RESOLVE: Robust local resolution estimation in micrographs, tomograms and 3D reconstructions

David Kartte[1], Carsten Sachse[1]
1) Ernst-Ruska Centre for Microscopy and Spectroscopy with Electrons, ER-C-3 Structural Biology, Forschungszentrum Jülich, Germany

Resolution estimation in **v**arying **e**nvironments

Introduction

Aims for optimal resolution estimation

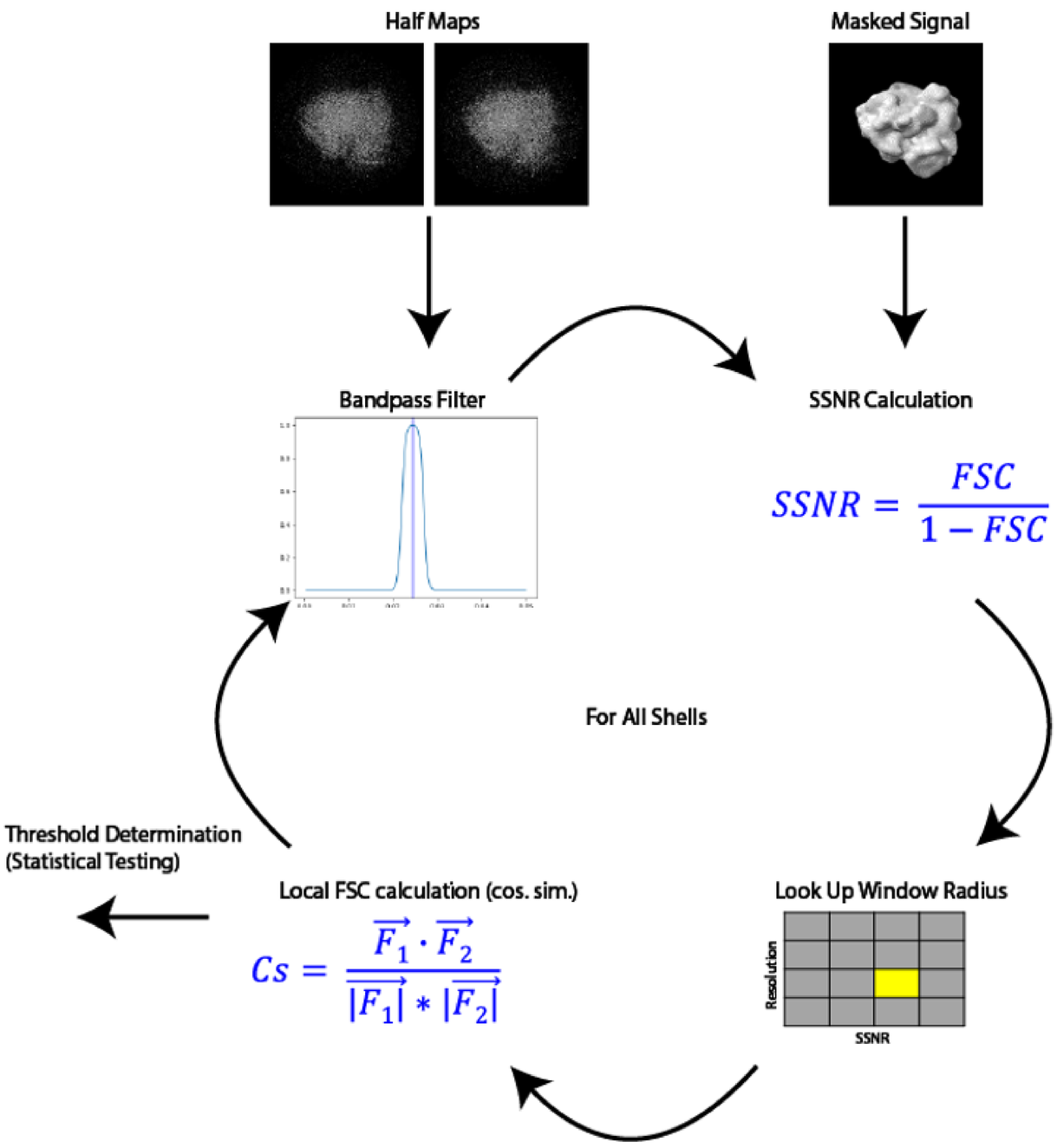
- Accurate
- Local
- Applicable to differing EM data types (3D reconstructions, tomograms, 2d micrographs)
- Robust and consistent (artifact free, independent of voxel size)
- Fast
- Easily usable with minimized parameter tuning

Extending the applicability of local resolution estimation

- Enhance analysis of tomograms.
- Estimate viability of data processing methods in 2D and 3D.
- Preselection of particles for SPA or STA.

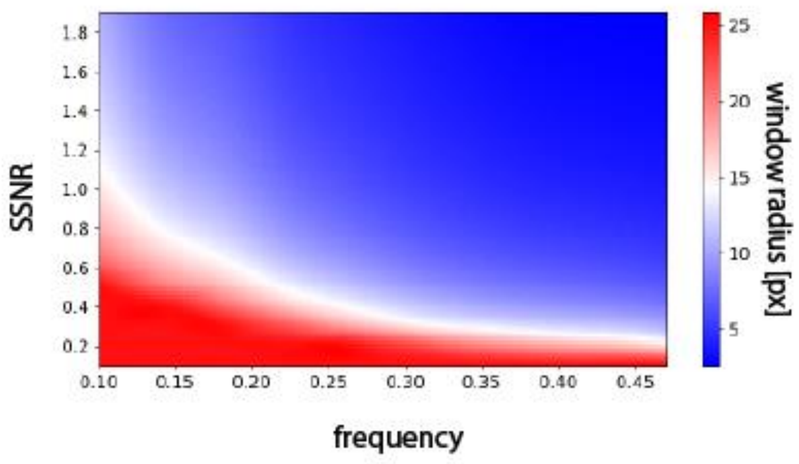
Methods

Overview



A broad overview of the method. For each shell: 1) The input half maps are bandpass filtered (hyp. tan.) for the current shell of interest 2) A signal mask is used to calculate the SSNR 3) According to current SSNR and resolution, the window radius is determined 4) FSC calculation as Cos. Sim. In real space. After all shells are testing, FDR-correction is conducted[1].

Empirical Determination of Window Size

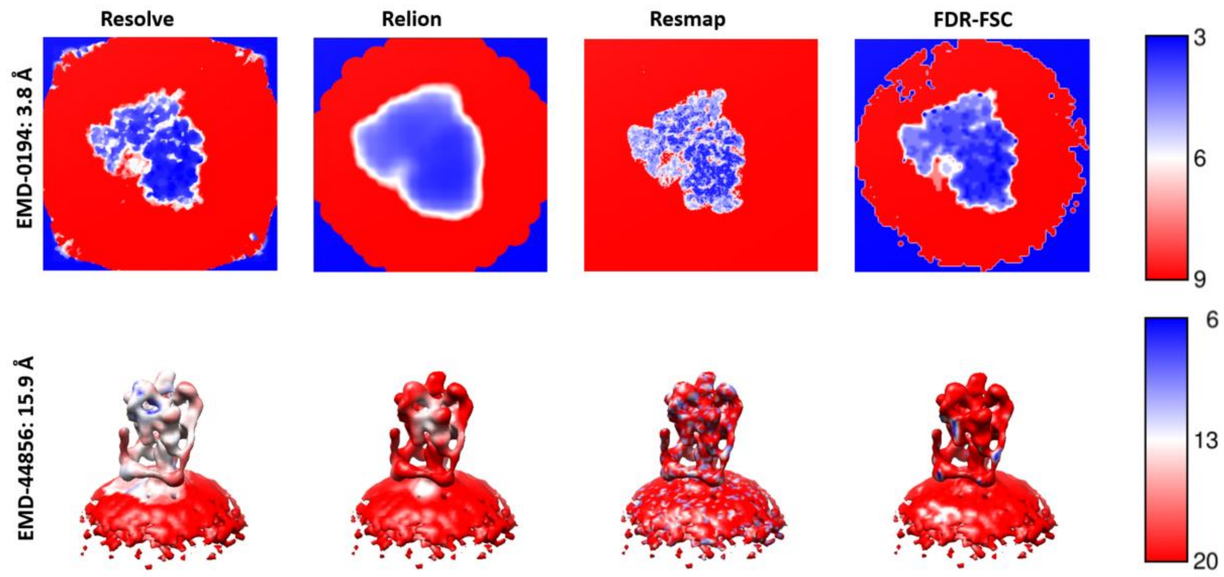


- High window size allows accurate measurement.
- Low window size allows more local measurements.
- Choose window size just large enough for accurate measurements. This is resolution dependent.

Simulation testing to determine the optimal window size, dependent on SSNR and resolution.

Results

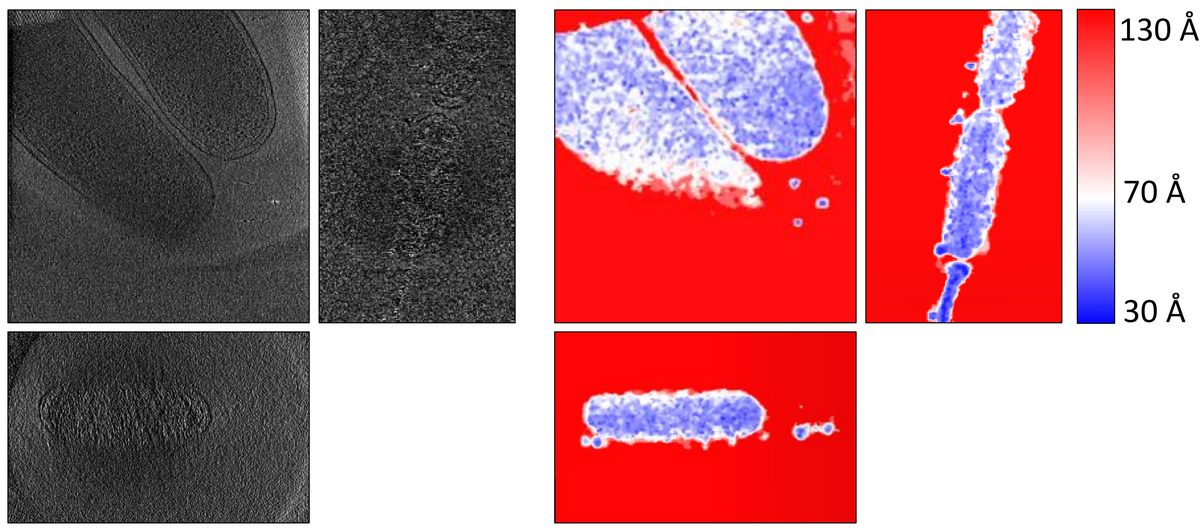
Benchmarking for single-particle structure



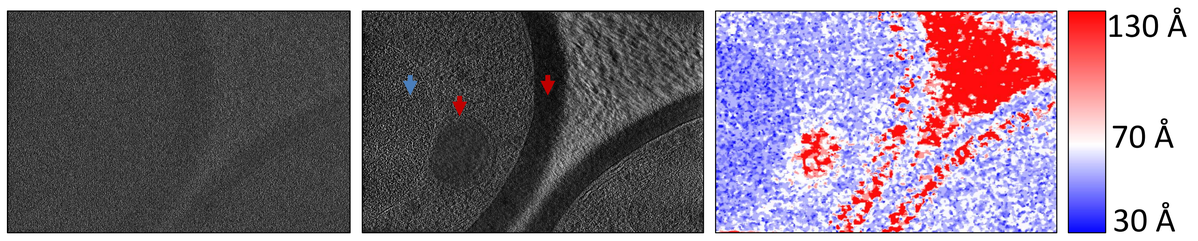
Top: Slice through EMD0194, colored by resolution. **Bottom:** Surface of EMD44856, colored by resolution. Measurements conducted by this tool, Relion[3], Resmap[2] and FDR-FSC[1]. Tools which do not optimize for window size fail to measure resolutions accurately for low SSNR environments. They also tend to lack locality.

Application to tomograms

A EMPIAR-10110

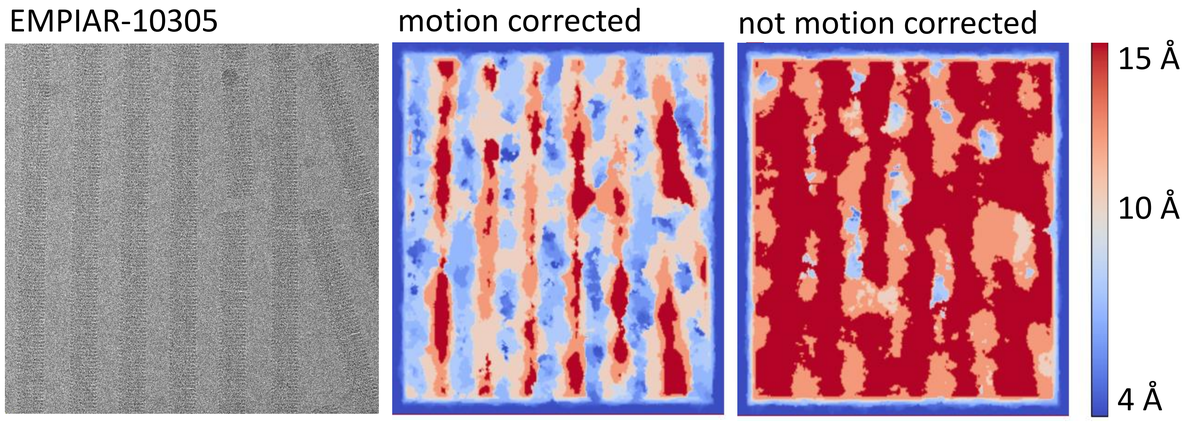


B Yeast cells



Measurements for tomograms. **A)** bacterial cells in solution. **Left**: raw tomogram. **Right**: measured resolution. Three different orientations. **B)** yeast cells. **Left**: raw tomogram. **Middle**: Denoised tomogram by cryoCARE. **Right**: measured resolution. Same color arrays indicate similar resolution signature (data provided by Claire Ortmann).

Micrographs



Left: Processed micrograph. **Middle**: Measured resolution, where motion correction was applied during processing. **Right**: No motion correction applied.

Conclusion

- Robust local resolution estimation with optimal, resolution dependent locality vs. accuracy trade-off.
- Applicable to different EM data types (single-particle structures, tomograms, micrographs).
- Local resolution estimation can help with data interpretation, method validation and particle picking.
- Efficient computation (GPU optimized).

Literature

1) Beckers et al., 2019, J. Struct. Biology
2) Kucukelbir et al., 2014, Nat. Methods
3) Zivanov et al., 2022, eLife

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