DOCTORAL DISSERTATION DEFENSE

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Epigenome-wide meta-analysis of gene function prediction across genomic features

COMMITTEE IN CHARGE: Jonathan Wren, Ph.D.; Ann-Louise Olson, Ph.D.; Karla Rodgers, Ph.D.; Hiroyuki Matsumoto, Ph.D., Willard Freeman, Ph.D.

ABSTRACT: Gene function prediction has been shown to be a useful methodology for leveraging publicly-available high-throughput datasets from open scientific repositories to identify previously unknown relationships between genes. Using hundreds of thousands of microarrays or transcriptomics data, gene function prediction has to this point mostly been applied in the context of gene coexpression. However, with the recent influx of DNA methylation microarrays, as well as publications on the regulatory role that DNA methylation plays in modulating gene expression, there is an open question to whether publicly-available DNA methylation microarrays can realize new information about the relationships between genes using methods for gene function prediction.

We have developed the methods for predicting gene function from DNA methylation using both a multi-tissue comethylation matrix constructed from publicly-available data, as well as a logistic regression method using the same dataset to increase predictive performance. We evaluate the dataset and model using a number of metrics including comparisons to gene expression predictions using the same methodology, as well the multifunctionality predictor as a baseline of the predictive performance inherent in the Gene Ontology’s representation of the connectivity between genes. We have shown that DNA methylation is effective at predicting gene function, and apply this to a systemic lupus erythematosus dataset as an application of the method on new data. Finally, we show that DNA comethylation clusters are enriched for permissive and repressive histone modifications, as well as development and differentiation terms.