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Genome replication dynamics in E. coli and Yeast and their effect on cellular growth

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To allow cells to proliferate successfully and efficiently, genome replication is governed by a sophisticated replication program which governs the time at which different parts of the genome are replicated. These programs are carefully synchronized with the cell cycle to ensure timely replication without undue interference with other cellular processes. We quantitatively study the replication program and its interactions with the cell cycle in both *E. coli* and yeast using replication timing data. Replication timing data are DNA abundance profiles measured in exponentially growing, asynchronous populations from which we infer a wide range of properties of the underlying replication program [1]. In *E. coli* a machine learning approach based on Gaussian Processes allows us to measure the temporal fluctuations of replication fork velocity in both wildtype and ectopic origin mutants with high precision. We observe that additional forks reduce population growth and fork velocity, which suggests mutual competition between forks and between forks and other cellular processes. Based on our observations, we introduce a model of resource allocation between replication and cellular growth and show that it is consistent with our data. In yeast we demonstrate that our method can infer the location and efficiency of origins of replication from replication timing data without any prior information except the (unannotated) genome. Since our method only requires organisms to be cultivable in the lab, this opens the door to studying replication programs and a wide range of single-cellular species.

[1] F. Pflug, D. Bhat, S. Pigolotti, *PLOS Computational Biology* **20**(1):e1011753, (2024).

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