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Open Complex Formation by Bacterial RNA Polymerase - a Quantitative Model

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Despite intensive research in the last two decades, the mechanism by which bacterial RNA polymerase (RNAP) forms open complex is still unknown. We here present the first quantitative model of open complex formation. We derive an explicit connection between transcription initiation rate and physical properties of the promoter sequence and promoter-RNAP interactions. We compare our model with both biochemical measurements and genomics data and report a very good agreement with experiments, with no free parameters used in model testing.

***Keywords* — RNA polymerase, transcription initiation, open complex formation, promoter melting, biophysical modeling**

I. Background

Bacterial RNA polymerase (RNAP) is the central enzyme of gene expression, and transcription initiation is both the first step and a major point in regulation of gene expression. Over the last two decades a large amount of data on initiation of transcription by bacterial RNAP has been obtained [1]. However, the mechanism by which RNAP forms open complex is still unknown, and several qualitative models have been proposed [2]. In order to provide a theoretical framework needed to analyze the assembled experimental data, we developed the first quantitative model of open complex formation by bacterial RNA polymerase [3]. The model is based on a theoretical biophysics approach, while statistical analysis and bioinformatic methods were used to test the model against available genomics and biochemical data.

II. Results

We first show that a simple model (which may follow from recent bioinformatic and experimental results), by which promoter DNA is melted in one step through thermal fluctuations, is inconsistent with experimental data. We next consider a more complex two step model. In this model the transcription bubble forms in -10 region, and consequently extends to transcription start site. We derive an explicit connection between the rate of transcription initiation and physical properties of promoter sequence and promoter-RNAP interactions.

We next compare our model with both biochemical measurements and genomics data. We first show that the biochemically measured transition rates from closed to open complex correlate very well with the values predicted from our model (R^2=0.75, with the P value of 10^{-3}). Furthermore, we report even better agreement of the parameters predicted by our model and those inferred from the experimentally confirmed core promoter sequences (correlation constant of R^2=0.93, with the P value of 10^{-11}). No free parameters are used in model testing.

III. Conclusion

The good agreement of our model with the experimental data strongly supports the qualitative view of the open complex formation on which our quantitative model is based. From a practical point of view, our results allow estimating the rate of transition from closed to open complex for a given promoter sequence, which would otherwise require performing quite demanding experimental measurements. This, in turn, allows efficient `engineering' of promoter sequences with desired kinetic properties. We therefore expect that our model will provide a better practical and conceptual understanding of the transcription initiation process.

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