ABSTRACT. Macrophages are immune sentinel cells that are distributed in every organ. Their physiological function is to detect pathogens, tissue damage, and immune cytokines to initiate and coordinate a multi-phased immune response that is appropriate for the immune threat. How macrophages specify the appropriate response remains unknown. Recent experimental studies suggest that the dynamics of the signal-responsive transcription factor, nuclear factor kappa B (NFkB), constitute a temporal code that conveys to the nucleus information about the presence and type of immune threat in the extra-cellular environment. In this project, I seek to construct a high resolution mathematical model of the NFkB signaling pathway to recapitulate single cell experimental data. This requires the development of novel methods as the data shows high cell-to-cell variability that includes technical noise, and distance metrics typically applied to time-series measurements over-penalize slight shifts in phase or frequency. To address these difficulties, I developed a feature based objective function for quantitative model fitting based on six so-called ‘signaling codons’ (i.e. duration, peak, total activity, oscillation content, etc.) identified as crucial for NFkB stimulus specificity using mutual information and classification analysis. Applications of this high-resolution model include identifying key circuit design principles that encode the observed stimulus-specific use of signaling codons and pinpointing crucial sources of molecular noise that diminish NFkB information encoding.

Abstract. The incorporation of mass spectrometry data to identify protein-protein interactions and associations has become extremely popular, and presents an exciting opportunity to exploit the protein interactome. However, the experimentation often produces large amounts of proteomic data that can be hard to handle, delaying scientific discovery. It has become clear that when handling the data, cleaning the data of false positives is as important as verifying associations. To address this issue, scientists have developed databases like the Contaminant Repository for Affinity Purification (CRAPome) that provide quantitative information for a collection of controls. However, the data can be hard to interpret without rigorous statistical analysis, differential expression via protein quantification still lacks full proteome coverage resulting in missing data points, and there is a lack of tools to biologically interpret and visualize the data. To address this issue, I have developed an open source proteomic pipeline that incorporates tools to identify false positives, analyze, and visualize interactions/associations in a user friendly manner. Taking advantage of R, a popular statistical programming language, and Shinny apps we developed a program that aims to standardize analysis of protein interaction/association experiments. The pipeline allows scientists to use quantified proteomic data and easily apply suggested significance tests to clean their experiments against their own control. Often these types of experiments are done through a purification step and so we have extended the platform to include machine learning to predict false positives based on intrinsic properties of proteins. After analysis, is carried out we couple the platform to protein interaction network visualization tools such as Cytoscape, and annotated biological databases such as Geneontology, BioGrid, IntAct, CORUM, and Reactome to create a user-friendly comprehensive analysis pipeline for protein association/interaction experiments.

Friday, May 31, 2019
3440 Molecular Sciences
3:30 p.m.

For more information, contact Marla Gonzalez marla@chem.ucla.edu