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Constrained suboptimal experiment design for HIV cryptic viremia model validation. Preliminary report.

In treated patients, HIV can continue to replicate in locations where combined antiretroviral therapy (cART) drugs do not penetrate. This is known as cryptic viremia. Cryptic viremia can be revealed by an experiment in which an integrase inhibitor is administered in addition to the background therapy. Virus replication inhibited results in the formation of 2LTR DNA circles. We have previously shown that the measured dynamics of these circles can be used as an indirect measure of the amount of cryptic replication. An experiment is being planned to validate the model developed in our previous work. Institutional Review Board (IRB) guidelines limit both the total number of blood measurements in human trials. In principle, we seek to optimize across the space of sampling schedules that meet the constraints to find the schedule that maximizes the expected Kullback-Leibler divergence relative to the broad priors obtained by fitting our model to data from previous experiments. We search the space using a Genetic Algorithm, and employ several approximations to make the problem numerically feasible. Preliminary results show that optimized schedules are expected to yield several times more information than uniform sampling schedules meeting the same constraints. (Received January 19, 2015)