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Heterogeneity and diversity of regulatory elements in the human genome

Over the last 4 years, the Encyclopedia of DNA Elements (ENCODE) project has generated massive amounts of diverse, genome-wide functional genomics data with the goal of obtaining a comprehensive functional annotation of the human genome. In this talk, I will start with a gentle introduction to the diversity of ENCODE data and a brief overview of robust, statistical methods that we developed for automated detection of potential regulatory elements from the massive collections of noisy, experimental data. The rest of the talk will focus on integrative analysis of these diverse datasets to understand functional heterogeneity of regulatory elements in the human genome. I will describe a novel machine learning approach that enabled us to obtain one of the most detailed context-specific maps of higher-order DNA binding interactions between transcription factors in humans. We discovered several novel co-associations and extensive heterogeneity of co-associations within and between cell-types linked to different functional categories of target genes. Next, I will present a novel targeted analysis that revealed extensive asymmetry and heterogeneity of patterns of nucleosome positioning and histone modifications at binding sites of 100s of transcription factors. The diverse patterns were related to the enrichment of specific sets of co-associating cofactors, the functional role of transcription factors as well as the effect of nucleosome positioning sequence elements. Finally, I will present a brief overview of my current work on understanding the variation of epigenomic chromatin regulation across multiple human cell types and across multiple individuals.