# Cryo-EM Validation Metrics in EMDA

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Cryo-EM is becoming an increasingly popular method of structure determination in structural biology. As the number of cryo-EM structures increases, it is important to maintain standards that measure the quality of those structures. The correctness of atomic models is very important because they often serve as targets for novel drugs or the knowledge base of such developments. Also, such standards are important to prevent the accumulation of errors of the structures in the databases. Thus, careful curation and validation of cryo-EM maps and derived atomic models are of utmost importance.

We have developed the EMDA Python package [1] that includes tools for cryo-EM map and model manipulation. In this presentation, the emphasis is given to those for validation. The majority of the current validation tools used in single-particle cryo-EM analyses are global metrics. They provide summaries of the global quality of maps or map-model fits. In order to reveal the local variation of the signal in maps and map-model fits, a new set of tools based on the local correlation have been developed. To calculate the local correlation, a spherical kernel is convolved with the map in image space to yield a correlation value at each voxel resulting in a three-dimensional (3D) correlation map. The variation of calculated correlation depends on the size of the kernel. The local correlation calculated using half maps captures the local variations in the signal, whereas the local correlation calculated between a map and a model indicates the quality of their fit. Map-model local correlation can be used to identify model regions outside the density or poorly fitted. Also, it can highlight unmodeled regions on the map. While the half map local correlation is useful to identify the presence/absence of the signal, its comparison with the map-model local correlation can be used to validate the map-model fit. In this presentation, we will demonstrate the use of local correlation through several examples. EMDA includes several tools based on the maximum likelihood method. EMDA's map-overlay and map magnification refinement are based on maximisation of the joint probability distribution between two maps by a quasi-Newton method. We will demonstrate the use of map overlay and magnification refinement implemented in EMDA through examples.

[1] Warshamanage, R. & Murshudov, G.N. (2021). Electron Microscopy Data Analytical toolkit- EMDA. https://emda.readthedocs.io/en/latest/

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