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Deep neural network algorithm identifies strength and location of transcription factor activation domains in eukaryotes

Researchers in Roger Kornberg's lab have developed a deep convolutional neural network algorithm that predicts the location and strength of transcription factor activation domains (ADs) in eukaryotes. Transcription factors are essential for modulating gene expression and when misregulated or mutated can lead to many human diseases including cancer. ADs are the regions of transcription factors responsible for increasing gene expression, however very few ADs in human or virus genomes are annotated because their sequences are poorly conserved. Researchers have developed a computational tool that predicts the locations and strengths of ADs with high accuracy, enabling rapid functional characterization of transcription factors across all newly sequenced genomes and genetic mutants. This trained neural network can predict the location and activation strength of a 53 amino acid long region with inputs of its (1) protein sequence and (2) secondary structure prediction. This is the only AD prediction algorithm that has been validated in an in vitro human system, where predicted high-strength ADs were 92% activating when tested in human cell lines. This is an effective tool for companies/researchers who are interested in engineering cells using transcriptional control systems and identifying disease-related AD mutations.

Applications

- Identification and characterization of ADs in eukaryotic cells
- Identification of disease-related mutations in human transcription factor proteins
- Cell engineering with carefully tuned transcriptional activity

Advantages

- High accuracy prediction of ADs in yeast and human cells
- Predicted ADs have been validated in an in vitro human system

Publications

- Sanborn et. al Simple biochemical features underlie transcriptional activation domain diversity and dynamic, fuzzy binding to Mediator eLife (2021)

Patents

- Published Application: 20220186401
- Issued: 11,732,381 (USA)

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