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Quantitative modeling and data analysis of SELEX experiments

MARKO DJORDJEVIC, Mathematical Biosciences Inst., Ohio State Univ., ANIRVAN M. SENGUPTA, Dept. of Physics and BioMaPS Inst., Rutgers Univ. — SELEX (Systematic Evolution of Ligands by Exponential Enrichment) is an experimental procedure that allows extracting, from an initially random pool of DNA, those oligomers with high affinity for a given DNA-binding protein. We address what is a suitable experimental and computational procedure to infer parameters of transcription factor-DNA interaction from SELEX experiments. To answer this, we use a biophysical model of transcription factor-DNA interactions to quantitatively model SELEX. We show that a standard procedure is unsuitable for obtaining accurate interaction parameters. However, we theoretically show that a modified experiment in which chemical potential is fixed through different rounds of the experiment allows robust generation of an appropriate data set. Based on our quantitative model, we propose a novel bioinformatic method of data analysis for such modified experiment and apply it to extract the interaction parameters for a mammalian transcription factor CTF/NFI. From a practical point of view, our method results in a significantly improved false positive/false negative trade-off, as compared to both the standard information theory based method and a widely used empirically formulated procedure. This work will appear in *Physical Biology*. This work was supported by NIH grant GM67794. Final parts of this work were supported by NSF under Agreement No. 0112050 and NSF grant MCB-0418891.

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