## Improved Machine Learning Strategies and Algorithms for Transmembrane Potential Estimation in Homogeneous Medium

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Introduction. Research on improved methods to provide accurate estimates of the inverse problem in cardiology and electrophysiology is active today. Recently it has been proposed the use of machine learning methods that can consider the biophysical equations of the problem. Still, the search for free parameters by generalization criteria can also be crucial. In this work, we propose to explore improvements in using kernel methods for estimating the inverse problem, with kernel given by the Green's function for the infinite homogeneous potential and with recently proposed cross-validation strategies for least squares estimation. Materials and methods. Three algorithmic solvers were implemented, namely, least squares with Zero-Order Thikhonov (ZOT) regularization, Support Vector Regression (SVR), and constrained L2 (CL2) optimization. The estimation of the transmembrane action potential from the extracellular potential was studied in 1D (fiber) and 2D (tissue) simulations. The reaction was generated using the Luo-Rudy model. Experiments and results. The ZOT method was the most unstable. The SVR method provided biased results, although intermediate and acceptable accuracy, except at the edges of spatial action potentials. The CL2 method provided better performance under certain conditions of the implemented cross-validation procedure. **Conclusions.** The presented work shows that the use of kernel methods, with appropriate algorithmic formulations and elaborated cross-validation criteria, provides an alternative way towards the estimation of the cardiac inverse problem in a homogeneous and infinite conductor, which can be improved by including the biophysical equations of the problem.

