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Towards a Quantitative Understanding of Single-Gene Transcription

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The transcription of the genetic information in DNA into RNA is the first step in protein synthesis. This process is highly regulated and is carried out by RNA polymerase (RNAP), a complex molecular motor. Here we discuss some of the consequences of a Brownian ratchet model of transcription, which incorporates internal structural degrees of freedom of RNAP and kinetic barriers to backtracking of RNAP resulting from steric clashes with co-transcriptionally folded RNA. This approach was previously used (a) to successfully predict sequence dependent positions of pauses during the elongation process [1,2]; (b) to study the behavior of a number of mutants of RNAP, with different elongation behaviors, believed to involve different internal motions of the enzyme [3]; and (c) to gain insight into the interpretation of single-molecule transcription elongation experiments [2]. The same model can be used to characterize the stability of the elongation complex at specific termination sequences, places along DNA where, with high probability, RNAP releases the RNA transcript and disengages from the template. Recent experimental results on termination reinforce a picture of the elongation complex as a flexible structure, not a rigid body [4]. In more general terms, some of the modeling to be presented raises fundamental issues related to "model comparison" and "model selection," the problem of identifying and characterizing quantitative models on the basis of limited sets of experimental data [5].

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