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# Emergence of the spatio-temporal replication program: from 1D signals to 3D chromatin structures

In the last few years, several models of the spatio-temporal replication program in eukaryotic cells were proposed in the literature. We proposed a simpler model with natural hypothesis that reproduces the frequency of new replication origin firing per length of unreplicated DNA along the S-phase, I(t), a fundamental quantity which present a universal bell shape in eukaryotes. Our model also predicts that the maximum value of I(t) is the product of the replication propagation speed with the squared density of origins. We verified this prediction in budding yeast, fission yeast, fly, frog and human cells which have very contrasted genome sizes and replication time (20 min to 8 hours).

In higher eukaryotes, the positioning of potential origins, their numbers and width are still under debate. This model with only one free parameter is a solid basis to study how observables such as Mean Replication Timing (MRT) profiles and Okasaky Seq (OK-Seq) profiles can emerge from spatial inhomogeneous distribution of potential origin. This distribution can be drawn from experimental signals that predict origin positioning (ORC2, SNS, Bubble Seq) or signals that are not related to the replication pathway (e.g. DNase I sensitivity) but that has been show to be good descriptors for origins positioning. We will present to which accuracy low and high resolution profiles (MRT ~100kb, OK-seq ~5kb) can be reproduced starting from these signals. We will also study the coherency between MRT and OK-Seq in the framework of this model by finding if a single optimized distribution of potential origin can reproduced both observables.

Potential origins of replication have been shown to bind on DNA in a sequence independent manner, and we will show in human how 3D spatial chromatin structures compatibles with Hi-C experiment can give rise by excluded volume to accessibility profile such as DNase I sensitivity, and naturally explain the observed MRT experiments.

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