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Potential and limits of minimal informative priors for hidden Markov Models to improve parameter inference

Inferring the complex functional dynamics of ion channels from ensemble currents is a daunting task. We previously addressed this problem by applying a parallelized Bayesian filter to specify kinetic schemes for macroscopic current and fluorescence data leeding to a more accurate likelihood than previous gold-standard algorithms (Muench 2022 eLife 11:e62714).

Using Bayesian statistics requires to define a prior distribution. When little information about the parameter is known, especially when the information content in the data is poor, the prior is crucial to make the posterior as sensitive as possible to the data. For ion-channel HMMs, a minimal informative prior may consist of a log uniform prior for the inverse dwell times of a state and a Dirichlet prior for the probability of each transition out of the state. Applying this prior reduces the number of ion channels required for a reasonable inference by one order of magnitude compared to the standard uniform prior, which is often considered mistakenly as uninformative.

Ion currents from patch-clamp experiments observe only partially the dynamics of interest in the chemical network. We show by simulated patch-clamp data that this partial observability causes the likelihood to become flat in many directions in the parameter space, causing a degree of practical parameter non-identifiability for most non-trivial hidden Markov models. The log uniform distribution of the minimal informative prior desensitizes the posterior to the non-identifiability problem of the likelihood for some part of the parameter space. Nevertheless, the posterior will always be dominated by the structure of the prior in the rest of the parameter space. Thus, all posteriors of HMM models will be improper if equipped with minimal informartive improper prior distributions. Here, we discuss how to recognize and treat this practical parameter non-identifiabilty problem, inherent in most HHMs and any statistical framework used. Including other
physically constraints further increases the inference quality and decrease the parameter unidentifiabilty problem.

We conclude that for a given data quality the quality of model inference can be significantly improved by selecting a minimal informative prior.

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