Abstract Submitted
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Inhomogeneous DNA replication kinetics is associated with immune system response[1] JOHN BECHHOEFER, MICHEL G. GAUTHIER[2], Dept of Physics, Simon Fraser University, Burnaby, BC, Canada, PAOLO NORIO, Department of Medicine, Albert Einstein College of Medicine, Bronx, NY — In eukaryotic organisms, DNA replication is initiated at "origins," launching "forks" that spread bidirectionally to replicate the genome. The distribution and firing rate of these origins and the fork progression velocity form the "replication program." Previous models of DNA replication in eukaryotes have assumed firing rates and replication fork velocities to be homogeneous across the genome. But large variations in origin activity and fork velocity do occur. Here, we generalize our replication model to allow for arbitrary spatial variation of initiation rates and fork velocities in a given region of the genome. We derive and solve rate equations for the forks and replication probability, to obtain the mean-field replication program. After testing the model on simulations, we analyze the changes in replication program that occur during B cell development in the mouse. B cells play a major role in the adaptive immune system by producing the antibodies. We show that the process of cell differentiation is associated with a change in replication program, where the zones of high origin initiation rates located in the immunoglobulin heavy-chain locus shift their position as the locus prepares to undergo the recombination events responsible for generating antibody specificity.

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