Local Resolution in cryo Electron Microscopy: Adding directionality

Carazo, J.[1]

[1] CSIC-CNB, Spain

Resolution has always being a key topic in cryoEM (1). The ability to calculate local (per pixel) resolution, first accessible with Blocres (2) and then with the very successful ResMap (3) approach, has had an important impact in the field. Building on the successful use of local resolution estimations, we introduced MonoRes (4), an approach that provided fully automatic and fast estimations, rendering a locally-filtered (per pixel) map that could be used as input to any modelling or docking approach.

In this work we introduce a new extension of this approach, so that we provide resolution estimations not only per pixel, but "per pixel and direction". We will show how this new approach allows us to differentiate between loss of resolution due to errors in image alignment, on the one hand, and due to macromolecular flexibility, on the other hand. Let us introduce with a simple example how this directional distinction is key for a proper understanding of the biological significance of local resolution estimations.

Let assume that our specimen is enclosed within a circle centered at the center of the macromolecule. Let imagine that we draw a whole set of circumferences using that center. We will refer to "tangential direction" to the one following the tangent of any of these circumferences. In this simple case, tangential resolution will have a linear relationship with the radius that will not have any biological significance, only geometrical. In other words, if we have a certain tangential local resolution X at radius R, at radius 2R we will have half that resolution, and this loss is due only to the linear relationship linking tangential resolution (to be visualized as an arch), angular accuracy of the alignment (independent of the radius) and the radius itself. In this contribution we will analyze these situations

MonoRes, ResMap and Blocres are available within the Scipion image processing framework (5), as well as freely served over the Web as part of Scipion Web Tools at the following directions:

Direct access from the CNB-CSIC: http://scipion.cnb.csic.es/m/myresmap
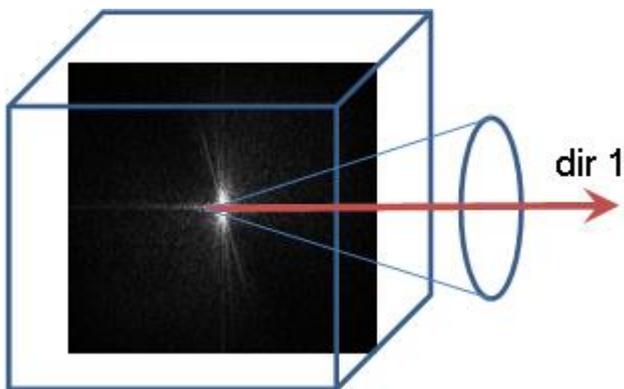Direct access from the EMDB: https://www.ebi.ac.uk/pdbe/emdb/validators.html

Figure 1. The main concept of "Directionality", showing a cone in Fourier space centered on a specific direction

References:

[1] C. Sorzano *et al*, A review of resolution measures and related aspects in 3D electron microscopy, Progress in Biophysics and Molecular Biology, **124**, (2017), 1-30.

[2] G. Cardone *et al*, One number does not fit all: Mapping local variations in resolution in cryo-EM reconstructions, Journal of Structural Biology **184** (2013) 226 - 236.

[3] A. Kucukelbir *et al*, Quantifying the local resolution of cry-EM density maps, Nature Methods **11** (2014) 63 - 65.

[4] Vilas et al., MonoRes: Automatic and accurate estimation of local resolution for electron microscopy maps, Structure, in press

[5] J. M. de la Rosa-Trevín *et al*, Scipion: a software framework toward integration, reproducibility, and validation in 3D electron microscopy, Journal of Structural Biology **195** (2016) 93 - 99.