

Statistical Inference and Community Detection in Proximity and Spatial Proteomics: Resolving the Organization of the Neuronal Proteome

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Technological advances in protein mass spectrometry (MS), aka proteomics, have enabled high-throughput and nearly complete quantification of spatially-resolved, subcellular-specific proteomes. Biological insight in these experiments depends upon sound statistical analysis. Despite the myriad of existing proprietary and open-source software solutions for statistical analysis of proteomics data, these tools suffer a drawback inherent in any general solution: a loss of specificity. These tools often fail to be easily adapted to analyze experiment-specific designs. I present a flexible framework for assessing differential protein abundance in MS experiments. Combined with methods to identify communities of proteins in biological networks, I extend this framework to perform inference at the level of protein groups or modules. Using these tools, I demonstrate how module-level insight from proximity and spatial proteomics generates hypotheses that identify foci of biological dysregulation underlying the neuropathology of disease.