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Genotype-to-phenotype mapping in post GWAS world

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Abstract

Understanding how metabolic reactions, cell signaling, and developmental pathways translate the genome of an organism into its phenotype is a grand challenge in biology. Genome-wide association studies (GWAS) statistically connect genotypes to phenotypes, without any recourse to known molecular interactions, whereas a molecular biology approach directly ties gene function to phenotype through gene regulatory networks (GRNs). Using natural variation in allele-specific expression, GWAS and GRN approaches can be merged into a single framework via structural equation modeling (SEM). This approach leverages the myriad of polymorphisms in natural populations to elucidate and quantitate the molecular pathways that underlie phenotypic variation. The SEM framework can be used to quantitate a GRN, evaluate its consistency across environments or sexes, identify the differences in GRNs between species, and compare health and disease states. Here, it will be illustrated with recent data combining the analyses of body weight, plus protein, sugar, and triglyceride content in a reference panel of natural *D. melanogaster*.

Biography

Sergey V. Nuzhdin combines expertise in Population Biology (Professor in Evolution and Ecology, UC Davis, 1997-2007) and in Molecular and Computational Biology (USC, 2007-present). He has published more than 100 papers in peer-review journals, including PLoS Biology, Science, Nature Genetics, and PNAS; has trained over a dozen of independent investigators; and is serving on several editorial boards, and on NIH panels.

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