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Identification and inference of transcription factor sequence preferences by DAP-seq and deep learning

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A long-standing goal of computational biology is to construct Gene Regulatory Networks (GRNs) to understand the regulatory process and mechanism of biological systems. The key component of a GRN is the Transcription Factors (TFs), each of which binds a set of similar DNA sequences, known as TF Binding Sites (TFBSs), in promoter regions. Some techniques have been proposed for identifying the TFBSs of TFs, such as ChIP-seq, Protein Binding Microarray (PBM), SELEX, etc. A powerful technique, called DAP-seq (DNA affinity purification sequencing), was recently introduced and demonstrated for the determination of many Arabidopsis TF genes. However, despite these advances in technologies, the portion of eukaryotic TFs whose motifs have been determined is still low, e.g. ~50% in human, ~40% in Arabidopsis and <~1% in non-model organisms. Fortunately, a study found that closely related DBDs from multiple eukaryotic clades have very similar DNA sequence motifs. It suggests that TF motifs can be inferred by representative TFs from the same or different species that have similar DBDs. Therefore, we studied maize TFs using the DAP-seq technique and developed a bioinformatics method to select the representative TFs with unknown motifs and predicted their potential target genes that enhance binding events for DAP-seq assay. Using the known and our identified TF motifs as a training set, we provided a tool to predict the TFBS of any given TF sequence by a convolutional neural network method.

Biography

Chun-Ping Yu has received his PhD degree in Physics from National Central University, Taiwan. He is currently working as a Postdoctoral Fellow at Biodiversity Research Center, Academia Sinica, Taiwan. His research interests include gene regulation, evolutionary genetics and systems biology. His current work focuses on developing NGS functional genomics applications for a large-scale determination of transcription factor binding sites using bioinformatics techniques, machine learning and artificial intelligence methods.

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