Contribution ID: **442** Type: **Talk**

【911】Transcriptional bursting and promoter cycles in mammalian cells

Wednesday 23 August 2017 17:00 (30 minutes)

Mammalian gene transcription occurs stochastically in short bursts interspersed by silent intervals. However, the underlying processes and consequences on fluctuations in gene products are poorly understood. In our lab we combine time-lapse imaging of a short-lived transcriptional reporter with stochastic modeling to quantitatively characterize transcriptional bursting. While bursting kinetics is generally gene-specific, we found that endogenous gene promoters typically exhibit refractory periods lasting about one hour before turning on again. Recently, we extended our models to identify minimal promoter cycles, which inform on the number and durations of rate-limiting steps responsible for refractory periods. We found that the structure of promoter cycles was promoter specific and independent of genomic location. Typically, five rate-limiting steps underlie the silent periods of endogenous promoters, while minimal synthetic promoters exhibit only one. In addition, certain promoter architectures, notably ones containing TATA boxes, show simplified two-state promoter cycles associated with increased intrinsic noise.
In addition, we observed large variability in burst sizes and frequencies between genes. To better understand the regulation of burst size and frequency, we followed the expression level of a Bmal1 transgene, a core circadian clock promoter, throughout the circadian cycle and inserted at different genomic loci. We observed both in living and fixed cells that the circadian phase predominantly modulated the burst frequency while the integration site mostly affected the burst size. Furthermore, we found that the clock-dependent modulation of burst frequency was associated with variations in histone acetylation levels. Additional experiments on other genes suggest correlation between acetylation levels and burst frequency likely may be a general feature of gene transcription. Thus, we begin to understand how gene expression modulation can occur both by tuning the burst size and frequency, involving different molecular mechanisms.

Author: NAEF, Felix (EPFL)

Presenter: NAEF, Felix (EPFL)

Session Classification: Biophysics, Medical Physics and Soft Matter

Track Classification: Biophysics, Medical Physics and Soft Matter