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BAYESIAN METHODS AND POLYNOMIAL CHAOS: APPLICATION TO FINDING CARDIAC BIDOMAIN PARAMETERS

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Electrophysiological simulations of ventricular cardiac tissue can provide valuable insights into the functioning of the heart that often cannot be achieved through experimental means alone. However, several crucial parameters that are required for accurate electrophysiological simulations are not known with certainty. This thesis develops a novel protocol, based on polynomial chaos and Bayesian inference techniques, which can be used to retrieve these crucial model parameters from experimental measurements.

The determination of accurate electrical properties for cardiac tissue is one of the significant challenges in realistically simulating cardiac electrophysiological behaviour. Insights gained through simulations of myocardial ischaemia, defibrillation, ST-segment deviation or ventricular fibrillation are essential for expanding current knowledge and can perhaps even inform or guide clinical decision-making. However, for these simulations to be helpful, a close match must exist between the system's true state and the output of the simulation.

Such electrophysiological simulations are often performed through the use of the bidomain model, which takes into account the differing electrical properties of the two interpenetrating domains of cardiac tissue, extracellular space and intracellular space, through the averaging of the electrical properties of each domain.

Cardiac tissue is arranged as sheets of fibres, in a laminar structure, which in turn are stacked with a slight offset relative to one another along a line between the outer wall of the heart and the inner wall of the heart, and thus introduces the notion of fibre rotation. The bidomain model, which is able to take this phenomenon into account,

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assumes that electrical current propagates in three directions: along the direction of the fibres (longitudinal), across the direction of the fibres within the sheet (transverse) and normal to sheets of the fibres (normal). Consequently, there are six conductivity values that are required to characterise the electrical behaviour of the cardiac tissue.

Despite efforts over the last fifty years, difficulties associated with making and interpreting experimental measurements have prevented researchers from determining conductivity parameters that are consistent, and account for the anisotropic nature of cardiac tissue. Studies in the past decade have proposed various techniques for retrieving all six bidomain conductivities and the fibre rotation angle through either experimental or theoretical means. One technique uses potential measurements, made on a multi-electrode array inserted in cardiac tissue, in conjunction with an inverse approach, to retrieve the cardiac conductivities and the fibre rotation angle. Our analysis shows that this protocol cannot adequately retrieve the cardiac conductivities and fibre rotation angle given the challenges associated with experimental measurements, such as the presence of outliers and the lack of sufficient data. Furthermore, this inversion protocol has inherent limitations that exacerbate the errors when retrieving a subset of the cardiac conductivities, as is shown using sensitivity and variance studies.

This thesis develops a novel inversion protocol, using Bayesian inference techniques, to obtain the cardiac conductivities and fibre rotation angle from experimental measurements. However, many forward solutions are required when solving inverse problems using Bayesian techniques and, given the computational costs of solving the bidomain model, implementation of this protocol is computationally infeasible. To obviate these computational restrictions, a surrogate model is developed, using polynomial chaos techniques, which approximates the solutions to the bidomain model. The resulting surrogate model is then used with Bayesian inference techniques to give the bidomain parameters. This new protocol is also designed to take into account outliers that might be present in experimental data and can incorporate the multiple datasets that are obtained using different current application electrodes on the multi-electrode array.

The novel inversion protocol is verified through the use of numerically simulated datasets of potentials measured on a multi-electrode array. Initially, we infer a single conductivity using a simulated isotropic medium, such as an electrolyte solution, from which a more thorough understanding of the protocol's capabilities is achieved. These studies indicate that the protocol can accurately infer the isotropic conductivity, even when the simulated datasets are populated with high noise levels and many outliers.

The inversion protocol is further used to retrieve the six cardiac conductivities and the fibre rotation angle using simulated noisy measurement sets. The simulated noisy measurement sets are populated with moderate levels of noise and many outliers. The results suggest that the three extracellular conductivities and the fibre rotation angle can be retrieved to a moderate degree of accuracy, given a single measurement set obtained using a single current-electrode configuration. However, the three intracellular conductivities are unable to be obtained under this specific scenario. Subsequently, it is shown that by using numerous measurement sets, obtained from

different current electrode configurations on the multi-electrode array, we can retrieve the intracellular conductivities accurately, as well as further refine the accuracy of the extracellular conductivities and the fibre rotation angle.

The inversion protocol is then used to infer model parameters from experimental measurements. We first used the protocol to infer the isotropic conductivity of an electrolyte solution of known conductivity from experimental measurements. However, it is found that the quality of the experimental potential measurements made by our collaborators degraded after each use of the multi-electrode array. Consequently, although the isotropic conductivity retrieved using the first trial of the measurements closely matches the true conductivity of the solution, subsequent experimental trials yield conductivities that are drifting away from the nominal conductivity value of the solution.

Twelve unique datasets of potential measurements were then made in rat cardiac tissue by our collaborators, using various different current-electrode configurations. The cardiac conductivities and fibre rotation angle are then inferred using these measurements. Despite the low quality of the experimental measurements and the reduced number of datasets available, we are able to obtain the extracellular conductivities and fibre rotation angle, but not the intracellular conductivities.

Since our studies with simulated noisy potentials show that it is possible to use the proposed new protocol to accurately retrieve all six bidomain conductivities, as well as the fibre rotation angle, we postulate that more datasets or improved datasets should make it possible to retrieve these parameters via our inversion protocol, provided that reliable and consistent experimental measurements of potential on a multi-electrode array are available.

Some of this research has been published in [1–3].

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