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Genotype to Phenotype Mapping of the E. coli lac Promoter[1]

JAKUB OTWINOWSKI, University of Pennsylvania, Biology Dept., ILYA NEMENMAN, Emory University, Physics Dept., Biology Dept.

— Genotype-to-phenotype maps and the related fitness landscapes that include epistatic interactions are difficult to measure because of their high dimensional structure. Here we construct such a map using the recently collected corpora of high-throughput sequence data from the 75 base pairs long mutagenized E. coli lac promoter region, where each sequence is associated with induced transcriptional activity measured by a fluorescent reporter. We find that the additive (non-epistatic) contributions of individual mutations account for about two-thirds of the explainable phenotype variance, while pairwise epistasis explains about 7% of the variance for the full mutagenized sequence and about 15% for the subsequence associated with protein binding sites. Surprisingly, there is no evidence for third order epistatic contributions, and our inferred fitness landscape is essentially single peaked, with a small amount of antagonistic epistasis. We identify transcription factor (CRP) and RNA polymerase binding sites in the promotor region and their interactions. We conclude with a cautionary note that inferred properties of fitness landscapes may be severely influenced by biases in the sequence data.

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Jakub Otwinowski
University of Pennsylvania, Biology Dept.

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