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Transcription Kinetics Heterogeneity of Highly Mobile Identical Genes Revealed by Simultaneous Measurement at the Single Cell Level

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Fluorescence microscopy was used in combination with molecular constructs to measure in real time and in living cells the transcriptional activity of individual genes and their displacement within the nucleus. The question whether local mobility of individual chromatin regions is correlated to their transcriptional output is still the subject of active research. There is a consensus that the local chromatin environment and physical accessibility may play a role in modulating transcription, possibly determining the large heterogeneity observed in RNA Polymerase II (PolII) elongation rates measured from fluorescence assays. Employing high-speed fluorescence nanoimaging we measure here at ms-temporal resolution PolII elongation and we are able to resolve the minute displacements of identical active genes surrounding a labeled transgene array. We observe a correlation between the transcriptional activity and sub-micrometer movements of the active genes that is evidence of an active molecular mechanism determining displacements of the active genes following transcriptional bursts. Furthermore, we detect a significant heterogeneity in the kinetics of identical genes measured simultaneously and at sub-second temporal resolution within the same cell. Together these observations rule out cell to cell variability as the underlying cause for the observed kinetic heterogeneity and point to the local chromatin environment and physical accessibility as the source of PolII elongation variability. Work supported in part by NIH P41-GM103540 and NIH P50-GM076516