***Hippocampal biomimetic model requires extensive computational power for model estimation and optimization***

Our team also aims to build a DARPA-sponsored hippocampal memory prosthesis, a biomimetic device developed for restoring or enhancing memory functions. It is designed to circumvent damaged hippocampal region by re-establishing the transformation of spike trains performed by a normal population of hippocampal neurons. At its core, lies a multi-input multi-output (MIMO) nonlinear dynamical model capable of predicting the outputs ensemble spike trains based on the ongoing input ensemble spike trains. Estimation of sparse MIMO nonlinear dynamical models using spike train data recorded from epilepsy patients performing memory dependent tasks (Song et al., 2018). The goal is to estimation sparse MIMO models from spike timings using a regularized generalized Laguerre-Volterra modeling approach. This modeling task involves iterative estimation of Laguerre-Volterra model coefficients and optimization of supra-parameters controlling the level of model sparsity, which is critical for achieving accurate out-of-sample prediction. In a typical experiment, we record hippocampal CA3 and CA1 signals from an epilepsy patient in the recording day. Data are preprocessed and sorted to generate spike train data for the MIMO modeling. Sparse MIMO nonlinear dynamical model of CA3-CA1 transformation is then estimated using the high-performance computer cluster within 3 days for the model-driven stimulation. One the stimulation day, a microstimulator is used to deliver MIMO model-predicted CA1 spatio-temporal patterns of spikes back to the hippocampus to enhance CA3-CA1 signal transmission and thus facilitate memory functions in the epilepsy patient. Since electrode implantations in these patients are temporary (approximately 7 days), the recording-estimation-stimulation paradigm cannot be achieved without the cluster.

The MIMO modeling methodology is computationally expensive and heavily relies on the high-performance computer cluster for estimation of parameters describing nonlinear dynamical properties of the hippocampus (Song et al., 2018). Notably, estimation of sparse MIMO nonlinear dynamical models is done using spike train data recorded from epilepsy patients while performing memory-dependent tasks. Access to these patients is usually limited to a 7-day window within which all model parameters must be estimated to enable testing of the model on the patient through electrical stimulation with the model predicted output. If this time window is exceeded (i.e. we do not have access to enough computational power to estimate all parameters in time), it becomes impossible to test the model predicted output.

For example, in one of the patients, the total estimation time is approximately 3700 hours without the cluster. Using the cluster and a specially developed parallelization scheme, we were able to reduce the estimation time to 29 hours (**Fig. 2.1.3**).

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|  | **Figure 2.1.3.** Parallelization of sparse MIMO model estimation for hippocampal memory prosthesis. Estimation of sparse MIMO model consists of three stages of computation. Stage 3 involves cross-validations with respect to sparsity parameter λ and is computationally the most extensive. Without parallelization, the total estimation time is 3700 hours. With Parallelization Scheme A, the total computation time is 237 hours; with Parallelization Scheme B, the total computation time is reduced to 29 hours, which makes it possible to perform the recording-estimation-stimulation paradigm of hippocampal prosthesis within the 7-day time window. |

Another example is to apply parallelization scheme on our Memory Decoding (MD) model, which can be used to understand how memories are encoded in the brain. The MD model for one decoding categories (memory labels) typically need to run multiple times (20 times) to reduce the randomness result from the used machine learning algorithm. And we have 27 categories need to check for one single patient’s data within 7-days’ time window. Through using the HPC cluster, we can enhance the speed of our model by 20 \* 27 times.

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