APPLIED MATHMATICS SEMINAR:
Quantifying Sequence Recognition by Regulatory Proteins Through Principled Analysis of High-Throughput Sequencing Data

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Date:
10/29/2021

Time:
3:00 PM-5:20 PM

Location:
COB2 170

About The Speaker:

H. Tomas Rube is an Assistant Project Scientist in the School of Engineering at University of California, Merced. In his research he develops computational methods that discover the rules whereby regulatory proteins read the genetic sequence. Previously, Tomas was a Postdoctoral Research Associate at Columbia University, and University of California, San Francisco. He obtained his Ph.D. in Physics from Stanford University.

Abstract:

Quantifying sequence-specific protein-ligand interactions is critical for understanding and exploiting numerous cellular processes, including gene regulation and signal transduction. Next-generation sequencing based assays are increasingly being used to profile these interactions with high-throughput. However, current computational methods do not provide the biophysical parameters that have long been used to uncover the quantitative rules underlying sequence recognition. In this seminar, I will introduce a highly flexible machine learning framework, called ProBound, that defines sequence recognition in terms of equilibrium binding constants or kinetic rates based on sequencing data. ProBound quantifies transcription factor behavior with models that accurately predict binding affinity over a range exceeding that of previous resources, captures the impact of DNA modifications and conformational flexibility of transcription factor complexes. When coupled with a new assay called Kd-seq, it determines the absolute affinity of protein-ligand interactions. It can also profile the kinetics of kinase-substrate interactions. By providing a biophysically robust foundation for profiling sequence recognition, ProBound opens up new avenues for decoding biological networks and rationally engineering protein-ligand interactions.

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