Project title: Accurate and fast Bayesian uncertainty quantification for personalized cardiac modelling

Project reference: DT4H_05_2022

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Aim of the project

Mathematical models play a fundamental role in computational cardiology in enhancing our understanding of patient's physiopathology and in guiding personalized treatments. Very accurate models are available, that represent phenomena at different scales and different physics. These are based on coupled systems of differential equations, with increasing complexity as we integrate more and more phenomenological details. In such framework, building a digital twin of a patient's heart corresponds to (i) fitting the model parameters (inputs) as individual functional measurements (data) become available through time, so to make the model (output) adhere to the data; (ii) understanding the interplay between parameters and model outputs, which can be indicative of both pathological conditions and targets for treatment. Achieving these goals requires a large number of model evaluations, and this can be computationally prohibitive. Popular methods are based on approximating computer models with low fidelity emulators, favouring computing speed at the expense of introducing unquantifiable bias in the estimates. The aim of this project is to develop statistical methods for exact uncertainty quantification but that require a low computing time, compatible with clinical needs.

Project description

We will adopt the Bayesian inference framework, that allows to incorporate expert elicited knowledge by treating the parameters as random variables with a set prior distribution, and to account for system un-identifiability if the Bayesian update leads to wide posteriors. In this framework, calibrating a cardiac computer model and propagating uncertainty through scales requires a large number of model evaluation in outer-loops, such as those involved in Markov Chain Monte Carlo (MCMC) algorithms or in the estimate of integrals of expensive functions of the samples.

To escape from prohibitive computations, existing methods perform calibration using low-fidelity emulators of the mathematical models, targeting certain quantities of interest (QoIs). These emulators can be used in exact calibration algorithms such as MCMC [1] where the likelihood incorporates both measurement error and an estimated additive noise term that accounts for the approximation introduced by the emulator. Alternative use of emulators in methods for iteratively reducing the parameter space by retaining non-implausible parameter values (History Matching [2]). The main drawback of these calibration techniques is the introduction of unquantifiable bias in the estimates, by making use of low-fidelity emulators of QoIs, instead of running numerical solvers for mathematical models that would fit all available data. The second method has the additional drawback of not providing formal (posterior) parameter distributions, but only non-implausible regions.
Similar issues are encountered in uncertainty propagation techniques, such as global sensitivity analysis (GSA) [1-2], if emulators are used instead of the full model.

Motivated by an inference problem in electrophysiology, we have recently developed a method (Stein thinning [3]) for postprocessing MCMC simulations in order to retain the parameter samples that give the best quantization of the posterior distribution, even when MCMC is targeting a biased posterior. This is achieved minimizing a discrepancy measure which, in the original formulation requires expensive gradient information of the posterior distribution, but for which recent work has provided a gradient-free formulation [4]. This opens to the possibility of removing the above-mentioned bias by:

i. Running MCMC that targets a `cheap' biased posterior – such as the one based on the emulator outputs [1], and postprocessing those samples
ii. Using only the Stein-thinned samples for evaluating the integrals involved in GSA [1-2]
iii. Incorporating online selection of points in existing multi-fidelity methods based on control variates, delayed acceptance in MCMC, psudo-marginal methods etc. [5-6]

The aim of this PhD project is to work on both the theoretical developments to provide convergence guarantees of such ideas, and apply them to digital twins in computational cardiology.

The desired background of the candidate is technical (applied mathematics, statistics, engineering, computer science etc.). They have an interest in developing novel statistical methodology driven by real data in cardiology, and applying the developed methods in High Performance Computing Settings.

[1] Salvador M, Regazzoni F, Dede L, Quarteroni A. Fast and robust parameter estimation with uncertainty quantification for the cardiac function. arXiv preprint arXiv:2210.03012. 2022 Oct 6.

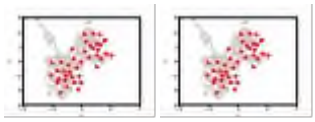
[2] Longobardi S, Lewalle A, Coveney S, Sjaastad I, Espe EK, Louch WE, Musante CJ, Sher A, Niederer SA. Predicting left ventricular contractile function via Gaussian process emulation in aortic-banded rats. Philosophical Transactions of the Royal Society A. 2020 Jun 12;378(2173):20190334.

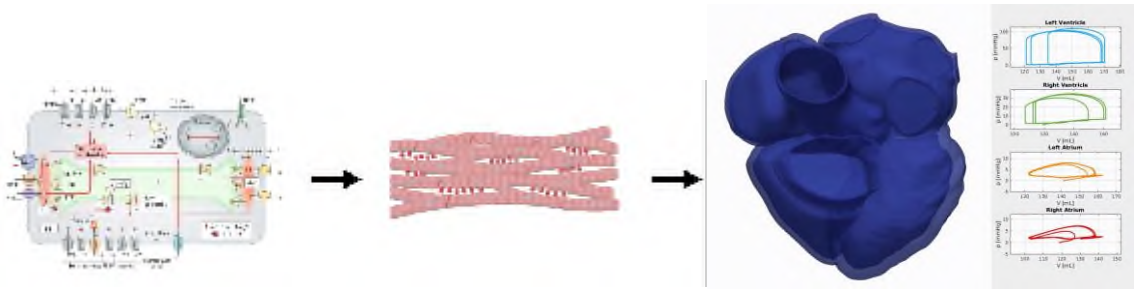
[3] Riabiz M, Chen W, Cockayne J, Swietach P, Niederer SA, Mackey L, Oates C. Optimal thinning of MCMC output. arXiv preprint arXiv:2005.03952. 2020 May 8.

[4] Fisher MA, Oates C. Gradient-Free Kernel Stein Discrepancy. arXiv preprint arXiv:2207.02636. 2022 Jul 6.

[5] Peherstorfer B, Willcox K, Gunzburger M. Survey of multifidelity methods in uncertainty propagation, inference, and optimization. Siam Review. 2018;60(3):550-91.

[6] Cai D, Adams RP. Multi-fidelity Monte Carlo: a pseudo-marginal approach. arXiv preprint arXiv:2210.01534. 2022 Oct 4.





Principled uncertainty quantification and propagation through layered computational scales, by selection of the most informative parameter samples via Stein thinning.