IST Faculty Candidate Lecture

Bringing big genomic data into focus for understanding multicellular function and disease

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11:10 a.m.
202 IST Building

Arjun Krishnan

Arjun Krishnan is an associate research scholar in the Lewis-Sigler Institute for Integrative Genomics at Princeton University. He earned a B.Tech in biotechnology from Anna University, India, and a Ph.D. in genetics, bioinformatics and computational biology from Virginia Tech. Arjun's research interests lie in developing computational genomic approaches that integrate large-scale data to tackle experimentally challenging/intractable aspects of multicellular biology and disease.

Abstract:

Our body has more than 200 types of cells and tissues, each performing a highly specialized function. This diversity emerges from how the 25,000 genes in our genome interact in distinct ways in different tissues/cell-types. Deciphering these tissue-specific gene networks is experimentally intractable, and yet, fundamental to our understanding of gene functions and disease-gene associations.

In this talk, I will describe a Bayesian framework that we recently developed that integrates thousands of genomic datasets to predict tissue-specific relationships between genes in each of 144 specific human cell-types and tissues (available at giant.princeton.edu). I will show examples to illustrate how the resulting networks predict tissue-specific molecular response to perturbation, and the changing roles of multifunctional genes.

I will use autism spectrum disorder (ASD) to further elaborate on how tissue-networks are valuable in generating hypotheses about the molecular basis of human diseases. Using an evidence-weighted machine learning approach that utilizes the human brain-specific functional gene network, we have produced the first genome-wide prediction of autism-associated genes. We have further established how the large set of ASD genes, including a host of novel candidates, converges on a smaller number of key cellular pathways and specific early developmental stages of the brain (available at asd.princeton.edu).

Manifesting in early development and being five times more common among boys than among girls, ASD is one among several diseases whose incidence/risk varies dramatically across the human lifespan and between the sexes. I will conclude by broadly laying out my future goals in expanding our genomics toolkit to address how genes and their interactions shape health, disease, and therapy in an age-, sex-, and tissue-specific manner.

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