CDB SEMINAR

Nick Luscombe

University College London / Cancer Research UK London Research Institute / Okinawa Institute of Science & Technology

Monday, April 22, 2013
16:00~17:00   C1F Auditorium

Transcriptional regulation in 3D: models of gene expression during fly development

Summary

Transcriptional control ensures that genes are expressed in the right amounts at the correct times and locations. A challenge is to understand quantitatively how regulatory systems precisely convert input signals to the appropriate outputs: what is the regulatory input function that determines a target gene's expression pattern? Making use of the Virtual Embryo dataset from the Berkeley Drosophila Transcription Network Project, for the first time, we successfully and accurately model the expression of even skipped (eve) stripes 2 and 3+7 across the entire embryo at cellular resolution. We show that a straightforward statistical relationship explains how the measured concentrations of transcription factors (TF) define the complex spatial pattern of eve expression, without the need for pairwise interactions or cross-regulatory dynamic processes. By simulating outputs from thousands of TF combinations, we recover known regulators and also suggest roles for new candidates. Finally, our models predict the intricate effects of regulatory perturbations including mutations in regulating TFs and misexpression experiments with remarkable accuracy. In contrast to many previous methods, we impose minimal assumptions on models; instead we identify those that best fit the data and then infer the underlying mechanistic features of the regulatory input function, such as the lack of TF-specific thresholds or the need for pairwise interactions, and the positional value of homotypic interactions. Overall, the study provides a generally applicable and quantitative approach for elucidating the regulation of diverse biological systems and developing experimentally testable hypotheses.

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