AI-Assisted Image Analysis for Structural Characterization of HIV-1 Capsids

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Introduction:

Cryo-Electron Microscopy (Cryo-EM) of HIV-1 allows for structural determination of the HIV-1 capsid. This makes it useful for studying virus-host interactions such as HIV-1 nuclear import, by capturing intact viral capsids within cellular environments. However, Cryo-EM faces several challenges:

Low Signal-to-Noise Ratio (SNR): Imaging conditions, including electron dose limitations to prevent sample damage, result in noisy data that complicates segmentation and analysis (Fig 1A).

Difficult Particle Identification: The structural variability of HIV-1 capsids, combined with crowded environments, makes distinguishing individual particles challenging, often requiring manual annotation.

To overcome these limitations, this project integrates artificial intelligence (AI) with Cryo-EM to automate capsid detection and classification. By leveraging convolutional neural networks (CNNs) and advanced image segmentation techniques, our approach enhances accuracy, accelerates analysis, and enables large-scale structural studies. AI-driven detection reduces human bias and improves the consistency of capsid identification, providing deeper insights into viral uncoating dynamics and host interactions. Ultimately, this work aims to refine computational tools for Cryo-EM, facilitating more efficient structural virology research in HIV-1.

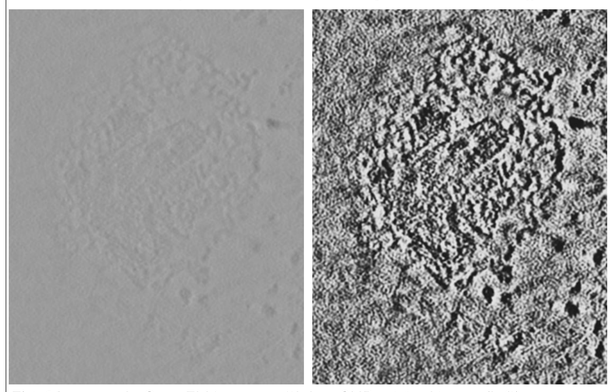

Fig. 1A: example Cryo-EM images with low SNR original image(left) versus processed and denoised image with high SNR (right).The low SNR causes low variability in the colors of the image making structural distinguishing difficult.

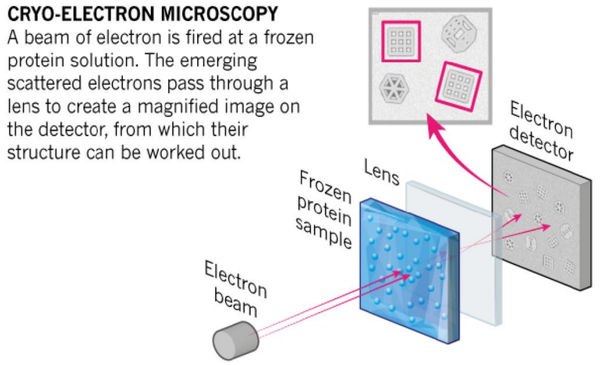

Fig. 1B: Cryo-EM explanation diagram. Taken from Wozniak, K.

Methods:

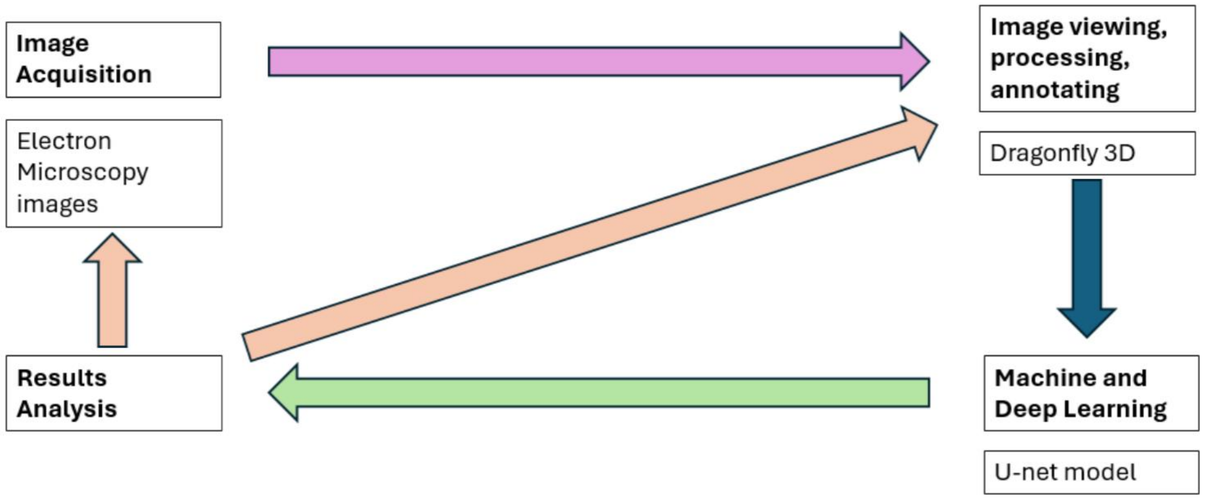

Fig. 2: Experiment methodology diagram. Cryo-EM images were taken of capsid-like particles (CLPs) to map capsids. Software (Dragonfly 3D) was used to denoise and process the images. The images were then manually segmented. A convolutional neural network (CNN) model was trained to recognize capsid structures. The model was tested on a series of images and its ability to segment intact, partially disassembled, and fully uncoated capsids were observed.

Results: Automatic segmentation of low magnification tomogram of CLPs

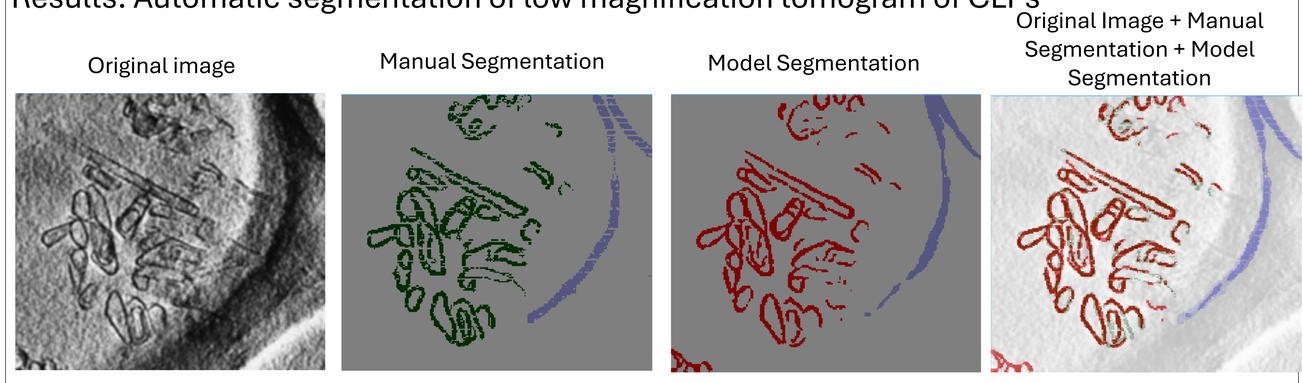

Fig 3: Example of Cryo-EM image segmentation done both manually and automatically for accuracy comparison. The segmentation of the capsids manually(in green) and automatically (in red) is shown, and the original image is also included for reference.

Discussion:

Key Findings

- Improved accuracy in capsid identification.
- Decreased image processing time consumption.
- Findings align with prior research supporting the integration of AI in biological image analysis to reduce human error and processing time.

Limitations

- Model accuracy depends on the quality of training data and accuracy of manual segmentation
- Capsid status (intact vs partially disassembled vs fully uncoated) affect model accuracy

Future Directions

- Further optimization of AI training datasets could improve segmentation accuracy.
- Expanding the model's application to different imaging techniques and biological samples would increase its utility.
- Application of CNNs to images of the HIV-1 virus capsid

References:

Bruch, R., Vitacolonna, M., Nürnberg, E., Sauer, S., Rudolf, R., & Reischl, M. (2024, August 29). *Improving 3D deep learning segmentation with biophysically motivated cell synthesis*. arXiv.org. https://arxiv.org/abs/2408.16471

Durkee, M. S., Abraham, R., Clark, M. R., & Giger, M. L. (2021, October). *Artificial Intelligence and cellular segmentation in tissue microscopy images*. The American journal of pathology. https://pmc.ncbi.nlm.nih.gov/articles/PMC8485056/

Gien, H., Morse, M., McCauley, M. J., Kitzrow, J. P., Musier-Forsyth, K., Gorelick, R. J., Rouzina, I., & Williams, M. C. (2022, January 25). *HIV-1 nucleocapsid protein binds double-stranded DNA in multiple modes to regulate compaction and capsid uncoating*. MDPI. https://www.mdpi.com/1999-4915/14/2/235

Maddalena, L., Antonelli, L., Albu, A., Hada, A., & Guarracino, M. R. (2022, August 31). *Artificial Intelligence for cell segmentation, event detection, and tracking for label-free microscopy imaging*. MDPI. https://www.mdpi.com/1999-4893/15/9/313

Wang, A., Zhang, Q., Han, Y., Megason, S., Hormoz, S., Mosaliganti, K. R., Lam, J. C. K., & Li, V. O. K. (2022, January 10). *A novel deep learning-based 3D cell segmentation framework for future image-based disease detection*. Nature News. https://www.nature.com/articles/s41598-021-04048-3

Winfree, S. (2022, March 10). *User-accessible machine learning approaches for cell segmentation and analysis in tissue*. Frontiers in physiology. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8960722/

Wozniak, K. (2024, October). (PDF) cryo-EM and Ed are driving structural studies at the University of Warsaw. https://www.researchgate.net/publication/385033712_Cryo-EM_and_ED_are_driving_structural_studies_at_the_University_of_Warsaw