MAR14-2013-020089

Abstract for an Invited Paper
for the MAR14 Meeting of
the American Physical Society

Real-time dynamics of RNA Polymerase II clustering in live human cells

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Transcription is the first step in the central dogma of molecular biology, when genetic information encoded on DNA is made into messenger RNA. How this fundamental process occurs within living cells (in vivo) is poorly understood,[1] despite extensive biochemical characterizations with isolated biomolecules (in vitro). For high-order organisms, like humans, transcription is reported to be spatially compartmentalized in nuclear foci consisting of clusters of RNA Polymerase II, the enzyme responsible for synthesizing all messenger RNAs. However, little is known of when these foci assemble or their relative stability. We developed an approach based on photo-activation localization microscopy (PALM) combined with a temporal correlation analysis, which we refer to as tcPALM. The tcPALM method enables the real-time characterization of biomolecular spatiotemporal organization, with single-molecule sensitivity, directly in living cells.[2] Using tcPALM, we observed that RNA Polymerase II clusters form transiently, with an average lifetime of 5.1 ($\pm$ 0.4) seconds. Stimuli affecting transcription regulation yielded orders of magnitude changes in the dynamics of the polymerase clusters, implying that clustering is regulated and plays a role in the cells ability to effect rapid response to external signals. Our results suggest that the transient crowding of enzymes may aid in rate-limiting steps of genome regulation.

[1]C. Rickman & W. A. Bickmore Science **341** (2013).
[2]I.I. Cisse et. al. Science **341** (2013).