

Deep-learning based 3D map sharpening in cryo-electron microscopy

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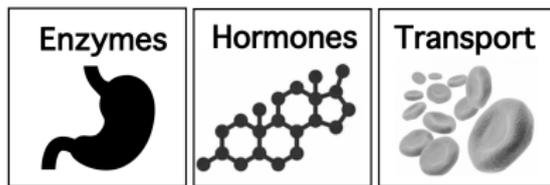
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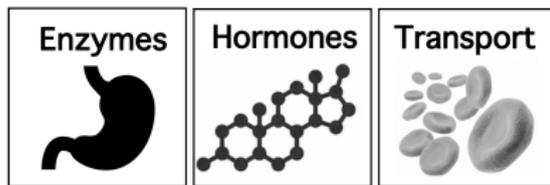
Motivation

- Proteins play a crucial role in our lives!



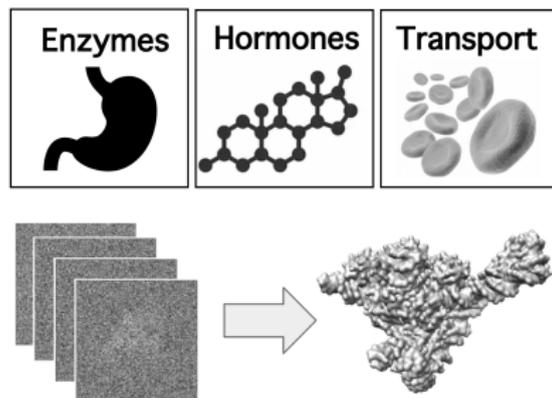
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- Proteins play a crucial role in our lives!
- Their functionality \iff 3D structure



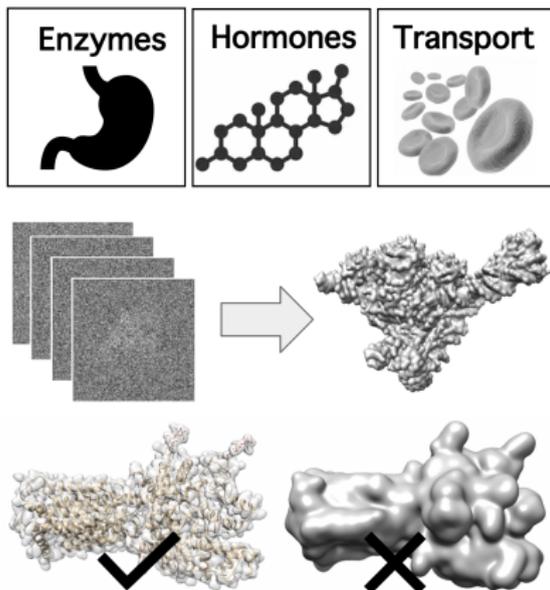
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- Proteins play a crucial role in our lives!
- Their functionality \iff 3D structure
- Cryo-Electron Microscopy:
Recovers the 3D structure



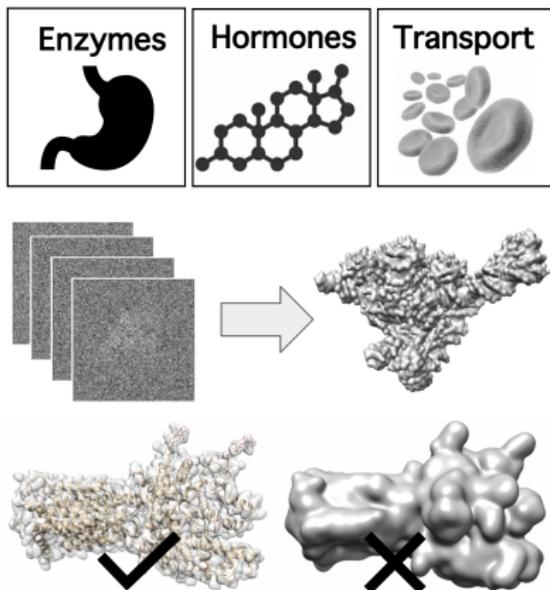
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- Cryo-Electron Microscopy: Recovers the 3D structure
- Shortcomings in reconstructing the structure \longrightarrow Harder to find atomic structure



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Need for methods to enhance the quality of maps

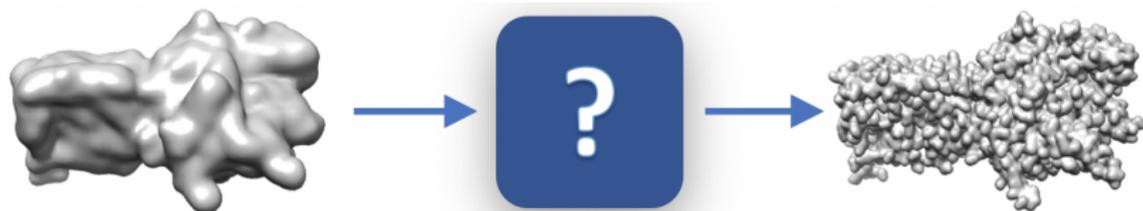


Outline

- Problem definition
- Related work
- Our approach
- Preliminary results
- Conclusion



Problem definition



Turn a low-resolution map in to a high-resolution one!



Problem definition



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Challenges:

Problem definition



Turn a low-resolution map in to a high-resolution one!

Challenges:

- Variable resolution across the map



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Challenges:

- Variable resolution across the map
- Unclear forward mapping between the low and high resolution pairs
- Computational complexity



Previous work

- Weighting low and high frequency terms of Fourier series to maximize connectivity and surface area¹²

¹Terwilliger et al, Automated map sharpening by maximization of detail and connectivity, 2018

²Optimal Determination of Particle Orientation, Absolute Hand, and Contrast Loss in Single-particle Electron Cryo-microscopy

Previous work

- Weighting low and high frequency terms of Fourier series to maximize connectivity and surface area¹²
- Use an atomic reference model to sharpen local patches of the density map³

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A data-driven model that maps low-res to high-res volumes.

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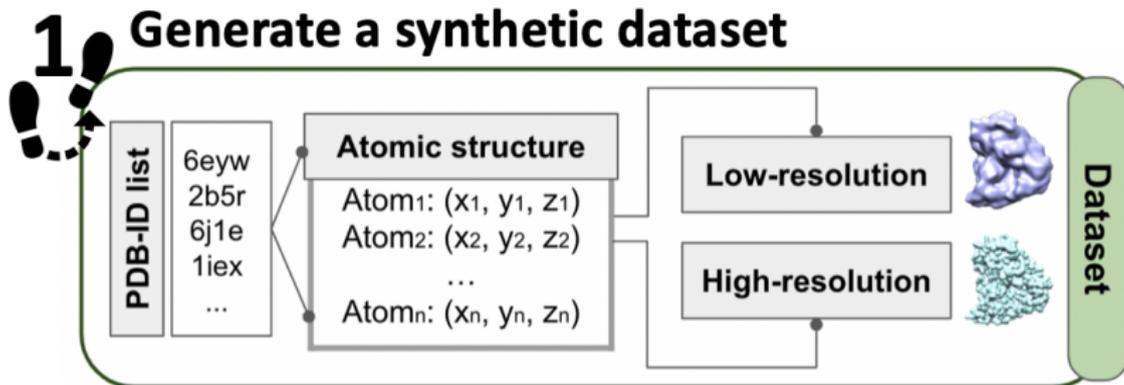
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Our approach

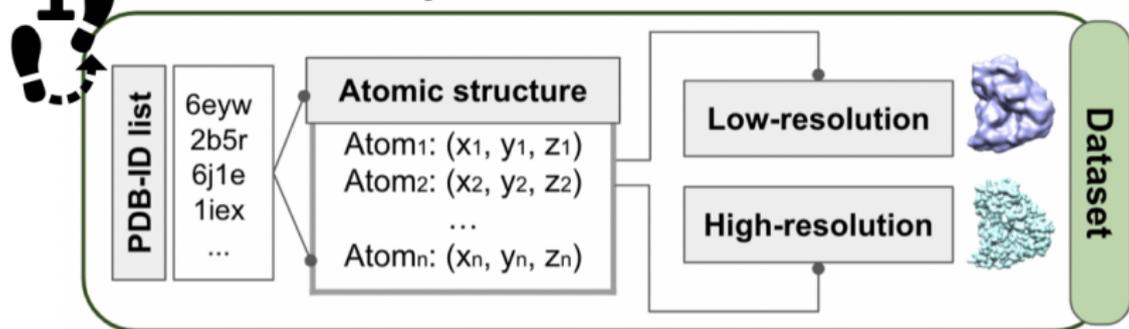


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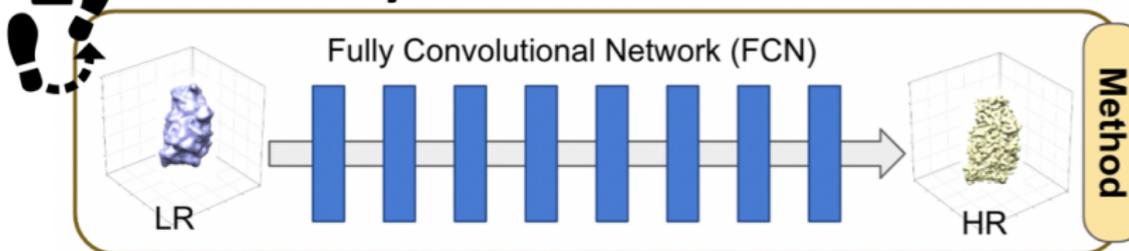


Our approach

1 Generate a synthetic dataset



2 Train a fully convolutional net.



Dataset



Dataset

- Protein structures from SCOPe database¹

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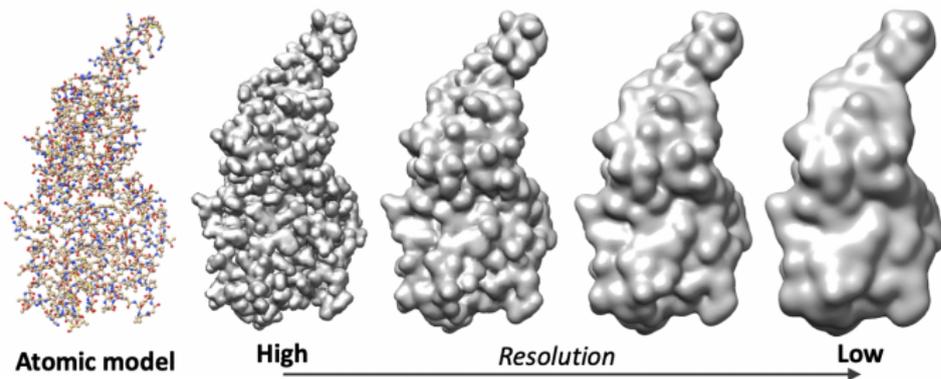
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Dataset

- Protein structures from SCOPe database¹
- ~ 15,000 protein structures
- Simulating atoms with Gaussian blobs with σ width and weight relative to their atomic number using Chimera²
- Generate samples with different resolutions



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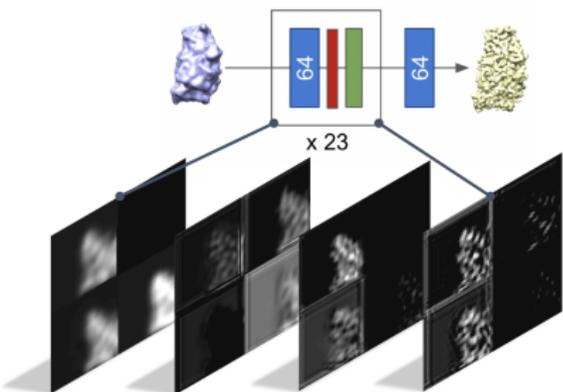
Network architecture

Fully convolutional architectures



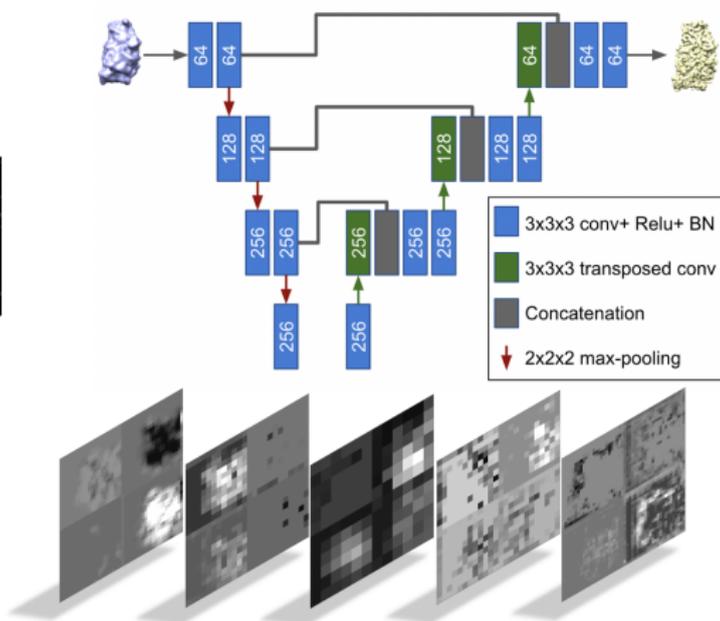
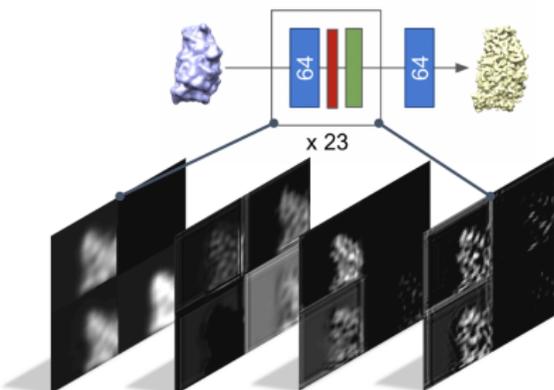
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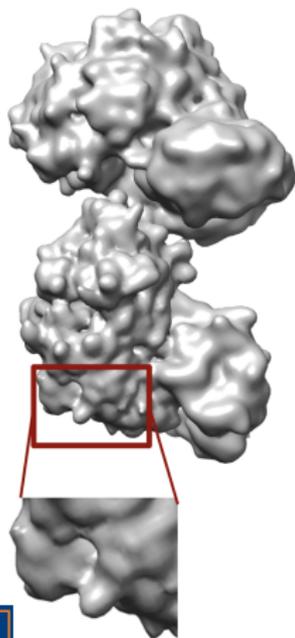
Fully convolutional architectures



Visual results—simulated

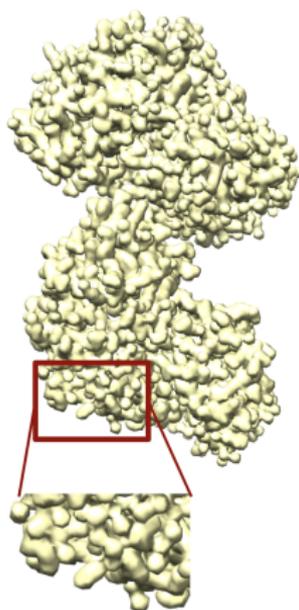
- PDB ID: 2b5r

Low-res (input)

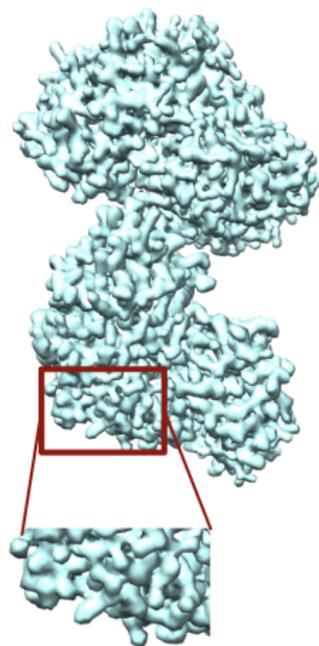


CC = 0.75

High-res (gt.)



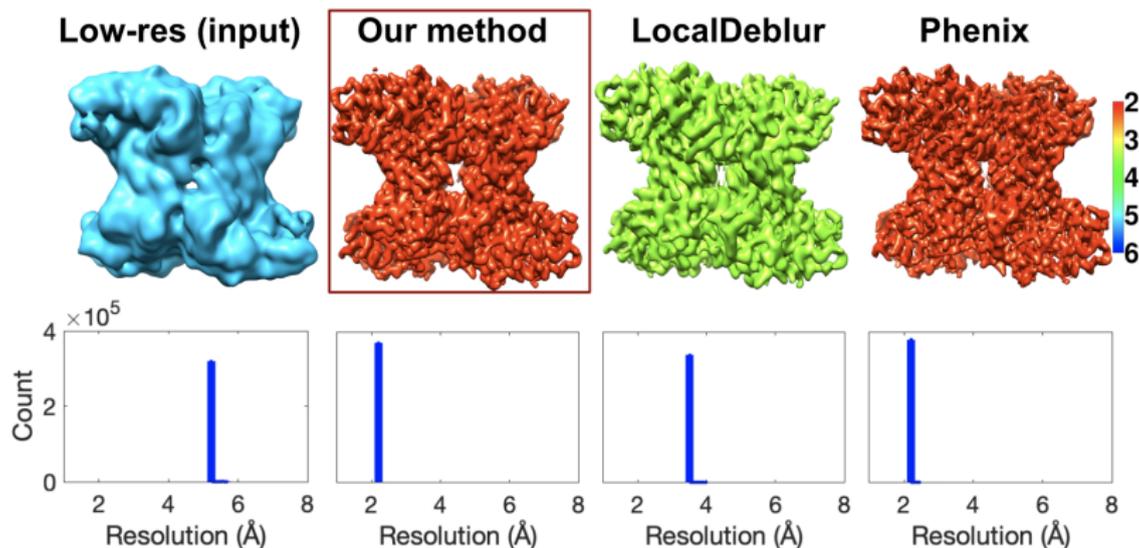
Ours



CC = 0.95

Visual results—experimental

- EMD-7550



Kucukelbir et al, Quantifying the Local Resolution of Cryo-EM Density Maps, Nature Methods., 2014.

Terwilliger et al, Automated map sharpening by maximization of detail and connectivity, 2018

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- Using the knowledge of protein sequence to better enhance the quality of the map



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- Using the knowledge of protein sequence to better enhance the quality of the map
- Consider other type of map degradation in experimental density maps

