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Inferring the Spatiotemporal DNA Replication Program from Noisy Biological Data<sup>1</sup> JOHN BECHHOEFER, ANTOINE BAKER, Simon Fraser University — We generalize a stochastic model of DNA replication to the case where replication-origin-initiation rates vary locally along the genome and with time. Using this generalized model, we address the inverse problem of inferring initiation rates from experimental data concerning replication in cell populations. Previous work based on curve fitting depended on arbitrarily chosen functional forms for the initiation rate, with free parameters that were constrained by the data. We introduce a model-free, non-parametric method of inference that is based on Gaussian process regression. The method replaces specific assumptions about the functional form of initiation rate with more general prior expectations about the smoothness of variation of this rate, along the genome and in time. Using this inference method, we show that we can recover with high precision simulated replication schemes with data that are typical of current experiments. The method of Gaussian process regression can be profitably applied to a wide range of physical and biological problems.

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