

## FSC-Q: Analyzing the quality of cryoEM-derived models

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In recent years, advances in cryoEM have dramatically increased the resolution of map reconstructions and, with it, the number of solved atomic models. Central to the task of CryoEM achieving a long term contribution to biomedical research is the fundamental issue of trusting the results obtained in the analysis. In this context, it is widely accepted that the quality of cryoEM maps varies locally; therefore, the evaluation of the maps-derived structural models must be done locally as well. In this contribution, a method for the local analysis of the map-to-model fit is presented. The rationale of the method is based on the differences between local resolution values calculated with blocres (2), providing local estimations of Fourier Shell Correlation (FSC) values. The process involves the subtraction of the local resolution map between the final full map and the map generated from the atomic model, from the local resolution map between the two half-maps (where a half-map refers to a map reconstructed from half of the data set). This latter subtraction, when properly statistically scaled, provides an estimation of the signal content of the map itself, that is then compared with the signal content implied in the fitting of the structural model. We call the new quality measure “FSC-Q”, and it is a quantitative estimation of how much of the model is supported by the signal content of the map. It is intuitive and, yet, very precise, introducing information that we have quantitatively shown is new.

To quantitatively analyze whether FSC-Q is capturing new information not present in other quality assessment metrics, we analyzed the information relationship between the global resolution and (for simplicity) volume-averaged value of FSC-Q and Q-Score (3) through Principal Component Analysis. There is a linear relationship between resolution and Q-score, and a non-linear one between FSC-Q and resolution. The first two principal components explain 98% of the variability and the information of the second principal component comes mostly from the FSC-Q, meaning that this new measure is bringing a new source of information that was not available before (even after considering the Q-Score), in particular, the quality of the fitting between the map and the model, especially for low resolution ( $>3\text{Å}$ ) maps

We are working towards offering FSC-Q as a Web Service for new maps and models before submission to public data bases, on the one hand, and on enhancing both PDB-Knowledge Base (4) and 3DBionotes (5) with extensive precomputed results on cryoEM quality, starting with 3DBionotes-Covid19 Edition

### References

- (1).- [FSC-Q: a CryoEM map-to-atomic model quality validation based on the local Fourier shell correlation](#). Ramírez-Aportela E, Maluenda D, Fonseca YC, Conesa P, Marabini R, Heymann JB, Carazo JM, Sorzano COS. Nat Commun (2021) Jan 4;12(1):42.
- (2).- [One number does not fit all: mapping local variations in resolution in cryo-EM reconstructions](#). Cardone G, Heymann JB, Steven AC. J Struct Biol. (2013). Nov;184(2):226-36.

3.-Measurement of atom resolvability in cryo-EM maps with Q-scores.Pintilie G, *et al.* (2020) *Nat Methods* 17(3):328-334.

4.- <https://www.ebi.ac.uk/pdbe/pdbe-kb>

5.- <http://3dbionotes.cnb.csic.es/ws/covid19>