

A local resolution in electron tomography and local directional resolution in Single Particle Analysis

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Introduction

Resolution has been discussed since the beginning of electron microscopy. It is well known that resolution is a spatially variant property and therefore it can be locally affected by heterogeneity, bad angular assignment, lack of data in certain orientations, among others reasons. In this regards the *MonoRes* [1] was proposed as a local resolution estimation algorithm. This issue is achieved in the robust mathematical framework of monogenic analysis. The root of this algorithm is an extension of the concept of analytic signal, called monogenic signal. Thus, a frequency sweep is applied to the original map from low to high frequency. At each frequency it is determined whether the local energy at a voxel is significantly different from the local energy expected for a noise voxel. The local resolution will be the first frequency for which the voxel of the macromolecule fails to be significantly above noise. This algorithm represents the operational core of the following results that this poster shows.

- 1) **MonoTomo**: Up to our knowledge the first method for estimating the local resolution in electron tomograms.
- 2) **MonoDir**: A local-directional resolution method for SPA reconstructions. The concept of resolution is extended as a tensor i.e. the resolution depends on the position and the direction. We expect that this concept opens new horizons in map quality, modeling and validation methods.

MonoTomo algorithm

MonoTomo estimates the local resolution of a tomogram using as input two independent tomograms reconstructed with the half of data. These independent tomograms can be obtained by 1) splitting alternatively the images of the tilt series in two subsets named odd and even that contains the corresponding images to the odd and even angles; or 2) creating two tilt series with the half of the movie frames at each tilt angle. The difference of both tomograms produces a tomogram of noise and provides a noise model that it is spatially variant. Thus, by means of a moving window, it determined the threshold of the monogenic amplitude [1] in each window. Then a B-spline fitting is carried out to obtain a noise model that allows to distinguish noise and signal at different frequencies. Where the signal is calculated as the tomogram considering the whole dataset.

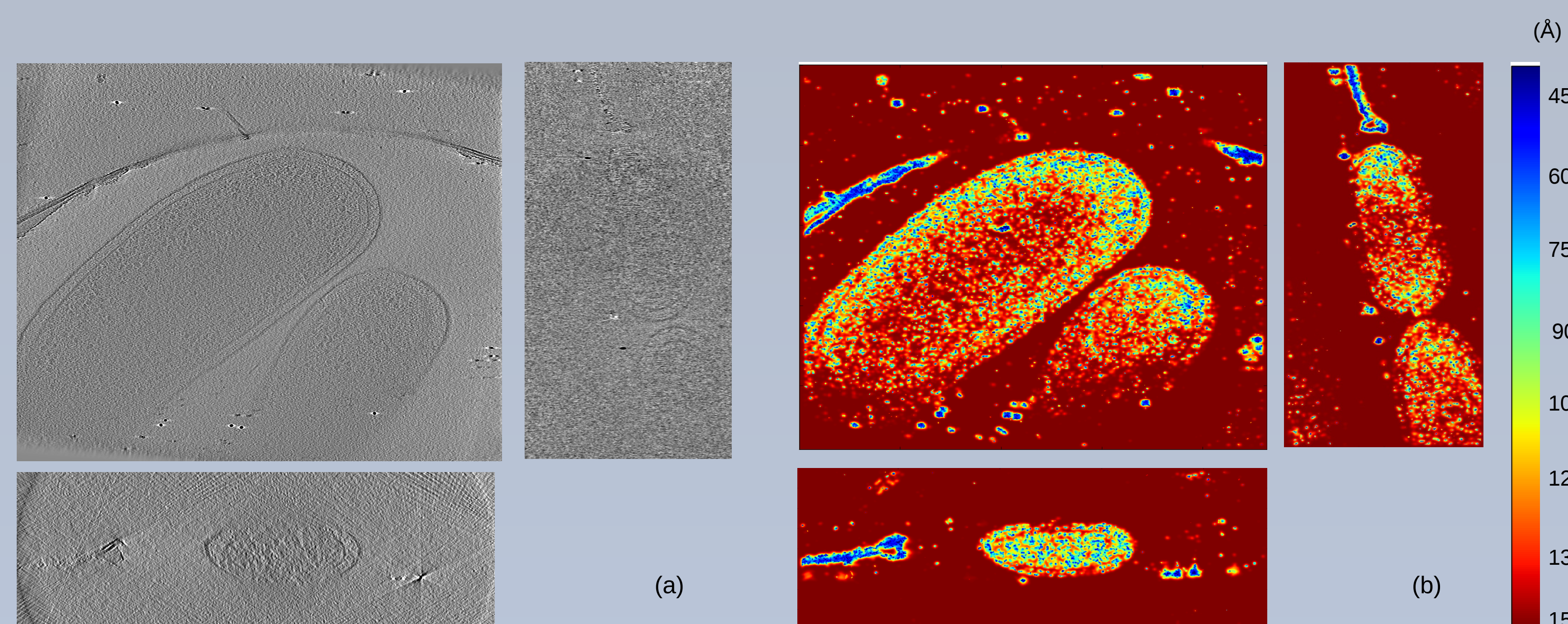


Fig. 1: (left) Tomogram of *Vibrio cholerae* cells obtained with a sampling of 1 degree and tilt angles from -60 to +60 degrees and a pixel size of 4.04 Å. (right) Corresponding slices of the local resolution map. Data taken from EMPIAR entry 10110.

MonoDir algorithm

MonoDir estimates the local-directional resolution of a SPA reconstruction along a set of directions. In a very simple manner this is achieved by a combination of the *MonoRes* algorithm with directional filters. The results are as many local-directional resolution maps as number of measured directions. The combination of these local-directional resolution maps allows to determine the existence of local resolution anisotropies, preferred directions, or angular assignment errors. This information is extracted only from the reconstructed map, it means without any kind knowledge of the set of particles that generated such density map. The existence of angular assignment error is identified as an slope in the radial average of the radial and tangential local resolution maps. The existence of preferred direction in the angular plot that represents the number of voxels which have their highest resolution along a given direction.

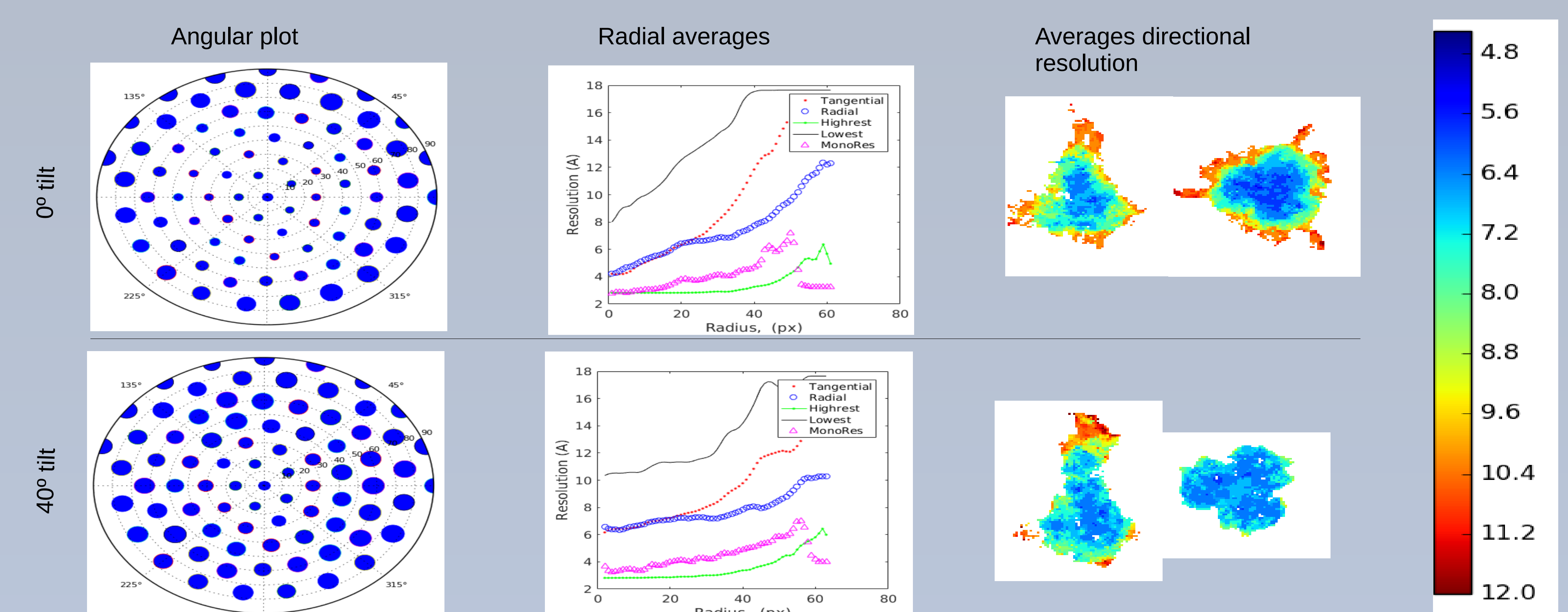


Fig. 2: MonoDir results for Influenza Hemagglutinin (HA) trimer when the sample is untilted and tilted showing the Angular plot (preferred directions), radial averages of tangential, radial, highest, lowest and MonoRes local resolutions (angular assignment errors as slope) and the average of directional resolution. Data taken from EMPIAR entries 10096 and 100097.

Conclusions

1. A fully automatic method for estimating the local resolution in electron tomography has been proposed. It makes use of two independent tomograms reconstructed with the half of data, i.e. by odd-even image splitting or by splitting the set of frame for each tilt angle.
2. A local-directional algorithm has been developed. This algorithm is able to provide information about map quality, existence of preferred directions, angular assignment error, and resolution anisotropy.

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References

- [1] J.L. Vilas et. Al, *MonoRes: Automatic and Accurate Estimation of Local Resolution for Electron Microscopy Maps, Structure*, 26(2):337-344 (2018)