Bayesian emulation and calibration of a stochastic computer model of mitochondrial DNA deletions in substantia nigra neurons

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Abstract

We consider the problem of parameter estimation for a stochastic biological model of mitochondrial DNA population dynamics using experimental data on deletion mutation accumulation. The stochastic model is an attempt to describe the hypothesized link between deletion accumulation and neuronal loss in the substantia nigra region of the human brain. Inference for the parameters of the model is complicated by the fact that the model is both analytically intractable and slow to sample from. We show how the stochastic model can be approximated using a simple parametric statistical model with smoothly varying parameters. These parameters are treated as unknown functions and modelled using Gaussian process priors. Several simplifications of our Bayesian model are implemented to ease the computational burden. Our models are validated using predictive simulations. We demonstrate the validity of our fitted model on an independent dataset of substantia nigra neuron survival.