Control of DNA replication by anomalous reaction-diffusion kinetics

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— DNA replication requires two distinct processes: the initiation of pre-licensed replication origins and the propagation of replication forks away from the fired origins. Experiments indicate that these origins are triggered over the whole genome at a rate $I(t)$ (the number of initiations per unreplicated length per time) that increases throughout most of the synthesis (S) phase, before rapidly decreasing to zero at the end of the replication process. We propose a simple model for the control of DNA replication in which the rate of initiation of replication origins is controlled by protein-DNA interactions. Analyzing recent data from Xenopus frog embryos, we find that the initiation rate is reaction limited until nearly the end of replication, when it becomes diffusion limited. Initiation of origins is suppressed when the diffusion-limited search time dominates. To fit the experimental data, we find that the interaction between DNA and the rate-limiting protein must be subdiffusive.

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