Modeling Promoter Escape

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***Short Abstract* — After RNA polymerase binds the promoter DNA and forms the open complex, it goes through cycles of production and release of short abortive transcripts before it is able to break the bonds with the promoter and enter the elongation phase. We use a three-pathway model to describe this process , compute the abortive profile obtained and compare the results with experimental data.**

***Keywords* — Escape, Scrunching, Abortive Transcripts, Transcription Initiation.**

I. Promoter Escape

Transcription is the complex process in which a DNA segment is copied into a messenger RNA. Transcription can be divided in three main processes: transcription initiation, elongation and termination. In transcription initiation, RNA polymerase binds to the promoter region in the DNA and gets ready to start copying the DNA. In transcription elongation, RNA polymerase moves along the DNA to create an RNA copy. In transcription termination, RNA polymerase falls off the DNA after completing the RNA copy.

Transcription initiation itself is a very complex process which consists of three main processes. First RNA polymerase binds the promoter resulting in a closed RNAP-promoter complex. Then RNA polymerase unwinds a short segment of DNA resulting in an open RNAP-promoter complex. Then, after abortive cycles of synthesis and release of short RNA segments, RNA polymerase escapes the promoter and enters the elongation phase.

Abortive transcripts were first observed in [1] in transcription reactions containing only the first two NTP substrates. Later experiments have shown existence of longer abortive transcripts. For a review on abortive initiation see [2].

While there is a lot of literature on models for transcription elongation and they seem to be in reasonable agreement with the experimental data [3,4], much less is available for transcription initiation models. Our work builds upon an initial sequence-dependent three-pathway kinetic model for promoter escape proposed in [5].

II. Model

Following [5] we assume that after RNA polymerase binds the promoter and forms the open complex, there are three competitive reaction pathways that can be followed. These are the abortive pathway, the scrunching pathway and the escape pathway. We define rates for the abortive, scrunching and escape reactions, and based on these rates we define abortive, scrunching and escape probabilities. With these probabilities we can calculate the model predicted abortive profile and compare the results with the experimental data available [6].

We start with the rates defined in [5], and we introduce several modifications in order to improve and make the model more realistic. In [5] the abortive rates are defined based on the hypothesis that abortive transcripts are released only when assisted by the first two complementary NTPs. We avoid this experimentally unsupported hypothesis by redefining the abortive rates. We also increase the size of the transcription bubble in the escape state and use optimized parameter values, including NTP-dependent values for the polymerization rate and NTP-dissociation constants.

After each modification we compute the predicted abortive profile and compare it to experimental data. Since we have not yet found a satisfactory match to the experimental data, we are studying the introduction of new parameters that will take into account two new features. The first one is the energy associated to DNA bending during the scrunching process, and the second the possible formation of DNA secondary structure in the single stranded scrunched DNA.

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