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The mean-ness of noisy biological systems

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Phenotypes are often noisy, sometimes varying dramatically around average effects. Body weight, insulin and triglyceride levels, colon cancer polyps, and many other traits sometimes show precise phenotypes and other times extreme variability, despite similar mean trait values. Does 'noise' simply result from stochastic variation and measurement error? Or does it have a biological (genetic) basis? With our obsession with mean effects, perhaps we have overlooked noise as a fundamental aspect of health and disease.

I will discuss the evidence that genetic and environmental factors control phenotypic variability in metabolic systems. Our work focused on diet-induced changes in metabolic features in engineered strains of mice whose progenitors differed in response to long-term high-risk diet exposure. These strains limit genetic heterogeneity as a source of phenotypic variability and enable focus on molecular and physiological regulatory mechanisms. We found that many genetic variants control noise either at baseline or in response to diet challenge. Propensity for noise appears to be set early during development, suggesting that small differences in molecular and physiological state early in life can have dramatic long-term consequences on disease risk.

I will consider the implications of phenotypic 'noise', with emphasis on the significance of normal and unusual phenotype distributions, whether means or variability are the primary drivers of phenotypic change, and whether induced changes in variability represent adaptation or dysfunction. With these ideas, metrics and evidence, the path is open to fully study the noisy well as well the average aspects of organismal biology.