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Title: How promoters optimally encode transcription factor concentrations under time and physics constraints

Cells must often make decisions in a rush based on limited observations of noisy molecular processes, such as binding activity of a transcription factor on a promoter. In addition, physics limits the speed at which certain processes used for such decisions can take place. We formulate this problem in terms of a constrained maximization of the Fisher information rate of the output of a promoter, namely mRNA transcription. The constrained optimization is carried out over the space of allowable molecular transition rates between the promoter's states, under the speed limits of diffusion and transcription activation time. Accounting for biophysical constraints in the search for fast promoters has interesting implications: optimal architectures transition from saturating one constraint (diffusion) to another (activation time) as a function of concentration, showing that encoding strategies and cooperativity are concentration-dependent. In the presence of spurious binders, the fastest architectures are not those that maximize selectivity against these decoys, leading to a "goldilocks zone" of selectivity. Finally, we show that optimal promoters are generically the farthest from equilibrium, but this energy expenditure is not a constraining factor with regard to decision speed.

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