Transcription Initiation Controls Skewness of the Distribution of Intervals Between RNA Productions

Most regulation in transcription controls when and with which intensity genes are expressed. However, recent evidence suggests that control is also exerted on the noiseness of this process. Here, we use an empirically validated stochastic multi-step model of transcription to explore how its steps kinetics affect the skewness of the distribution of intervals between consecutive RNA productions in individual cells. From the simulations, we show that skewness is independent of the mean transcription rate, but differs widely with the fraction of time the RNA polymerase spends in the steps following open complex formation. Next, from qPCR and live, time-lapse, single-RNA microscopy measurements of multiple promoters, we validate our model predictions. Using the validated model, we then show that skewness affects, e.g., the fraction of time protein numbers are below a threshold. We conclude that skewness in transcription kinetics can be tuned by the rate-limiting steps in initiation and, thus, may be an evolvable decision-making parameter of genetic circuits.