28. JOINT STATE AND PARAMETER ESTIMATION OF AN ORDINARY DIFFERENTIAL EQUATION MODEL OF THE CARDIOVASCULAR SYSTEM FROM SIMULATED MONITORING DATA USING PARTICLE FILTERS

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Introduction:
Clinicians in acute care environments such as the anaesthesia workplace or the intensive care unit (ICU) are faced with an ever increasing amount of quantitative data about patient physiological state derived from monitoring and imaging technology. Full exploitation of the large amounts of quantitative information contained in these data is limited by the human operators' capabilities, in particular in view of the highly nonlinear, dynamic interactions between different physiological observables. This suggests an opportunity for computer- ized decision support. In this context, data interpretation, patient state prediction, and, eventually, therapy optimization based on mechanistic mathematical models of physiology may offer an alternative to traditional rule based or purely statistical approaches [3]. Computing full posterior distributions on parameter and state space rather than point estimates may not only offer a resolution of the difficulties typically encountered when attempting to solve the inverse problems of state and parameter estimation from observations arising in this context, but also has the potential to provide a direct link between the clinical concept of differential diagnosis and the quantitative representation of patient condition in joint parameter/state space via mode identification in the joint posterior distribution [4]. The obvious algorithmic choice for the sequential assimilation of data acquired in real-time in the case of non-normality and multimodality of the posterior distributions are Sequential Monte Carlo

Methods [1]. The performance of parallelized particle filtering algorithms may be sufficient to allow real-time estimation of states for highly nonlinear models of the cardiovascular system in a simulation setting where the parametersareknown[2].In this study,I extend this work to the more practically relevant scenario of simultaneous parameter and state estimation from realistically available monitoring data for a model of the cardiovascular system including baroreflex via a state augmentation approach.

Methods: The highly simplified model of the cardiovascular system employed consists of 5 ordinary differential equations describing arterial (Va) and venous volume (Vv), sympathetic activation, and enddiastolic (EDV) as well as endsystolic volume, respectively and 19 static parameters [4] and was simulated using the CVODE solver from the Sundials package. Filtering was performed using a parallelized sequential importance sampling/resampling algorithm with deterministic local particle exchange, distributed resampling with non-proportional allocation, and global weight normalization at each iteration implemented in C using the Message Passing Interface (MPI) standard[2]. Following a standard state augmentation approach, parameters were constrained to vary from 1/3 to 3 times the true value under an artificial stochastic evolution with additive Gaussian noise with standard deviation 1/200 of the allowed range, while the deterministic evolution of states was also stochastically perturbed with additive Gaussian noise. In a first step, artificial observations of arterial pressure (AP), central venous pressure (CVP) and heart rate (HR) as well as cardiac output (CO) were generated from a simulated experiment of bleeding followed by fluid resuscitation using the parameter set from [4]. Trajectories of posterior distributions when assimilating AP,CVP,andHRwerecomputedandthe1-dimensional marginal distributions of states and parameters evaluated and compared to the scenario where CO was additionally observed.

Results: With sufficient numbers of particles (250,000 were used for the reported results), sequences of parameter/state distributions were found that closely reproduced the trajectories of observables within the limits of the assumed measurement error after an initial settlement phase. When examining the posterior distributions of states, we found that while Va and Vv exhibit wide scatter consistent with non-identifiability in particular when CO was not observed, EDV qualitatively tracked the preload alterations induced by simulated bleeding and resuscitation. Properties of marginal posterior distributions of parameters ranged from relatively tightly constrained to widely spread. In a subset of parameters, the posterior probability mass tended to concentrate at the boundaries of the allowed ranges.

Discussion: Distribution of parameters and states closely reproducing the trajectories of observables can be found even in this underdetermined scenario. From a technical perspective, particle overdissipation will need to be controlled using more advanced algorithms, while the observed tendency of certain marginal parameter distributions to concentrate at the boundaries of the allowed ranges is suggestive of the need to compensate for distortion introduced by the fundamental underdeterminedness of the inverse problem [5].

As exemplified by the procedure's ability to identify preload reduction manifested as reduction of EDV as a possible cause of the observed trajectories in spite of the simplistic computational approach applied here, inferring full posterior dis tributions of parameters and states for a fairly complex nonlinear model of cardiovascular system dynamics from clinically available physiological observables under minimal a priori assumptions has the potential to yield physiologically meaningful results that may allow for clinically meaningful interpretation. Furthermore, these results are encouraging with respect to applying the proposed methodology to a combination of more complex models with richer datastreams. First application of the described approach to experimental data is currently under way.

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