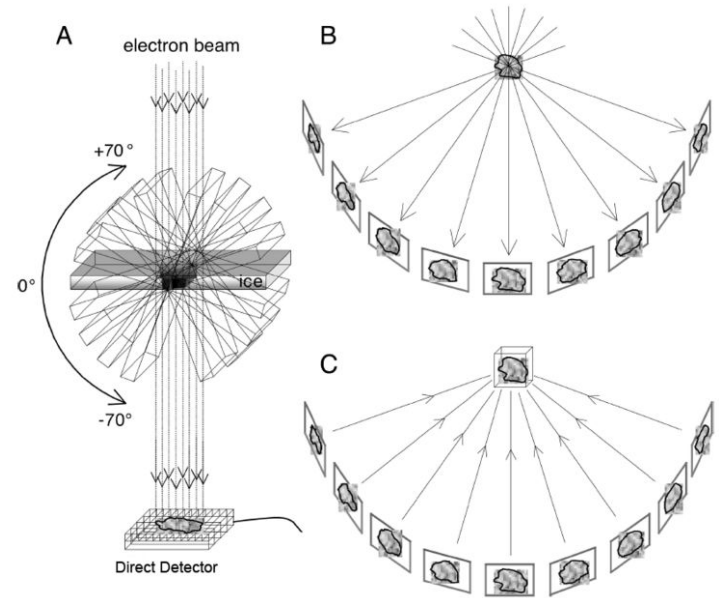

Automated Particle Picking Tool for Cryo-EM Tomograms

By
Manaz Kaleel

Cryo electron microscopy and tomography

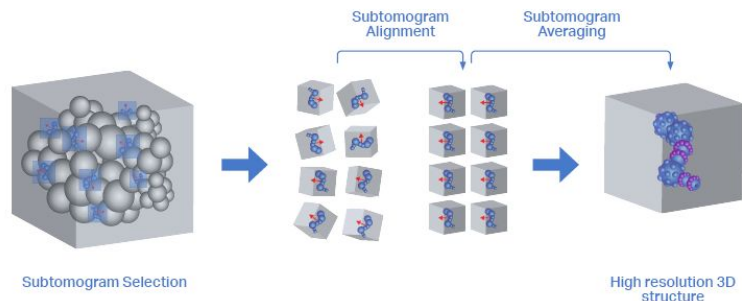
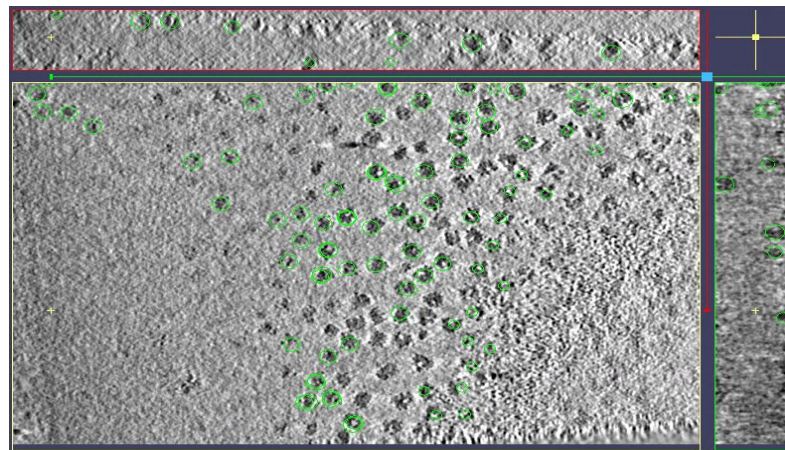
- Cryo electron microscopy (CryoEM) is an electron microscopy technique used to image samples of interest at cryogenic temperatures ($< -150\text{ }^{\circ}\text{C}$) that are embedded in an environment of vitreous ice
- Cryo-electron tomography (CryoET) is an imaging technique to reconstruct 3D views of samples from a series of 2D images obtained from tilting the sample
- The resulting image is a detailed 3D reconstruction of a cellular, macromolecular or material specimen



Principle of Cryo-Electron Tomography

Particle picking and Subtomogram averaging

- Identifying molecular components from a 3D reconstruction (tomogram) remains challenging due to the crowded nature of the environments these molecular components reside and the low signal to noise ratio
- Once the components/particles are located, they can be averaged to provide a higher resolution picture of the particle of interest (“subtomogram averaging”)



Our aims and what do we do

- Create a tool to identify particles of interest from a 3D tomogram
- Make the tool as automated as possible with minimal human labor
- Make the tool as user friendly as possible
- For this, we harness the power of Deep Learning
- The engine of the particle picking mechanism is powered by a deep Residual network

Dataset

- Herpesvirus (pseudorabies or PRV) dataset
- Vesicle covering the virus
- The virus capsid is enclosed by nuclear egress complex (NEC) proteins attached to the inner side of the vesicle membrane
- Picking the **hexamers** (made of 6 heterodimers) that form the NEC pseudo-lattice
- Tomograms are binned and low pass filtered

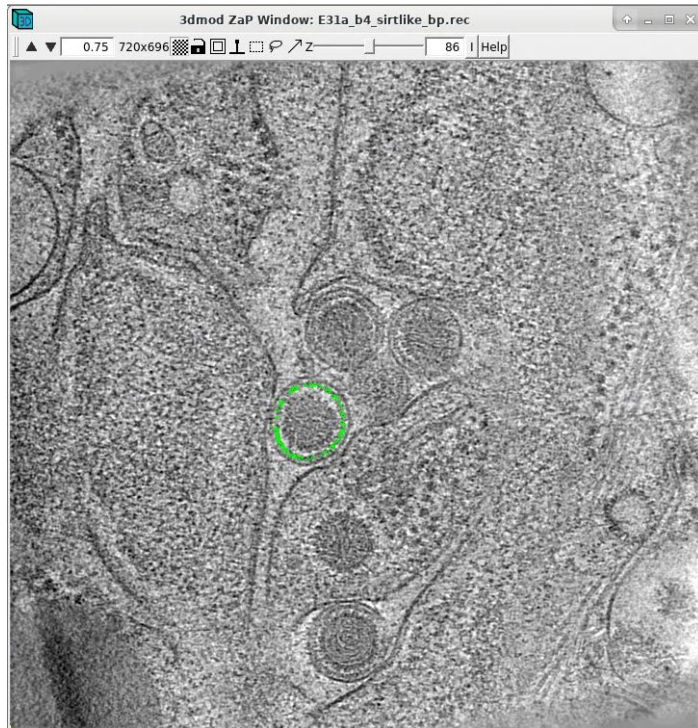
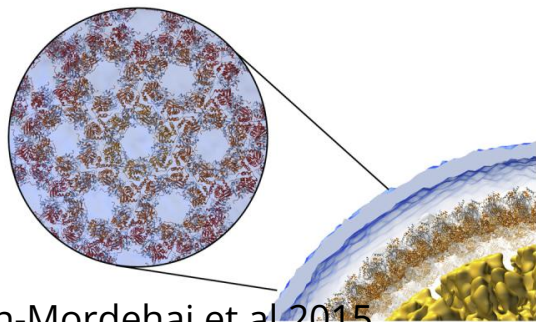


Image source: Topf-lab & Zeev-Ben-Mordehai et al 2015

Initial results

- Performance of the machine learning models for test set
- Top model picks nuclear egress complex with the MCC of 0.8 and nearly 90% accuracy

Configuration	MCC	ACC	F1-Score
config_19	0.8	89.88	0.9
config_21	0.8	89.88	0.9
config_30	0.77	88.25	0.88
config_24	0.74	87	0.87
config_27	0.73	86.25	0.86
config_33	0.73	86.38	0.86
config_31	0.72	85.5	0.85
config_43	0.72	85.94	0.86
config_23	0.71	85.06	0.85
config_39	0.71	85.44	0.85
config_40	0.7	85.19	0.85
config_32	0.69	84.06	0.84
config_35	0.69	84.38	0.84
config_25	0.68	83.44	0.83
config_29	0.67	83.19	0.83
config_34	0.67	83.38	0.83
config_38	0.67	83.44	0.83
config_28	0.65	82.06	0.82
config_36	0.65	81.94	0.82
config_44	0.65	81.94	0.82
config_22	0.64	81.5	0.81
config_26	0.62	80.31	0.8
config_41	0.61	79.81	0.8
config_42	0.61	80.31	0.8
config_37	0.6	79	0.79

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