

Cologne Evolution Colloquium

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Molecular Basis of
Evolutionary Innovations
SFB 680

Limits to gene regulation by global crosstalk

Gene regulation relies on the specificity of transcription factor (TF) – DNA interactions. In equilibrium, limited specificity may lead to crosstalk: a potentially detrimental regulatory state where a gene is either incorrectly activated due to noncognate TF-DNA interactions or remains erroneously uninduced. We present a tractable biophysical model of crosstalk in a global setting, where many genes are simultaneously regulated by many TFs. We show that in the simplest regulatory scenario, a lower bound on crosstalk severity can be analytically derived solely from the number of (co)regulated genes and a suitable parameter that describes binding site similarity. In the first part of the talk, I will show that crosstalk could present a significant challenge for organisms with low-specificity TFs, e.g. metazoans, and ask how far these limits can be relaxed by combinatorial regulation schemes in equilibrium.

In the second part of the talk, I will present a proposal for an out-of-equilibrium, kinetic-proofreading-like regulatory scheme that is significantly more robust to crosstalk, explore the tradeoffs in this proposal, and suggest that we should revisit the equilibrium assumption for multicellular eukaryotes. Our results suggest that crosstalk imposes a new type of global constraint on the functioning and evolution of regulatory networks, which is qualitatively distinct from the known constraints acting at the level of individual gene regulatory elements.

Wednesday, June 24, 2015, 17:00
University of Cologne, Institute for Genetics
Seminar Room 0.46

Hosted by Michael Lässig