refinement.html) – Automatic Refinement Library for HOL Platform.

[e] <http://www.jikesrvm.org/> ; <http://www.scala-lang.org/> ; <https://imagej.nih.gov/ij/> ;

[f] <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3537914/>

## **Acknowledgements :**

Special thanks to all those who have made this possible. The author declares no conflict of interest and no competing financial interest/s. This short note or technical communication is for non-profit academic research work.

## **References :**

[1]. <https://patentimages.storage.googleapis.com/af/02/69/d83dd8e6e8dcb9/US20020143779A1.pdf>  
[Data structures and methods for imaging computer readable media]

[2]. Understanding JikesRVM in the Context of Cryo-EM/TEM/SEM Imaging Algorithms and Applications – A General Informatics Introduction from a Software Architecture View Point  
D.N.T. Kumar, Gagik Shmavonyan; Article DOI:10.5958/0975-8089.2016.00001.4

[3].An Insight into Cryo-EM Imaging Process Architecture Using GENTLE Compiler Construction System with an Informatics Design Paradigm - Nirmal Tej Kumar ;  
Article DOI:10.5958/0975-8089.2016.00008.7

[4].A Technical Note on Hilbert Spaces as Mathematical Tools to Probe and Process Cryo-EM Images – An Architectural and Computational Point of View Using Higher Order Logic (HOL)/Scala/Java/JVM Software Environment ; N.T. Kumar;  
Article DOI:10.5958/0975-8089.2016.00016.6

[5].<http://cryoem.berkeley.edu/> - Cryo-Electron Microscopy Website.

[6]. Aransay J., Divasón J. (2015) Generalizing a Mathematical Analysis Library in Isabelle/HOL. In: Havelund K., Holzmann G., Joshi R. (eds) NASA Formal Methods. NFM 2015. Lecture Notes in Computer Science, vol 9058. Springer, Cham.  
[[https://link.springer.com/chapter/10.1007/978-3-319-17524-9\\_30?no-access=true#citeas](https://link.springer.com/chapter/10.1007/978-3-319-17524-9_30?no-access=true#citeas)]

[7]. <https://yunhokim.wordpress.com/research/cryogenic-electron-microscopy/>