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Application of Maximum Caliber to Infer Rates in Genetic Circuits[1] TAYLOR FIRMAN, KINGSHUK GHOSH, Department of Physics and Astronomy, University of Denver — Learning the underlying details of a gene network is a major challenge in cellular and synthetic biology. We address this challenge by building a chemical kinetic model that utilizes information encoded in the stochastic protein expression trajectories typically measured in experiments. The applicability of the proposed method is demonstrated in an auto-activating genetic circuit, a common motif in natural and synthetic gene networks. Our approach is based on the principle of Maximum Caliber (MaxCal) – a dynamical analogue of the principle of maximum entropy – and builds a minimal model using only three constraints: i) protein synthesis, ii) protein degradation, and iii) positive feedback. The MaxCal model was benchmarked against synthetic data generated using a Gillespie algorithm on a known reaction network. MaxCal accurately predicts underlying rate parameters of protein synthesis and degradation as well as experimental observables such as protein number and dwell time distributions. This 'top-down' methodology based on minimal information – in contrast to traditional 'bottom-up' approaches that require ad-hoc knowledge of circuit details – provides a powerful tool to accurately infer underlying details of feedback circuits that are not otherwise visible in experiments.

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