Filtering, Segmenting, and Quantifying Caveolin-1 Protein Clusters in 3D Super-Resolution Microscopy via Machine-Learning and Network Analysis

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1 Background

- Caveolae are omega-shaped small (50-100 nm) invaginations of the plasma membrane. Their formation requires both caveolin-1 (Cav1) and CAVIN1/PTRF (Polymerase I and transcript release factor) proteins
- Scaffolds are non-caveolar oligomers of Cav1 only (absence of CAVIN1)
- Super-resolution microscopy is used to localize the blinks of Cav1 protein with ~20 nm lateral resolution (X-Y), and with 40-50 nm axial resolution (Z)

2 Objectives

- To extract the heterogenous clusters of Cav1 proteins from 3D SMLM big-data
- To find the biological signatures from the extracted clusters and then utilize the signatures to discriminate between the different groups of clusters
- Determine the molecular architecture of Cav1 in caveolae and scaffolds

3 Method

- We designed a modular computational pipeline to identify the biological structures and their signatures from SMLM data

4 Data

- We validated our approach on GSD/STORM datasets of 80 PC3, PC3-PTRF and 10 HeLa cells labeled with primary rabbit anti-caveolin-1 antibodies and Alexa647 conjugated anti-rabbit secondary antibodies.

5 Results

6 Conclusion

- We identified caveolar and non-caveolar domains in PC3 cell lines as well as in HeLa cells
- We categorized more than one type of scaffolds
- Our approach could be generalized to other SMLM data and, at the same time, could be used to analyze different proteins and different cellular structures
- We designed a pipeline that allows us to identify the biological structures and their signatures from aforementioned datasets

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