

# CryoRes: Local Resolution Estimation of Cryo-EM Density Maps by Deep Learning

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- A cryo-EM density map can have varying extents of resolvability in different local regions, owing to factors including sample heterogeneity and radiation damage.
- Estimate from half maps: blocres, ResMap.
- Estimate from a single final map: ResMap, MonoRes, DeepRes.

# Introduction

Table 1 Comparison and summary of local resolution estimation methods.

Method	Theory	Input	Output	Disadvantage	Time
<i>blocres</i>	Fourier shell correlation	1. Half-maps; 2. Mask; 3. Parameters (Kernel width in voxels, step size <i>et al.</i> );	1. Resolution map;	1. Requiring half-maps; 2. Requiring parameters; 3. Spectral leakage 4. Huge number of calculations;	Several hours
ResMap	Signal and noise comparison	1. Single final map / Half-maps *; 2. Mask *; 3. Parameters (step size <i>et al.</i> ); 4. Step of manually adjusting frequency conversion;	1. Resolution map;	1. Preferring half maps; 2. Preferring mask; 3. Requiring parameters;	Dozens of seconds / Several minutes
MonoRes	Signal and noise comparison	1. Single final map; 2. Mask or Half-maps; 3. Parameters (resolution range <sup>#</sup> );	1. Resolution map;	1. Requiring mask or half-maps; 2. Requiring parameters;	Dozens of seconds/ Several minutes
DeepRes	Deep learning	1. Single final map; 2. Mask;	1. Resolution map;	1. Requiring mask; 2. Requiring sharp-ened map; 3. Estimating only 1.5 Å – 13 Å;	Dozens of minutes
CryoRes	Deep learning	1. Single map;	1. Resolution map; 2. Mask;	1. Estimating only 1 Å – 10 Å;	Several seconds/ Dozens of seconds

\* means “prefer”.

# means compulsory user parameters, without default value.

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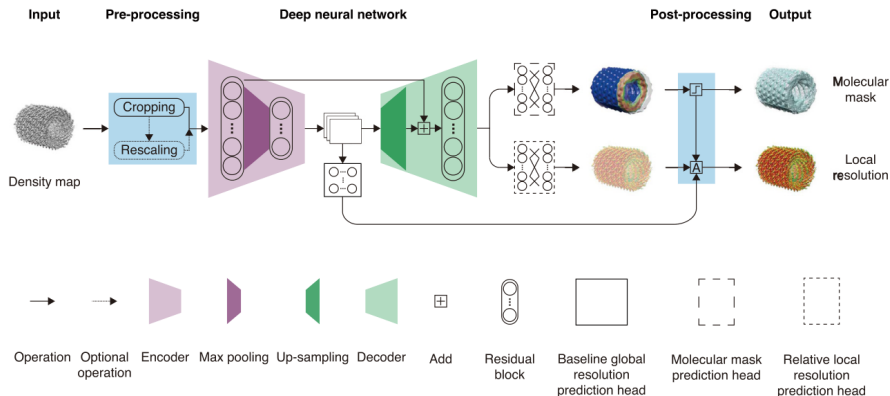
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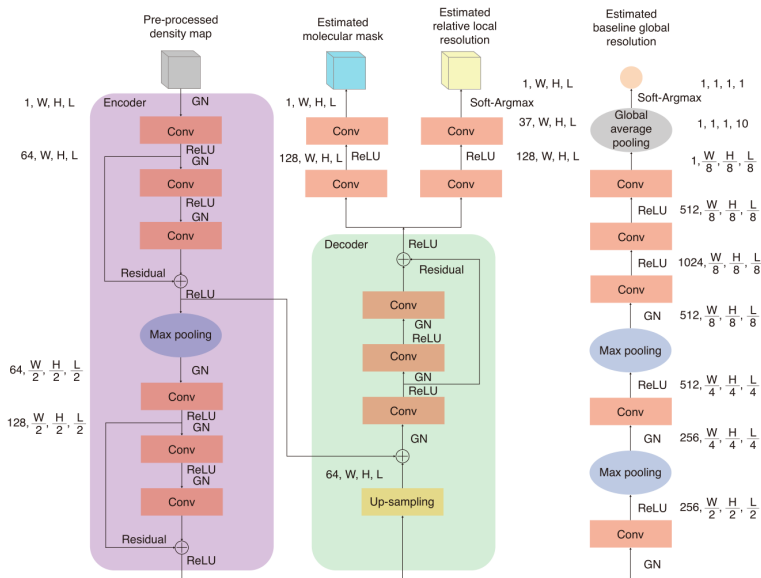
# Algorithm

- The CryoRes algorithm comprises three modules: pre-processing, network inference, and post-processing.



- Cropping: extracting the minimum bounding cube. Ensure that those voxels outside of the cube have a density value less than or equal to  $\mu \pm 3\sigma$ .
- Rescaling: Down-sampling the density map to a size of  $W \times H \times L$  with interpolation.

# Network Inference





- Labels:
  - The global resolution: the global resolution deposited in EMDB.
  - Relative local resolutions: estimated by ResMap.
  - Molecular mask: calculating a  $4\text{\AA}$  simulated map from the corresponding atomic model in PDB.
- Loss function:  $L_{global}, L_{rel}, L_{mask}$ 
  - $L_{global} = (\hat{y}_b - y_b)^2$ .
  - $L_{rel} = \frac{1}{N} \sum_{i=1}^N (\log_{10} |\hat{y}_i^r - y_i^r| + 1)$ .
  - $L_{mask} = -\frac{1}{N} \sum_{i=1}^N [y_i^m \log(\hat{y}_i^m) + (1 - y_i^m) \log(1 - \hat{y}_i^m)]$ .
  - $L_{total} = L_{global} + \lambda L_{rel} + L_{mask}$ .
- SGD optimizer, learning rate 0.0000001, momentum 0.8, 500 epochs.

## Post-processing:

- The post-processing includes two steps: aggregating and rescaling.
- Aggregating: add the predicted baseline global resolution to the relative local resolution and then multiply it with the predicted molecular mask.
- Rescaling: rescale the aggregated local resolution to the same size as the original input density map.

## Evaluation:

- Local resolution:  $\text{RMSE} = \sqrt{\frac{1}{N}(\hat{y}_i - y_i)^2}$ .
- Mask:  $\text{mIoU} = \frac{1}{N} \sum_{i=1}^N \frac{\hat{y}_i \cap y_i}{\hat{y}_i \cup y_i}$ .

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