A Hierarchical Graph-Based Method for Single-Molecule Localization Microscopy Clustering

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Clustering of point-cloud data that originate from single-molecule localization microscopy (SMLM) plays a significant role in identifying the spatial organizations of protein complexes. Existing methods for SMLM clustering rely on some priors either on the shape of the structures of interest and/or on the noise distribution and do not provide a solution for multi-scale clustering. We propose a novel SMLM clustering method, named GrapHiC, that can infer a hierarchical structure from the data. It takes a particular relevance when quantitatively analyzing the biological particles of interest at different scales. It does not assume any prior neither on the shape of particles nor on the background noise. We build our multi-scale clustering pipeline upon graph theory. At each scale, we first construct a weighted graph that represents the SMLM data. We perform a preprocessing step to omit isolated points from the graph. Moreover, we use the uncertainty of localizations for calculating the graph weights to improve the clustering and denoising steps. Next, we find clusters using spectral clustering. We then use the output of this clustering algorithm to build the graph in the next scale; in this way, we ensure consistency over different scales. Our method suits very well with the clusters of various labeling densities and shapes. We provide an example of our method in Figure 1.

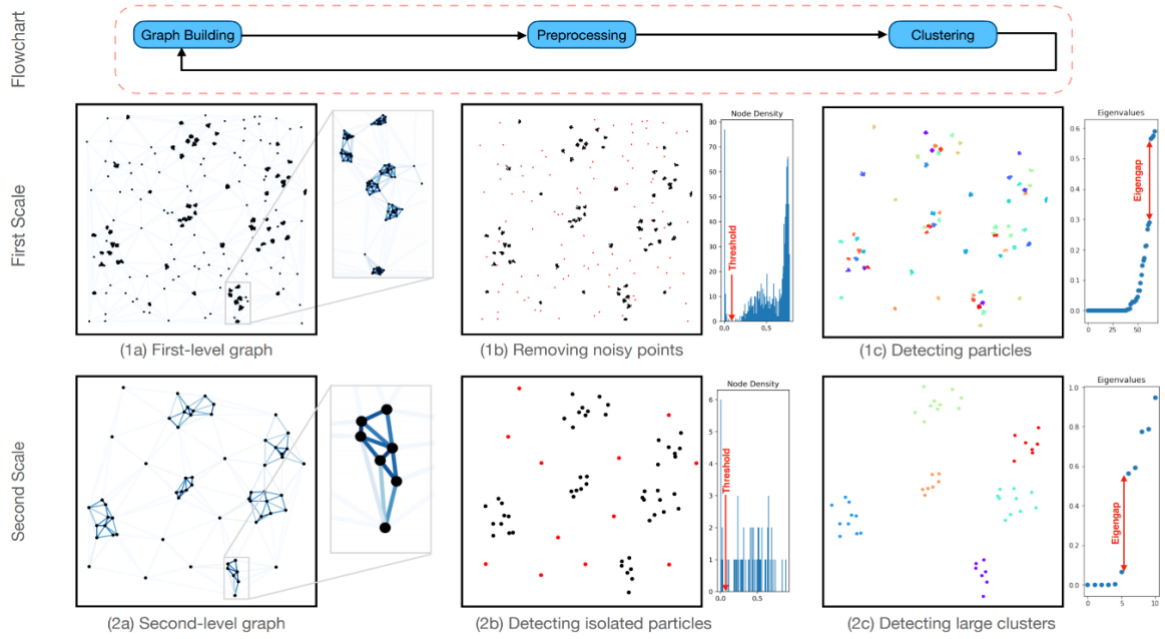

Figure 1. Steps of our method over two scales